
# Dosimetry for Small Animal Studies

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# Disclosure

I am a part of a commercialization agreement with Precision X-Ray, Inc. for XRad225Cx.

# Acknowledgments


**PMH XRad Team**

- Steve Ansell
- Richard Clarkson
- Paul DeJean
- Richard Hill
- David Jaffray
- Salomeh Jelveh
- James Stewart
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**Users and Collaborators**

- Bristow Lab (Christina Schutze and Carla Coackley)
- **James Chow**
- **Caroline Chung**
- Ralph DaCosta Lab
- **Hill Lab (Naz Chaudary)**
- Andrew Hope
- Doug Moseley
- Taylor Lab (Livia Garzia)
- Robert Weersink

# Outline

- Systems for small animal irradiation
  - Image-guided, conformal irradiation
- Dosimetric guidelines for small animal irradiation
  - Input data/system characterization
  - Examples of small animal irradiations & dose calculations
  - Sources of Error
  - Validation
  - Monte Carlo studies

# Small Animal Irradiation Experiments

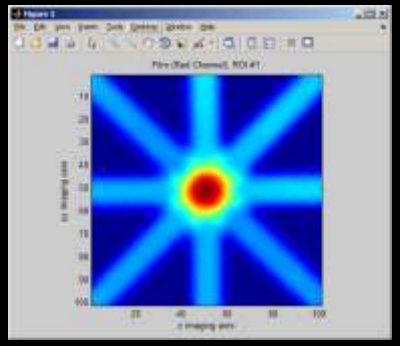
Whole Body

**Gammacell 40**
**(Best Theratronics)**

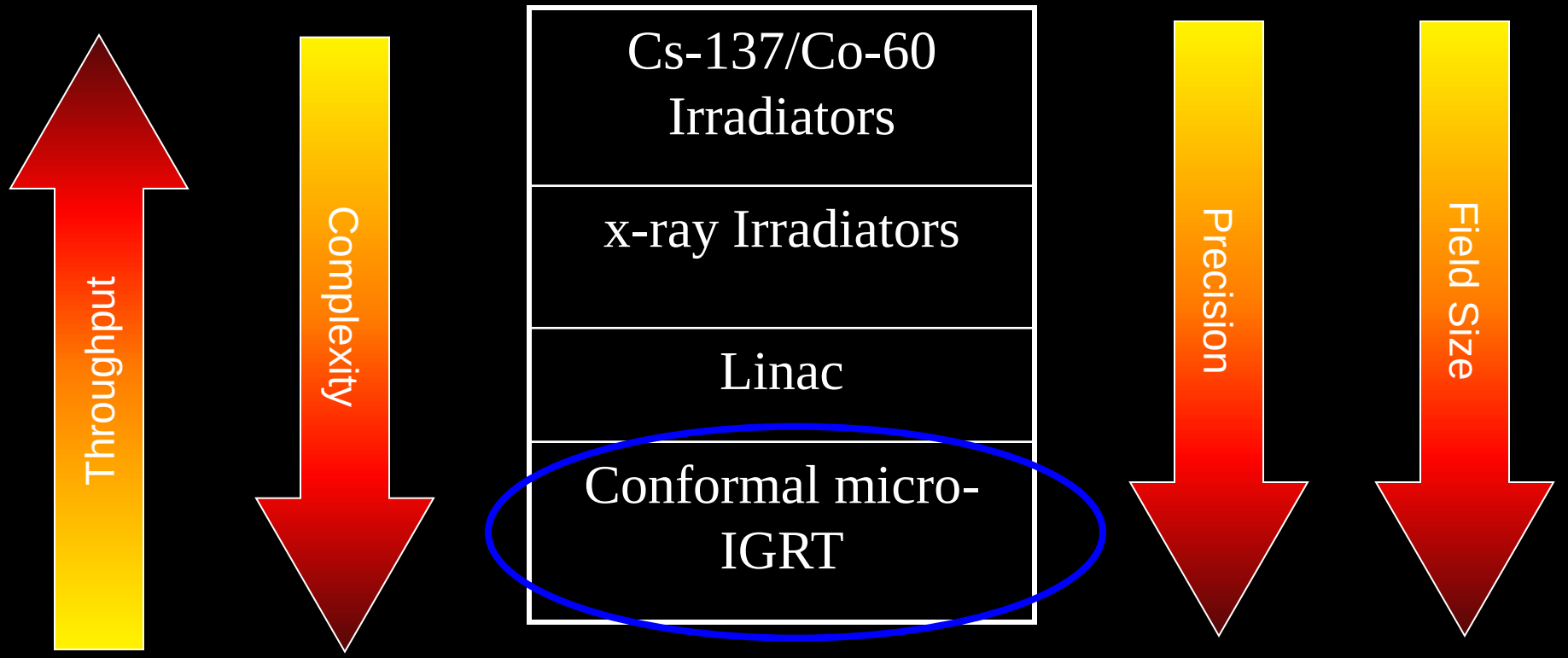
Hind Leg

**In house x-ray irradiator**

Conformal, orthotopic, image-guided, multi-beam

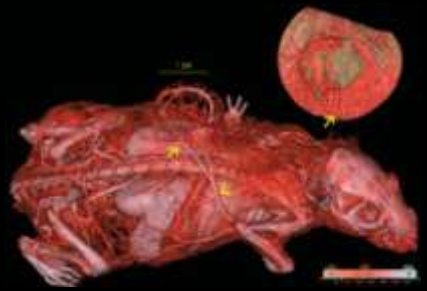


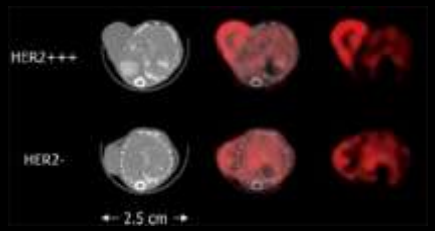
# Systems for Animal Irradiation

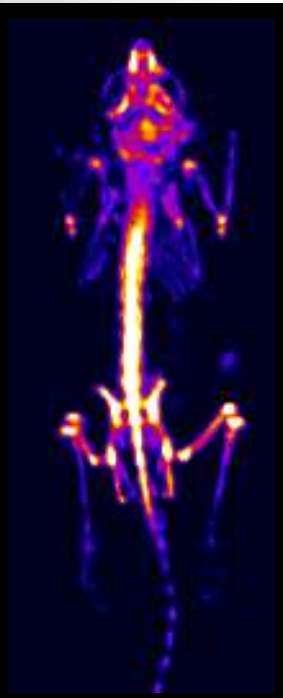


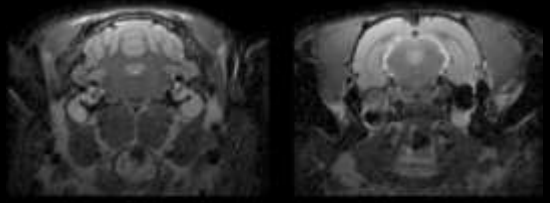
# Pre-clinical imaging modalities

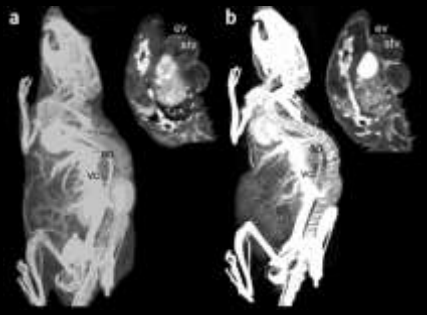
**μCT** **μSPECT** **μPET** **μMR – 7T**

