Biodosimetry Bloopers: Why Radiation Biology Needs Radiation Physics

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INTRODUCTION

- Concerns about the risk of large-scale exposure of the civilian population in a radiological terrorist incident following 9/11 led in 2005 to establishment of a network of Centers for Medical Countermeasures against Radiation (CMCR)

- Funded through NIAID, these CMCR were created to serve as multidisciplinary, extramural research centers focusing on a number of areas

CMCR: Focus Areas

- Development of agents for prophylaxis, mitigation, and treatment of radiation injury
- New or expanded educational resources to improve expertise in the radiation sciences, particularly radiation biology (previously acknowledged by NCI and ASTRO)

CMCR Educational Efforts

- Initial efforts focused on radiation biology education and the need for standardized animal models
- Jointly sponsored a workshop, “Animal Models for Medical Countermeasures” held Jan 18-19th 2008, San Antonio, Texas

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Animal Models for Medical Countermeasures to Radiation Exposure

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Focused primarily on the most appropriate species and rodent strains to use to assess countermeasures in particular organ systems

Need to consider radiation quality and dosimetry was recognized, but little detail as to impact of these radiation physics-based factors on biological response to irradiation was included

Radiation Dosimetry

- To the non-expert, the irradiation component of any radiobiological study appears trivial
- Without ensuring accurate, reproducible dosimetry, the time, effort, and expense of conducting experiments to develop/assess the efficacy of putative countermeasures is wasted
- However, would appear that little coordinated effort has gone into ensuring a standardized approach to radiation dosimetry across the CMCR

NY Times Articles
Medical Cases Reviewed

- Imaging Overdoses: October, 2009
  - 206 stroke patients: pre-sets edited to other settings
  - Pediatric CT case: operator error with older CT

- Radiation Treatment, January, 2010
  - IMRT delivery error: field open, no MLC operation
  - Breast delivery error: wedge reversed – OUT, not IN
  - Prostate brachytherapy: poor implantation technique
  - Linac SRS overdose x 1.5: calibration error in spreadsheet

The New York Times

October, 2009

October 16, 2009

Radiation Overdoses Point Up Dangers of CT Scans

By WALT BOGDANICH

At a time when Americans receive far more diagnostic radiation than ever before, two cases under s
involving a large, well-known Los Angeles hospital, the other a tiny hospital in the northern part of t
risks that powerful CT scans pose when used incorrectly.

A week ago, Cedars-Sinai Medical Center in Los Angeles disclosed that it had mistakenly administer
normal radiation dose to 206 possible stroke victims over an 18-month period during a procedure ir
of the brain. State and federal health officials are investigating the cause.

Hundreds of miles north at Mad River Community Hospital in Arcata, the other case — involving a
of neck pain after falling off his bed — has led to the revocation of an X-ray technician's state license
more than an hour of CT scans. The procedure normally takes two or three minutes.

The hospital's radiology manager at the time, Bruce Fleck, called the overdose a "rogue act of insani

Photo: NY Times, Aug 1, 2010

The New York Times

January, 2010

January 24, 2010

THE RADIATION BOOM

Radiation Offers New Cures, and Ways to Do Harm

By WALT BOGDANICH

As Scott Jerome-Parks lay dying, he clung to this wish: that his fatal radiation overdose — w
unable to swallow, burned, with his teeth falling out, with ulcers in his mouth and throat, nau
unable to breathe — be studied and talked about publicly so that others might not have to liv

Sensing death was near, Mr. Jerome-Parks summoned his family for a final Christmas. His f
the beach where they had played as children so he could touch it, feel it and remember bette

Mr. Jerome-Parks died several weeks later in 2007. He was 43.

A New York City hospital treating him for tongue cancer had failed to detect a computer err
blast his brain stem and neck with errant beams of radiation. Not once, but on three consecu

Soon after the accident, at St. Vincent's Hospital in Manhattan, state health officials cautione

