Radiation Sources

External Beam and Isotopes

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Outline

- External Beam Equipment
  - X-ray beams
  - Sealed radioisotope sources
  - Research examples
- Irradiators: Sealed radioisotope sources
  - Research examples
- Internal Sources
  - Sealed radioisotope sources
  - Unsealed radioisotope sources

Production of Ionizing Radiation

- Photons: electromagnetic radiation, no mass, $E = h\nu$
- X rays: origins are from atomic energy transitions
  - Bremsstrahlung (braking) and characteristic x rays
  - Bremsstrahlung – the "x ray" we know - electronically produced when accelerated electrons hit a high-Z target: $E_{ke-} \rightarrow$ photon (x ray)
  - Can be turned "ON" and "OFF" with a switch – an exotic lightbulb
- Gamma (γ) rays: origins are from nuclear energy transitions
  - The result of (following) radioactive decay
  - Always "ON" with radioactive decay – cannot be turned "OFF"
  - Radioisotope material is usually encapsulated as a "sealed source"
- Both types: low to high energy ($10\text{ keV} > h\nu > 1\text{-}20\text{ MeV}$)

Irradiation Devices

Irradiation Device	Radiation, Energy	Distinctions
Orthovoltage X-Ray	X rays, 200 - 300 kV	Ease of use, can use field shaping, can be operated by researcher
Linear Accelerator	X rays, 6 MV & higher	Highest energy source, high quality setup tools, high quality assurance, irradiation planning. Operation only by selected users (clinical device).
Cesium Irradiator	γ rays, 662 keV	Ease of use, simple operation, relatively high dose rate. Operation only by selected users, limited access.
Gamma Radiosurgery	γ rays, 1.25 MeV	Focal radiation source, high quality setup, requires stereotactic imaging and irradiation for each individual irradiation. Operation only by selected users (clinical device), limited access.

External Beams: X-ray Beams
Two methods of x-ray production

- Diagnostic medical and small animal work: The X-ray Tube
  - Energy: 20-300 kV
  - Dose rate: 50 to 300 to 1,200 cGy/min
  - Operating distance: 30-50 cm
- Therapeutic medical and large animal work: The Linear Accelerator
  - Energy: 4-20 MV
  - Dose rate: 50 to 300 to 1,200 cGy/min
  - Operating distance: 100 cm

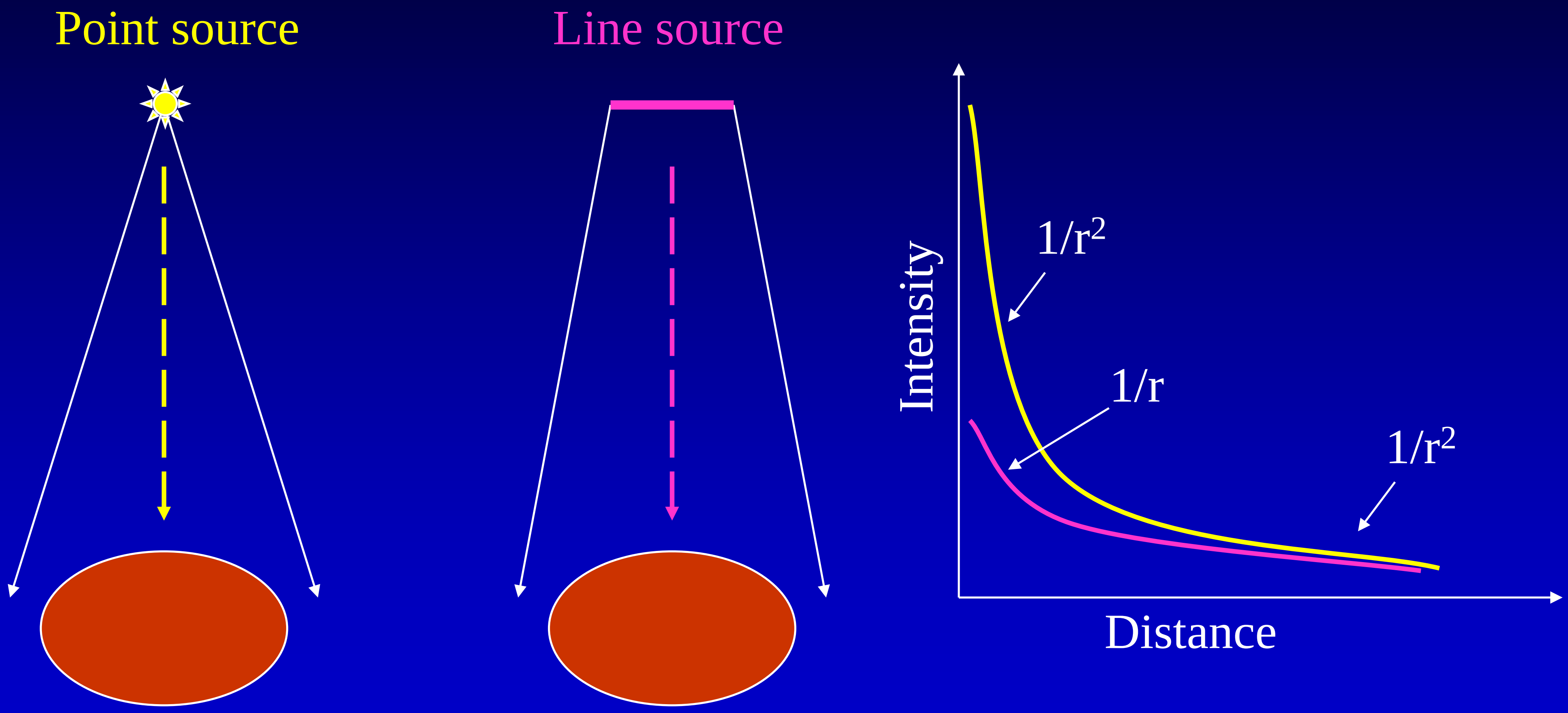
X-ray Beam Characteristics

- X rays undergo exponential attenuation in matter: $e^{-\mu d}$
- Beam energy: energy ↑, depth of penetration ↑
- X-ray energy chosen to match target thickness or depth
- Dose rate varies with distance as $1/r^2$ (ISL)
- Dose rate varies with x-ray settings and geometry
- Irradiation parameters of beam filtration, beam current, source-to-target distance, and field size - affect depth dose, dose rate, surface dose, amount of scatter

Unique radiation research problems require unique irradiation solutions: geometry and radiation sources

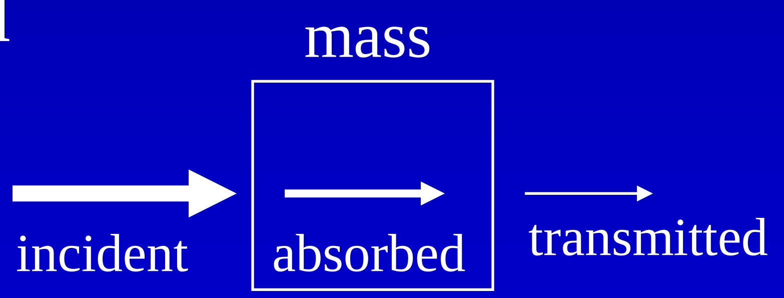
Once irradiation parameters are chosen and validated, consistency is the key!

Point and Line Source Models



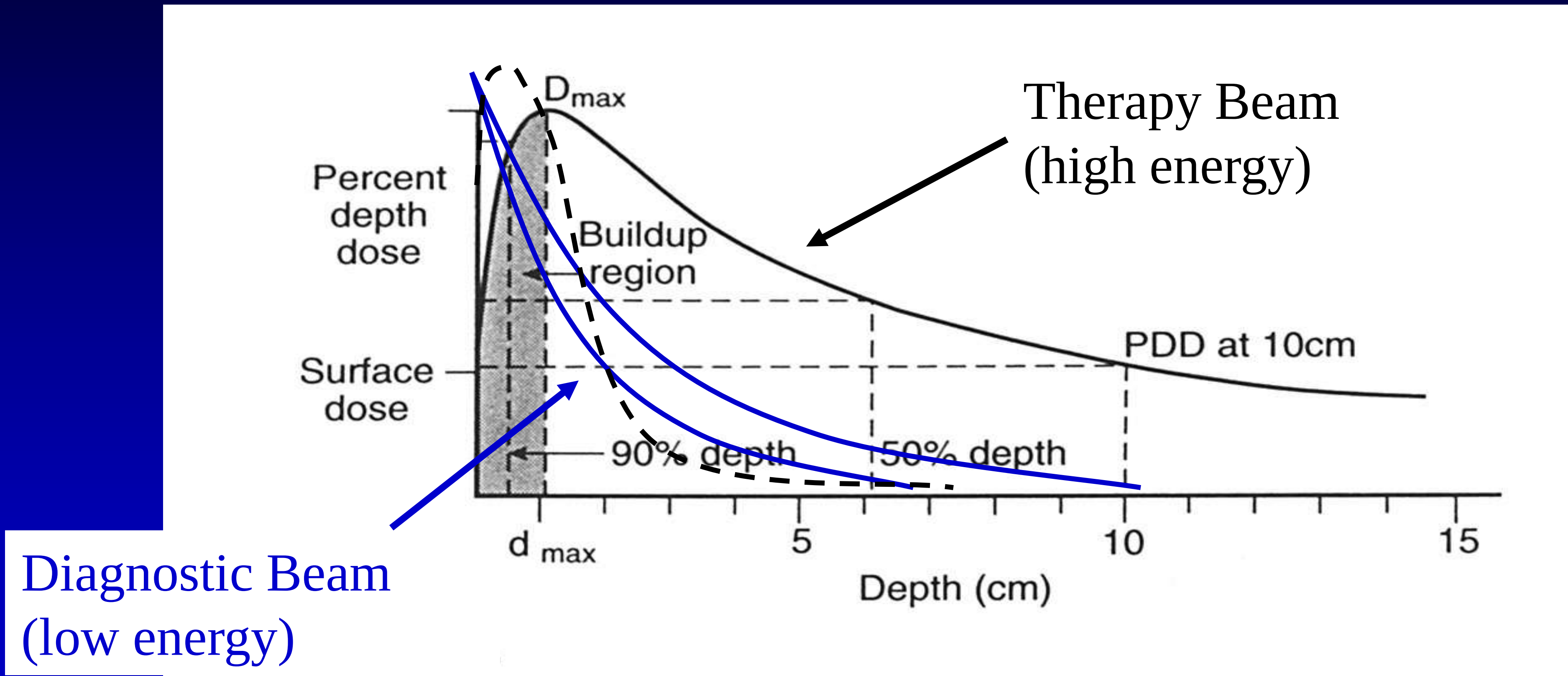
Ionizing Radiation Dose

- Dose: energy absorbed per mass: energy/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



X-Ray Photon Beam

Percent Depth Dose Curves



A typical photon percent depth dose curve, characterized by surface dose, a buildup region, a point of maximum dose, and an exponentially attenuated region.