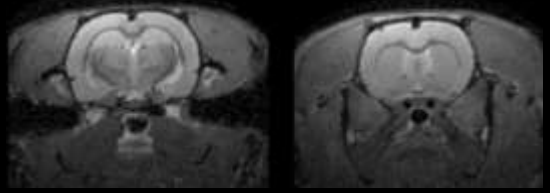






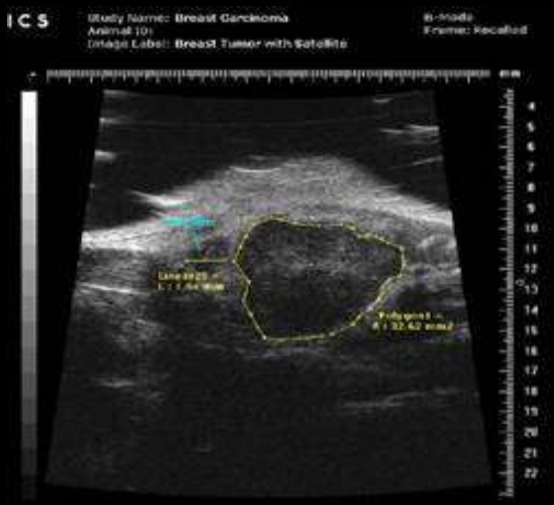


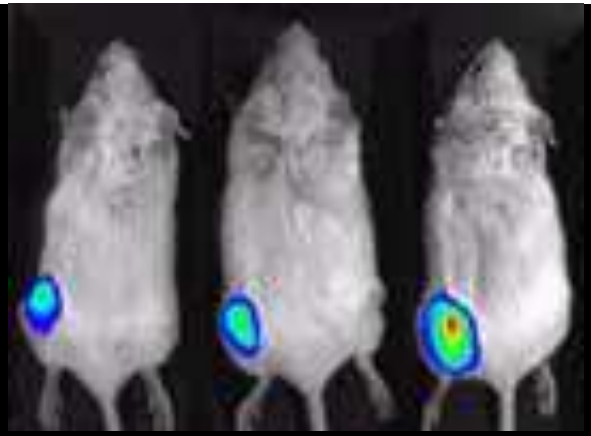
Gruene et al., Gamma Medica, Nature Medicine