Photo: NY Times, Jan, 2010

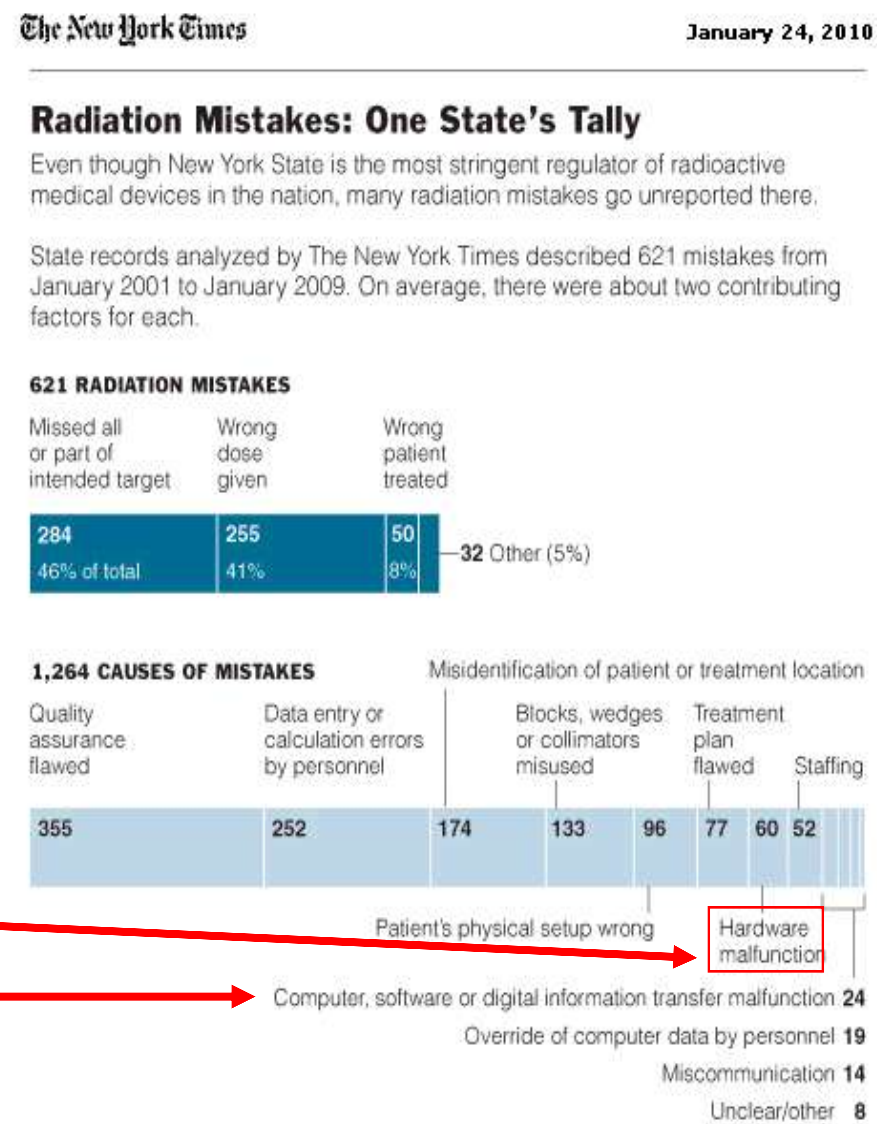
Classes and Causes of Events

Classes of Errors

- **Missed all/part of target**
- **Wrong dose**
- Wrong patient
- Other

Causes of Errors

- **QA flawed (improper checks)**
- **Data entry & calc errors**
- Misidentification: patient, site
- Device setup error (blocks, wedges)
- Flawed treatment plan
- Hardware malfunction
- Software, data transfer malfunction, software overrides, communication



Radiation Dosimetry Education

- Education and Training Core of the Radiation Countermeasures Center of Research Excellence (RadCCORE, PI Nelson Chao, MD) based at Duke organized a 1-day workshop for its members

- "Small Animal Dosimetry: Current Sate and Future Directions" held on May 20th 2010

- Included RadCCORE members from Duke, Univ Arkansas for Medical Sciences, UNC Chapel Hill, and Wake Forest

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informa
healthcare

Notice of Acknowledgement:

This paper Specific Issues in Small Animal Dosimetry and Irradiator Calibration, was supposed to be part of the Special Issue published in August 2011 titled "Overview of research from the Centers for Medical Countermeasures against Radiation". Due to an error on the part of the publishers, the paper was omitted. The publisher wishes to apologize to the authors and readers for any inconvenience caused.

