

Experience and Dosimetry Standardization for Total Body Irradiations in Research

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**Council on Ionizing Radiation Measurements and Standards
NIST, Gaithersburg, MD, April 17, 2018**

Disclosures

Research funding:

- NIH/NIAID, U19 AI67798 (subcontract 131714)
- DOD, PR141508, GRANT 11779583
- Asell LLC/BARDA, HHSO100201700022C Subcontract

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Broad Agency Announcements for Advanced Research and Development of Medical Countermeasures for Pandemic Influenza and Chemical, Biological, Radiological and Nuclear Threats.

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BARDA seeks to launch a novel partnership, a product accelerator to address antimicrobial Resistance
- +

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BARDA

CBRN

CHEMICAL, BIOLOGICAL, RADIOLOGICAL, AND NUCLEAR (CBRN) THREAT PROGRAMS

The Pandemic and All Hazards Preparedness Act (PAHPA) established BARDA as the focal point within HHS for the advanced development and acquisition of medical countermeasures to protect the American civilian population against CBRN and naturally occurring threats to public health. CBRN accomplishes this by supporting advanced research and development of medical countermeasures against CBRN threats and establishing stockpiles of vaccines, drugs and diagnostics against these threats. Ultimately, these medical countermeasures are used to help the Nation prepare to respond to and recover from public health emergencies. Using its advanced research and development authority, BARDA strengthens HHS efforts to bridge the valley of death funding gap that exists between the early stages of product development and the acquisition of approved or approvable medical countermeasures for the Strategic National Stockpile.

The CBRN programs within BARDA span a number of threat areas:

Anthrax

Anthrax is an acute infectious disease caused by the spore-forming bacterium Bacillus anthracis, which can cause human disease via gastrointestinal, cutaneous, or inhalational (pulmonary) routes.

Smallpox

Smallpox is a potentially deadly infectious disease and is considered a high-priority biological threat agent.

Botulism

Botulism is a serious paralytic illness caused by neurotoxins produced by several Clostridium botulinum strains.

Chemical Threats

Chemical threats include nerve agents.

Radiological and Nuclear Threats

The acquisition and ready availability of medical countermeasures for radiation-induced illnesses is essential to our Nation's preparedness and response capabilities.

Broad Spectrum Antimicrobials

Broad Spectrum Antimicrobials (BSA) Program was established in January 2010 and is focused on developing novel antibacterial and antiviral drugs for the treatment or prevention of disease caused by currently defined and future biological threats.

CBRN Diagnostics and Dosimetry

CBRN oversees the development of

BARDA

U.S. Department of Health and Human Services • National Institutes of Health

Temas de Salud

NIH

National Institute of Allergy and Infectious Diseases

Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases

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Organizations and Universities

Food and Drug Administration (FDA) Corner

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Pegfilgrastim Approved for Treatment of Acute Radiation Syndrome

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Radiation and Nuclear Countermeasures Government Sites

Centers for Disease Control and Prevention (CDC)

What To Do in an Emergency

Radiation Studies

Acute Radiation Syndrome—A Fact Sheet for Clinicians

Strategic National Stockpile

Executive Office of the President (EOP)

Office of Science and Technology Policy (OSTP)

Federal Emergency Management Agency (FEMA)

Nuclear Blast

Nuclear Power Plants

Food and Drug Administration (FDA)

For a listing of FDA resources, see FDA Corner.

National Aeronautics and Space Administration (NASA)

The Health Risks of Extraterrestrial Environments (THREE) Website

Space Radiation Analysis Group

National Cancer Institute (NCI)

Division of Cancer Epidemiology and Genetics

Radiation Research Program

National Institute of Standards and Technology (NIST)

Radiation Physics Division

National Laboratories

Armed Forces Radiobiology Research Institute (AFRRI)

Brookhaven National Laboratory (BNL): Space Radiation Program

Lawrence Berkeley National Laboratory (LBNL): Life Sciences Division

Lawrence Livermore National Laboratory (LLNL)

Los Alamos National Laboratory (LANL)

Oak Ridge National Laboratory (ORNL)

Pacific Northwest National Laboratory (PNNL)

Sandia National Laboratories (SNL): Nuclear Weapons

U.S. Department of Defense

Defense Threat Reduction Agency

U.S. Department of Energy (DOE)

Low Dose Radiation Research Program

U.S. Department of Health and Human Services (HHS)

Public Health Emergency Medical Countermeasures Enterprise

Project BioShield

Office of the Assistant Secretary for Preparedness and Response

Biomedical Advanced Research and Development Authority (BARDA)

U.S. Department of Homeland Security (DHS)

Be Informed—Radiation Threat

U.S. Environmental Protection Agency (EPA)

Radiation Protection

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Related Links

Division of Allergy, Immunology, and Transplantation (DAIT)

Biodefense and Related Programs

Chemical Countermeasures

Radiation: the delivery of energy to a distant point by some mechanism; “effect at a distance”

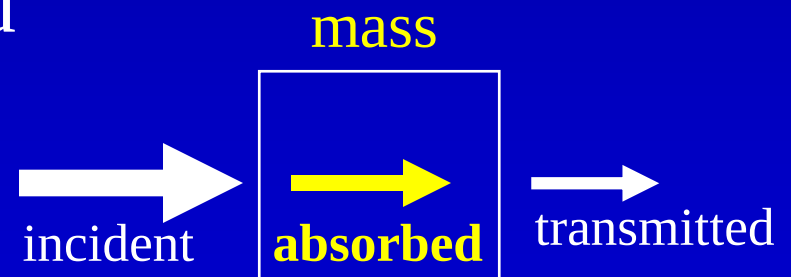
Ionizing Radiation

- That radiation which is capable of ionization
 - Radiation energy must be greater than the binding energy of the atomic electrons, ie, 13.6 eV - ~100 keV
- Radiation may be photons ($E=h\nu$) or particles
 - x rays, γ rays, UV; $E > 13.6$ eV
 - electrons, protons, neutrons, etc

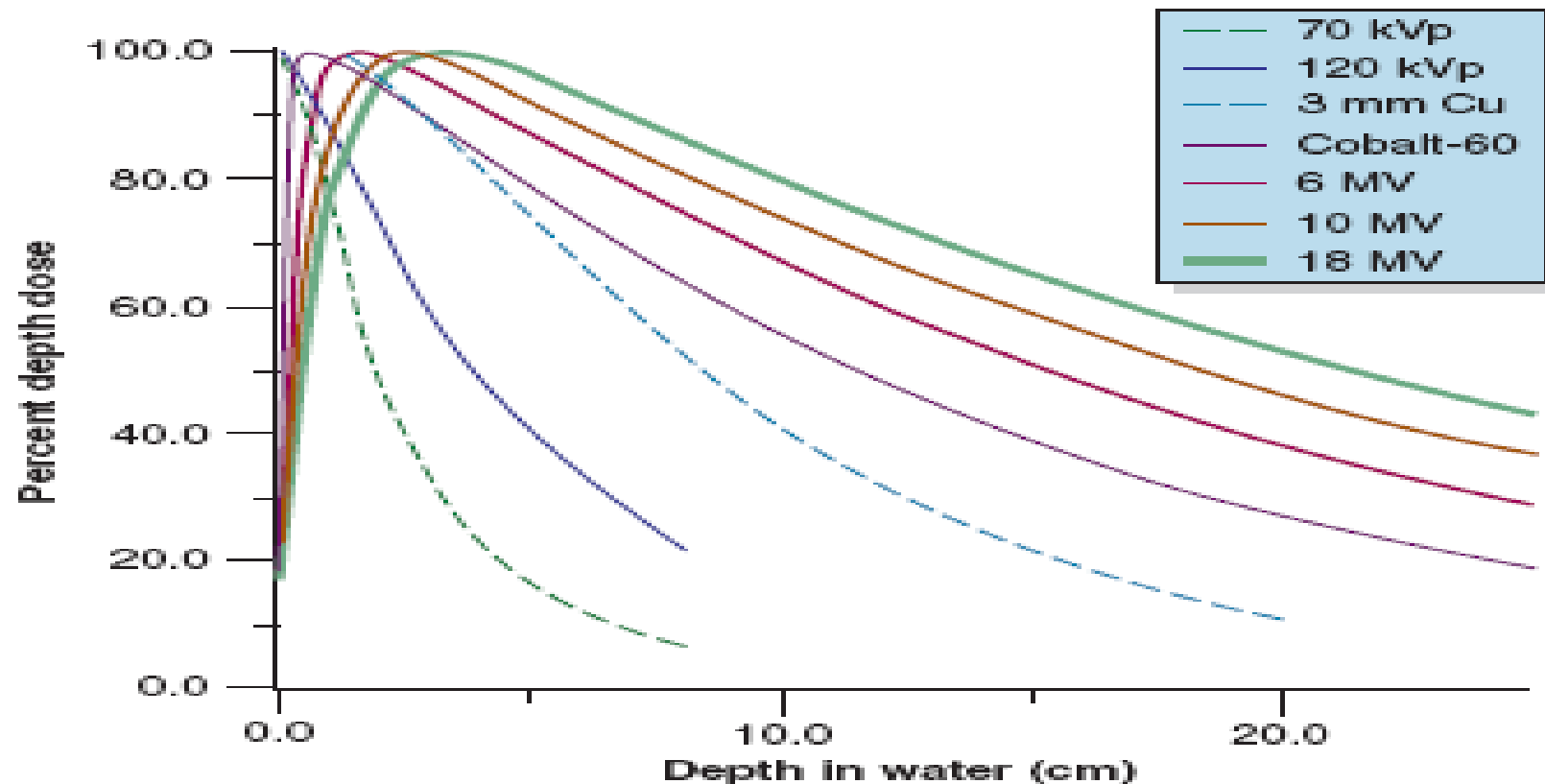
Communication Challenge

Radiation Dose: E / mass, and Dose Distributions (dose / organ)

- **Dose: energy absorbed per unit mass**
 - Unit: rad 1 rad = 100 erg/g
 - SI Unit: Gray 1 Gy = 1 J/kg
 - Conversion: 100 rad = 1 Gy
- Measured by ionization, calorimetry, or chemical
- Calibration protocols defined
- Great detail in practice
- **See your local physicist**



MV vs kV Radiation Beam Depth Dose Curves



Communication Challenge

Radiation Response Sequence

Physical



Chemical



Biological



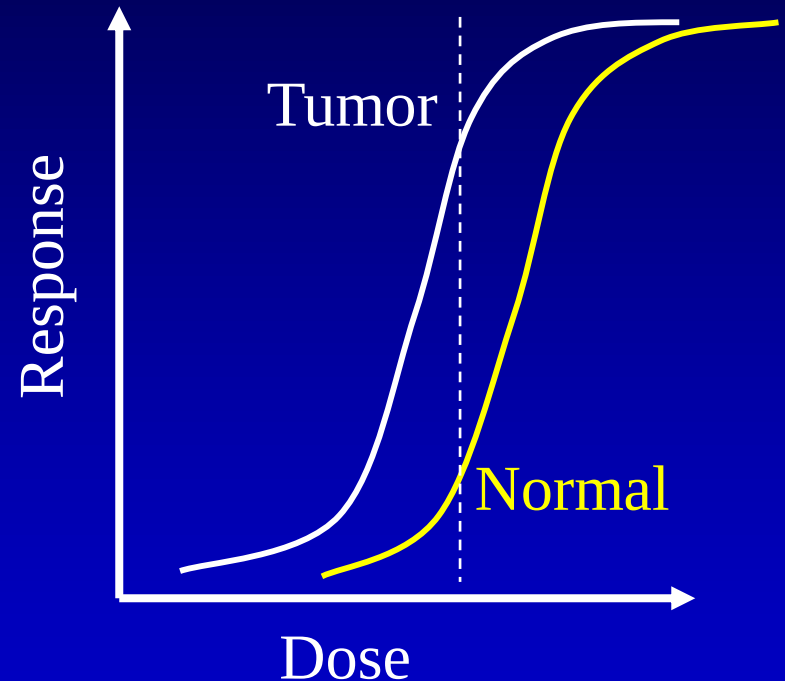
Clinical

(responses, changes, consequences)

Radiation Biology and “Treatment”

Radiobiology of Tumor and Normal Tissues

- Radiation Biology “is complicated”
- Sigmoidal dose-response curve
- Response is dependent on
 - Total radiation dose
 - Fractionation regimen (# of fractions, dose per fraction)
 - Dose rate
 - Radiosensitivity of target
 - Radiosensitivity of nearby normal and/or critical structures, etc



WFU Radiation Survivor Cohort JM Cline, PI

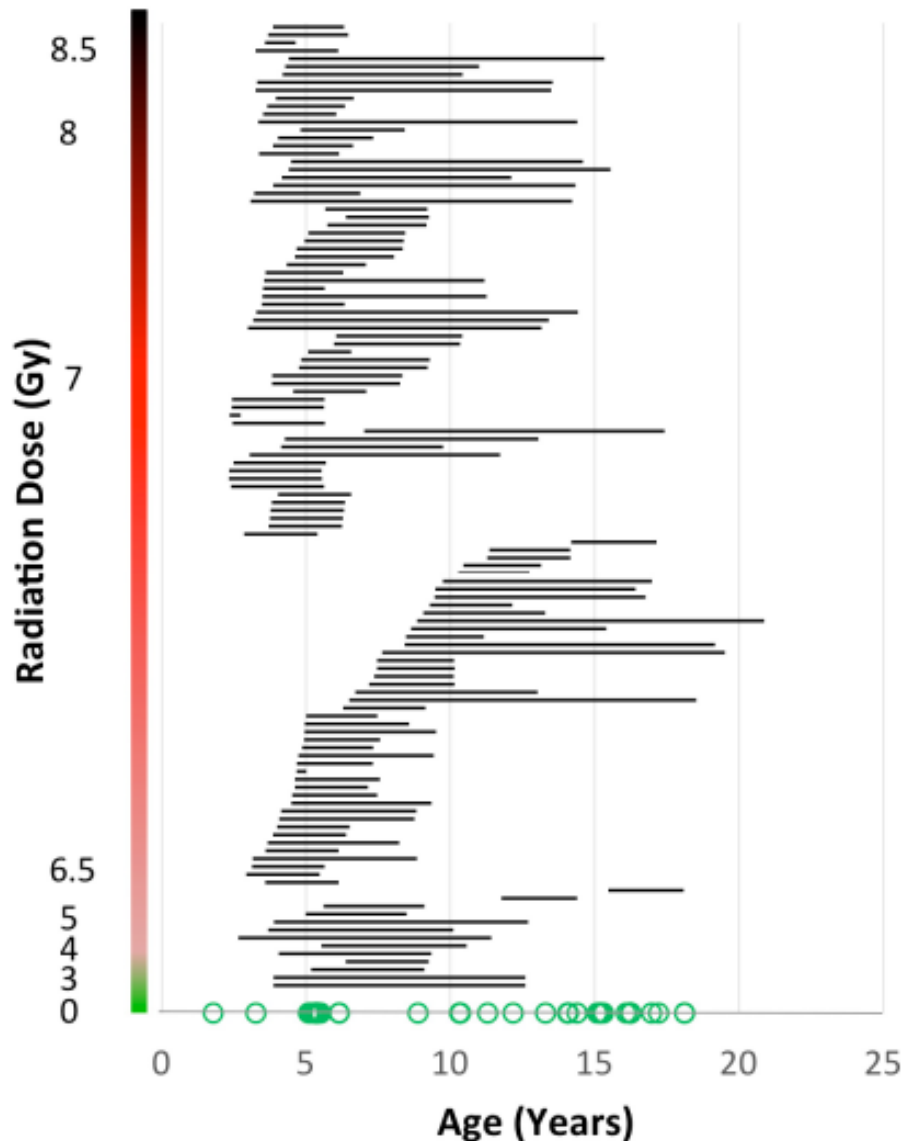


Figure 0.1: Age and dose distribution of the Radiation Survivor Cohort. Each horizontal bar represents a single animal; the left end of the bar is the age at which the animal was irradiated, and the right end of the bar is the animal's current age or age at time of death. Green circles represent the current age of non-irradiated controls. For rhesus monkeys, the typical age at puberty is 3.5 years; typical lifespan is 30 years.