# Pre-clinical imaging modalities

**μUS**



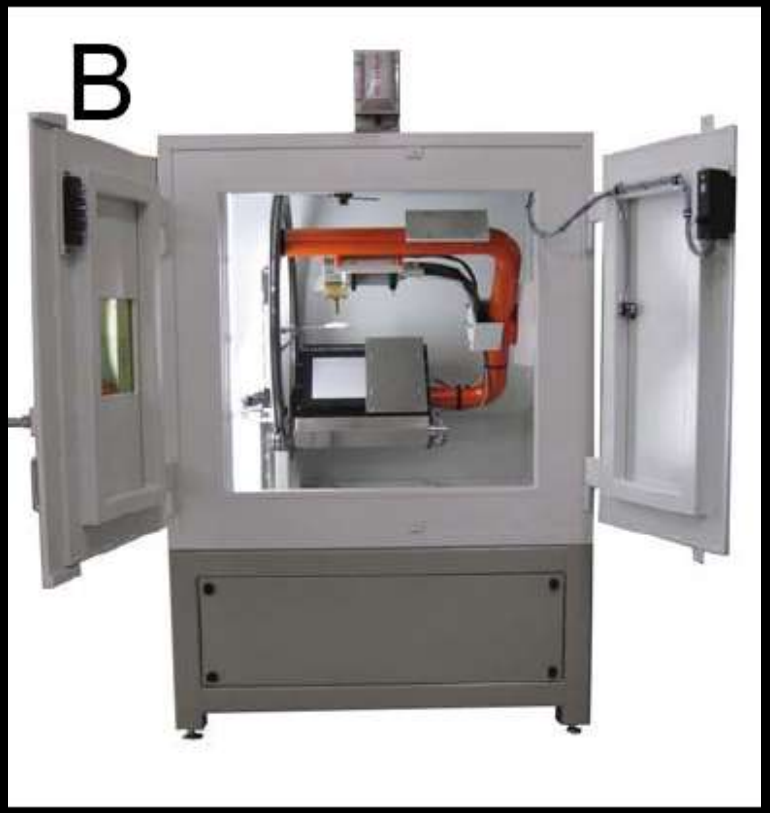

**μOptical**

Images courtesy of Visualsonics, Xenogen

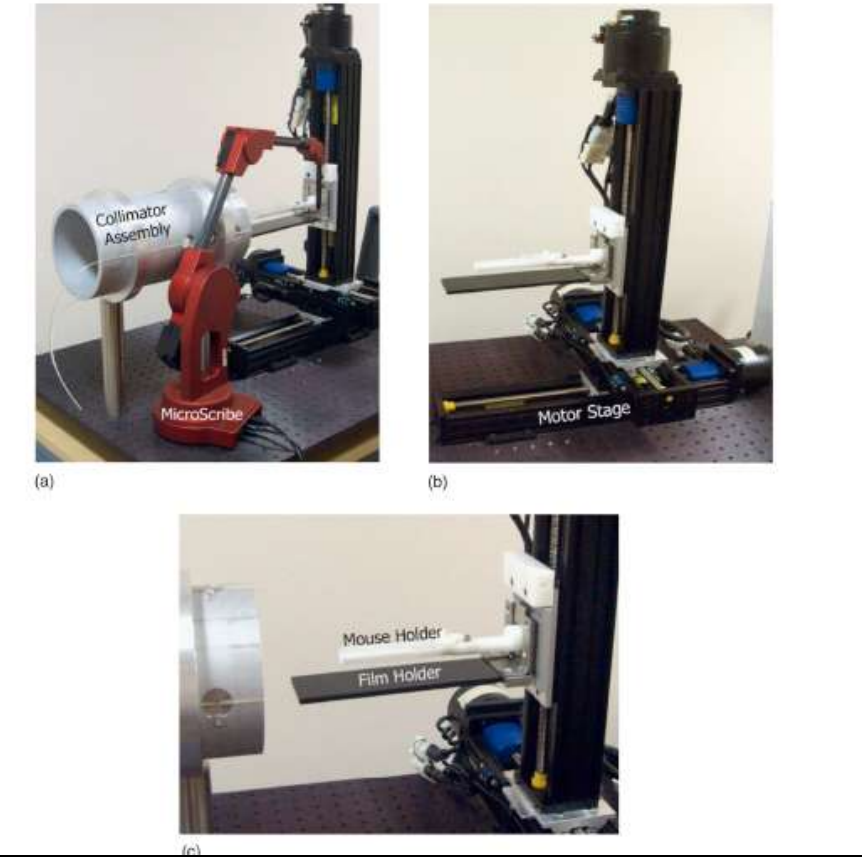
# SARRP (XStrahl/Johns Hopkins)