RECOMMENDATIONS

- A user training program for new irradiator users
- Subsequent training updates
- Establishment of a national small animal dosimetry center for all CMCR members

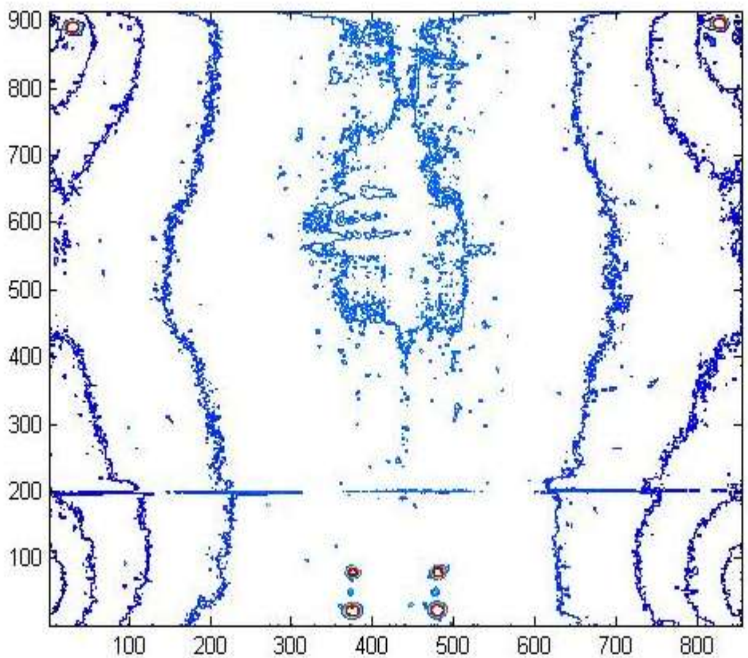
DOSE VERIFICATION (2010-2011)

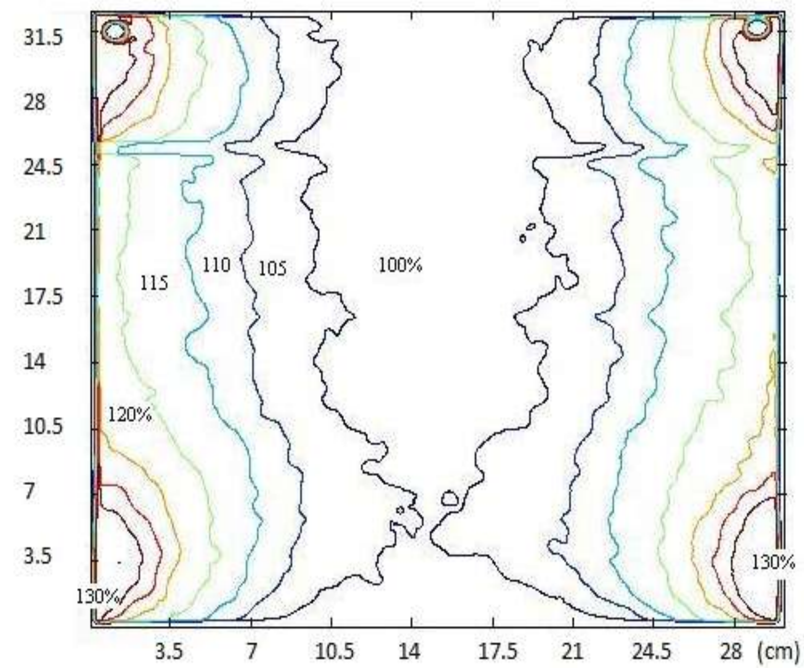
PI	ANIMAL	TIMELINE	Machine
LAB A	MICE	May-June 2011	Xrad225 orthovoltage (Image Guided therapy machine)
LAB B	MICE	2010-11	JL Shepherd Cs-137
LAB C	MICE	2011	Xrad320 orthovoltage
LAB D	MICE	July 2011	JL Shepherd Cs-137 (External Consultation)