Isodose Curves

Representing a Radiation Dose Distribution

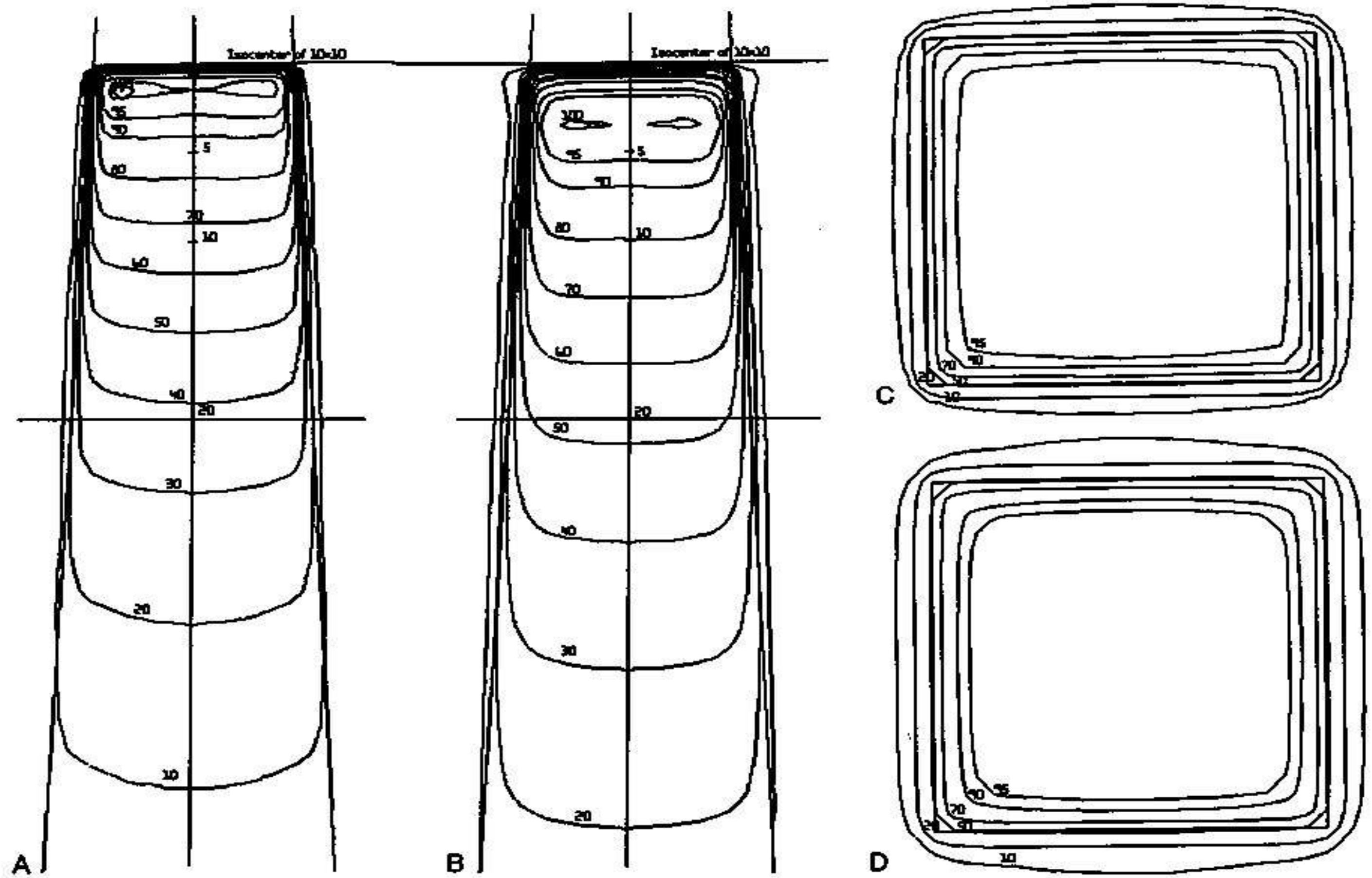
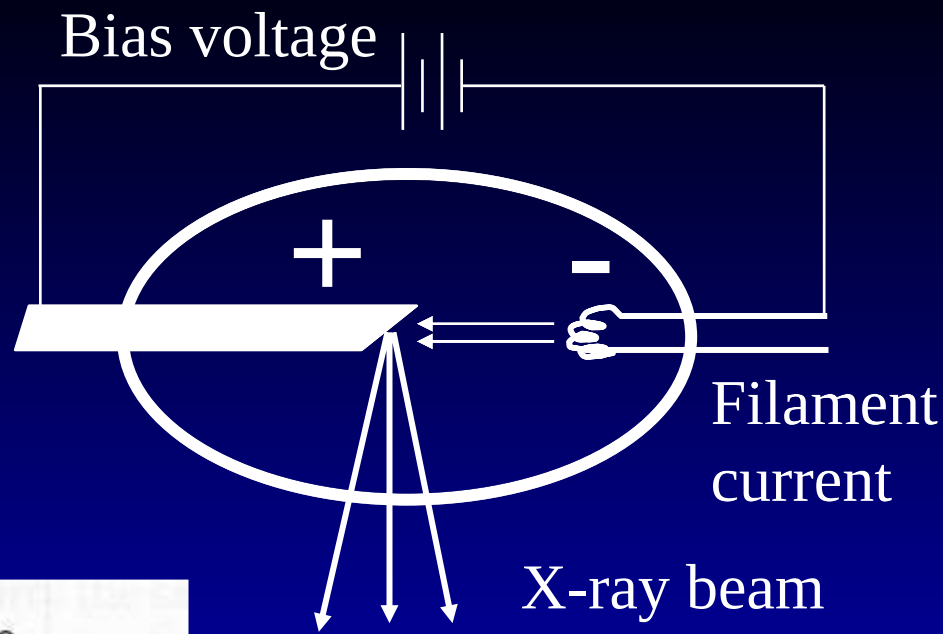
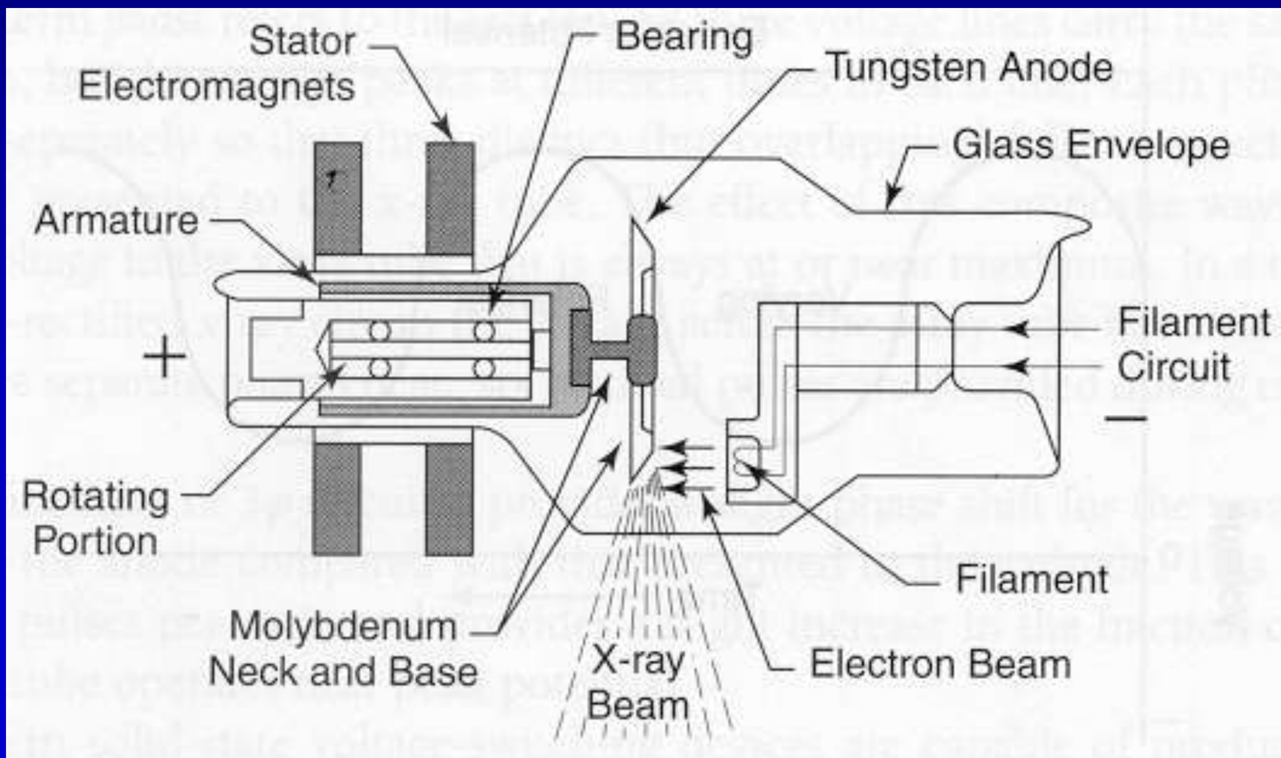


FIGURE 3–37.

Photon isodose curves, 10 × 10 cm² fields. *A*, 6 MV, cross plane. *B*, 18 MV, cross plane. *C*, 6 MV, orthogonal plane. *D*, 18 MV, orthogonal plane. (Data courtesy of Wake Forest University Baptist Medical Center, Winston-Salem, NC.)

X-ray Equipment and Research Examples

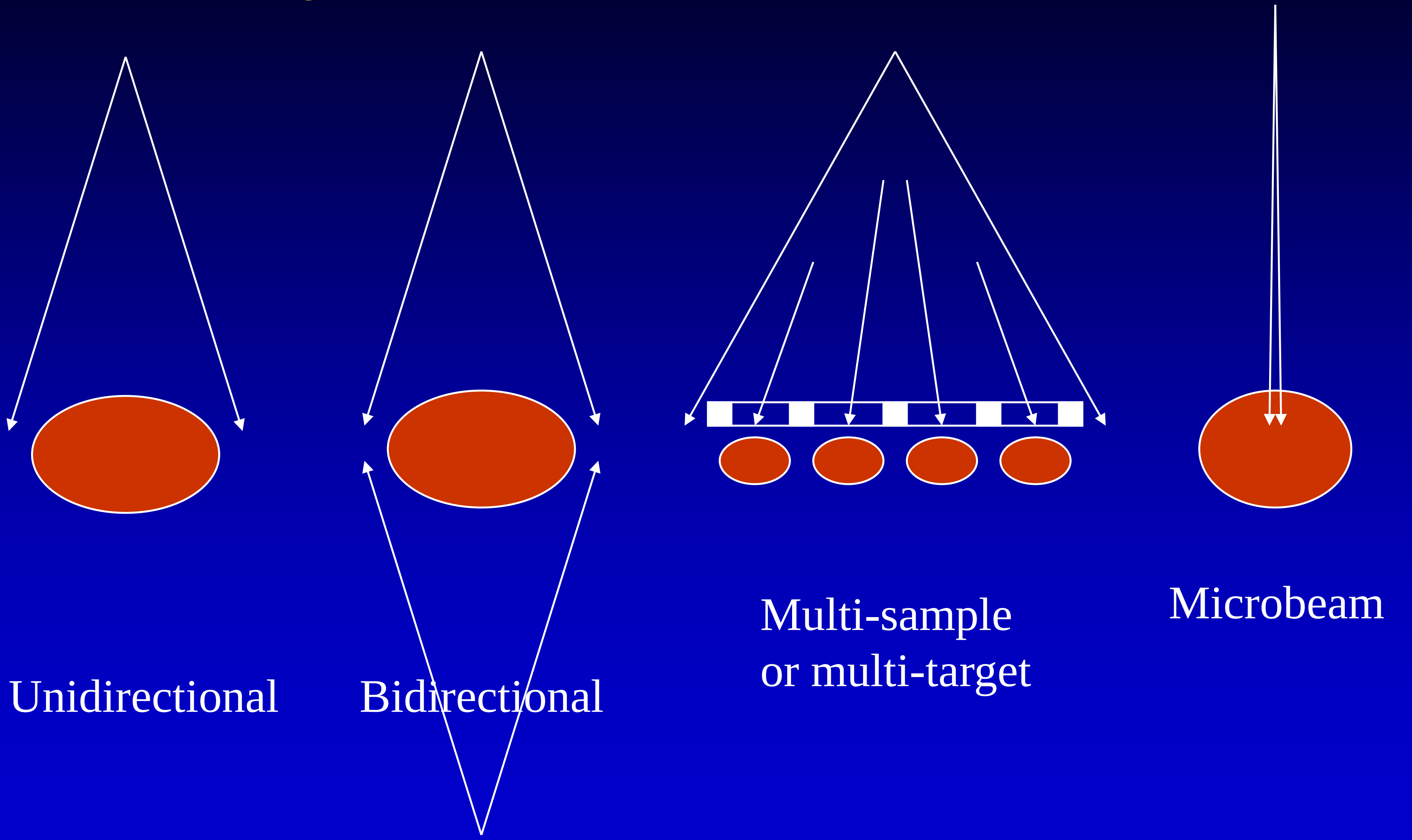




X-ray Tube Characteristics

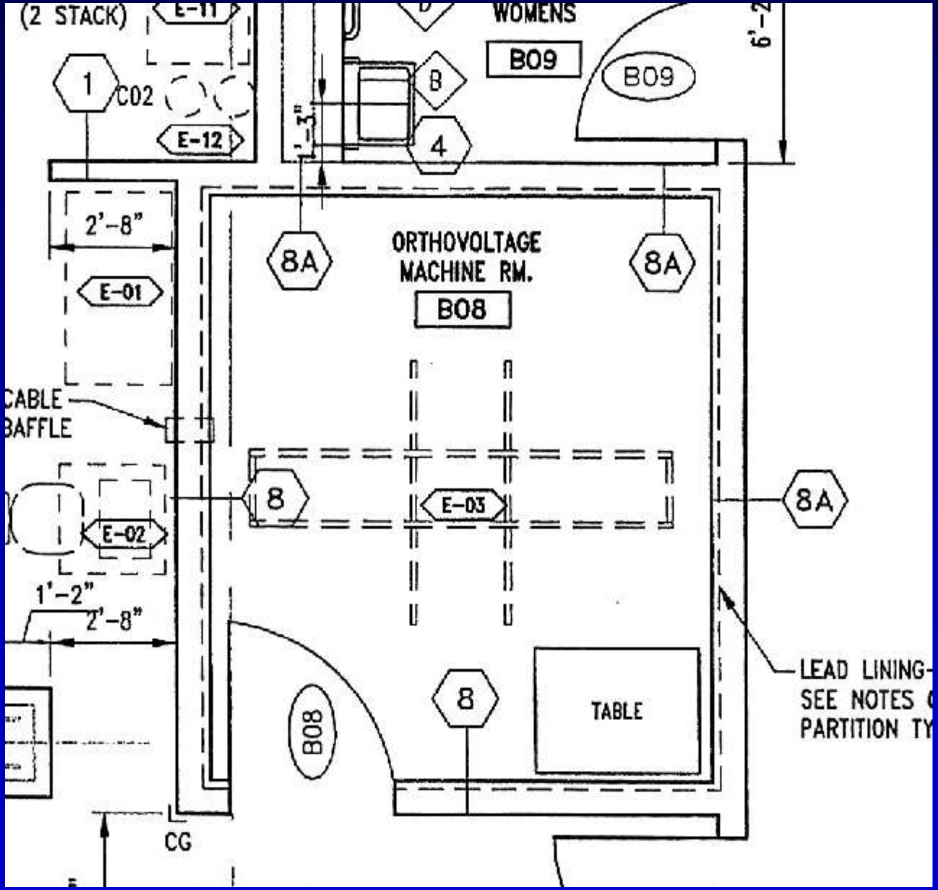
Radiation Source (Energy)	Dose Rate	Small Animal Applications	Comments
X rays (30 – 320 kV x rays) Note: Orthovoltage x-ray energy range is 130-320 kV. A timer controls the irradiation time.	1 – 5 Gy/min @ 50 cm from source. Dose rate varies with energy (kV), filtration, source-to-sample distance, and tube (beam) current.	Whole-body irradiation. Partial-body or single-organ irradiations using collimated fields. Irradiation of one or more animals possible, depending on size and geometry.	A variety of beam energies is possible with depths of penetration from 0 – 2 cm. Can be used in single- or opposed-field geometries. Field sizes can be collimated to a specific size. Requires either a shielded enclosure or a shielded room. Dose rate calibration required to determine irradiation times.