# XRad225Cx (Precision X-Ray/Princess Margaret Hospital)



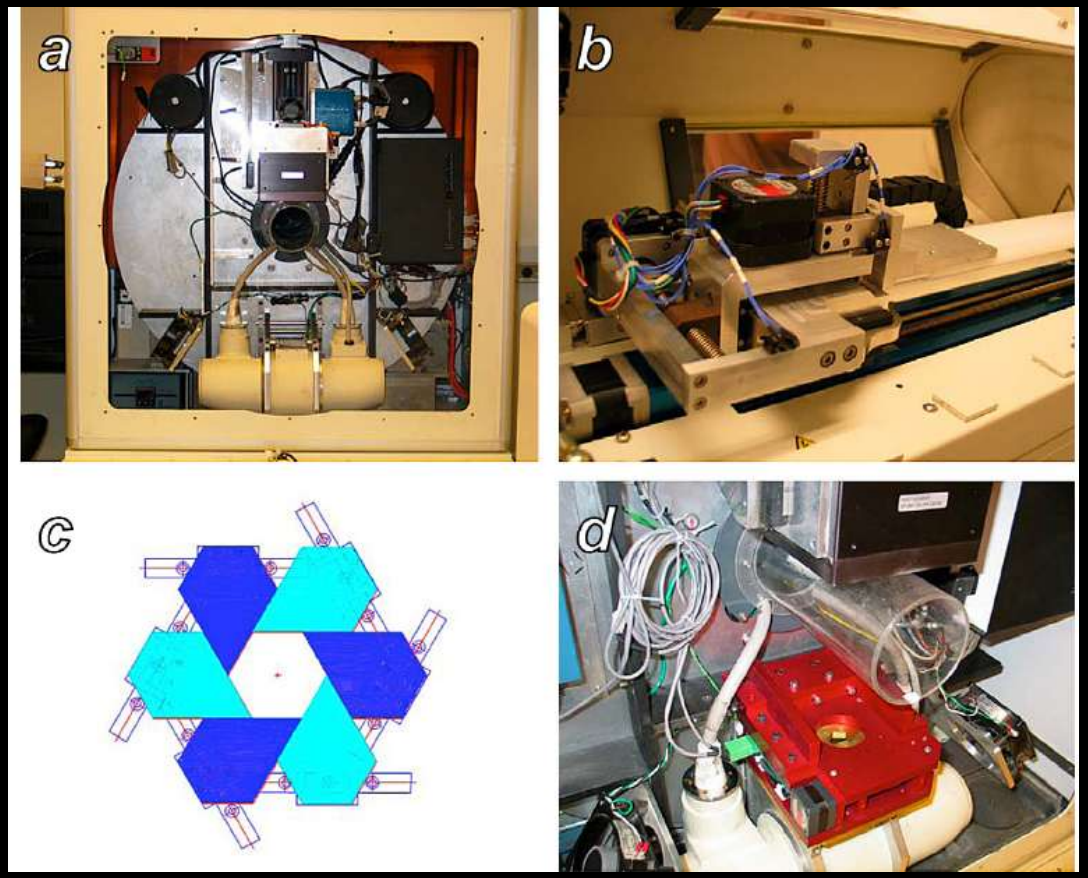

Verhaegen, Granton and Tryggestad, Phys. Med. Biol. 56 (2011) R55-R83, *Small animal radiotherapy research platforms*

# Washington University - microRT




Stojadinovich et al, Med Phys 34 (12), 2007, *MicroRT—Small animal conformal irradiator*

# Stanford – GE RS120 microCT




Zhou et al, IJROBP 2010, *DEVELOPMENT OF A MICRO-COMPUTED TOMOGRAPHY–BASED IMAGE-GUIDEDCONFORMAL RADIOTHERAPY SYSTEM FOR SMALL ANIMALS*

# Systems for Conformal Image Guided Small Animal Irradiation

Technical Requirements

- Depth of irradiation ≤ 5 cm
- Small field sizes (0.5 mm – 5 cm)
- High dose gradients (penumbra < 1mm)
- High dose rate (>1 Gy/min, < 15 min treatment)
- High precision and accuracy of field placement

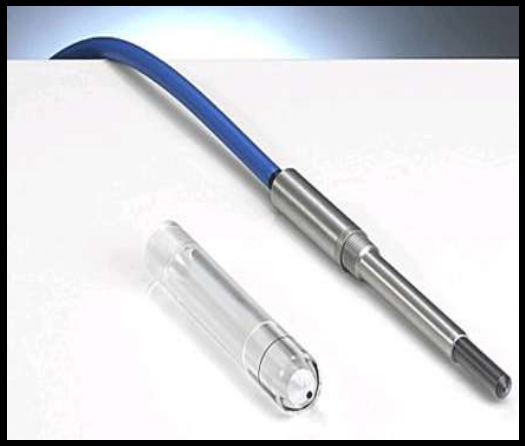
System Commissioning

- Dosimetric
- Mechanical
- Image-guidance

Kilovoltage Radiation Sources (100-320 kVp)