LAB B: J L Shepherd Cs-137

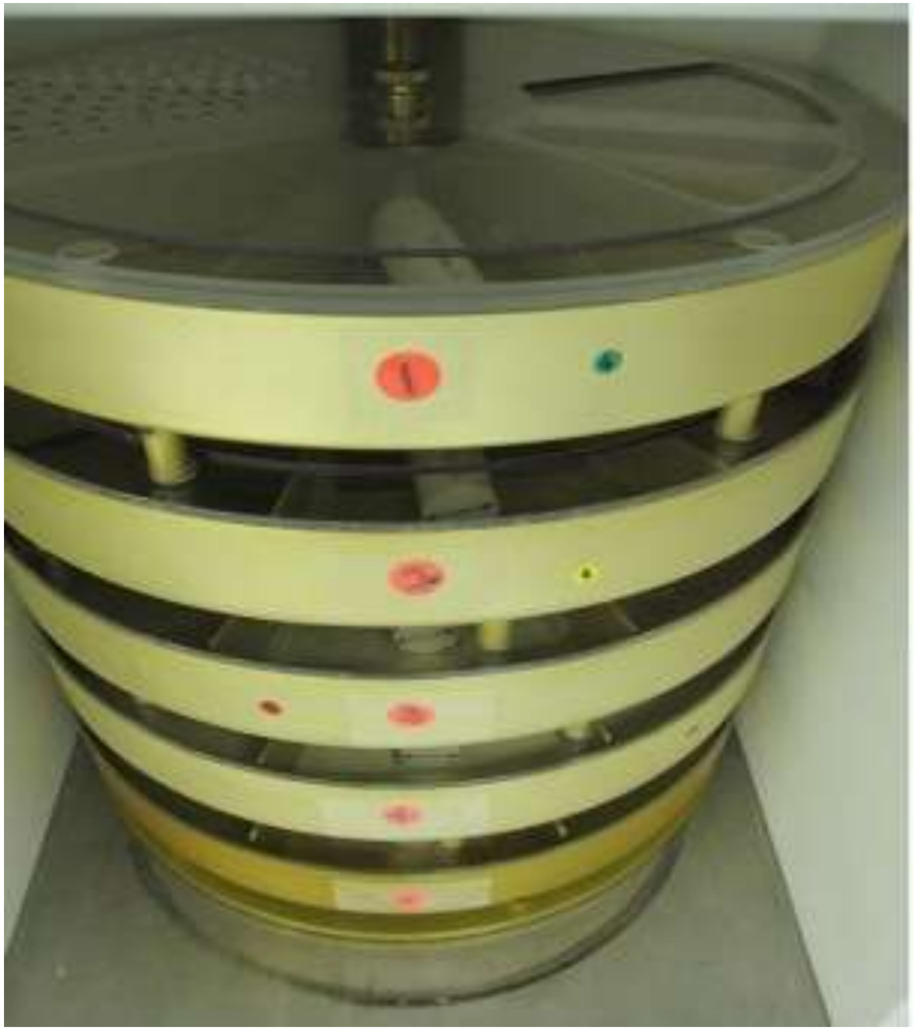
- RADCCORE MEMBER INSTITUTION

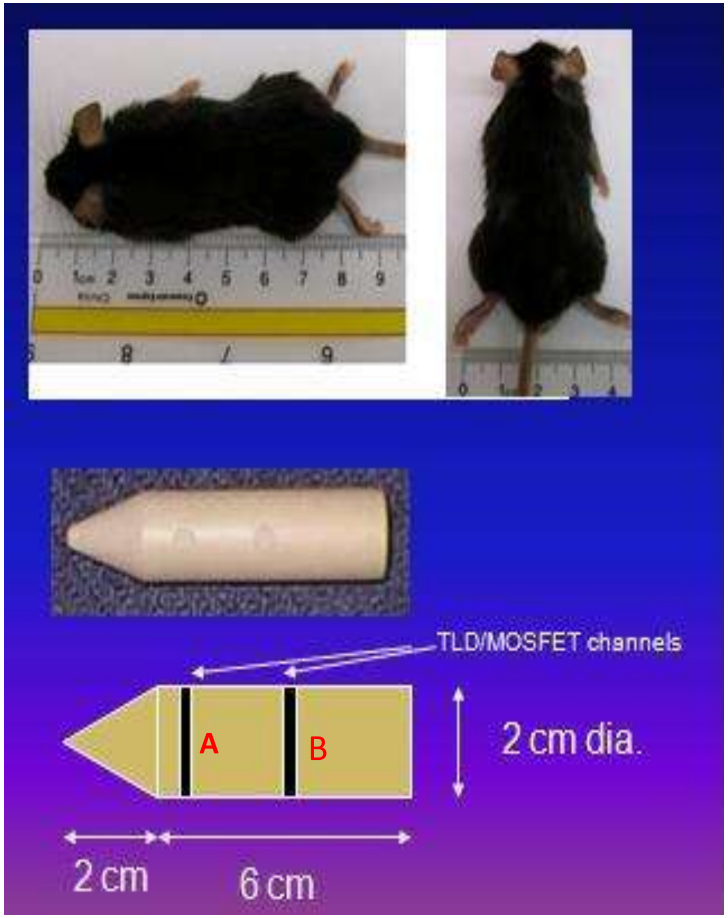
Radiochromic Film Dose Distributions





LAB B Experimental Set-up





LAB B: RESULTS
TARGET DOSE = 9 Gy; variation range:-2% to -26%

HOUSING LEVEL/2 LOCATIONS IN MOUSE	TARGET DOSE (Gy)	Average dose per location (Gy)	% difference
1 -B	9.00	6.63	-26
1 -A	9.00	7.57	-16
2 -B	9.00	6.99	-22
2 -A	9.00	7.51	-17
3 -B	9.00	6.82	-24
3 -A	9.00	7.55	-16
4 -B	9.00	7.33	-19
4 -A	9.00	8.23	-8.5
5 -B	9.00	8.18	-9.1
5 -A	9.00	8.80	-2.2

Researchers use only lower levels for their experiments (smaller % diff)