X-ray Beam Irradiation Geometries



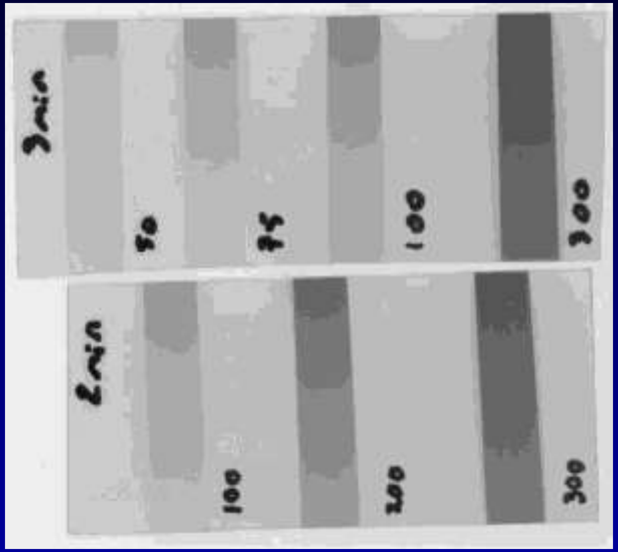
XRad 320 Orthovoltage X-Ray Unit
Wake Forest University

- X-ray tube has a single source, produces a rectangular beam
- Beam energies from 60 to 320 kVp
- Field sizes from 0 x 0 to 20 x 20 cm^2
  - X and Y field widths are variable over the range
- Treatment distance 50 cm (source-surface) – moveable unit
- Two calibrated energies: 250 kVp and 300 kVp
- Safety systems, manual, logbook
- **YOU get to run it (with training)**



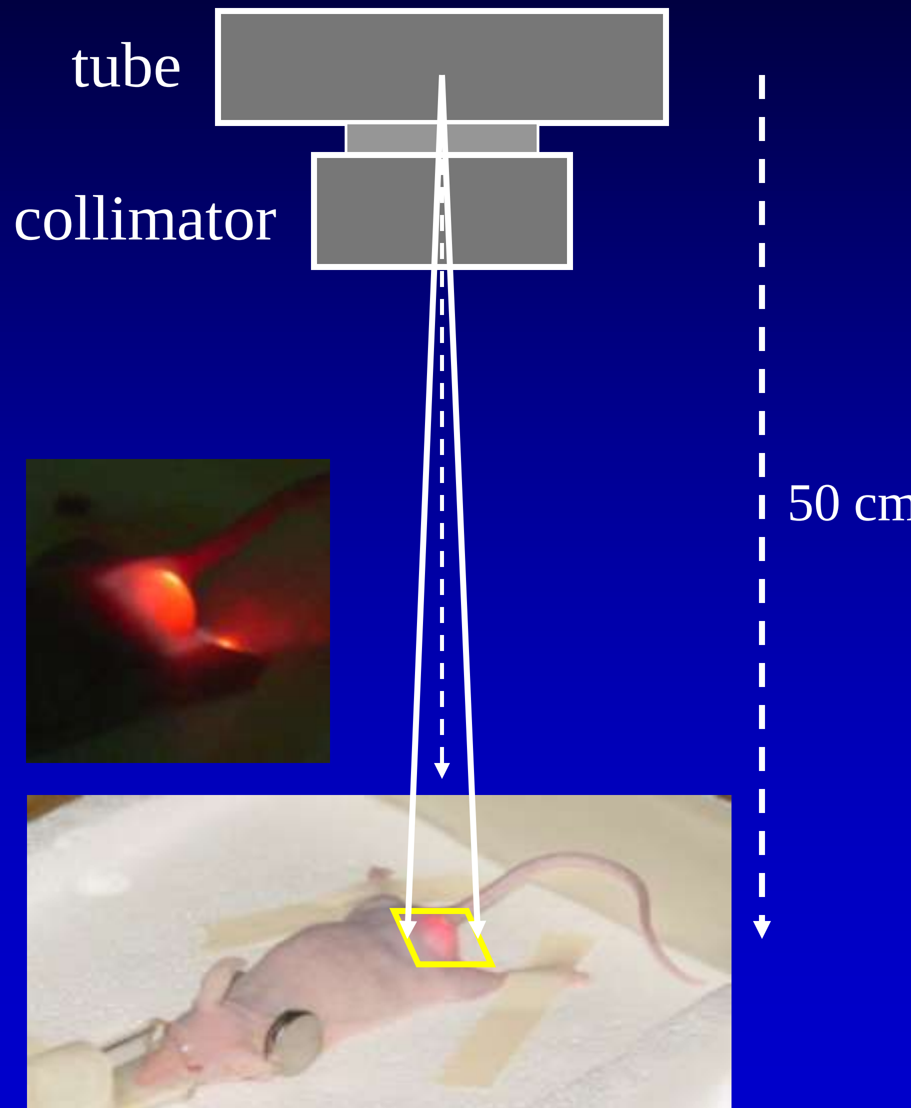
Shielded room
(or smaller shielded enclosure)

Orthovoltage X-Ray Unit



Orthovoltage X-Ray Unit

Flank tumor geometry



Research

Open Access

Use of an orthovoltage X-ray treatment unit as a radiation research system in a small-animal cancer model

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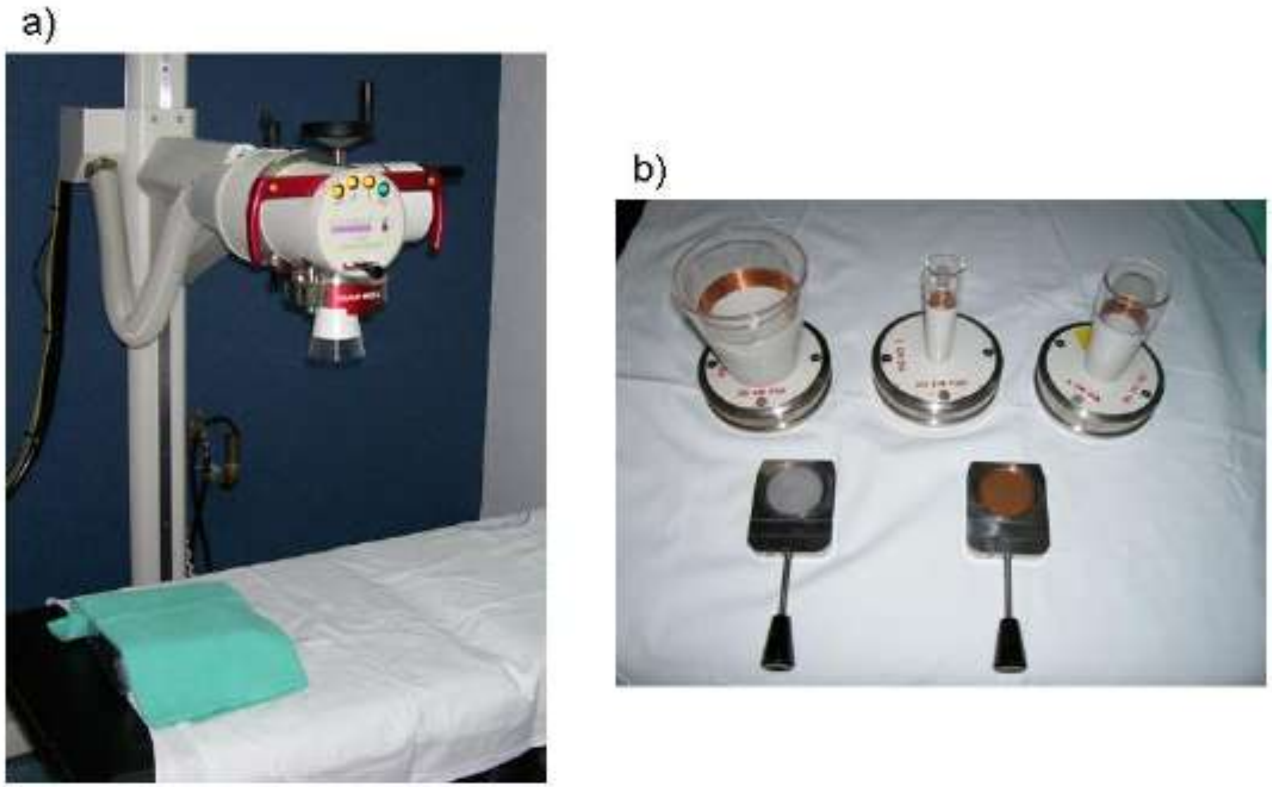


Figure 1
a) Orthovoltage X-ray unit (Gulmay D3225); b) filters and applicator cones.

Older, clinical device, re-tasked for research purposes with success

Figure 2
Tumor xenograft of cervical cancer developed by subcutaneous injection of 5×10^6 HeLa cells at the lower limbs of nude mice. Arrows indicate the tumor lobes.

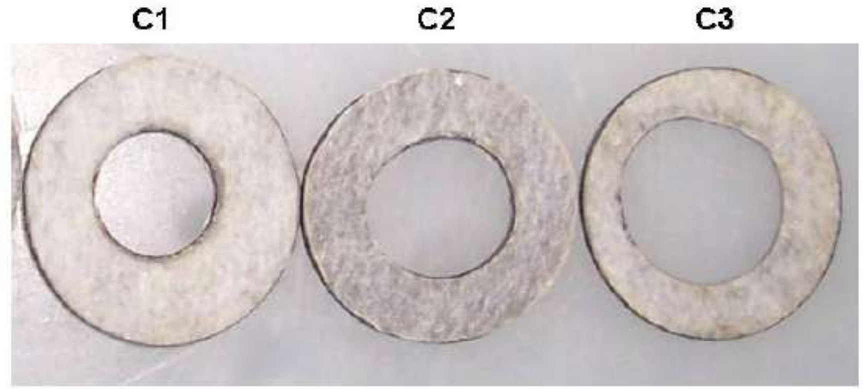


Figure 3
Lead collimators with different diameters (0.5, 1.0, 1.5 cm) and a thickness of 2 mm, used to restrict the X-ray beam onto the tumor lobes.

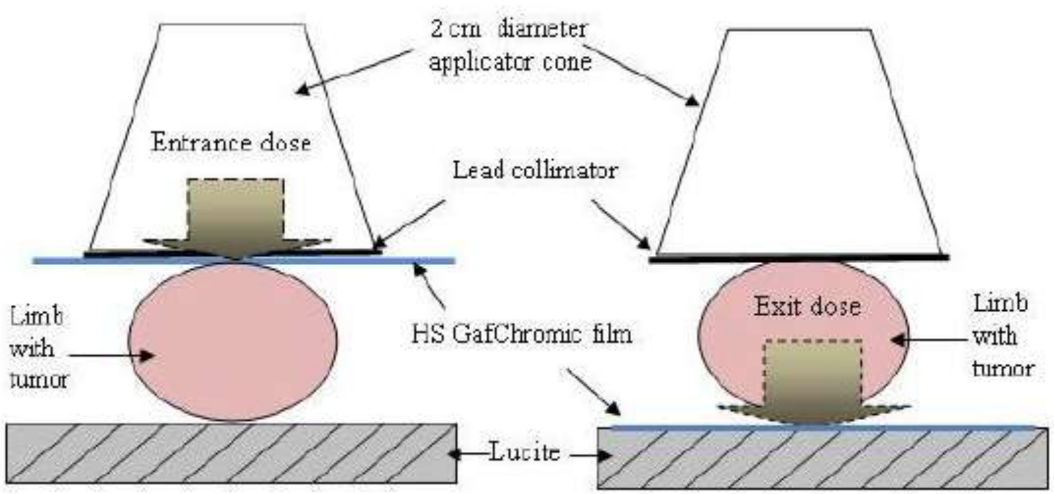


Figure 4
Experimental setup to evaluate the entrance and exit dose in the tumor lobe, using HS Gafchromic film.

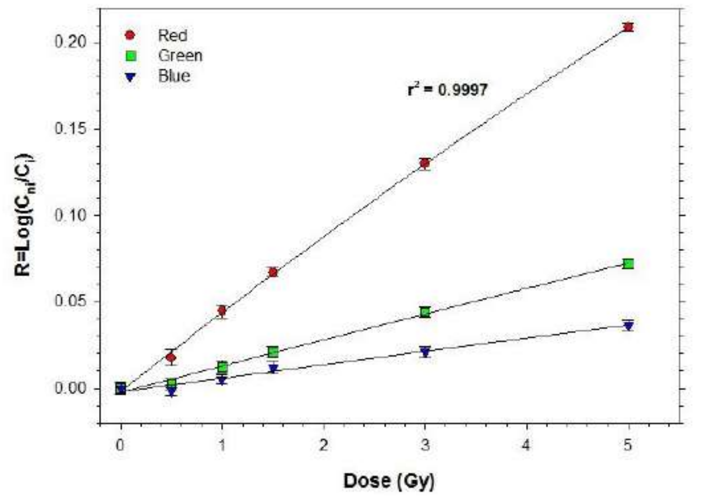


Figure 6
Calibration curve (Response vs. Dose). This curve shows the lineal response of the red, green and blue components (RGB mode) as function of the dose. Values are given as means ± SEM.