Table 1: Threshold-based determinations of morbidity in the long-term Radiation Survivor Cohort.

Organ or Disease	Irradiated	Control	Fisher's Exact p value	Criteria for Diagnosis of Abnormality
Body Condition Obese	44.4% (20/45)	80% (9/15)	NSD	Waist Circumference > 45 cm or DEXA Body Fat > 30% after 7 years of age
Body Condition Underweight	15.6% (7/45)	13% (2/15)	NSD	Waist Circumference < 25 cm or DEXA Body Fat < 12.3% after 7 years of age
Bone (osteopenia)	34.10% (15/44)	0% (0/13)	0.0129	DEXA BMC < 274g BMD < 0.373 g/cm ³ after 7 years of age CT: Fracture or other abnormality
Brain	12.50% (12/96)	0% (0/15)	NSD	Any MRI lesion Neurologic abnormality
Cardiovascular	25.30% (21/83)	20% (3/15)	NSD	Murmur/valvular insufficiency on echo Stroke volume < 5 mls/stroke Cardiac output < 0.5 L/min Hypertension MAP > 120 Other
Diabetes	13.10% (16/122)	0% (0/38)	0.013	HbA1c > 6.5 Fasting Blood Glucose > 100 mg/dL x 3 Non Fasted Blood Glucose > 200 mg/dL
Gastrointestinal	6.00% (5/83)	6.70% (1/15)	NSD	Any lesion on endoscopy Chronic diarrhea (severity code > 2 for > 5 days) Other GI signs
Lung	10.80% (9/83)	13.30% (2/15)	NSD	CT densities (any amount) Emphysema > 25% of lung volume Hypoxia under sedation (SPO2 < 80%)
Neoplasia	13.10% (16/122)	0% (0/38)	0.0125	Biopsy with histologic diagnosis
Ocular (cataracts)	21.70% (18/83)	0% (0/15)	NSD	Ophthalmologic exam (slit lamp); lens opacity
Renal	35.80% (31/87)	0% (0/24)	< 0.001	Bun > 30 mg/dl Cr > 1.1 mg/dl Loss of renal volume > 50% Urolithiasis
Skin	22.90% (19/83)	6.70% (1/15)	NSD	Biopsy diagnosis of dermatitis Other significant disease (e.g. alopecia, depigmentation)
Testicular atrophy	56.70% (17/30)	6.30% (1/16)	0.0253	< 10 ml testis volume after 5 years of age

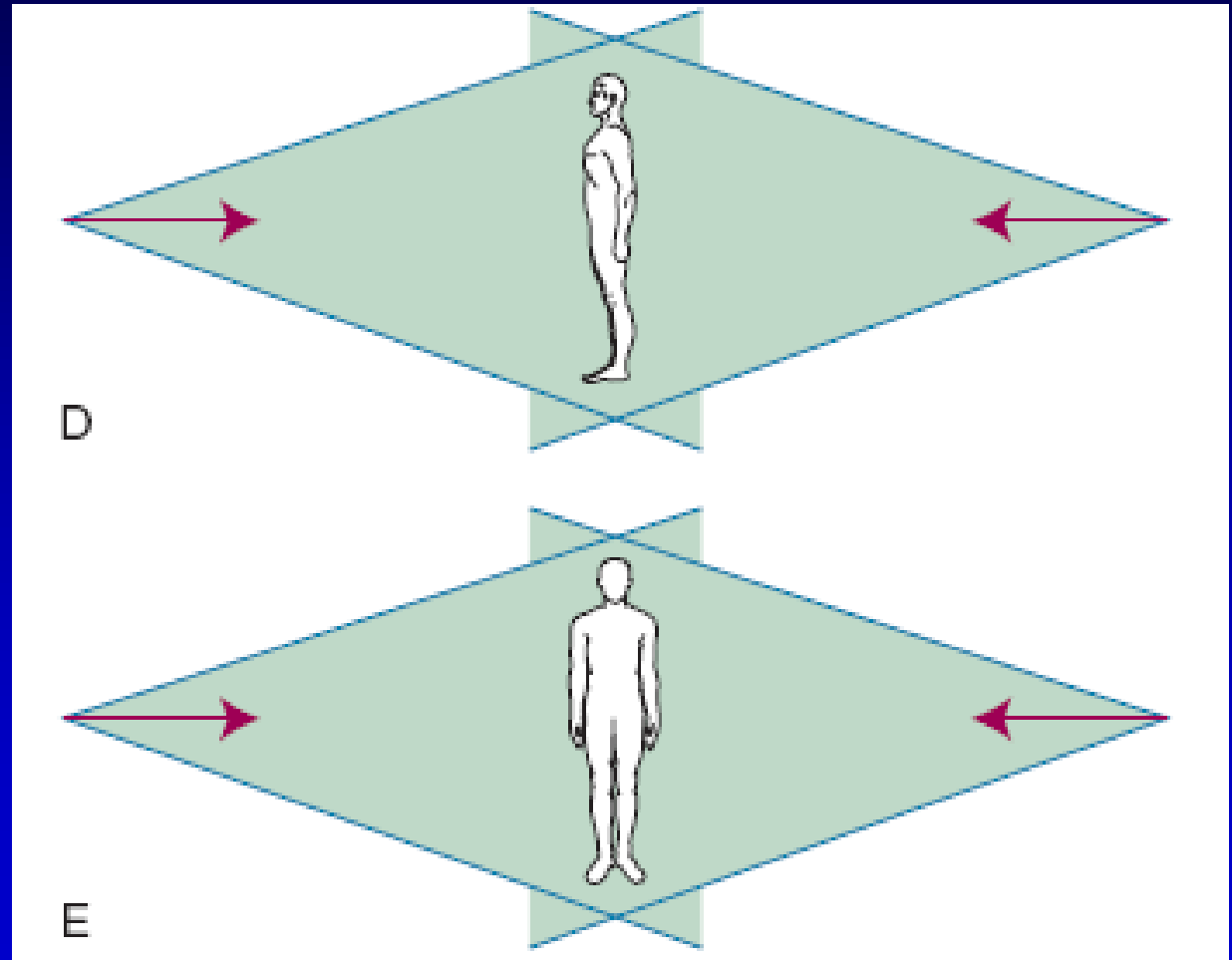
Abbreviations: BUN = blood urea nitrogen; Cr = serum creatinine; CT = computed tomography; DEXA = dual emission x-ray absorptiometry; HbA1c = hemoglobin A1c; MRI = magnetic resonance imaging; NSD = no significant difference; SPO2 = oxygen saturation.

Irradiation Geometry

Total Body Irradiation

Characteristics

- Extended distance
 - 150 – 500 cm
- Large fields
- Parallel-opposed pairs
 - AP-PA or RT-LT
- Photons, $E \geq 6\text{MV}$
- Geometry similar to human TBI protocols



TBI Pilot Geometry

6 MV x ray

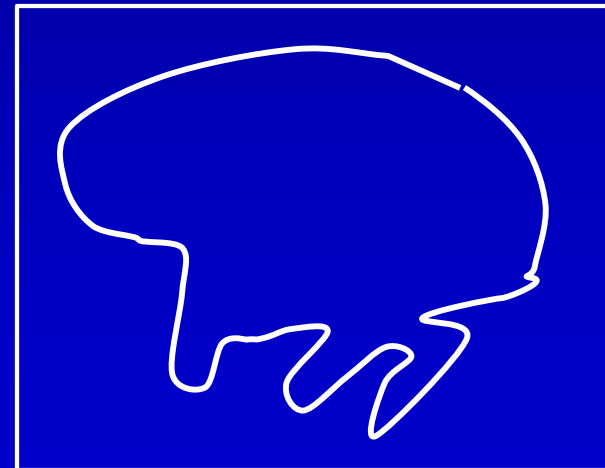
SOURCE

Dose rate ~ 4 Gy/min
field size 40×40 cm²
@ 100 cm

120 cm

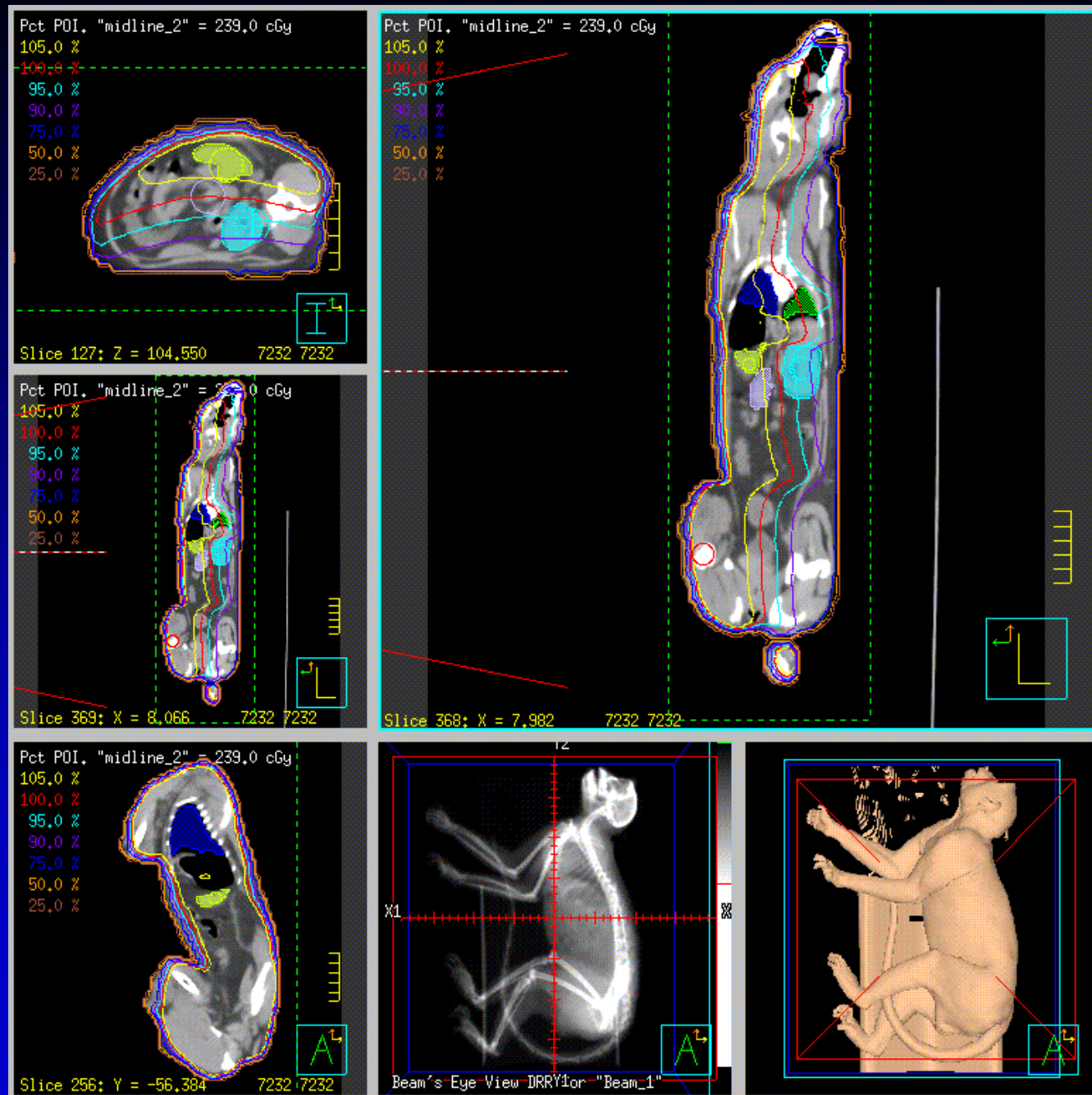
subject

table



Dose Distribution

- Single Field
- Obtain CT scans in irradiation positions
- Segment (outline) “all” anatomy
- Simulate the radiation geometry
- Calculate dose
- Evaluate dose
- CT scan size a challenge for supine animal



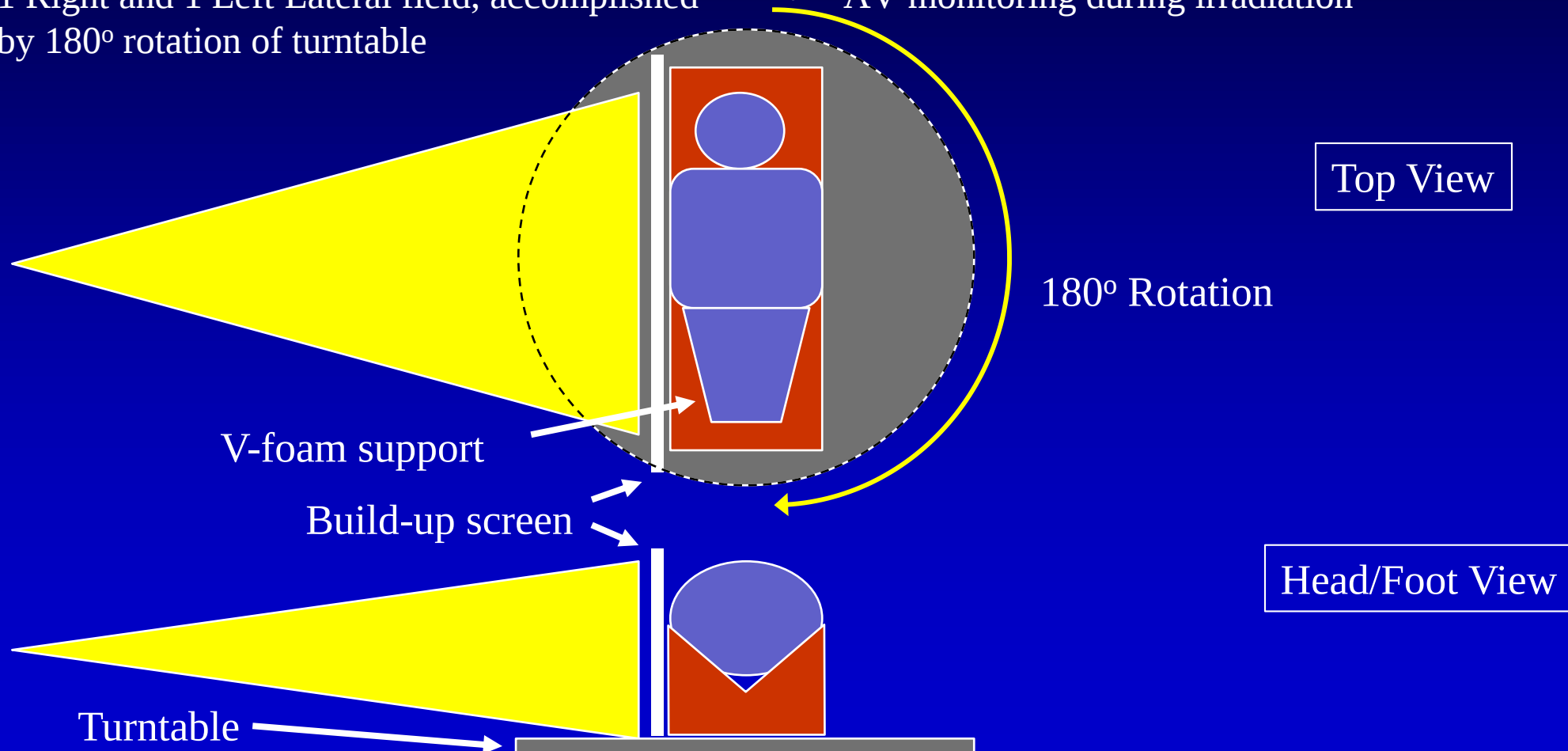
L1 TBI Dose Parameters: NHP

- 6 MV x rays, Opposed Pairs of Fields
 - Left-Right Laterals, with build-up screen
- Extended SSD to include whole body: 1.4 to 1.8m
 - Knees bent/legs retracted; arms at side, wrists at midline
- Dose rate of 0.8 Gy/min at midline
- Dose per protocol, MU calculated to midline, equal weights, no inhomogeneity calculations
- Specific irradiation geometry measured/validated
- Linear accelerator clinically used, QA per natl stds