This is an unusual case, i.e., max dose rate is located lower level of the housing (normally we find max dose rate at the height of 15 cm from the floor of the housing)

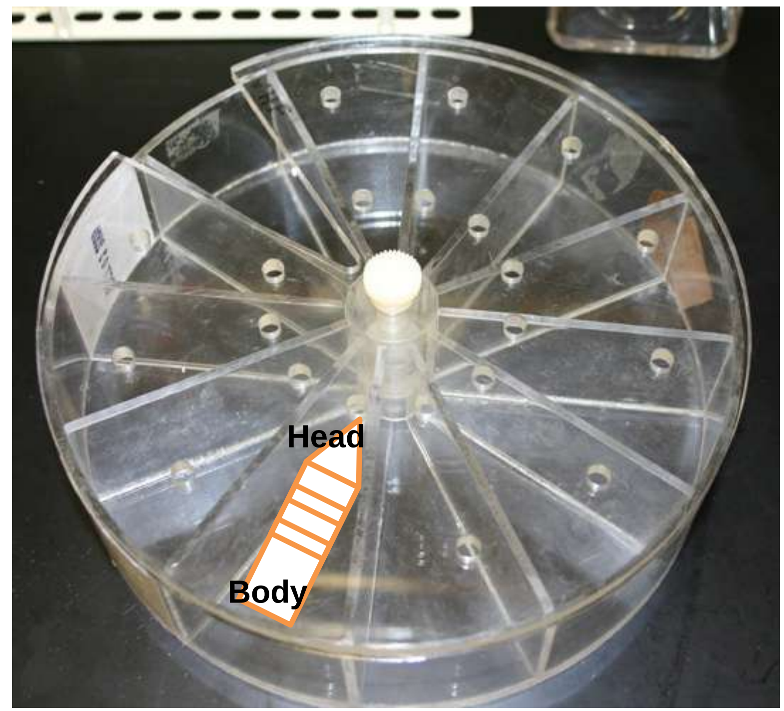
LAB D: J L SHEPHERD Cs-137

- Non-affiliated major academic institution

- Dosimetry consultation requested by PI
  - No quality assurance on dosimetry; History of irradiator calibration sketchy
  - PI did not believe current calibration factor; needed verification

LAB D: J L SHEPHERD Cs-137 NON-AFFILIATED ACADEMIC INSTITUTION (WEST COAST)

Inside irradiator

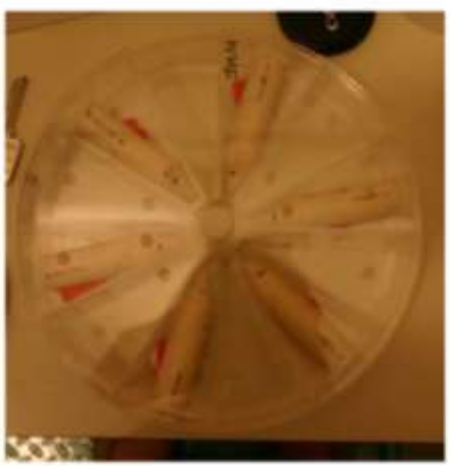


LAB D: J L SHEPHERD Cs-137
NON-AFFILIATED ACADEMIC INSTITUTION
(WEST COAST)