Used, Clinical X-ray Units

The challenges of old technology – it can work (?)

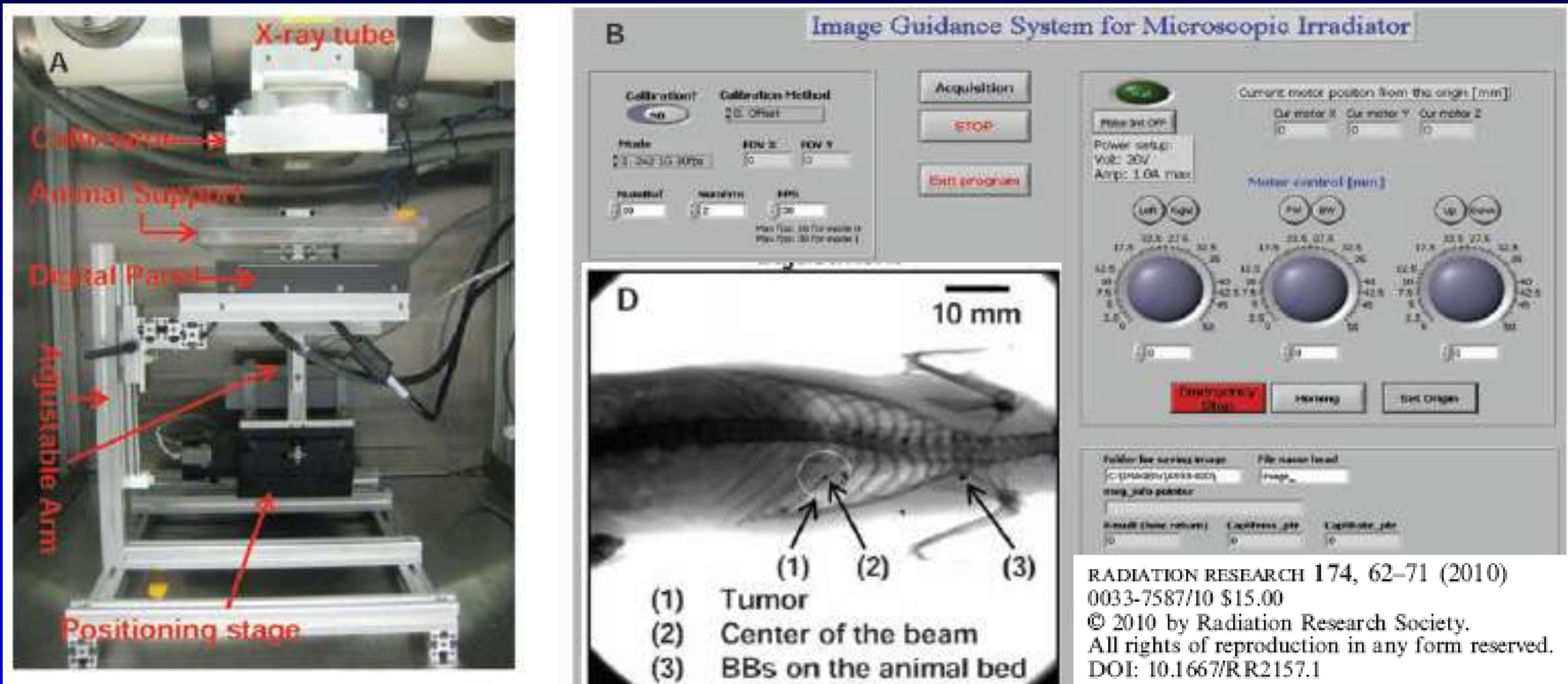
- **One example: email from 1994**
- **We are seeking information and parts for a General Electric Maxitron 250 X-ray unit. The unit which had operated for years, mostly with the help of rubber bands and bubble gum, is now pushing up daisies.** Specifically, we are looking for a new tube, or info on having one reconditioned (?). **The last tube in it imploded** (The cylindrical tube is now an elliptical tube !!! BOOM, SIZZLE, SMOKE). We have one other tube, but have been told that it might be to gassy to use now. This is the tube they would like to get reconditioned. … We would very much like to get in touch with you if you are still in the market. Thank you again for your help. DJB (**Call him first, he knows the unit better than GE, i.e. Mr. Rubber-bands and Bubble-gum**)
- **WFU has a similar story**
  - clinically used orthovoltage unit retired from service and stored for 3 years.
  - 6 months install → no success. Called in the experts → no success
  - Bought new – much success! Reliability, easy service, consistency, etc

Image-guided Irradiations

- Current technique for human radiation treatment
  - Image-guided radiation treatment (IGRT)
- Adapted for animal research

An Orthotopic Lung Tumor Model for Image-Guided Microirradiation in Rats

Debabrata Saha,[a] Linda Watkins,[b] Yi Yin,[b] Philip Thorpe,[b] Michael D. Story,[a] Kwang Song,[a] Pavithra Raghavan,[a] Robert Timmerman,[a] Benjamin Chen,[a] John D. Minna[c] and Timothy D. Solberg[a,1]



RADIATION RESEARCH 174, 62–71 (2010)
0033-7587/10 $15.00

DOI: 10.1667/RR2157.1

FIG. 1. The image-guided small animal irradiation device (panel A) with major components indicated, positioned beneath a commercial X-ray source. Panel B: Software for image acquisition and positioning. Panel C: Initial localization image with beam center and tumor indicated. Panel D: Final localization verified by a second image. Panel E: Calibration and centering relative to the beam axis.

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0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.04.025

HIGH-RESOLUTION, SMALL ANIMAL RADIATION RESEARCH PLATFORM WITH X-RAY TOMOGRAPHIC GUIDANCE CAPABILITIES

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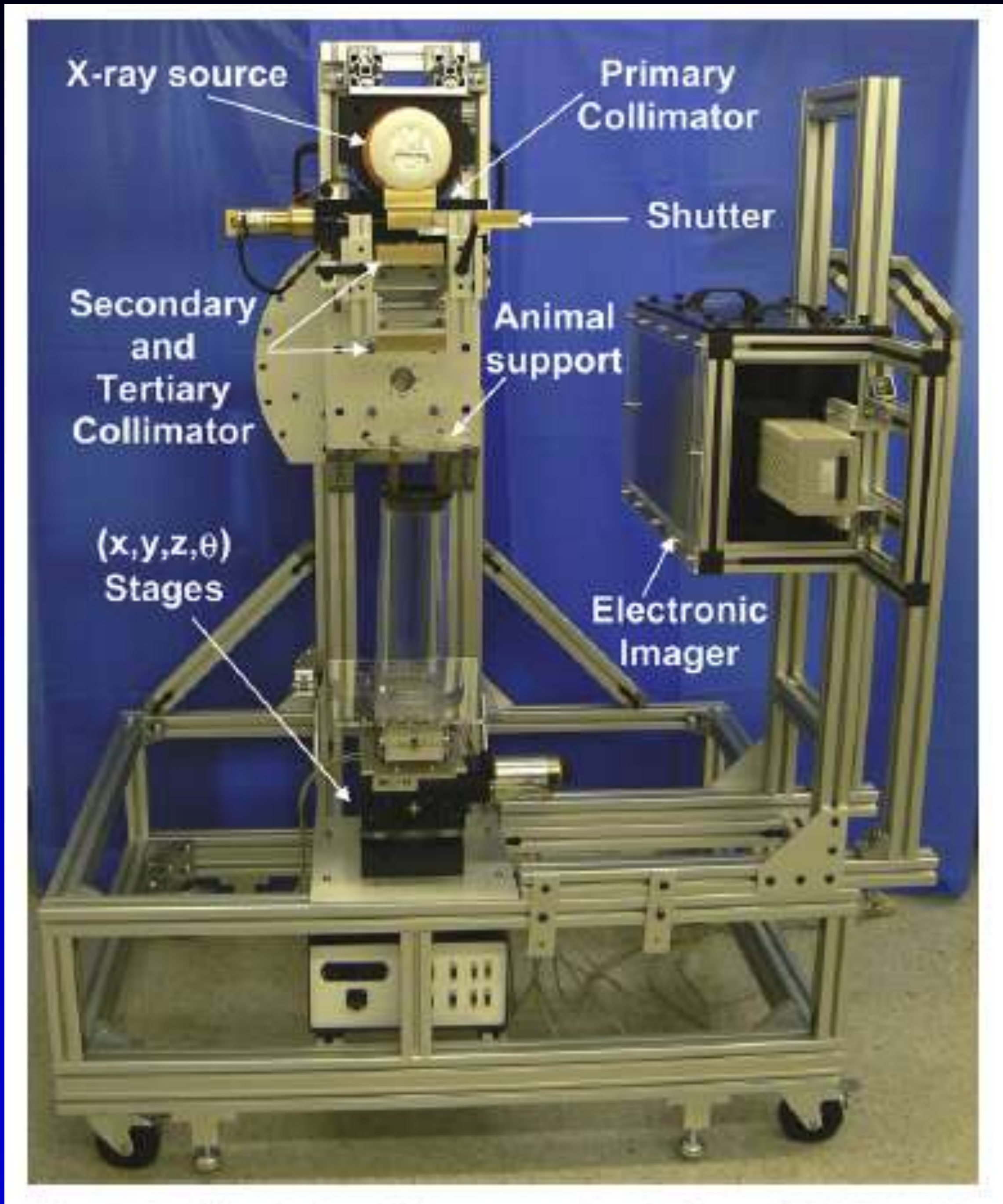
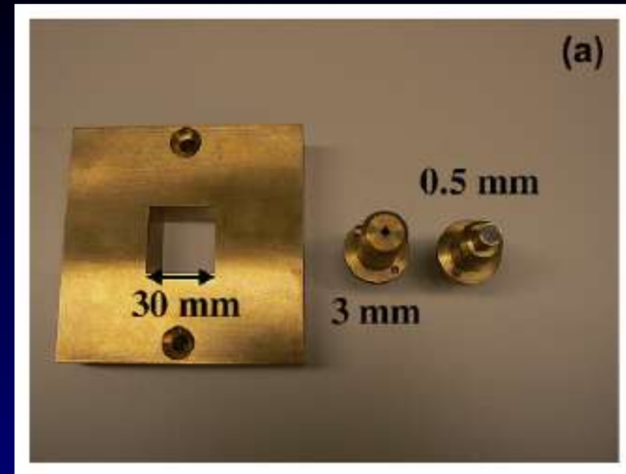
ERIK TRYGGESTAD, PH.D.,* HUA DENG, PH.D.,* MOHAMMAD MATINFAR, M.S.,†
CHRISTOPHER KENNEDY, PH.D.,* ZEJIAN LIU, PH.D.,* TIMOTHY CHAN, M.D., PH.D.,* OWEN GRAY, B.S.,†
FRANK VERHAEGEN, PH.D.,‡ TODD MCNUTT, PH.D.,* ERIC FORD, PH.D.,*
AND THEODORE L. DEWEESE, M.D.*





IGI

Wong et al. IJROBP 71(5) 1591-99 (2008)

Image-guided Irradiation

Wong et al. IJROBP 71(5) 1591-99 (2008)

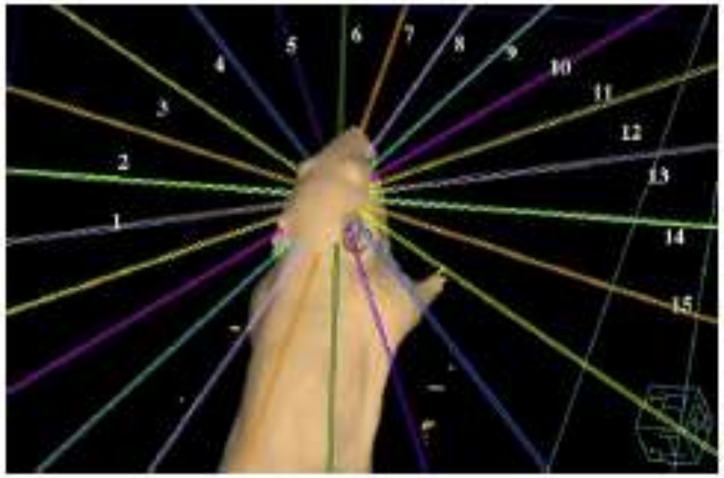
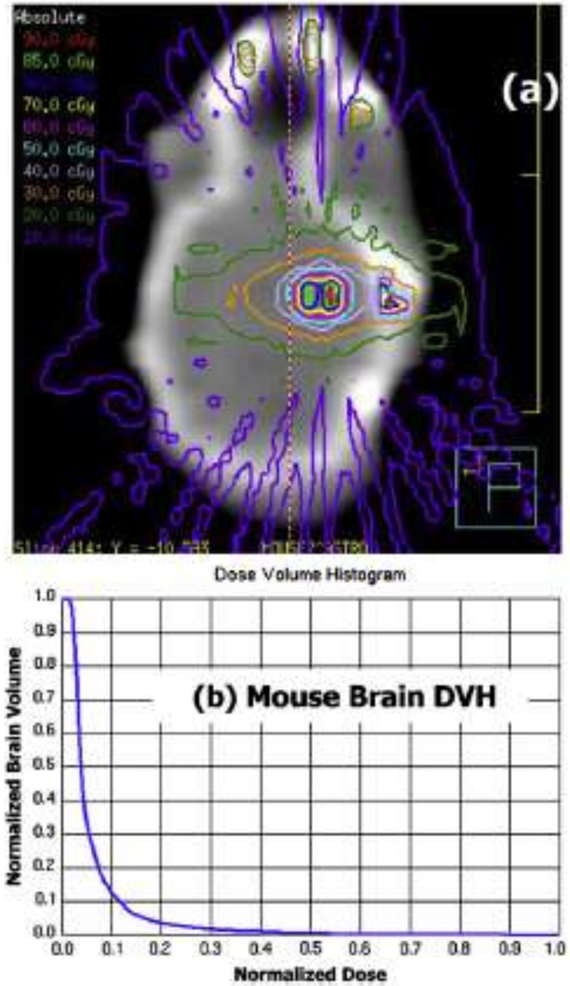


Fig. 4. Surface-rendered display of Pinnacle[3] three-dimensional treatment planning system showing irradiation of mouse brain using 15 beams equally spaced in a coronal arc arrangement. Each beam is 1 mm in diameter.