L1 Irradiation Geometry: 2007

- 6MV x rays, 161cm SSD, 40x20² @ 100cm, diameter of 10-13cm, depth of 5-6.5cm
- DR of 200 MU/min → 0.8 Gy/min at midline
- 1 Right and 1 Left Lateral field, accomplished by 180° rotation of turntable

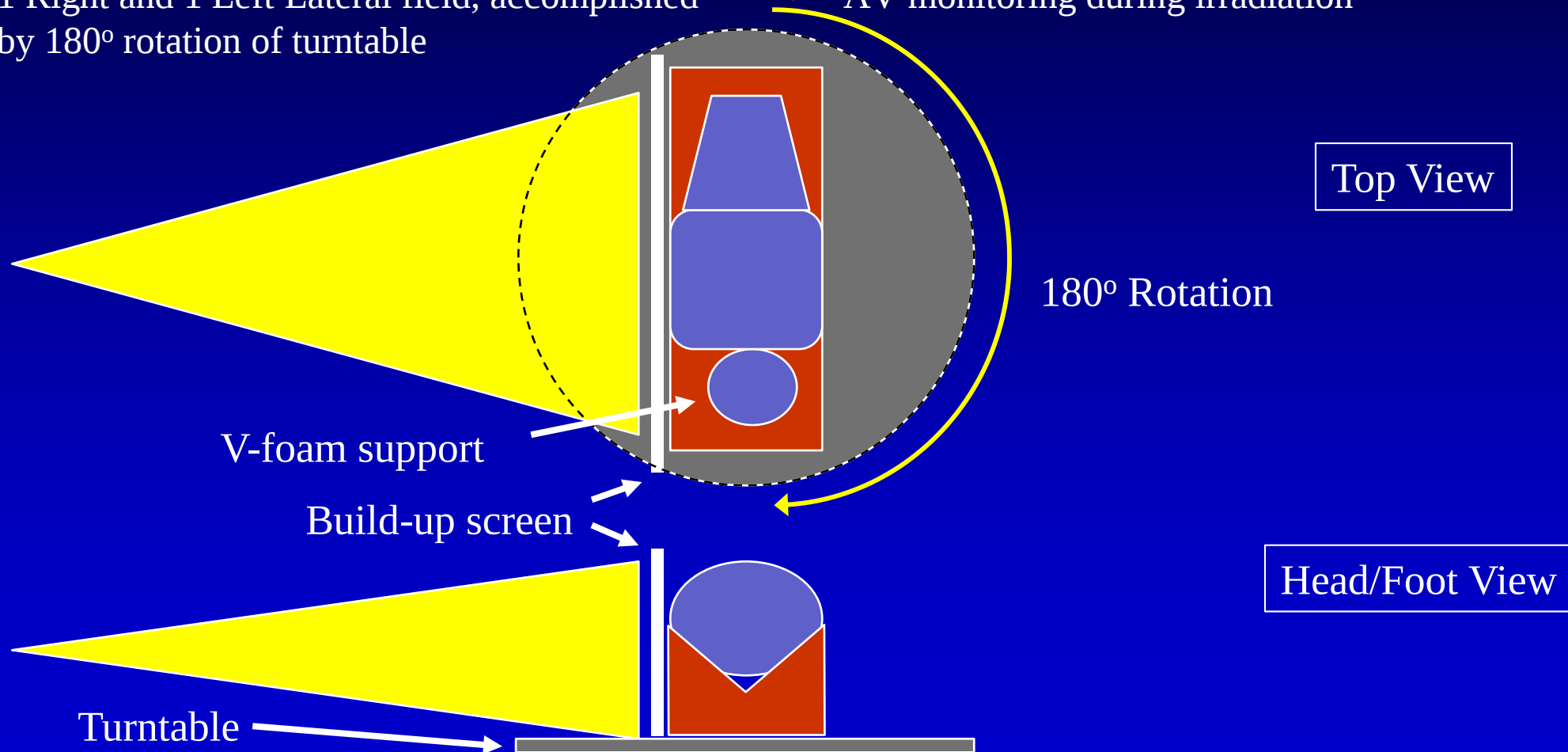
- 1 Build-up Screen
- Average midline depth, adjust for outliers
- Dose measurement prior in phantom
- AV monitoring during irradiation



L1 Irradiation Geometry: 2007

- 6MV x rays, 161cm SSD, 40×20^2 @ 100cm, diameter of 10-13cm, depth of 5-6.5cm
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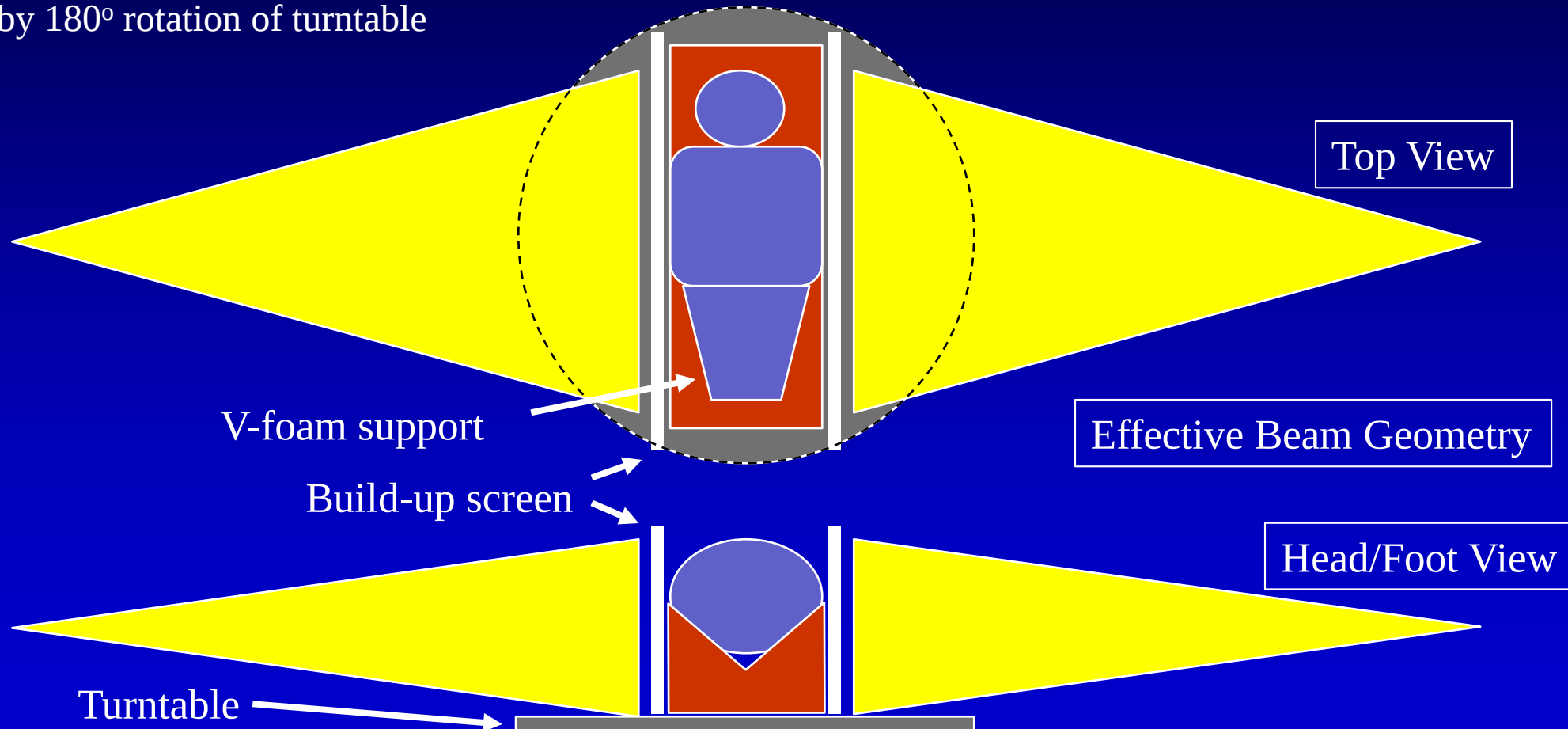
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L1 Irradiation Geometry: 2007

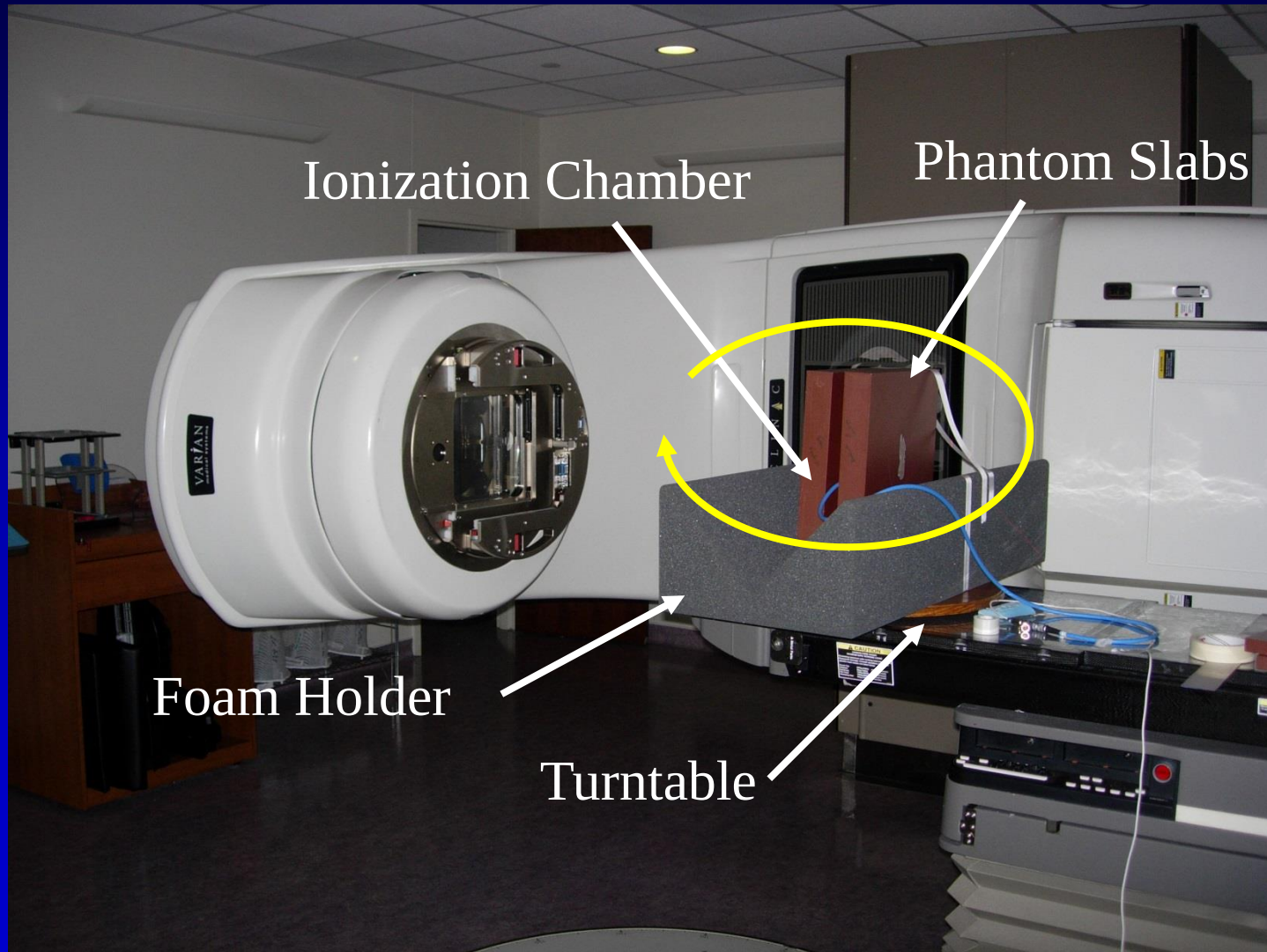
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DoseVerification