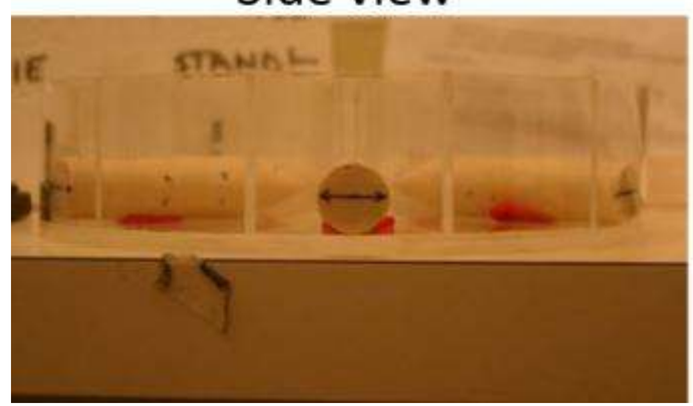
- RESULTS

TARGET DOSE	MEASURED DOSE AT DUKE (TLD)	% DIFFERENCE
750 cGy	463 cGy	-38%

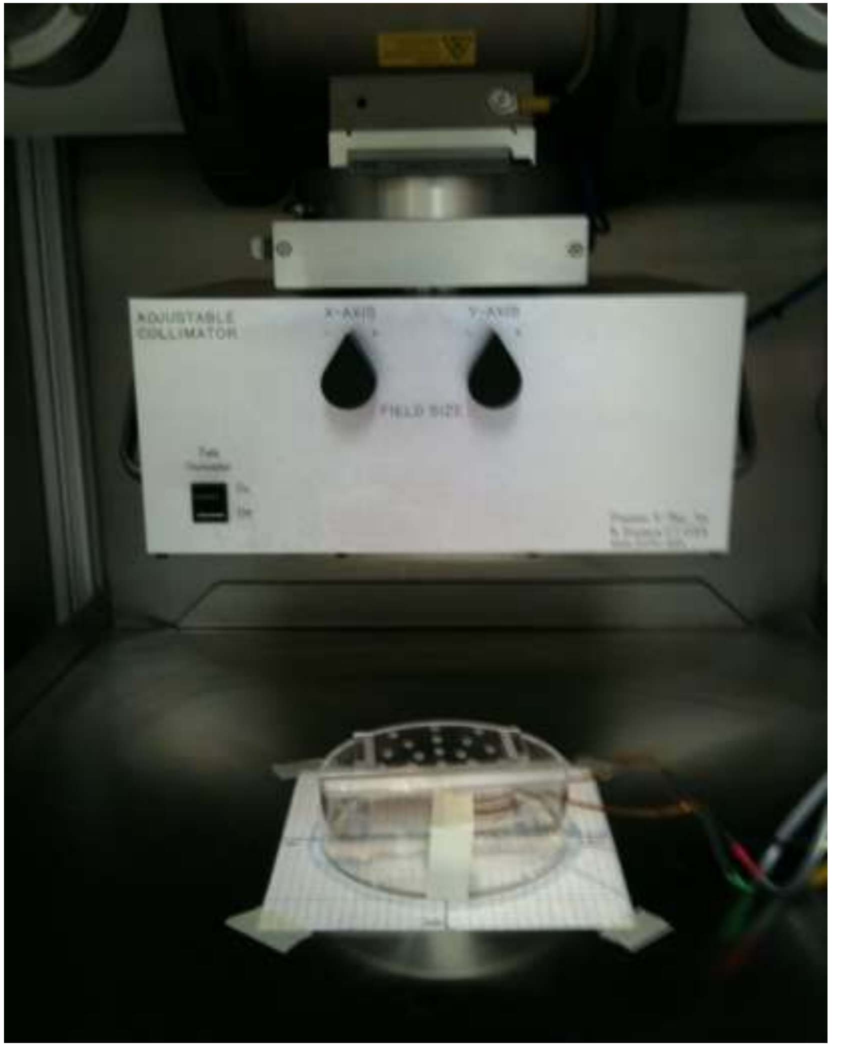
top view



Side view



LAB C: XRAD 320 ORTHOVOLTAGE IRRADIATOR



RESULTS

- Results discussed with PI and his staff
  Problems: All mice died

- Dose rate used by technician was fairly close to the measured dose rate.