# Absolute Dosimetry

- Absolute dosimetry following AAPM TG-61 protocol
- 0.6 cc farmer chamber, calibrated at NRCC
- Chamber placed in air at isocenter
- Measuring exposure (air kerma) in air
- Output depends on kVp (HVL) and mA
- Calculate dose at surface of water under full scatter conditions



| 10 x 10 cm field, at isocenter (30 cm from the source) | |
|---|---|
| 225 kVp, 13 mA | **4.2 Gy/min** |
| 100kVp, 29 mA | **4.0 Gy/min** |

# Dosimetric verification - RDS TLDs

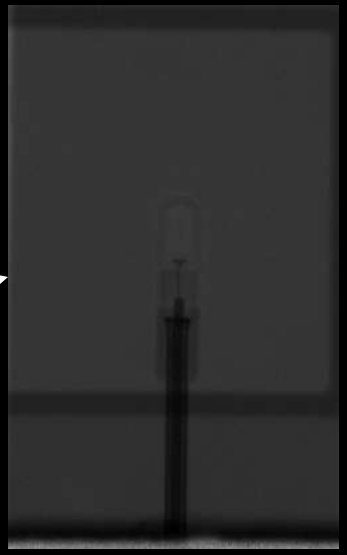
Irradiated April 6 and 7th, 2011

Results Read April 20th, 2011

| System | Energy<br>HVL | MDACC/Institution |
|---|---|---|
| PMH | 100 kVp<br>3.1 mm Al | 1.02 |
| PMH | 225 kVp<br>0.9 mm Cu | 0.98 |
| STTARR | 100 kVp<br>2.93 mm Al | 1.01 |
| STTARR | 225 kVp<br>1.02 mm Cu | 1.01 |

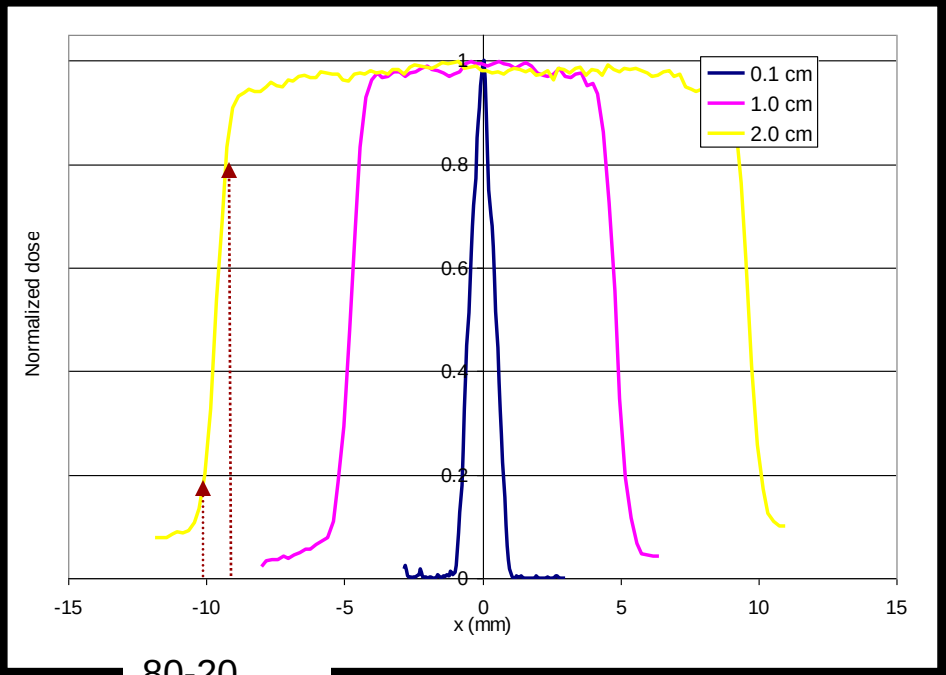
# Relative Dosimetry

- Percent depth dose (PDD) and relative output factors (ROF)
  - Small volume (0.07 cc) ion chamber in water, and water-equivalent plastic (solid water)
  - Radiochromic film (EBT/EBT-2) in solid water