Table 1. Radiation output of small animal radiation research platform for range of field dimensions at 35-cm source-surface distance

Field dimension	Added filtration	Dose output (cGy/min)
Tertiary collimators		
60 mm × 60 mm*	4 mm Al	378
30 mm × 30 mm*	4 mm Al	334
13 mm diameter*	4 mm Al	206
10 mm × 10 mm	0.5 mm Cu + 2 mm Al	131
5 mm × 5 mm	0.5 mm Cu + 2 mm Al	124
1 mm diameter	0.5 mm Cu + 2 mm Al	102
"Nozzle" collimators		
5 mm × 5 mm	0.5 mm Cu	146
3 mm × 3 mm	0.5 mm Cu	122
1 mm diameter	0.5 mm Cu	92
0.5 mm diameter with 0.4 mm focus	0.5 mm Cu	22



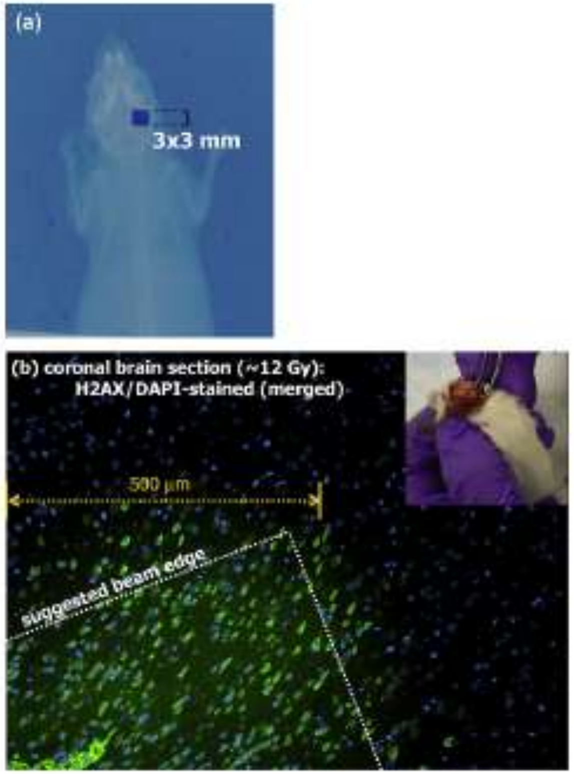
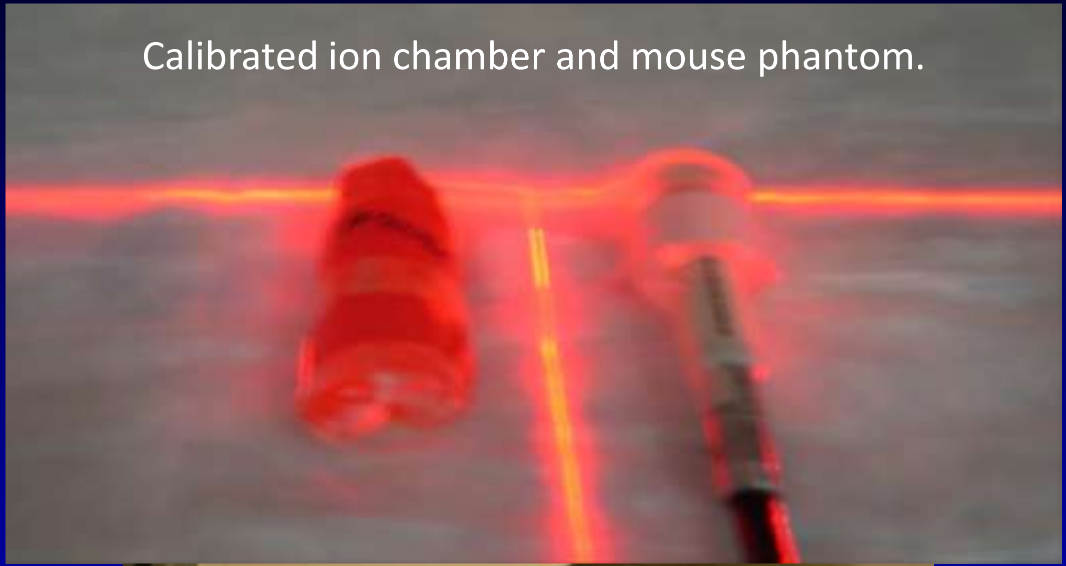


Fig. 8. (a) Double-exposed EBT film of mouse irradiation for which single 3-mm × 3-mm beam was directed posteriorly to right hemisphere. (b) Merged image of sectioned mouse brain stained with 4′6′-diamidino-2-phenylindole-2 HCl for cell nuclei and with antibody against γ-H2AX for correspondence with radiation-induced DNA strand breaks. Entire section shows 4′6′-diamidino-2-phenylindole-2 HCl (DAPI) staining, with sharp demarcation of region also showing γ-H2AX staining apparent. Beam edge suggested on image because experiment did not include geometric validation of

Clinical CT Scanner for Irradiation



Whole body irradiation with 100 kVp x rays.

MT Munley, Wake Forest School of Medicine

High Energy (Megavoltage) X Rays

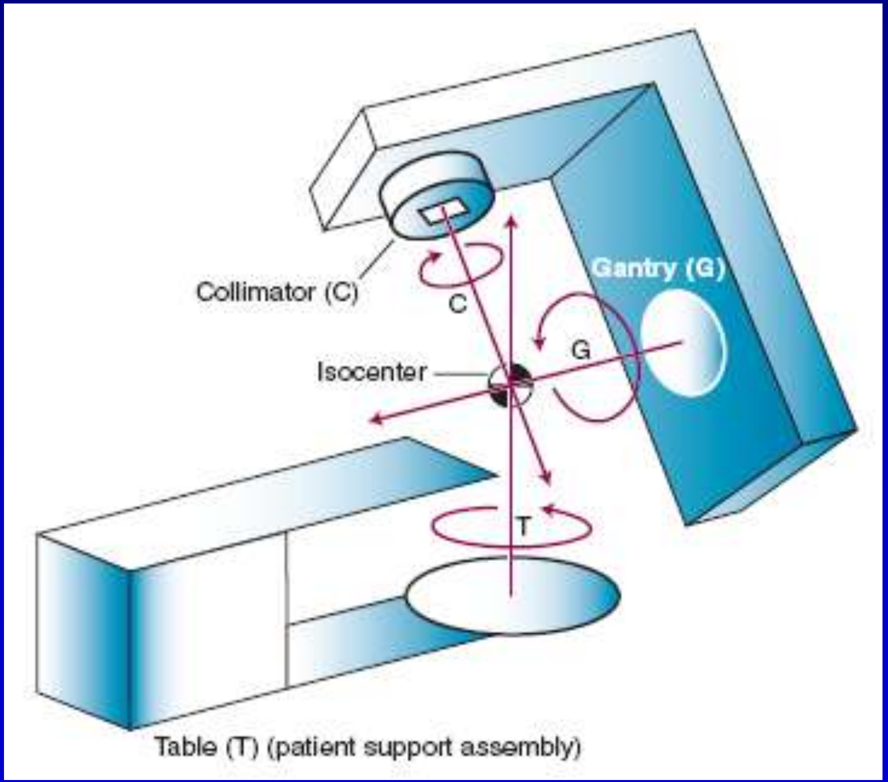
The Electron Linear Accelerator

Radiation Treatment Geometry

Six Degrees of Freedom about the Isocenter

3 rotations, 3 translations, 1 mm radius precision

Best match for large animals (second talk)

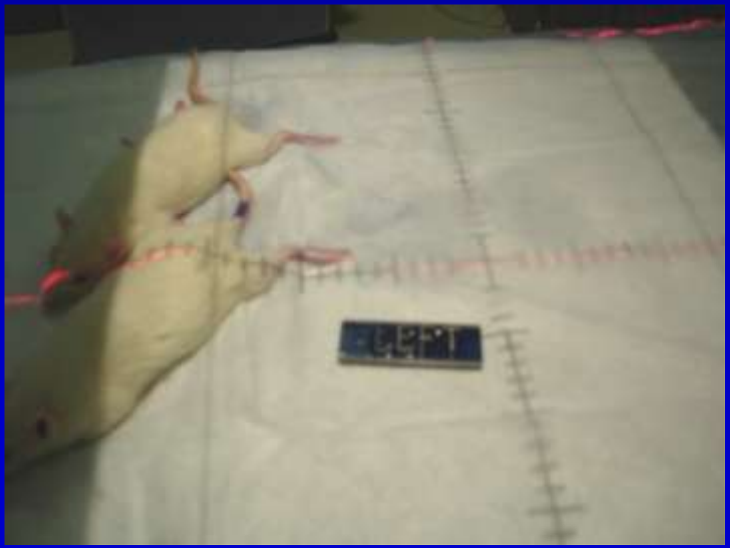


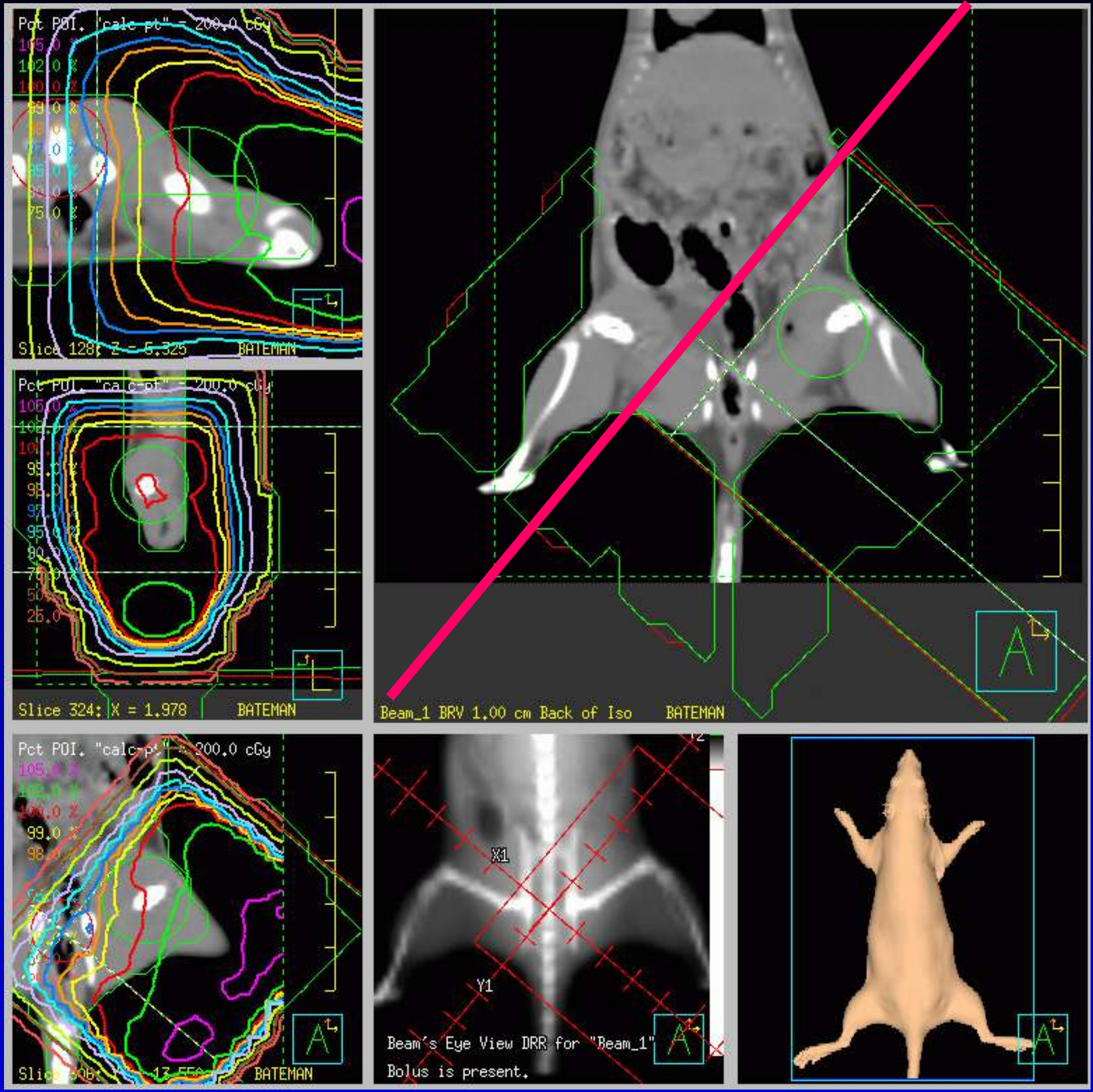
Linear Accelerator

In general, too high energy for small animals, however, depends on geometry.