Dose rate used by PI group	Dose rate measured by us (Filter #4)	% difference
150 cGy/min	160 cGy/min	6%

- Target dose, expected dose, and delivered dose

Target dose	Expected dose	Actually delivered dose (possible source of error)
5-6 Gy	4.39 Gy	UNKNOWN due to unknown set-up, e.g., type of filter used – unable to verify

- Possible sources of errors
  - Human errors (failed to verify filter types, possibly no filter used)
  - User was not familiar with the filter system and physics (in-service provided)

LAB A: XRAD225 (Image Guided Radiation Therapy)

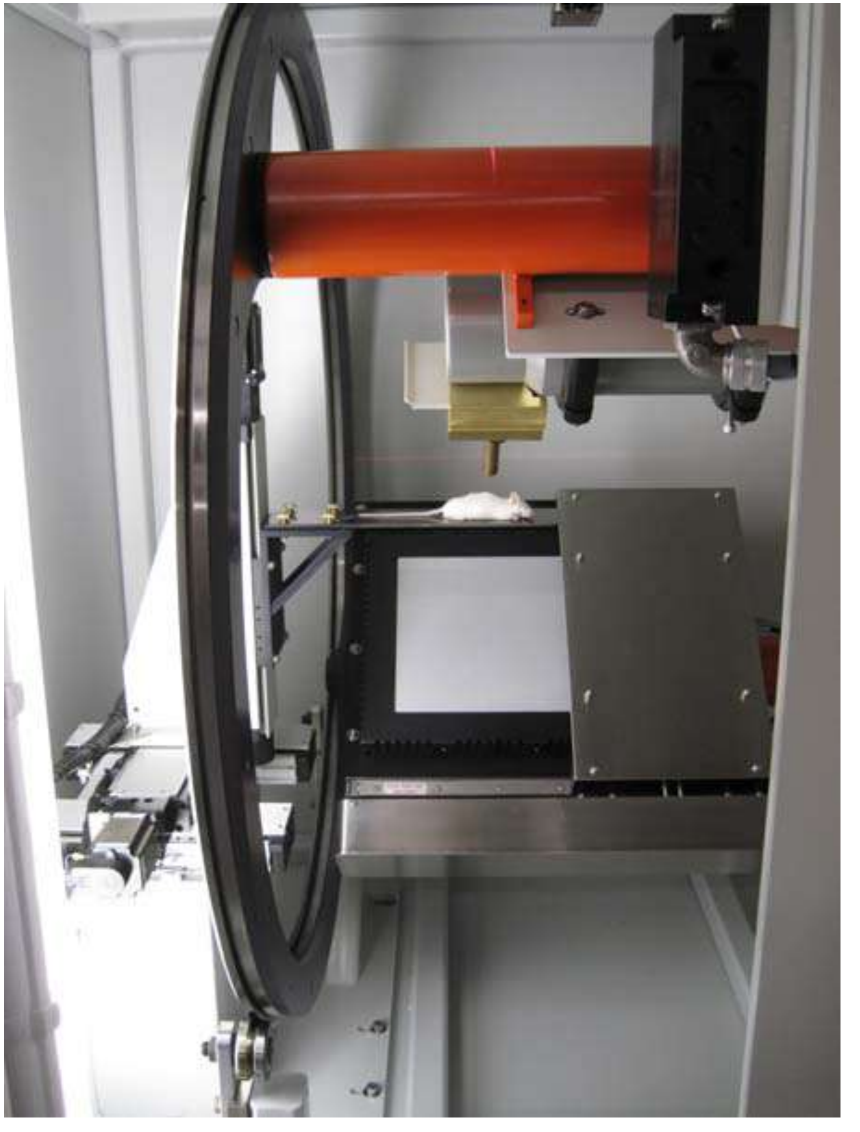
- RADCCORE MEMBER INSTITUTION

X-RAD225Cx

Doors Open

Conventionally, pre-clinical irradiation is typified by large volume irradiations or crude confinement of dose to the extent of a fixed irradiating beam.