Prior to Research Procedures

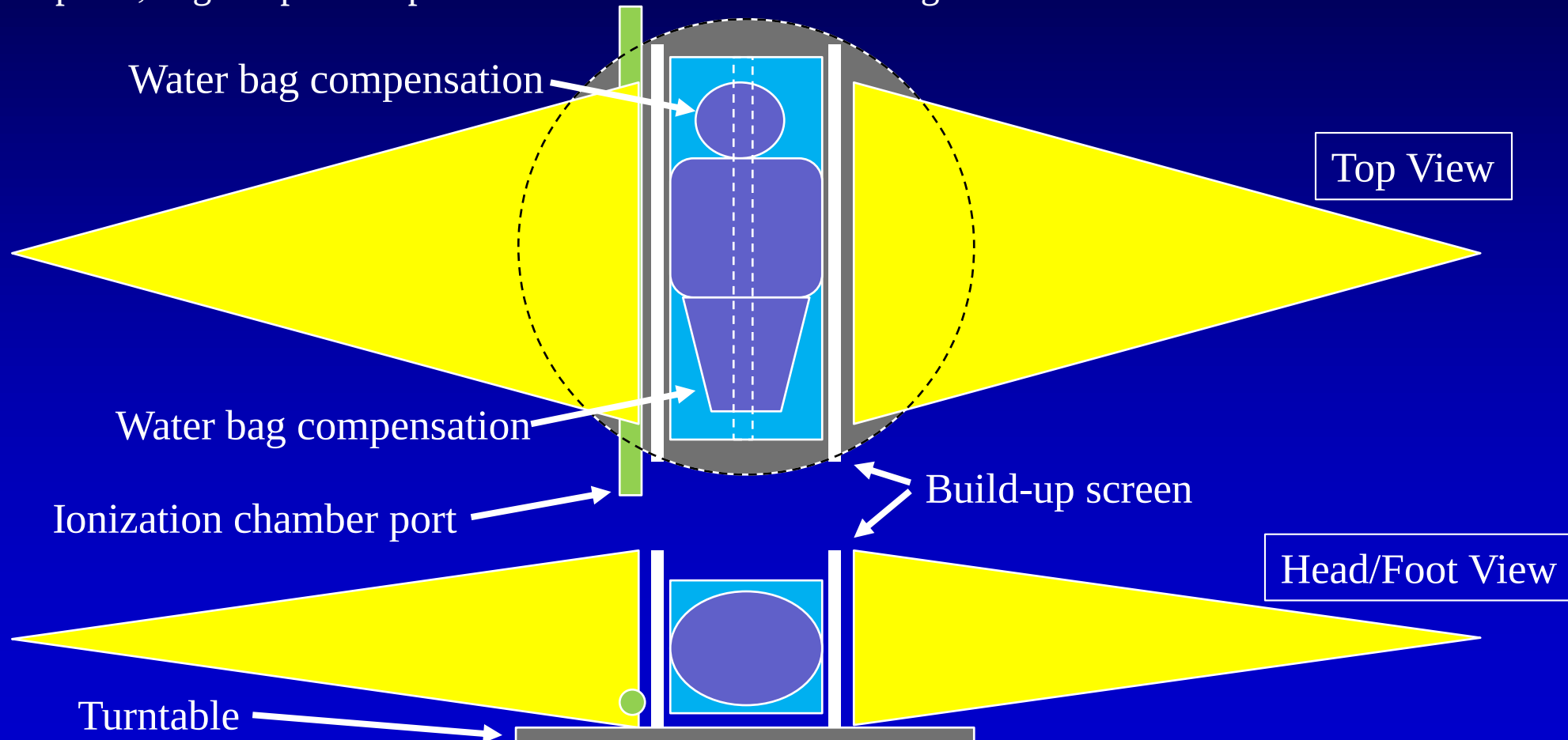


Irradiation Record

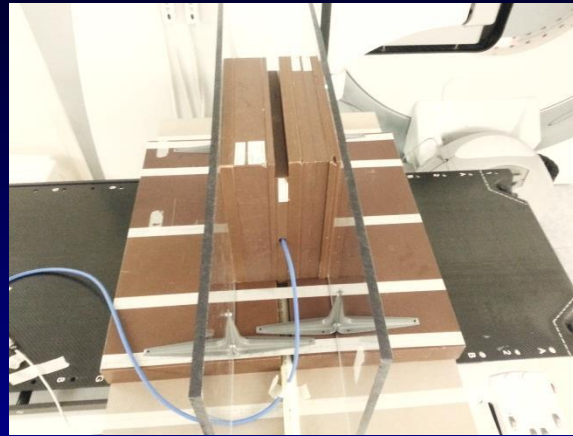
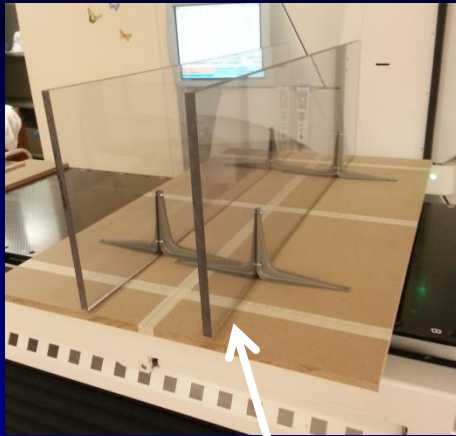
Animal #	Time In / Out (AM)	MU Rt	MU Lt	SSD	Field Size 40x20 @ 100 cm	Nominal Diameter (cm)	Mid-Plane Depth (cm)	Bolus Screen	Weight (kg)	Comment
7487 C1	8:10 / 8:55	291	291	161.3	Y	13	6.5	N / Y	6.3	First animal for set-up. Tail radius limited. Adjusted nominal SSD to 161.3 cm. Screen on Lt side only. DRlow on Rt side and 168/291 of Lt side. Animal awoke.
7492 C2	9:15 / 9:21	291	291	(163.1)	Y	(13)	(6.5)	Y	7.0	T = 1.46 min per side
7495 C2	9:24 / 9:32	291	291	(163.1)	Y	(13)	(6.5)	Y	5.5	T = 1.46 min per side
7499 C3	9:49 / 9:55	291	291	(163.1)	Y	(13)	(6.5)	Y	6.1	T = 1.46 min per side
7493 C3	10:00 / 10:07	291	291	(163.1)	Y	(13)	(6.5)	Y	6.8	T = 1.46 min per side
7494 C4	10:23 / 10:29	291	291	(163.1)	Y	(13)	(6.5)	Y	6.8	
7501 C4	10:32 / 10:40	281	281	162.8	Y	10	5.0	Y	4.2	Pee Wee – Revised MU for size
7486 C5	11:00 / 11:07	291	291	(163.1)	Y	(13)	(6.5)	Y	6.55	
7489 C5	11:09 / 11:16	291	291	(163.1)	Y	(13)	(6.5)	Y	6.0	
7498 C5	11:19 / 11:25	286	286	162	Y	11.5	5.8	Y	5.3	Revised MU for size. Lt side at DRhigh

WFU L2A Irradiation Geometry

- Lazy Susan, 2 Build-up Screens
- Dose measurement prior in phantom
- 174 cm SSD, 6MV x rays, 80 cGy/min @ midplane, avg midplane depth of 11cm
- Dose measurement during irradiation at an exit reference point, all fields
- Water bag compensation for head, ankles
- 1 Right and 1 Left Lateral field

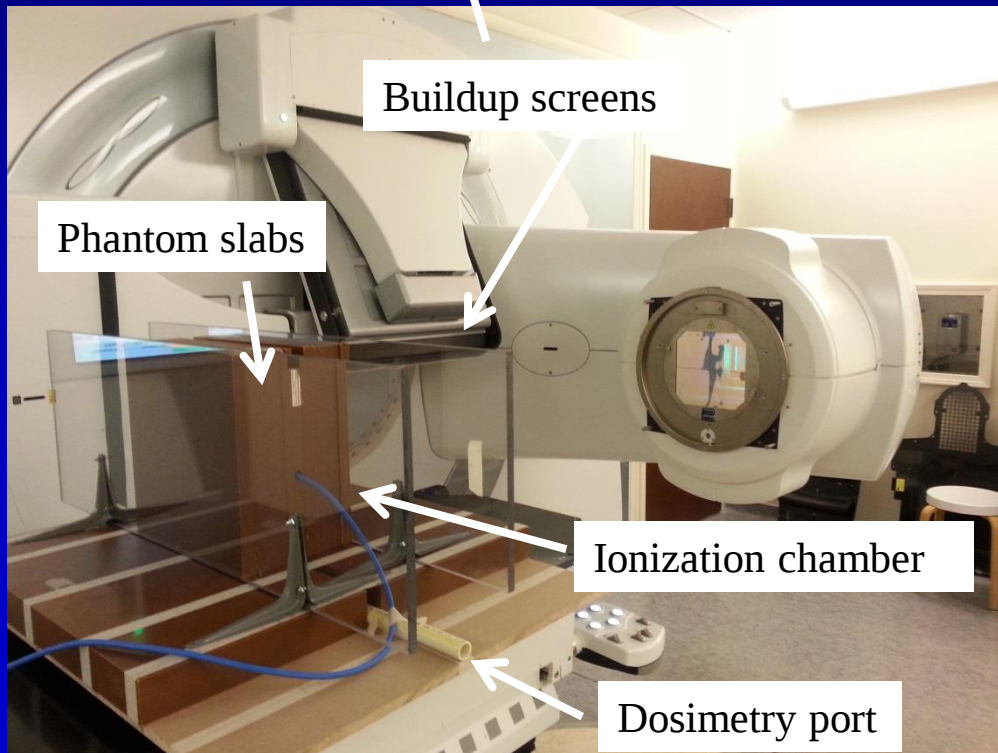


L2A Irradiation Geometry: 2015



In vivo Dose Results

592.34	620.06	-0.01	1732
579.97	616.45	-0.03	1763
579.33	615.77	-0.03	1765
578.99	630.50	-0.04	1784
585.37	613.12	-0.02	1788
583.17	615.82	-0.03	1790
583.20	618.62	-0.03	

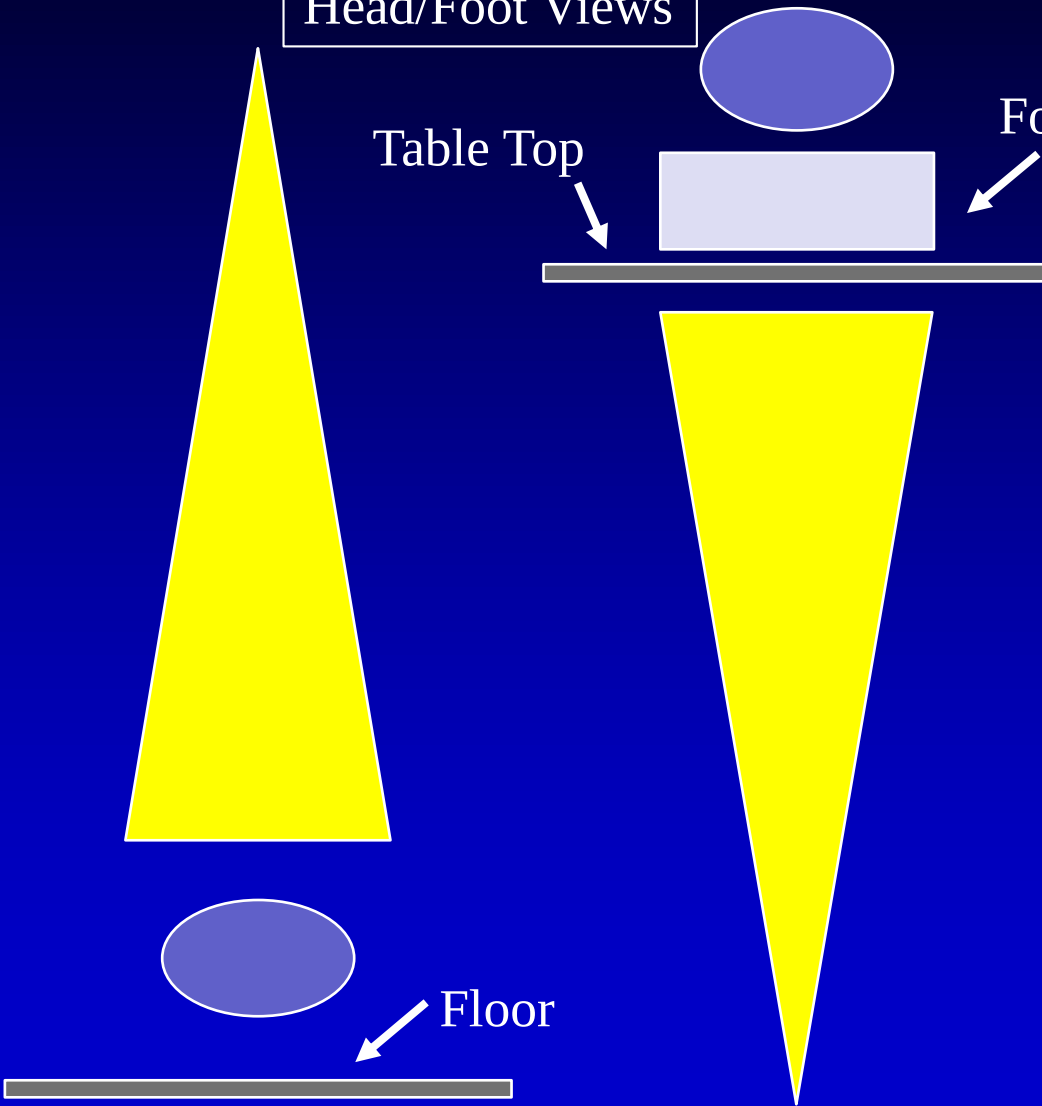


Irradiation Geometry: Site 1: 6 MV X Rays

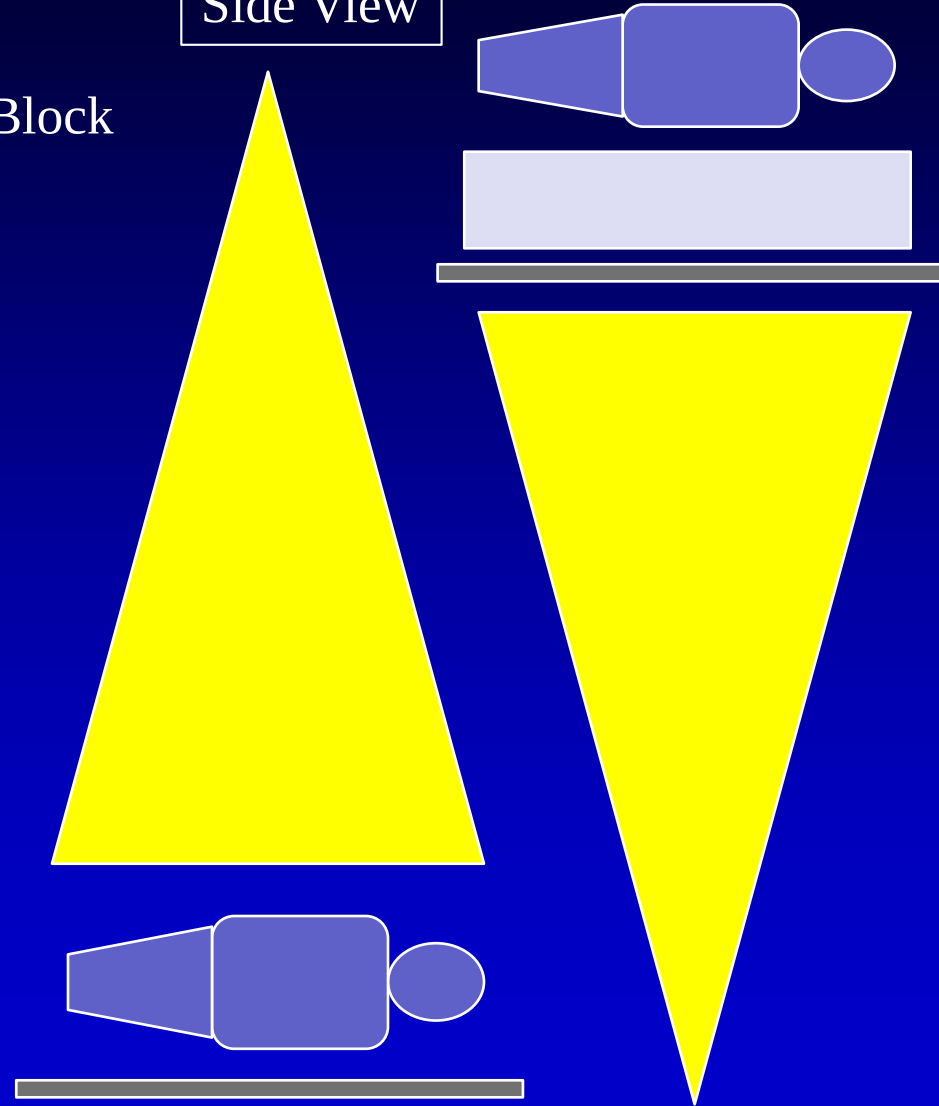
Head/Foot Views

Table Top

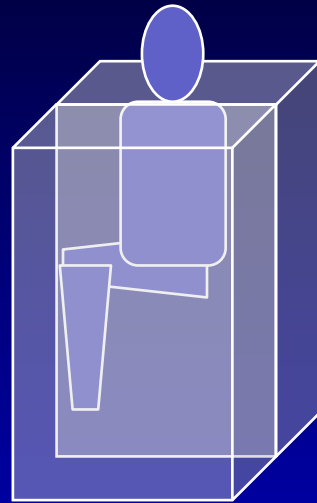
Foam Block



Side View

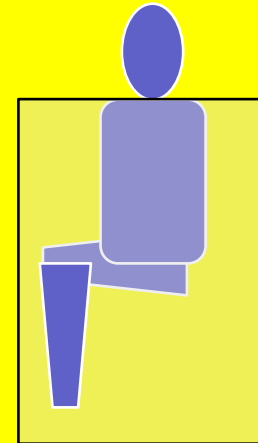


Irradiation Geometry: Site 2: Cobalt-60 Flood

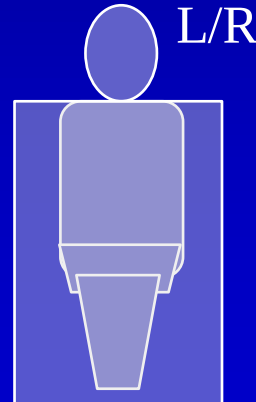


Seated,
Plastic Box

Side View

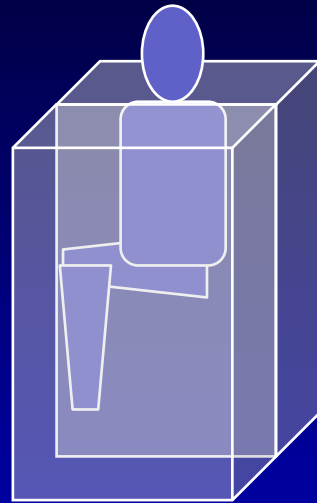


Anterior/Posterior View



L/R

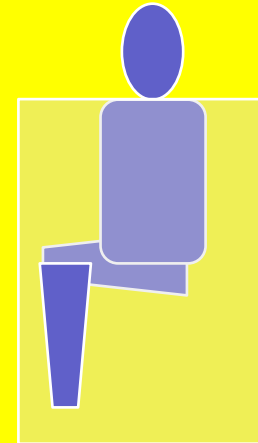
Irradiation Geometry: Site 3: 6 MV X Rays