Advantages: excellent modeling and set-up tools.

Example: Bone Loss Irradiations





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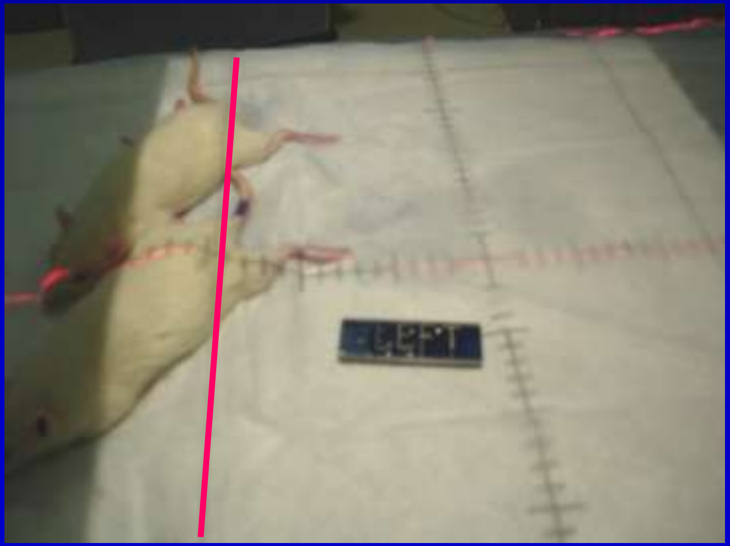
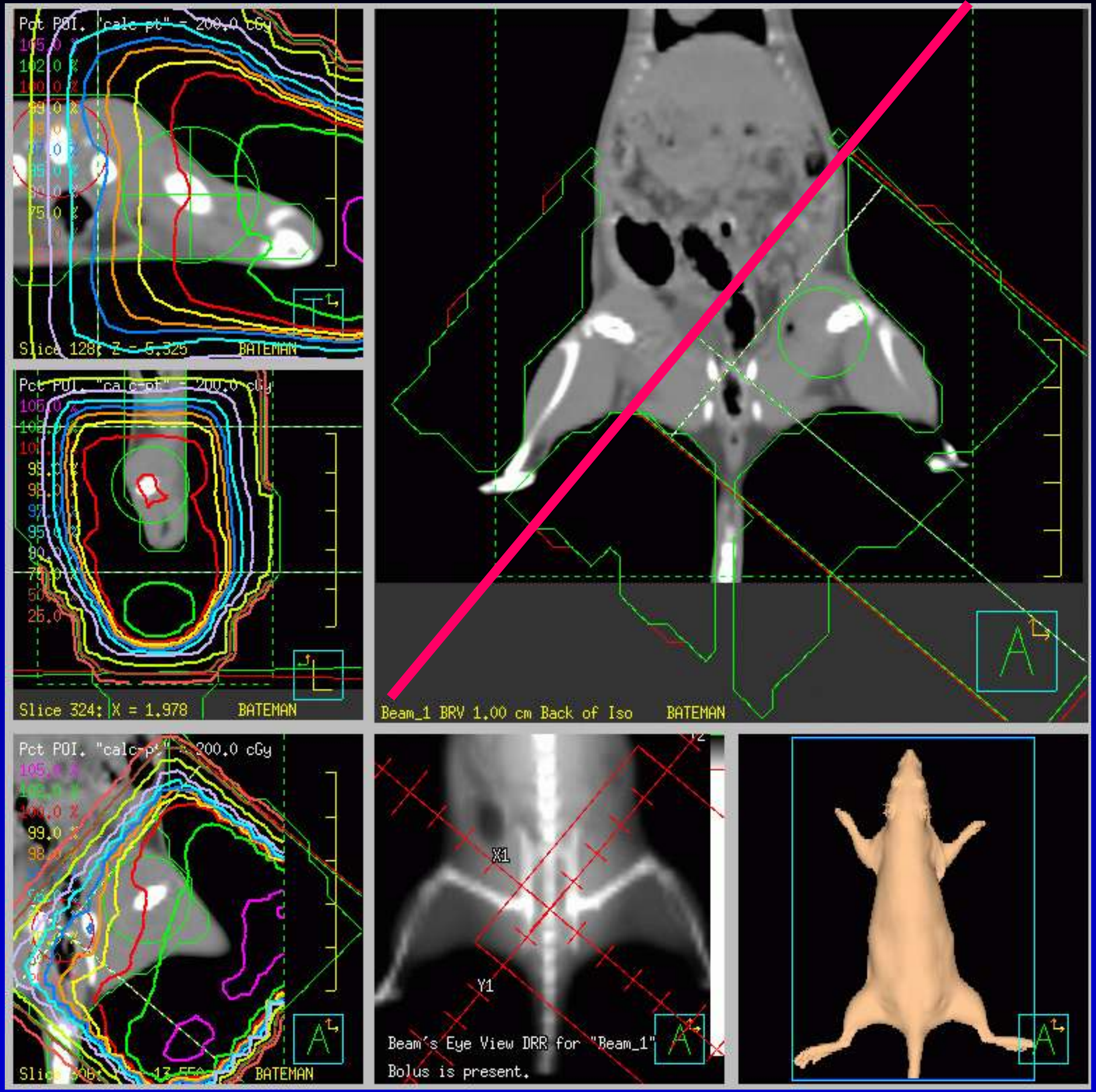
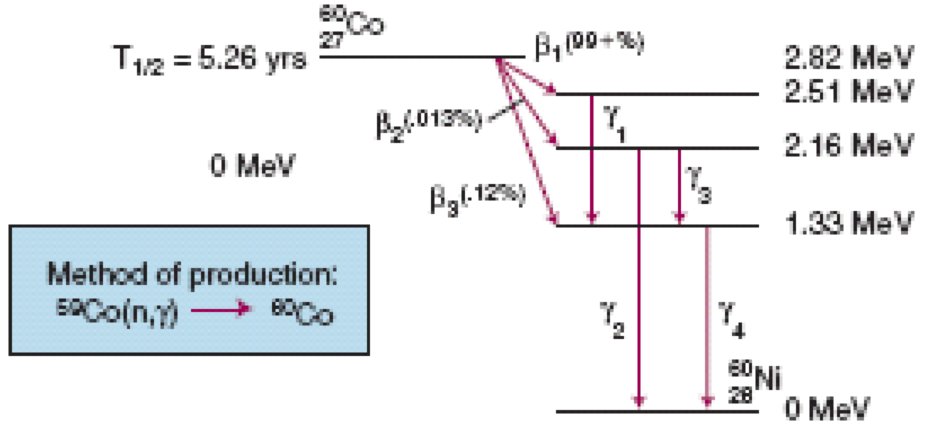




Radionuclide Generators

- D-T Generator: low energy deuterons
- Cobalt-60 γ rays: teletherapy

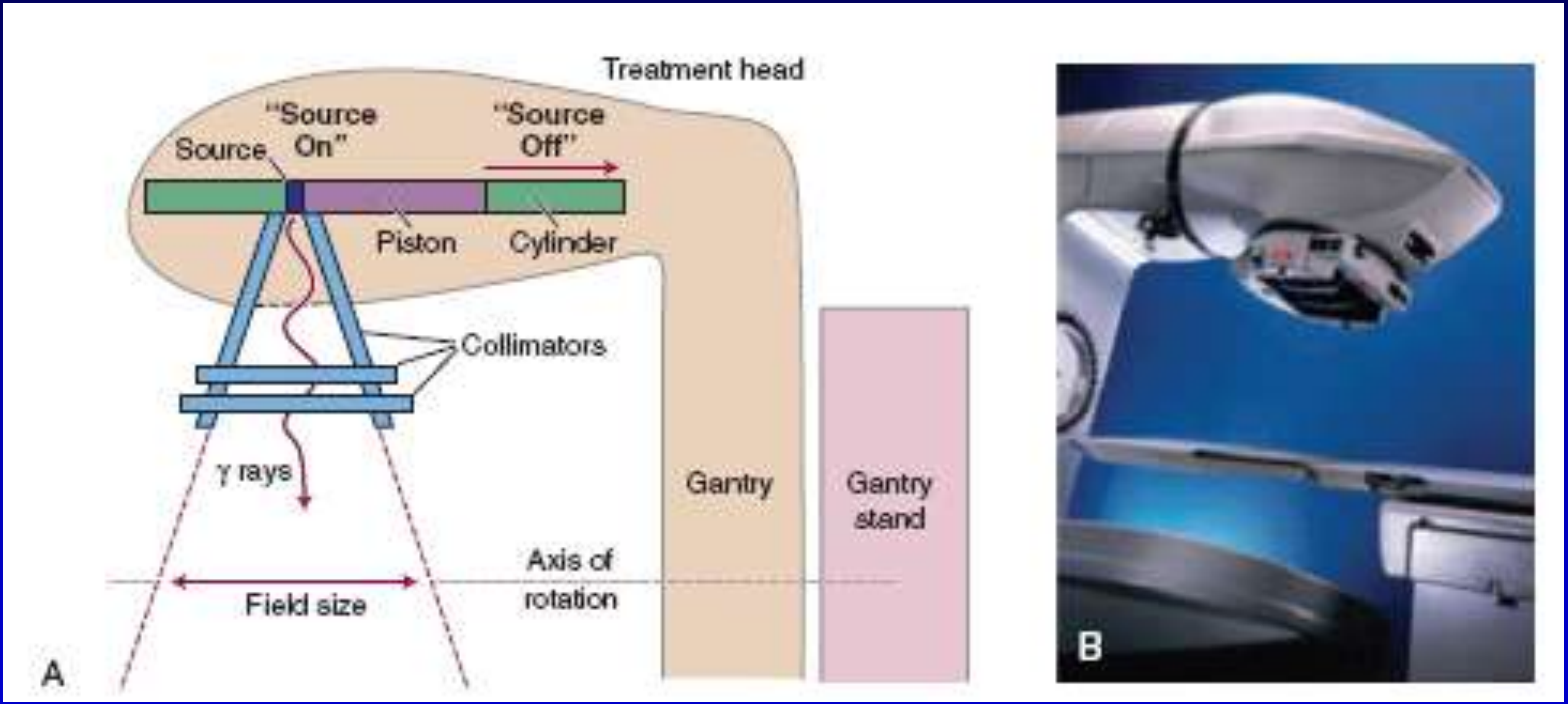


Emitted radiation	Energy (MeV)	Mean number per disintegration
γ ray (Nickel-60 γ rays)	1.173	0.998
γ ray (Nickel-60 γ rays)	1.332	1.0

Figure 6-69 A ^{60}Co decay scheme.
CREDIT LINE: Data from Lederer CM, Hollander JM, Perlman I: Table of Isotopes, ed 6, New York, Wiley & Sons, 1967; schematic courtesy of E.L. Chaney.

Cobalt-60 Teletherapy: "Beam"

Many of these devices retired from clinical service and used for radiobiology studies. Geometry and setting very similar to linear accelerators, but usually with an extremely decayed source and possibly an unacceptable dose rate.



Bourland JD. In Gunderson & Tepper, 3rd edition (in press)

Cesium and Other Isotope Irradiators

- Very common, easily operated, and subject to increased security
- Cesium-137, 30 yr $t_{1/2}$, 662 keV γ rays
  - Alternates include Cobalt-60 and Iridium-192
- Single and dual source trains
- Added filters can improve dose homogeneity
- Horizontal and vertical designs
- Static and rotating sample positions for dose homogeneity
- High (1-100 Gy/min) dose rates possible
- Depth of penetration matches well with small animal size
- Linear source train produces “flood field” of 1/r
- Large field can be used as is or collimated to “beams”
- Versatile: Irradiation geometries limited only by creativity

Isotope Irradiator Characteristics

Radiation Source (Energy)	Dose Rate	Small Animal Applications	Comments
Cesium-137 gamma (γ) rays (0.662 MeV γ ray) Less common: Cobalt-60 gamma (γ) rays (1.17 and 1.33 MeV γ rays) Both designs use linear, steel-encapsulated radioactive sources. A timer controls the irradiation time.	1 – 5 Gy/min @ defined positions within irradiation chamber. Nominal radioactivity of 2,000 Curies (Ci). Dose rate varies with source-to-sample distance and dose distribution uniformity may vary across the irradiated volume depending on sample size and position in the irradiation chamber.	Whole-body irradiation. Partial-body irradiations using specially-designed collimators. Irradiation of one or more animals possible, depending on size and geometry.	Simple design makes for ease of use. Source moves from the shielded condition to irradiate a chamber with enclosed sample. Designs are horizontal or vertical operation. Irradiation geometry can be customized for required experimental conditions. Dose rate calibration required to determine irradiation times. Radiological security must be insured.