The X-RAD Roto 225Cx provides image-guided placement of irradiation distributions within pre-clinical subjects. The isocentric design, combined with an amorphous silicon flat-panel detector, permits high-performance cone-beam CT soft-tissue imaging of the subject in situ prior to irradiation. The cross-calibration of imaging and treatment isocenters allows targeting of the radiation field through three-dimensional (3D) translation of the subject to align target or avoid normal structures. Typically setup, imaging, guidance and irradiation time is completed in 15 minutes for single isocenters and reasonable doses (<10 Gy). The compact rotational gantry is housed within a self-shielded assembly and controlled by a Windows XP application.

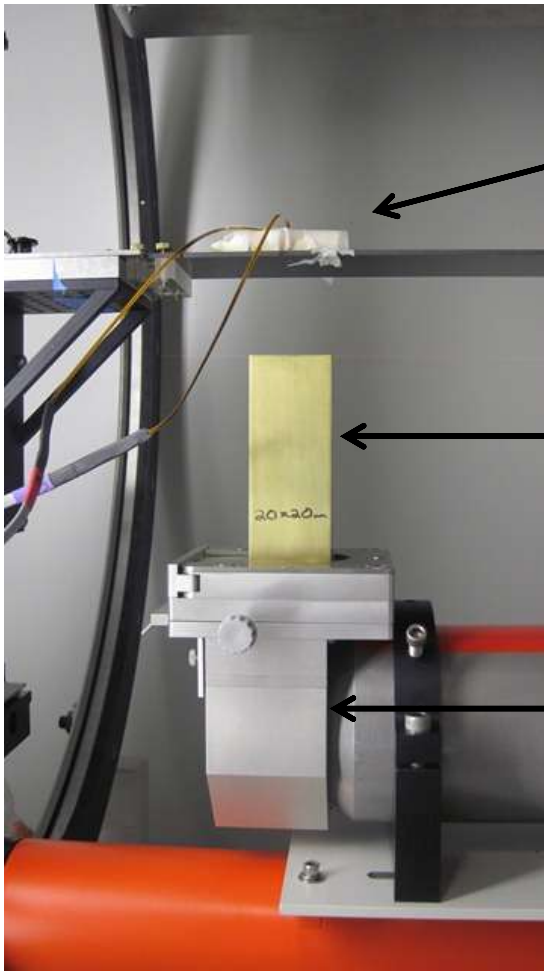


LAB A: XRAD225 (Image Guided Radiation Therapy)

- Dose Look-up Table generated by Dr. Shiva Das (based on film dosimetry with small tissue block)

- Accuracy of the Look-up table was measured with MOSFET technology (Terry Yoshizumi)

LAB A: XRAD225 (Image Guided Radiation Therapy)



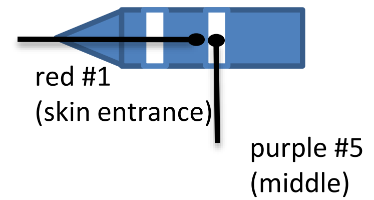
Mouse phantom

Collimator 20 x 20 mm

X-ray tube housing

LAB A - RESULTS

- Therapy Mobile MOSFETs
- 225 kVp 13 mA
- AP projection
- Taking $f_{chamber}$ = 1.02 in to account



Collimator	Dose at center (Gy)	Irradiation time (mins)
20x20 mm	**2**	0.6

	Center (Gy)
Mean	**1.61**
SD (%)	**0.6**
Percent diff (%)	**19.42**

Collimator	Dose at center (Gy)	Irradiation time (mins)
10 mm circ	**3**	1.1

	Center (Gy)
Mean	**2.97**
SD (%)	**0.0**
Percent diff (%)	**1.06**

→ Larger the collimator field, the % diff increases

Collimator	Dose at center (Gy)	Irradiation time (mins)
15 mm circ	3	1.1

	Center (Gy)
Mean	**2.83**
SD (%)	**0.6**
Percent diff (%)	**5.82**

Collimator	Dose at center (Gy)	Irradiation time (mins)
10x20 mm	2	0.7

	Center (Gy)
Mean	**1.97**
SD (%)	**0.6**
Percent diff (%)	**1.4**

CONCLUSIONS

- Commonly used γ- and X-ray irradiators are robust devices that can be used in a variety of experimental conditions and easily operated by lab personnel

- However, technical and logistical challenges exist for determination of individual dose calibration factors prior to various experimental set-ups

CONCLUSIONS

- Physics support is often the weakest link in the small animal dosimetry chain
- Lack of physics support is a norm rather than exception in many of the US small animal radiation research facilities
- Need to establish a national small animal dosimetry center

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