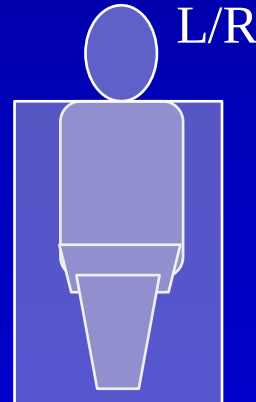
Seated,
Plastic Box



Side View



Anterior/Posterior View



L/R

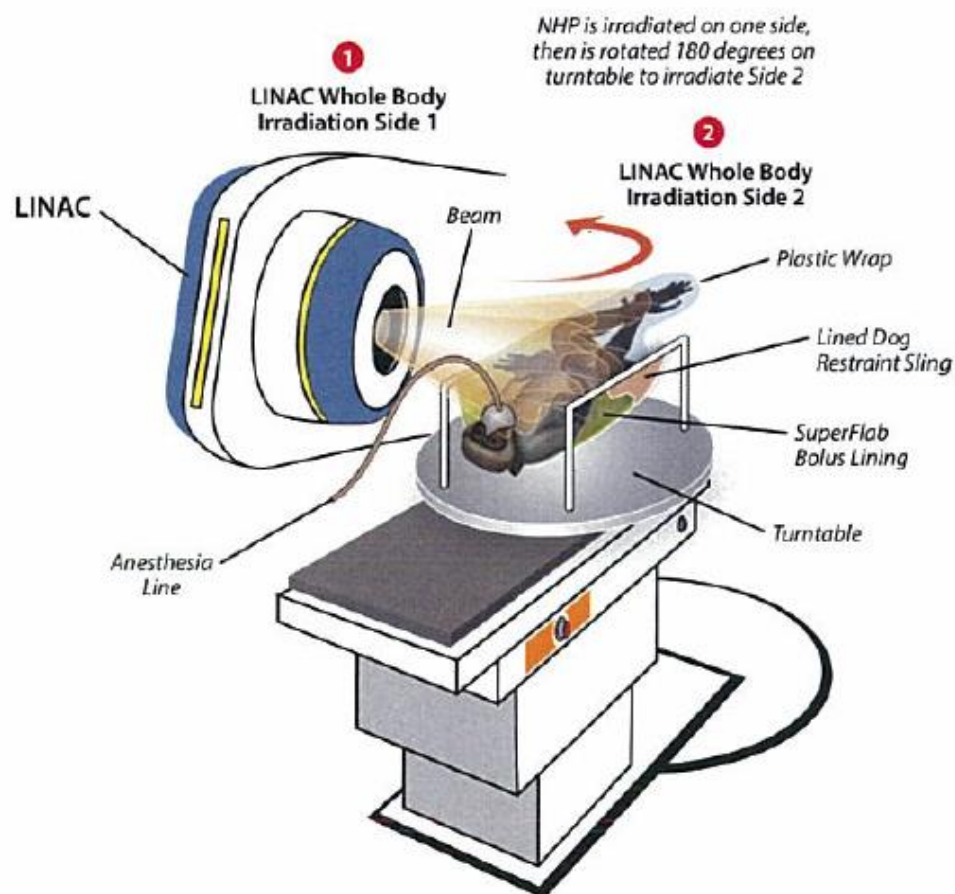


Comparison of Dosimetry Techniques in Rhesus Macaques

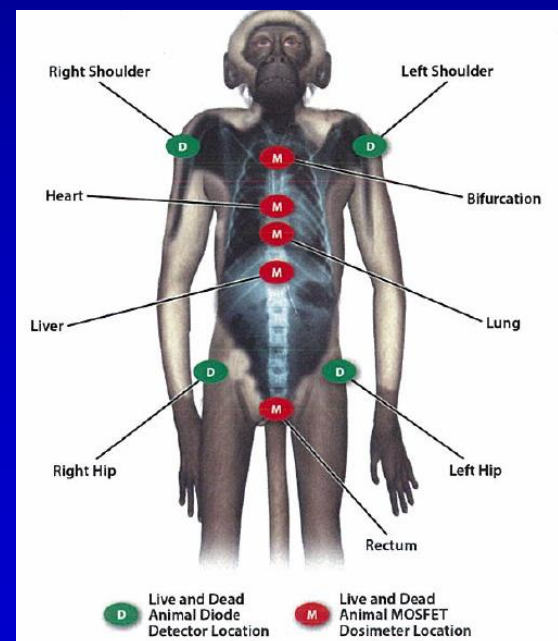
Dunstana Melo¹, Waylon Weber¹, Daniel Sandoval²,
Melanie Doyle-Eisele¹, A. Matchett¹, J. Bayardo¹, Philip Heintz², Ray Guilmette¹

Lovelace Respiratory Research Institute, Albuquerque, NM; ²University of New Mexico, Albuquerque, NM

LINEAR ACCELERATOR (LINAC) ANIMAL EXPOSURE SETUP NON-HUMAN PRIMATE (NHP) EXPOSURE

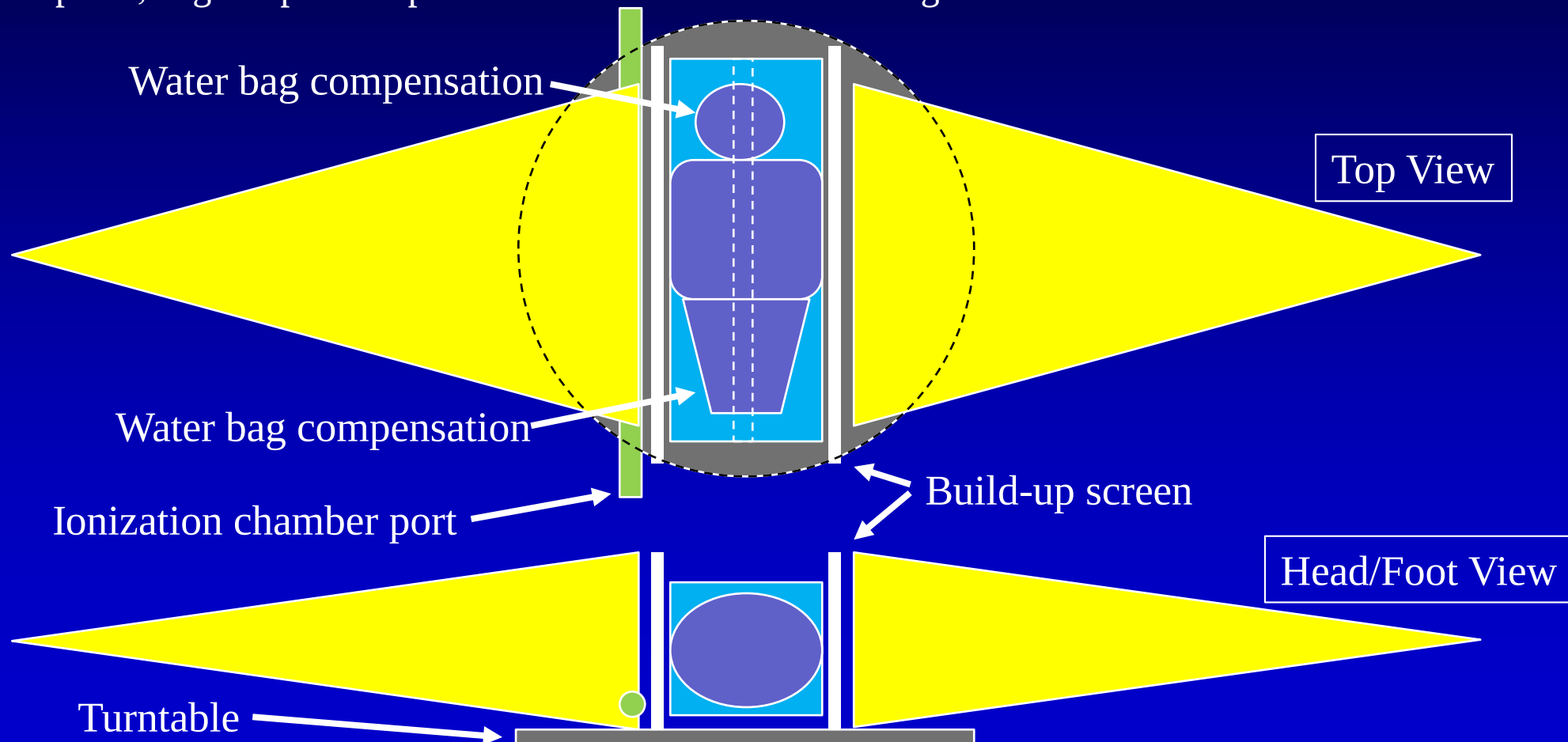


Animal	Average $\pm$ SD % planned dose diode detectors (range)	Average % planned dose measured with MOSFET dosimeters				
		Bifurcation of trachea	Heart	Lung	Liver	Rectum
Live	99 $\pm$ 1 (98 – 101)	98 $\pm$ 5 (93 – 105)	108 $\pm$ 6 (102 – 115)	105 $\pm$ 4 (100 – 109)	104 $\pm$ 2 (102 – 107)	105 $\pm$ 2 (102 – 108)
Dead	100 $\pm$ 2 (98 – 102)	100 $\pm$ 4 (96 – 106)	104 $\pm$ 1 (103 – 105)	104 $\pm$ 2 (101 – 105)	101 $\pm$ 2 (98 – 105)	103 $\pm$ 2 (102 – 104)



WFU L2A Irradiation Geometry: 6 MV X Rays

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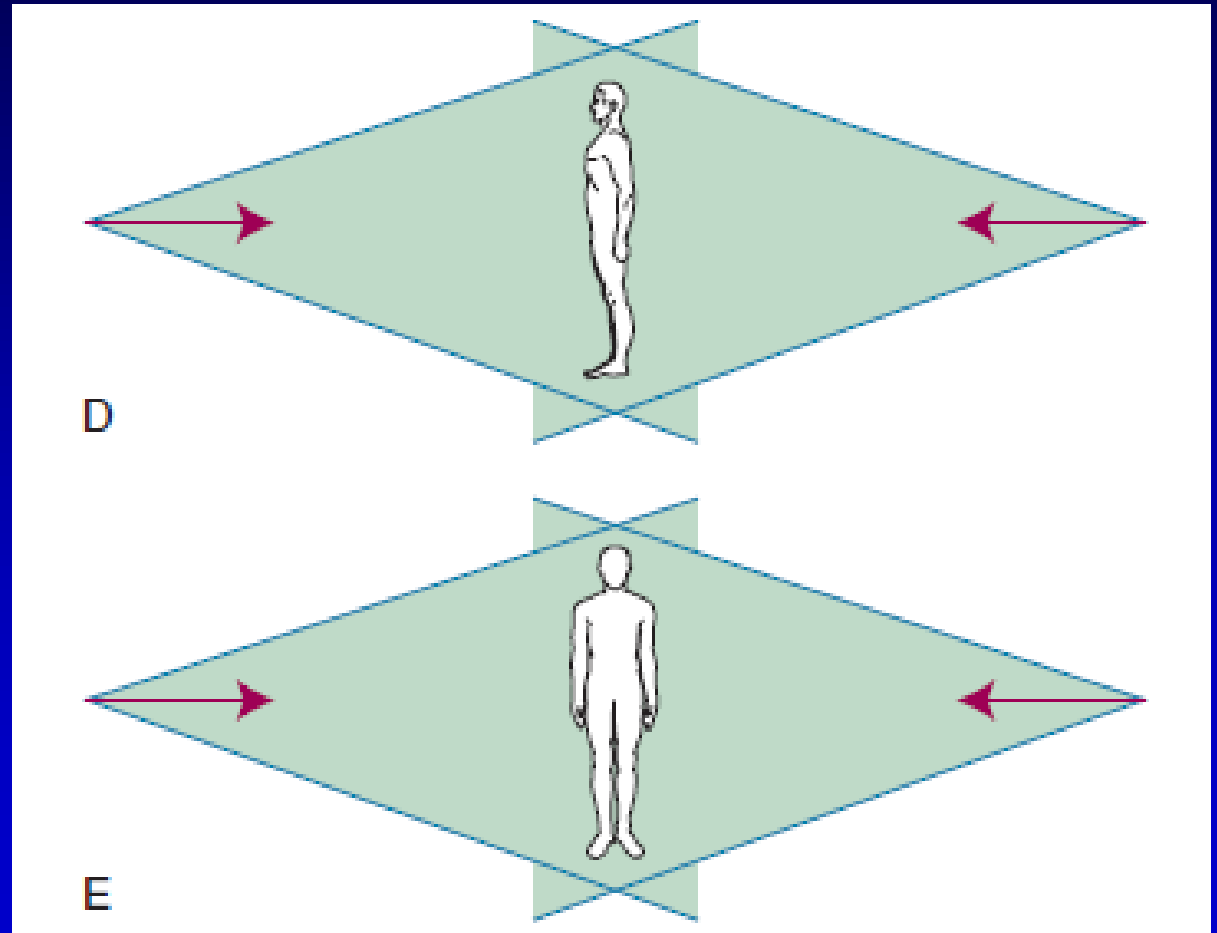


Physics Challenge

Whole Body Irradiation Geometry

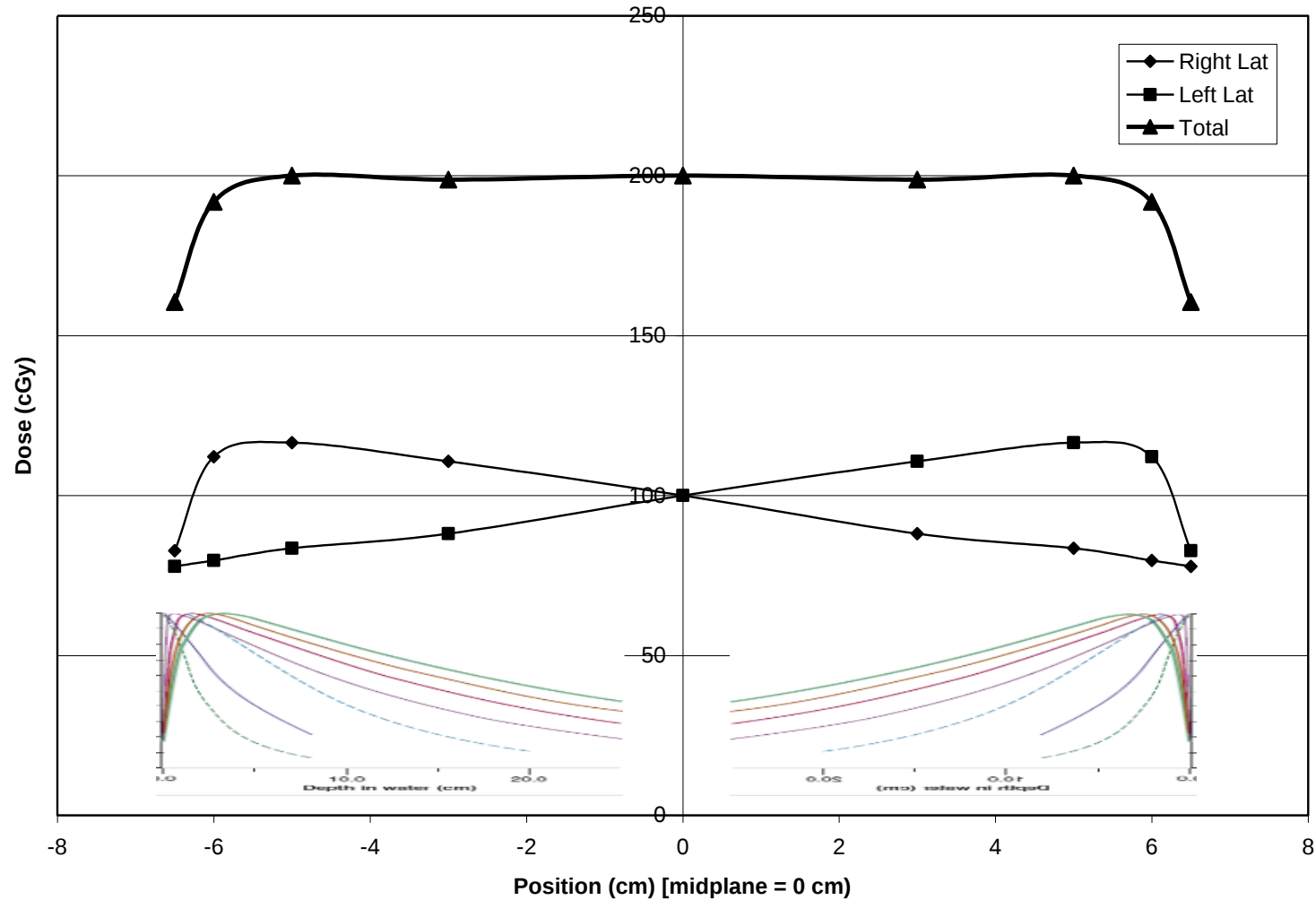
Two Most Commonly Used Geometries

- Which technique best?
- Animal species in use?
- Photon energy?
- Dose calc point?
- Dose rate?
- Y/N Buildup?
- Y/N Compensation?
- Overall dose homogeneity?
- Dose monitoring?
- **Shall we standardize TBI?**