NRC-Mandated Increased Controls

- Directly related to 9/11/01
- Source security measures
- User security measures – vetting process
- Must have been implemented as of ~2010

Table 1: Radionuclides of Concern

Radionuclide	Quantity of Concern[1] (TBq)	Quantity of Concern[2] (Ci)
Am-241	0.6	16
Am-241/Be	0.6	16
Cf-252	0.2	5.4
Cm-244	0.5	14
Co-60	0.3	8.1
Cs-137	1	27
Gd-153	10	270
Ir-192	0.8	22
[illegible]	[illegible]	[illegible]

A Cesium-137 Irradiator for Small Laboratory Animals[1]

E. B. Hranitzky, M.S., Peter R. Almond, Ph.D., Herman D. Suit, M.D.,[2] and E. B. Moore, B.S.

Radiology 107:641–644, June 1973

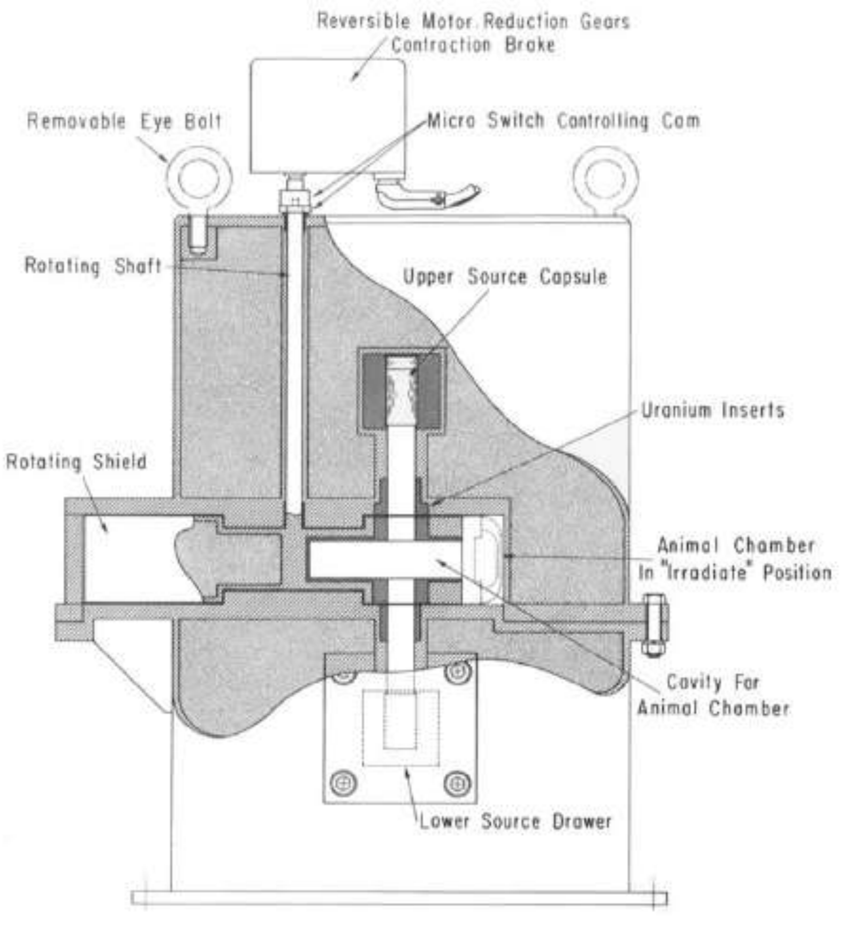


Fig. 1. Sagittal cutaway of the irradiator.

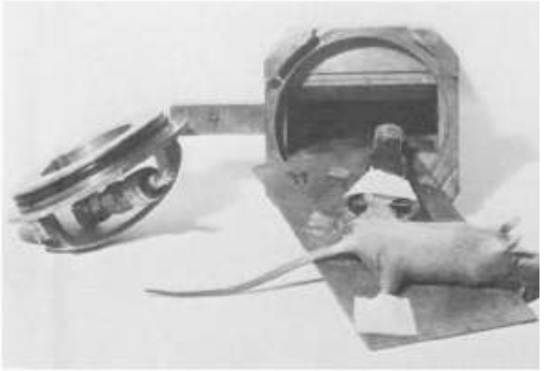


Fig. 3. Animal chamber with adaptor for anoxic exper

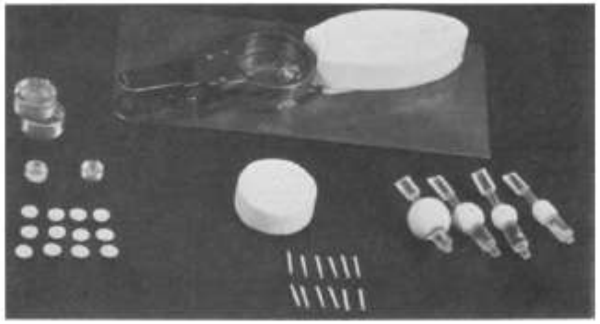


Fig. 4. Thermoluminescence dosimeters and phantom material.

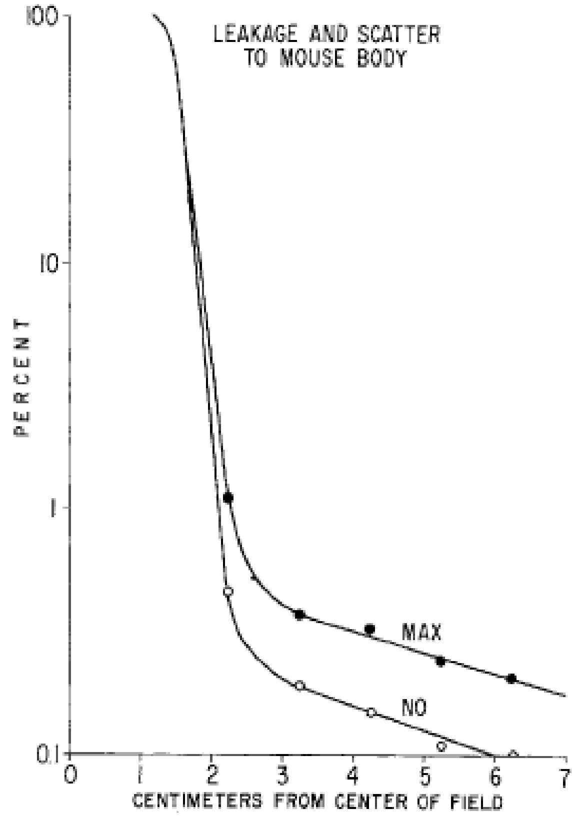
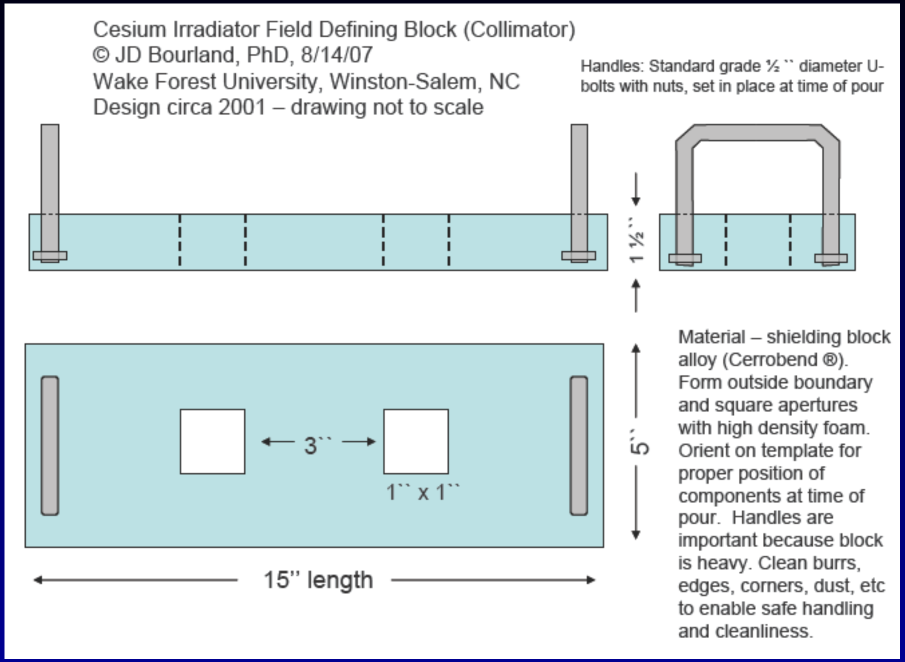


Fig. 5. Leakage and scattered radiation with extreme variation of tissue within the beam. Max and No refer to scattering material in the field.

- Animal chamber rotates into irradiation position
- Dose homogeneity of 1-4%
- TLD and Fricke dosimetry
- Built by AECL

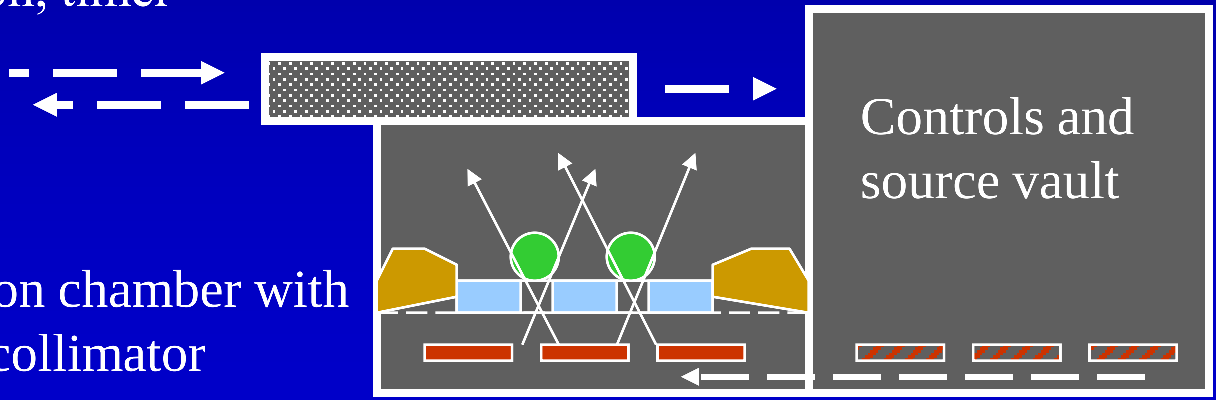
Cesium Irradiator

Horizontal configuration
3-source train



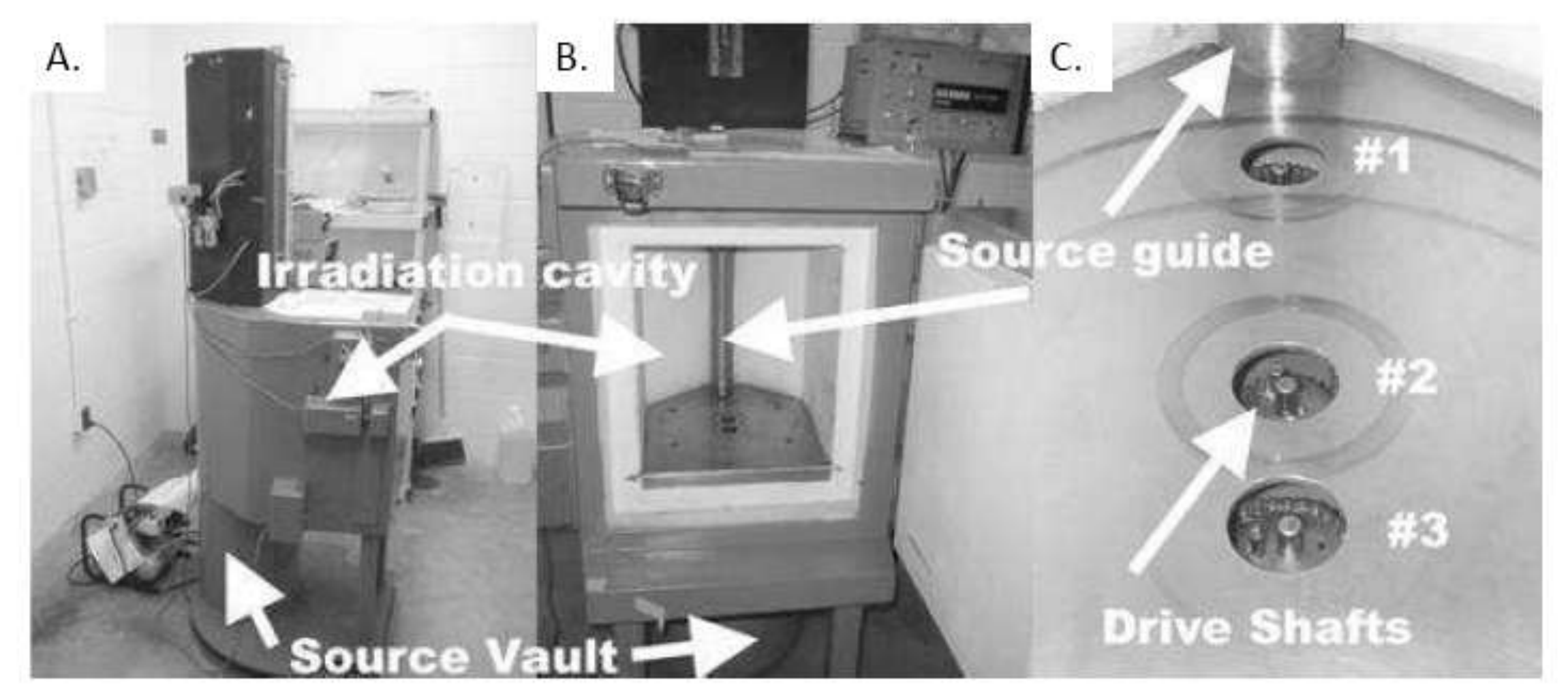
- Linear Cesium-137 tubes (0.662 MeV γ rays)
- Custom apertures for whole brain or other irradiations (rat, mouse) – HEAVY
  - do not drop on your foot
  - Do not drop on your friend's foot either
- Geometries for cells, dishes, flasks
- For a specific geometry the setup must be consistently reproduced – this means "height", "width", specimen position, timer setting, etc.
- Radiological security measures