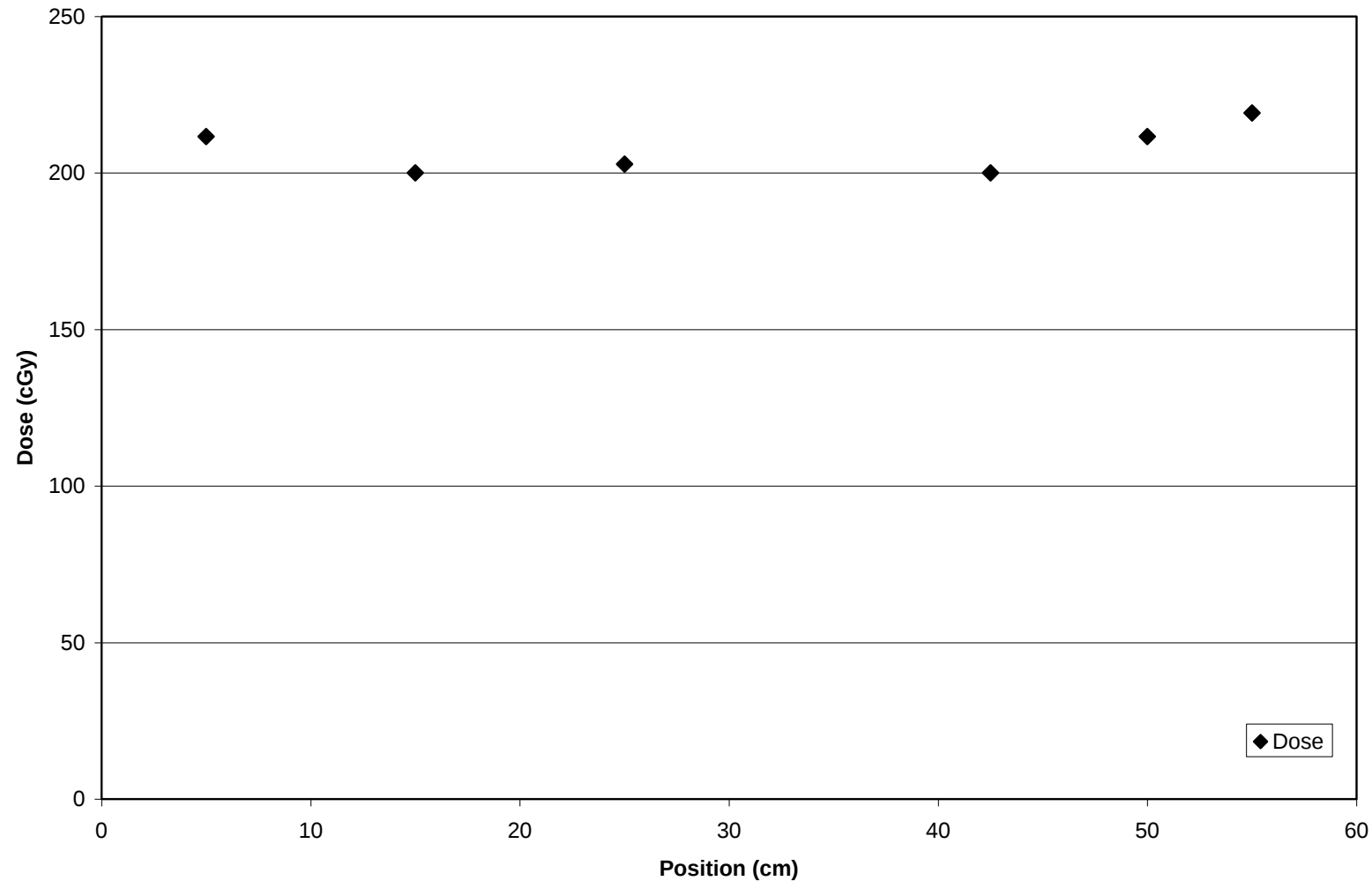
Dose Homogeneity: 14cm diameter

Graph 1: Dose Homogeneity: Right (neg) to Left (pos)



Dose Homogeneity: S-I Level

Graph 2: Dose Homogeneity: Superior (0 cm) to Inferior (55 cm)



Measurements for Dose Calculations

AP, RL Diameters, Length, Weight

Animal ID#	Gender (M/F)	Body Weight (kg)		Anterior-Posterior Diameters														
				Head To Toe Length (cm)		Head To Knee Length (cm)		Head (cm)			Shoulder s (cm)		Pelvis (cm)		Knees (cm)		Ankles (cm)	Total %Diff
8410	F	3.9	8.5%	74	-0.5%	51	1.4%	11	1.4%	9.3	0.4%	7.7	15.7%	3.2	-10.7%	3.1	0.9%	17.5%
8411	F	3.95	9.9%	77	3.5%	53	5.4%	11.3	4.2%	9	-2.8%	6.3	-5.3%	3.4	-5.1%	3.5	13.9%	-4.0%
8412	F	3.75	4.3%	75	0.9%	51	1.4%	10.9	0.5%	9.9	6.9%	8.3	24.7%	3.8	6.1%	3.3	7.4%	32.1%
8413	F	3.5	-2.7%	74	-0.5%	49	-2.5%	10.5	-3.2%	9.4	1.5%	5.8	-12.8%	3.6	0.5%	3.2	4.1%	-14.6%
8414	F	3.2	-11.0%	72	-3.2%	48	-4.5%	10.5	-3.2%	8.4	-9.3%	6.6	-0.8%	3.3	-7.9%	2.7	-12.1%	-13.3%
8415	F	3.2	-11.0%	71	-4.5%	47	-6.5%	11.5	6.0%	10.7	15.5%	6.8	2.2%	3.6	0.5%	3	-2.4%	23.7%
8416	F	3.55	-1.3%	78	4.9%	53	5.4%	11.1	2.3%	8.8	-5.0%	6.1	-8.3%	4.2	17.3%	2.7	-12.1%	-11.0%
8417	F	3.9	8.5%	78	4.9%	54	7.4%	11.3	4.2%	9.4	1.5%	6.6	-0.8%	4.2	17.3%	3.2	4.1%	4.8%
8418	F	4.65	29.3%	76	2.2%	53	5.4%	10.9	0.5%	9.7	4.7%	7.6	14.2%	3.8	6.1%	3.4	10.7%	19.4%
8419	F	3.05	-15.2%	71	-4.5%	47	-6.5%	10	-7.8%	8.2	-11.5%	6.1	-8.3%	3.7	3.3%	3.1	0.9%	-27.6%
8420	F	2.9	-19.3%	72	-3.2%	47	-6.5%	10.3	-5.0%	9.1	-1.8%	5.3	-20.4%	2.6	-27.4%	2.6	-15.4%	-27.2%
		3.6		74.4		50.3		10.8		9.3		6.7		3.6		3.1		
Cohort 1	F	3.9	8.9%	76.3	2.6%	52.7	4.8%	11.2	3.3%	9.2	-0.3%	6.9	3.2%	3.6	0.5%	3.3	6.3%	6.1%
Cohort 2	F	3.9	7.5%	74.0	-0.5%	50.3	0.1%	11.1	2.3%	10.1	9.0%	7.6	13.7%	3.7	4.2%	3.2	5.2%	25.1%
Cohort 3	F	3.4	-5.0%	74.7	0.4%	50.0	-0.5%	10.7	-1.3%	8.9	0.0	6.2	-7.3%	3.7	3.3%	2.9	-6.7%	-13.0%
Donors	F	3.0	-17.3%	71.5	-3.9%	47.0	-6.5%	10.2	-6.4%	8.7	-6.6%	5.7	-14.3%	3.2	-12.1%	2.9	-7.2%	-27.4%
8421	M	5.3	-16.2%	76	-6.6%	52	-5.1%	12.2	-3.9%	13.1	6.5%	9.5	-12.8%	4	-9.3%	2.9	-12.8%	-10.2%
8422	M	5.2	-17.8%	80	-1.7%	54	-1.5%	11.9	-6.2%	14.3	16.3%	10.5	-3.7%	4.5	2.1%	3.6	8.2%	6.4%
8423	M	5.5	-13.8%	79	-2.9%	53	-3.3%	12.2	-3.9%	11.1	-9.8%	10.7	-1.8%	4.2	-4.7%	2.8	-15.8%	-15.5%
8424	M	5.8	-8.3%	80	-1.7%	54	-1.5%	12.8	0.9%	10.2	-17.1%	11	0.9%	4.9	11.1%	3.4	2.2%	-15.3%
8425	M	6.8	6.8%	84	3.2%	57	4.0%	13.2	4.0%	12.9	4.9%	8.3	-23.9%	4.3	-2.5%	3.2	-3.8%	-15.0%
8426	M	7.9	24.9%	83	2.0%	55	0.3%	14	10.3%	12.7	3.3%	11.5	5.5%	4.5	2.1%	3.1	-6.8%	19.1%
8427	M	8.2	28.9%	87	6.9%	57	4.0%	13.4	5.6%	12.6	2.4%	9.6	-11.9%	5.3	20.2%	3.4	2.2%	-3.9%
8428	M	7.6	20.2%	80	-1.7%	54	-1.5%	13.2	4.0%	12.3	0.0%	13.4	22.9%	3.8	-13.8%	3.6	8.2%	26.9%
8429	M	5.5	-13.8%	84	3.2%	56	2.2%	11.5	-9.4%	14.3	16.3%	10.5	-3.7%	4.5	2.1%	3.4	2.2%	3.2%
8430	M	5.6	-12.2%	80	-1.7%	55	0.3%	12.1	-4.7%	11.4	-7.3%	11.8	8.3%	4.6	4.3%	3.4	2.2%	-3.7%
8431	M	6.4	1.2%	82	0.8%	56	2.2%	13.1	3.2%	10.4	-15.4%	13.1	20.2%	3.9	-11.5%	3.8	14.2%	8.0%
		6.3		81.4		54.8		12.7		12.3		10.9		4.4		3.3		
Cohort 1	M	6.3	0.2%	81.0	-0.4%	54.7	-0.3%	12.6	-1.0%	12.4	0.5%	10.3	-5.5%	4.6	5.1%	3.2	-2.8%	-5.9%
Cohort 2	M	5.7	-10.1%	82.0	0.8%	55.3	0.9%	12.2	-4.1%	13.0	5.7%	11.4	4.3%	4.3	-2.5%	3.6	8.2%	5.8%
Cohort 3	M	6.0	-5.1%	81.0	-0.4%	54.7	-0.3%	12.7	0.3%	11.4	-7.3%	10.0	-8.3%	4.5	1.3%	3.1	-5.8%	-15.2%
Donors	M	7.8	22.6%	81.5	0.2%	54.5	-0.6%	13.6	7.2%	12.5	1.6%	12.5	14.2%	4.2	-5.9%	3.4	0.7%	23.0%

Date: _____

Animal: _____

Weight: _____

Head-to-Toe Length (cm): _____

Head-to-Knee Length (cm): _____

Anterior-Posterior Diameter (cm)

Head: _____

Shoulders: _____

Pelvis: _____

Knees: _____

Ankles (both): _____

Head-to-Toe Length (cm): _____

Head-to-Knee Length (cm): _____

Left-Right Diameter (cm)

Head: _____

Shoulders: _____

Pelvis: _____

Knees: _____

Ankles (both): _____

Initials: _____

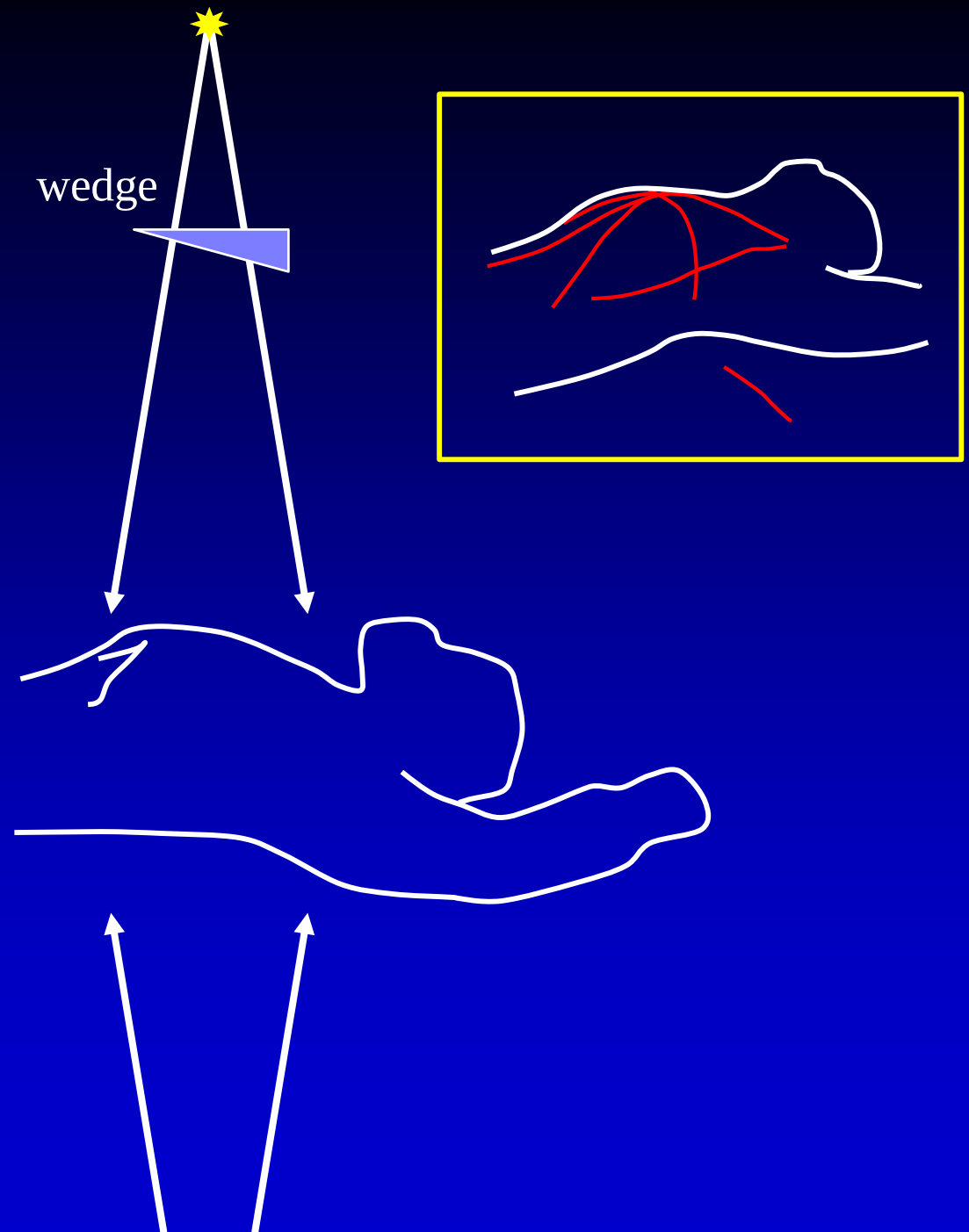
Monitor Unit (Time) Calculations

- NHP measurements, dose, and geometry parameters used to calculate monitor unit (timer) settings for the linear accelerator
- Validated with specific experiment measurements

$$MU = \frac{TD}{D_o \cdot \left[\frac{(SAD + dm)}{(SSD + d)} \right]^2 \cdot Sc \cdot Sp \cdot TMR \cdot OAF \cdot WF \cdot TF \cdot OF}$$

L2B: Irradiation Geometry Partial Body: Lungs

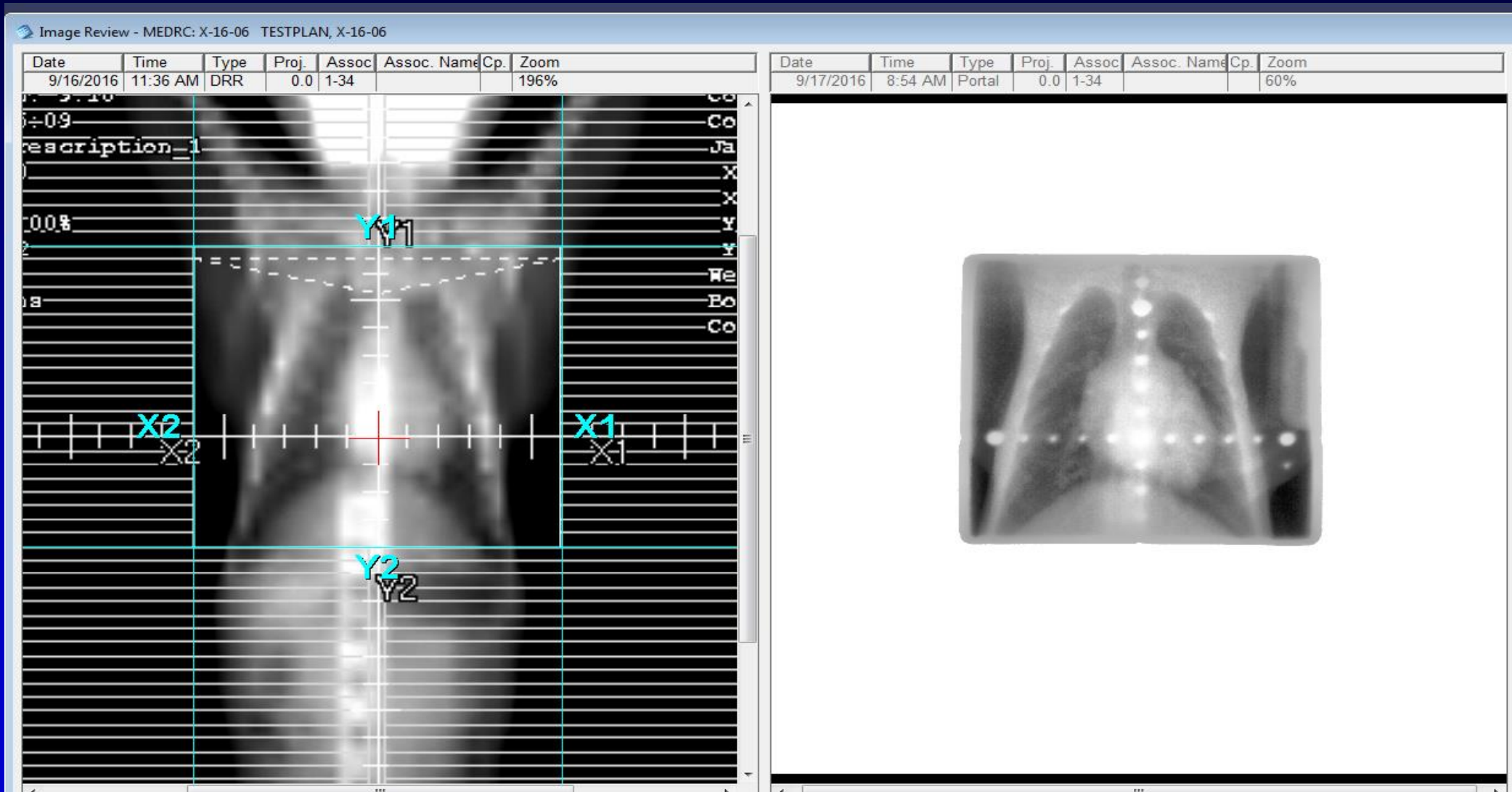
- AP-PA, 6 MV x rays
- 96 cm SSD (average)
- FS: 10.0 x [5.0, 7.5] cm²
- 1 cm bolus, AP field
- Table + post tissue, PA
- Calculated to midplane, no lung corrections
- Non-ketamine anesthesia – aid for flexibility of positioning without rigidity



AP-1934

DRR-Planned

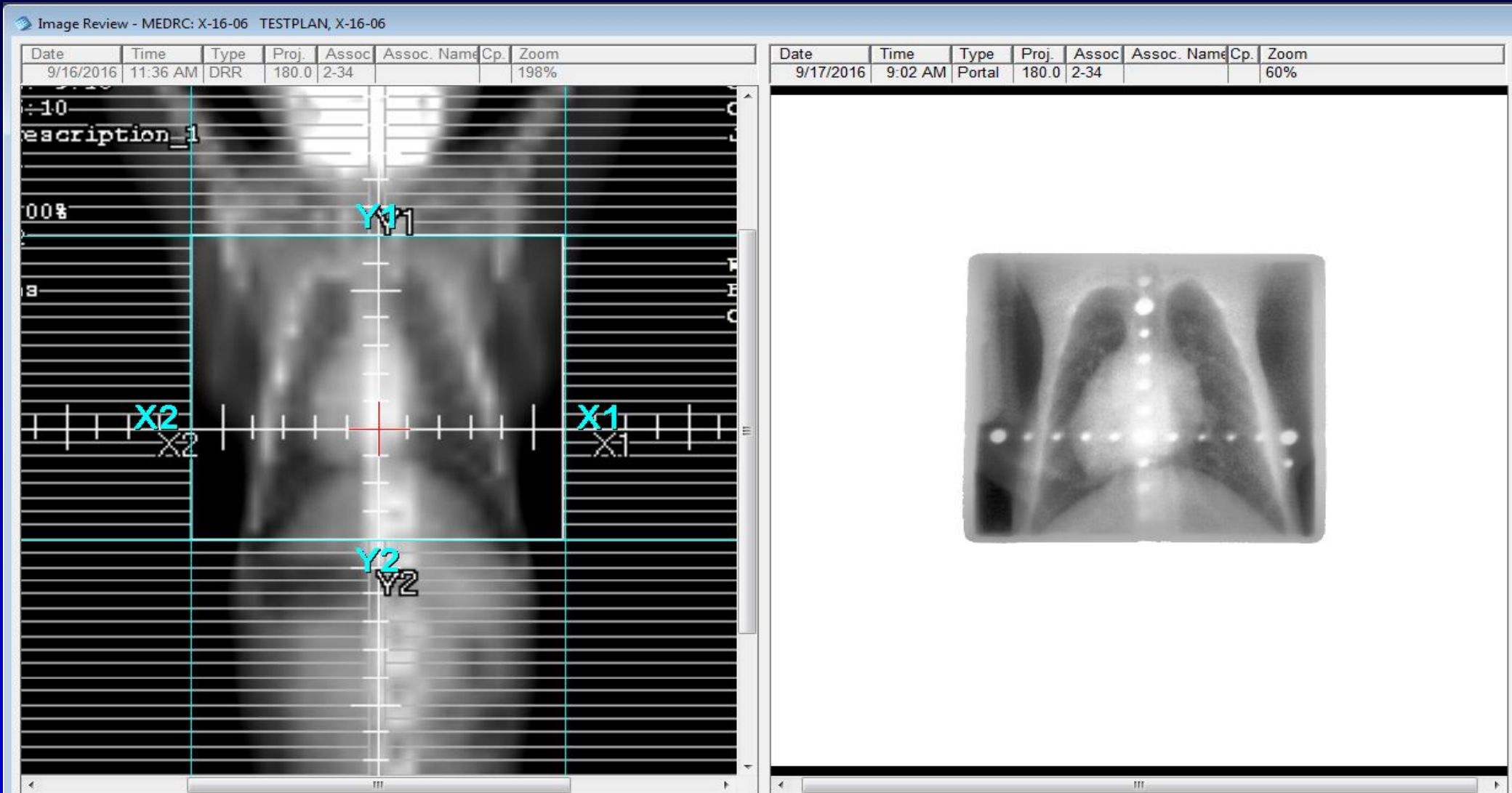
Port-Delivered



PA-1934

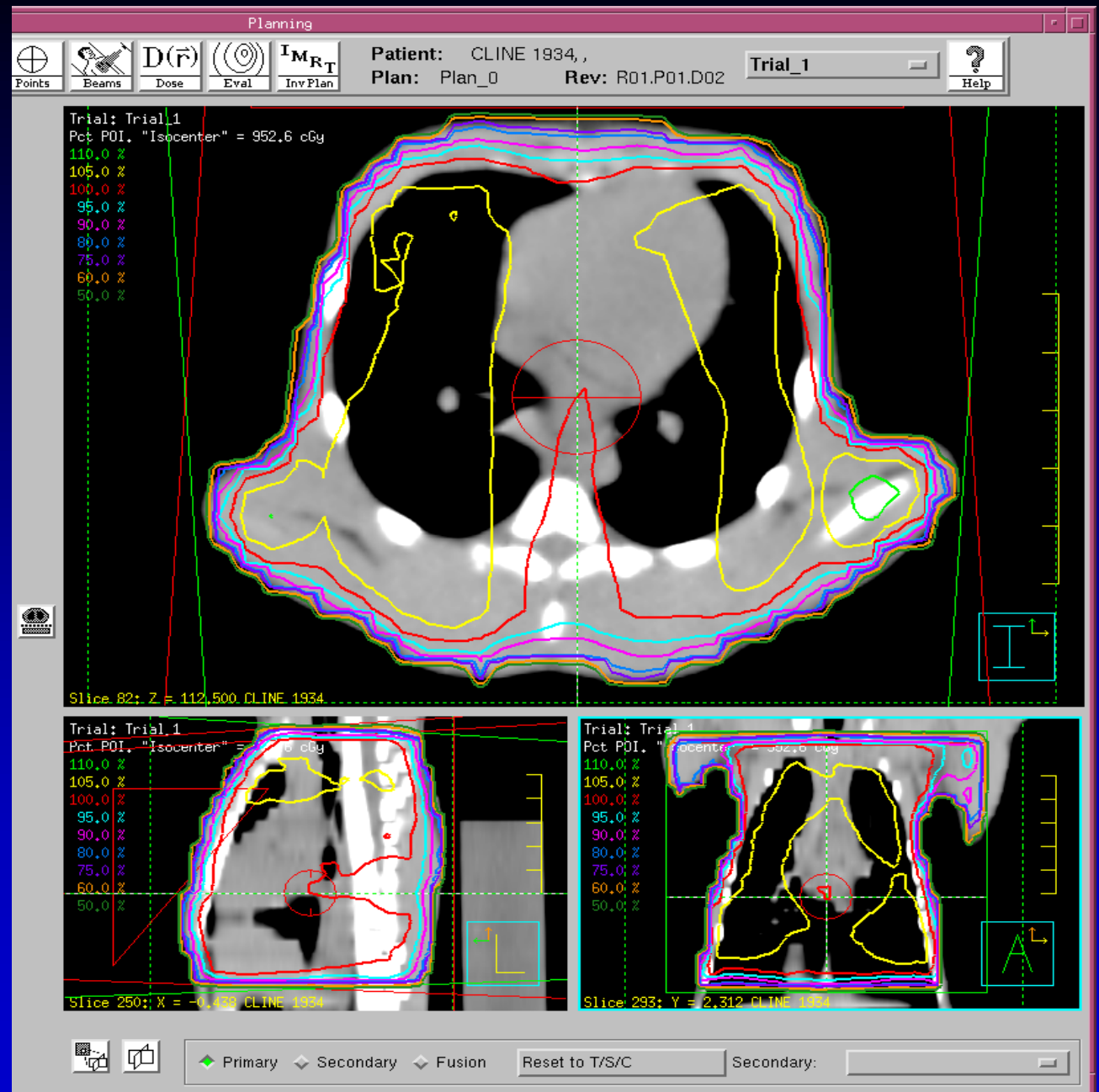
DRR-Planned

Port-Delivered



Radiation Plan - 1934

- 10 Gy @ 105% of dose at isocenter
- Isocenter dose of 9.5 Gy
- Lung dose of 10 Gy
- 12 deg wedge Ant
- 55:45 AP:PA beam weights



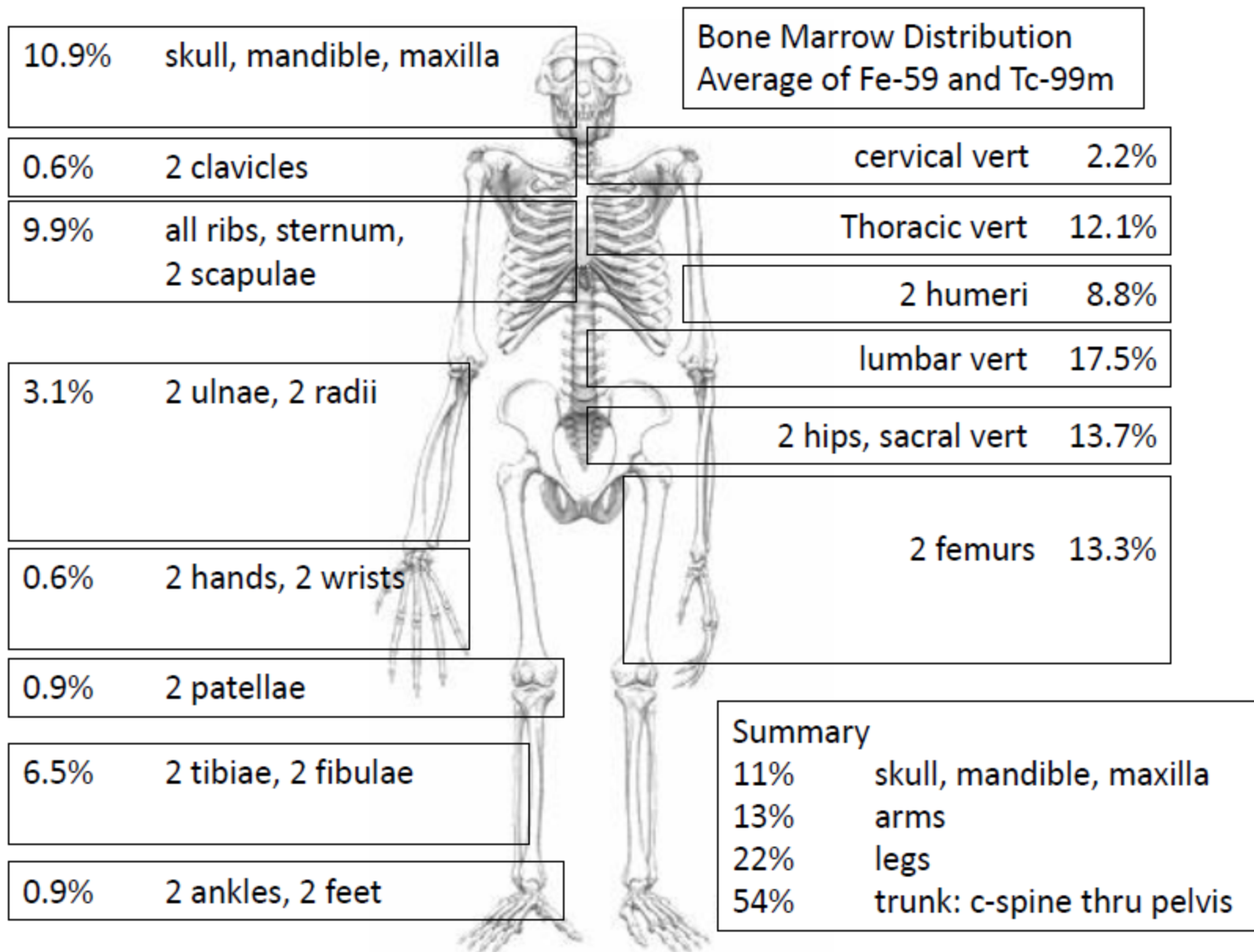
Research Study Design

- IACUC-approved protocols
- Linear accelerator QA: TG-51, other
- Validation of research geometry dosimetry