Removable access lid, interlocked



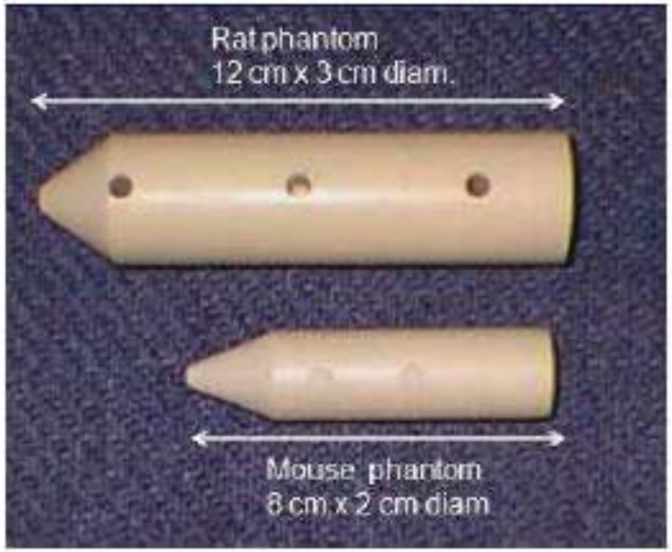
Irradiation chamber with custom collimator

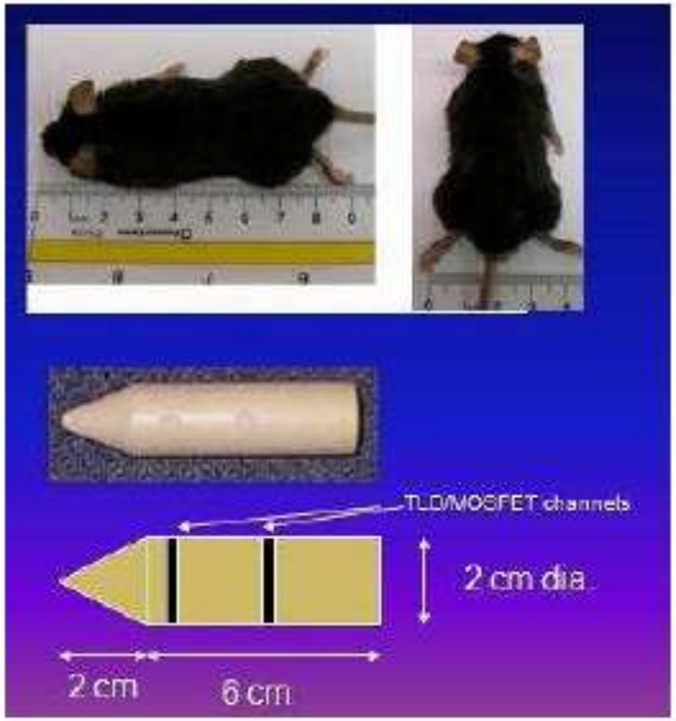
Vertical Configuration
two-source model with rotating sample carousel

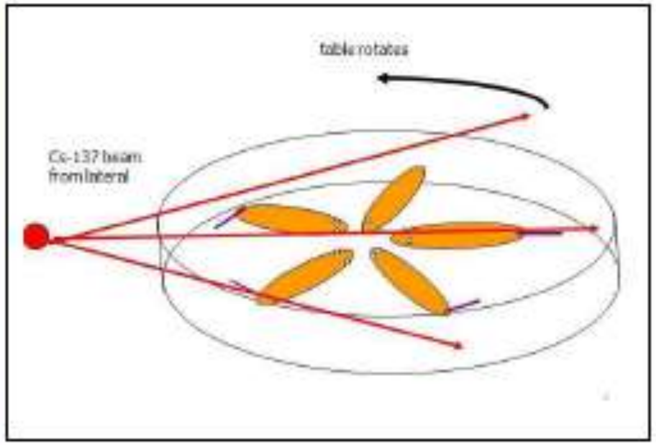


Specific Issues in Small Animal Dosimetry and Irradiator Calibration
Yoshizumi T, Brady SL, Robbins ME, Bourland, JD. IJRB (in press)

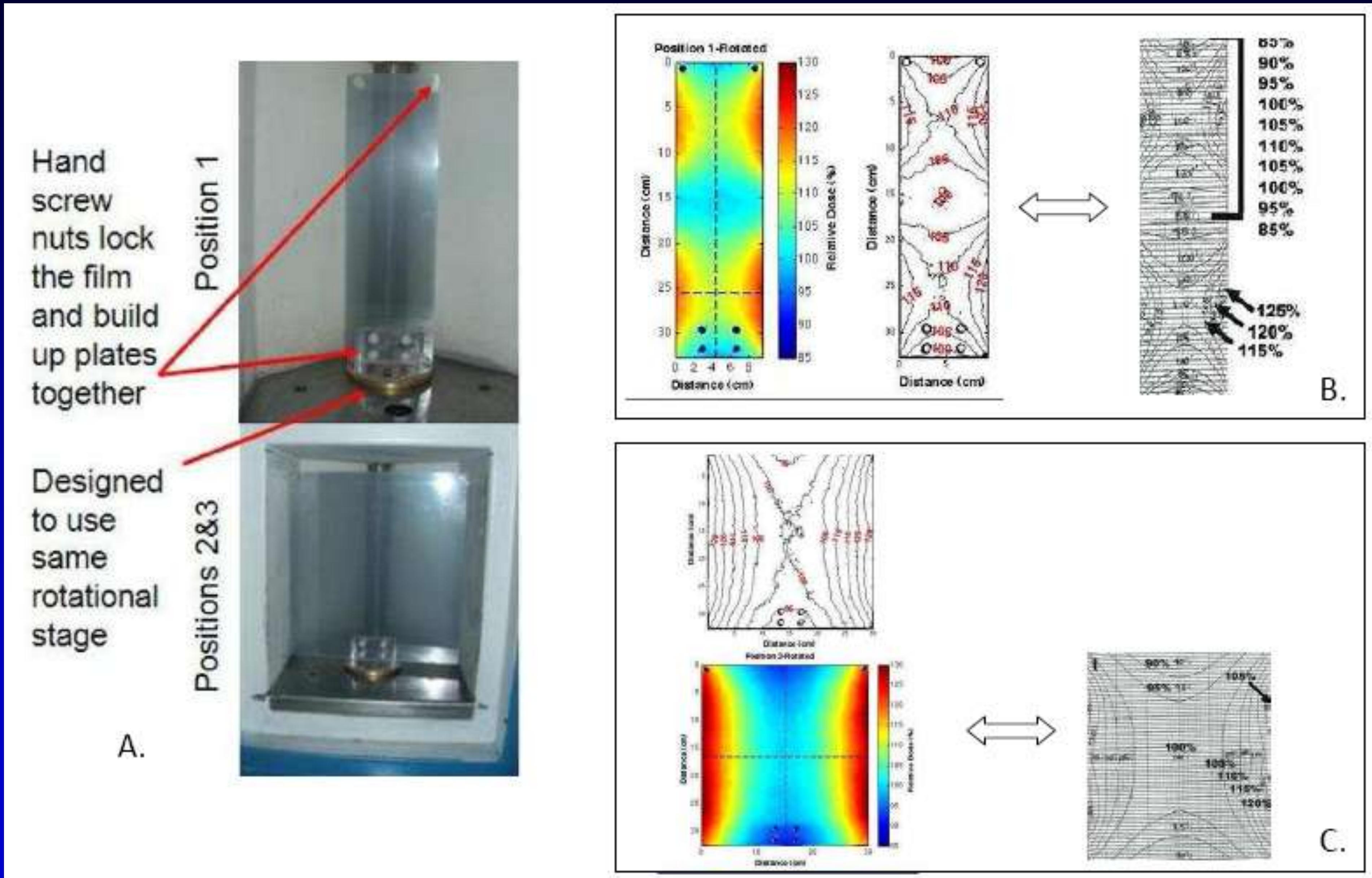
Mouse Phantom Dosimetry







Radiochromic Film Dosimetry



Irradiation Curator (Physics) Role

- Meet with researcher, discuss research project
  - Species, target depth and thickness, non-target tissues
- Develop irradiation geometry and jigs
- Validate dose for possible unique conditions
- Train researcher on device operation, radiation safety, and irradiation geometry setup
- Perform trial irradiations with researcher
- After confirmation, researcher is independent

Things To Do

- Basic Calibration at a point or points
  - Dose Rate for specified reference conditions
  - Energy, field size, distance, depth, and material
- Field Characterization – "2D/3D dose distribution"
- Decay Correction for Radioisotopes
- Communicate this information
- Verify on regular basis

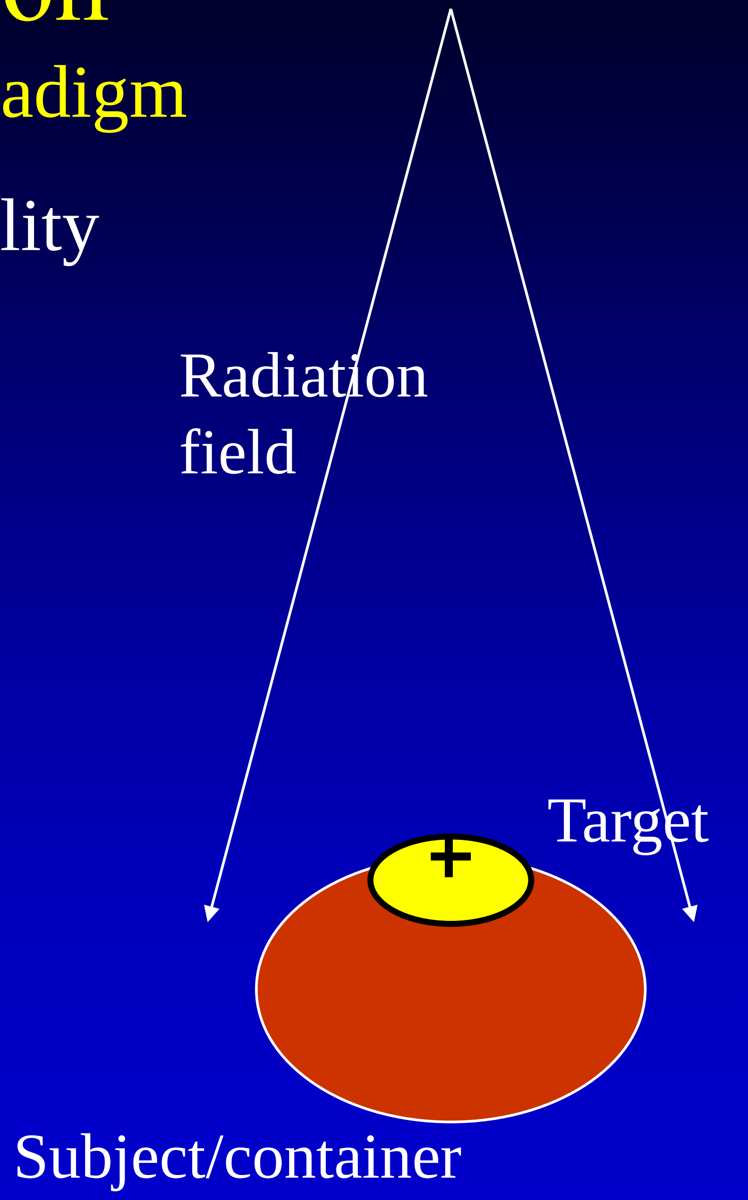
- Particular Calibrations for Specific Geometries

Things to Be Careful About

- Specification of dose – how much and where
  - Communication is key for researcher and physicist
- Irradiation geometries with poor reproducibility
- User training – hi & lo user abilities
- Small field calibrations – very challenging
  - Instrumentation “too big” for field size
- High dose rate calibration conditions
- High dose gradient geometries – setup points

Dose "Prescription"
Radiation Treatment Paradigm

- Radiation type/mode; energy/beam quality
- Beam/field geometry
- Dose defined at a point
  - Description of the point – it's location
  - Amount of dose to the point (value, range)
- Dose defined to a volume
  - Description of the volume – it's boundary
  - Amount of dose to the volume (range)
- Dose/fraction and number of fractions
- Dose rate at the point
- Values have error bars +/- ranges



Summary

- Two common small animal irradiation devices
  - Orthovoltage x-ray unit and Cesium-137 irradiator
- Calibration of dose rate and dose distribution
- Constancy of sample positioning per validated irradiation geometry is key: ISL effect is steep
- Further characterization required and desired for unique irradiation geometries
  - Instrumentation and geometric and species-morphic phantoms

Summary

- Ease of use is high with proper training
- Isotope irradiators require increased security controls
- Multi-disciplinary / team science important for delivery of consistent dose distribution
- Communication and consistency of all irradiation parameters is key to consistent results

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