Logistics: Irradiation Procedures

Irradiation Day

- Warm up linear accelerator, verify in-vivo dosimetry
- Set up specific geometry (previous evening)
- Verify anesthesia unit
- Animal transport of 1, then 2 at a time after 1st setup
- Verify animal ID, verify positioning
- Verify anesthesia: Anesthesia time < 45 min
- Recording form for MUs, dose, time in, time out
- Radiation On time 3-10 min; Total In-room time < 15 min
- Linac operator at control console, Linac personnel for positioning
- Animal handlers at housing and irradiation locations
- Backup plan – next day

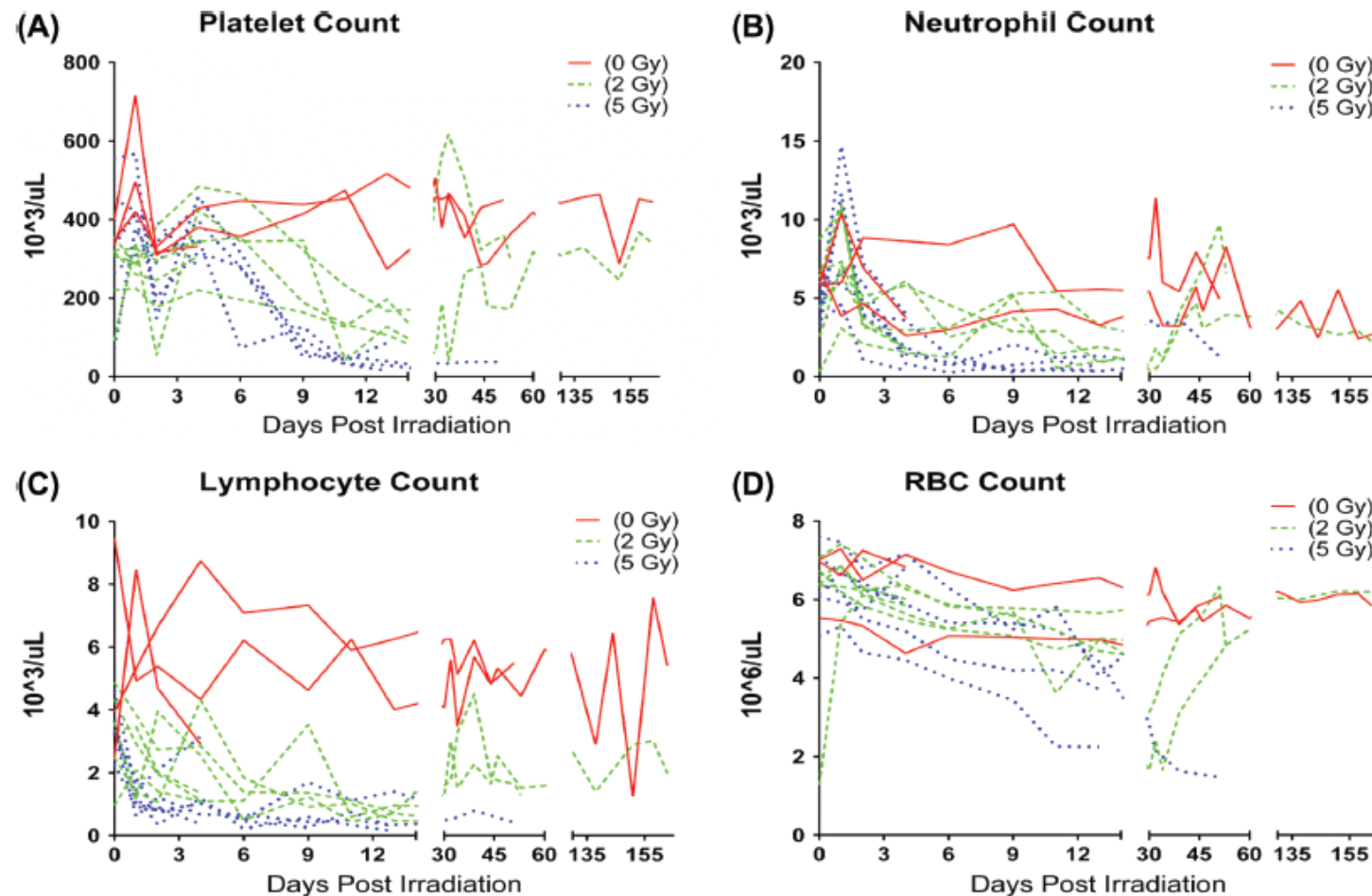


References: Drawing © of Jay H. Matternes. Data from Taketa et al., Life Sciences 9:Part II:169-174, 1970.

Molecular and cellular profiling of acute responses to total body radiation exposure in ovariectomized female cynomolgus macaques

Ryne J. DeBo¹, Thomas C. Register¹, David L. Caudell¹, Gregory D. Sempowski^{2,3,4}, Gregory Dugan¹, Shauna Gray¹, Kouros Owzar⁵, Chen Jiang⁶, J. Daniel Bourland⁷, Nelson J. Chao⁸ & J. Mark Cline¹

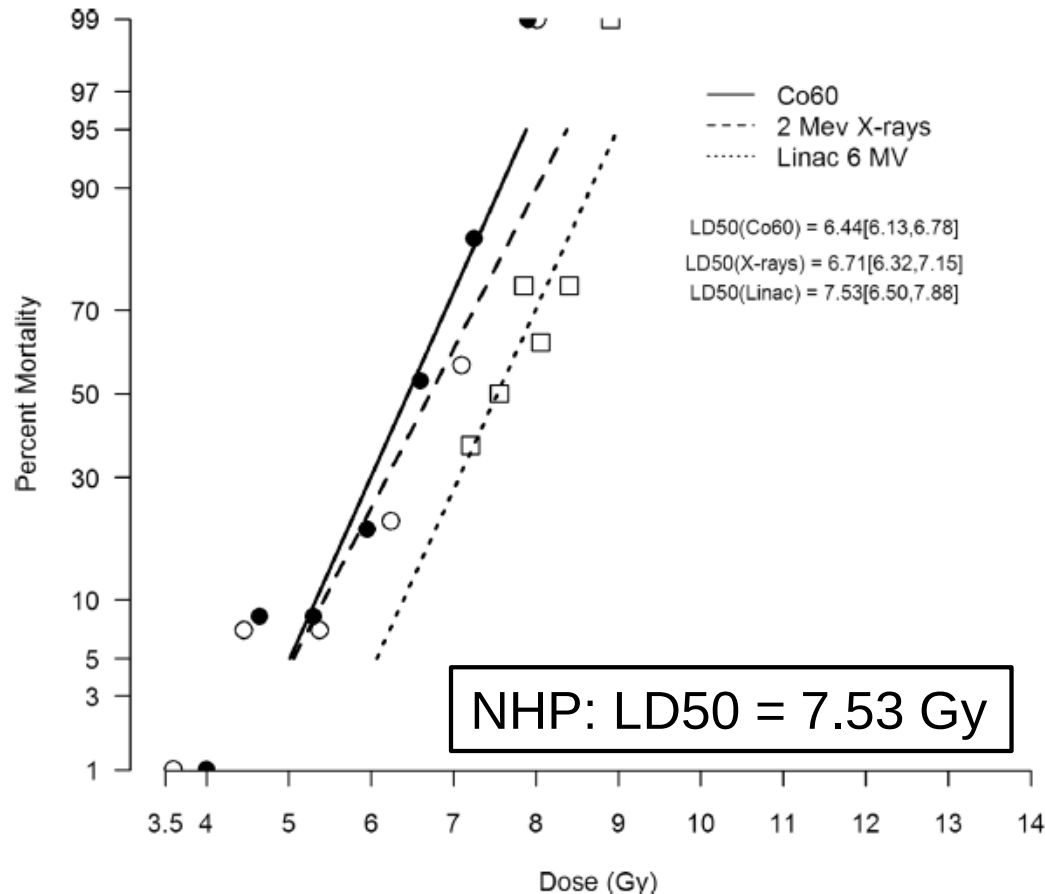
International Journal of Radiation Biology, June 2015; 91(6): 510–518



A Nonhuman Primate Model of the Hematopoietic Acute Radiation Syndrome Plus Medical Management

A.M. Farese^{*}, M.V. Cohen[†], B. P. Katz[‡], C. P. Smith^{*}, W. Jackson III[§], D. M. Cohen^{*}, and T.J. MacVittie^{*}

Health Phys. 2012 October ; 103(4): . doi:10.1097/HP.0b013e31825f75a7.

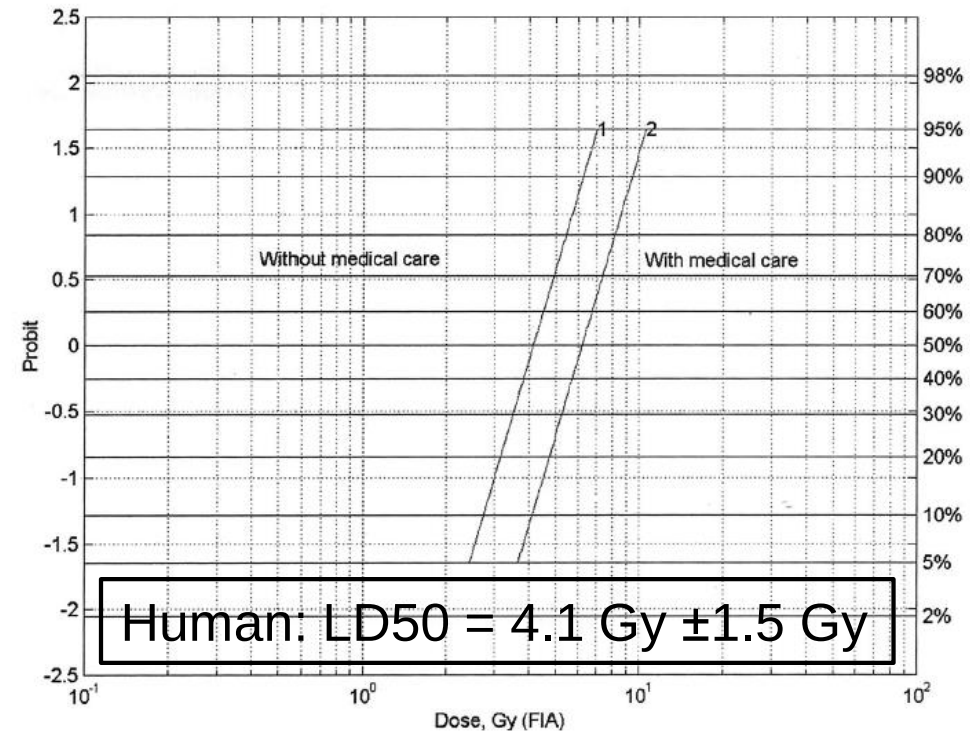


DOSE RESPONSE RELATIONSHIPS FOR ACUTE IONIZING-RADIATION LETHALITY

Health Physics

May 2003, Volume 84, Number 5

G. H. Anno,^{*} R. W. Young,[†] R. M. Bloom,^{*} and J. R. Mercier[‡]



QUANTEC Papers

“Quantitative Analysis of Normal Tissue Effects in the Clinic”

- ASTRO and AAPM: This series of papers offers focused summaries of the dose/volume/outcome data for many of the organs potentially impacted by radiation treatment and gives physicians and treatment planners excellent resources to assist in determining acceptable dose/volume constraints.
- **Topics:** [**Science:** Accumulation of dose, Scientific issues, Biomarkers, Imaging for assessment, Improving complication models]; [**Organs:** Brainstem, Penile bulb, Rectum, Brain, Esophagus, Heart, Larynx/pharynx, Lung, Spinal cord, Stomach/SB, Optic nerve/chiasm, Bladder, Hearing, Kidney, Liver, Salivary gland]; [**Guidance:** Users Guide, Model use in the clinic]
- IJROBP, Vol 7, No. 3, Supplement, 2010 – publically available at:
- <https://www.astro.org/Clinical-Practice/Quantec/QUANTEC.aspx>

CMCR TBI Parameter Survey

1. Institution name
2. Radiation source: Cobalt-60 or Linear accelerator
3. Radiation source energy
4. Radiation beam geometry and techniques
 - a. 1 field at a time or 2 fields at a time
 - b. Anatomical pose: supine, prone, decubitus, seated, other
 - c. Anterior-posterior or lateral or other
 - d. Distance to mid-plane of animal
 - e. Field size at mid-plane of animal
 - f. Use of build-up material and/or compensation material - describe
 - g. Nominal dose rate setting on the radiation device – at the control console: cGy/min or MU/min
 - h. Dose rate at mid-plane of animal
 - i. Radiation dose prescription
 - j. Irradiation time per field
 - k. Elapsed irradiation time to deliver prescribed dose
 - l. Elapsed time for anesthesia and/or sedation
5. Dose computation algorithm or methods
6. Radiation source calibration protocol: TG-51 or TG-21 or other
7. Instrumentation used for in-vivo dose confirmation
8. Medical supportive care provided in the peri-irradiation phase

Experience and Dosimetry Standardization for Total Body Irradiations in Research

Summary

- Physics integral to RCM work
- Multi-disciplinary communications imperative
- TBI parameters vary and specific to available resources
- Validation, quality assurance and constancy are keys
- Analysis of techniques and standardization for reporting of results necessary
- Standardization, inter-comparison of techniques are important opportunities

Physics → Chemistry → Biology → Clinical

Acknowledgements

- WF School of Medicine
 - Sue Appt, DVM
 - Dave Caudell, DVM, PhD
 - Mike Chan, MD
 - Mark Cline, DVM, PhD
 - Sam Deadwyler, PhD
 - Waldemar Debinski, MD, PhD
 - Greg Dugan, DVM
 - Rob Hampson, PhD
 - Nancy Kock, DVM, PhD
 - Bob Kraft, PhD
 - Linda Metheny-Barlow, PhD
 - Mike Munley, PhD
 - Anne Peiffer, PhD
 - Tom Register, PhD
 - Mac Robinson, PhD
 - Mike Tytell, PhD
 - Jeff Willey, PhD
- WF Graduate School
 - Physics, SBES grad students
- WFU Radiation Oncology
- CCCWFU / BTCOE / TSI
- WF Innovations
- WFU-Duke DEARE
- Duke Univ RadCCORE
- VMRCVM - VaTech
- NCBioTech
- NIH/NIAID, U19 AI67798 (subcontract 131714)
- DOD, GRANT 11779583
- Asell LLC/BARDA, HHSO100201700022C