# Film Dosimetry

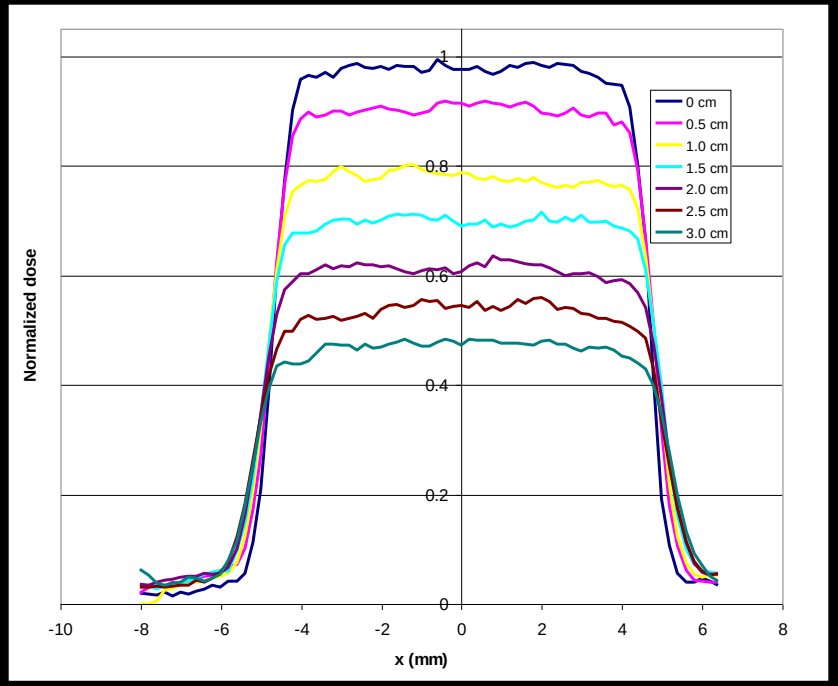
Profiles for 3 collimator sizes




80-20 penumbra

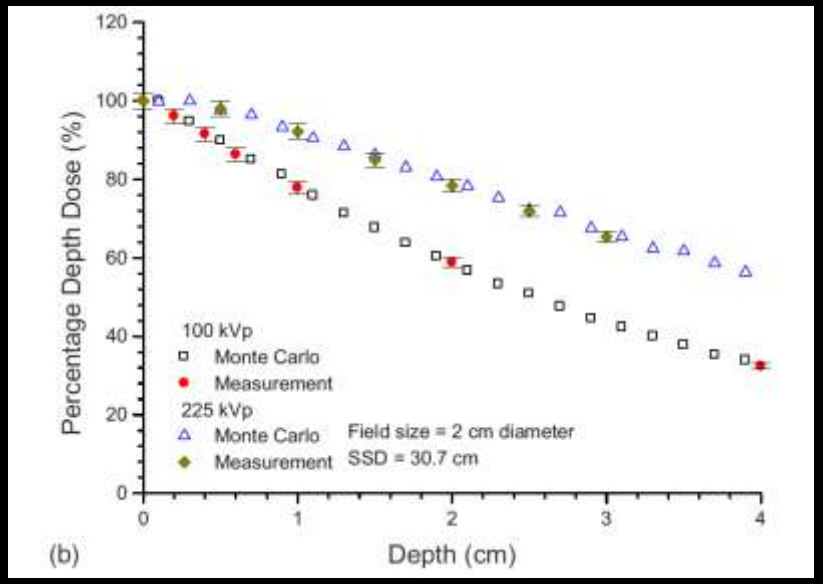
<1 mm

Profiles vs depth for 1.0 cm collimator



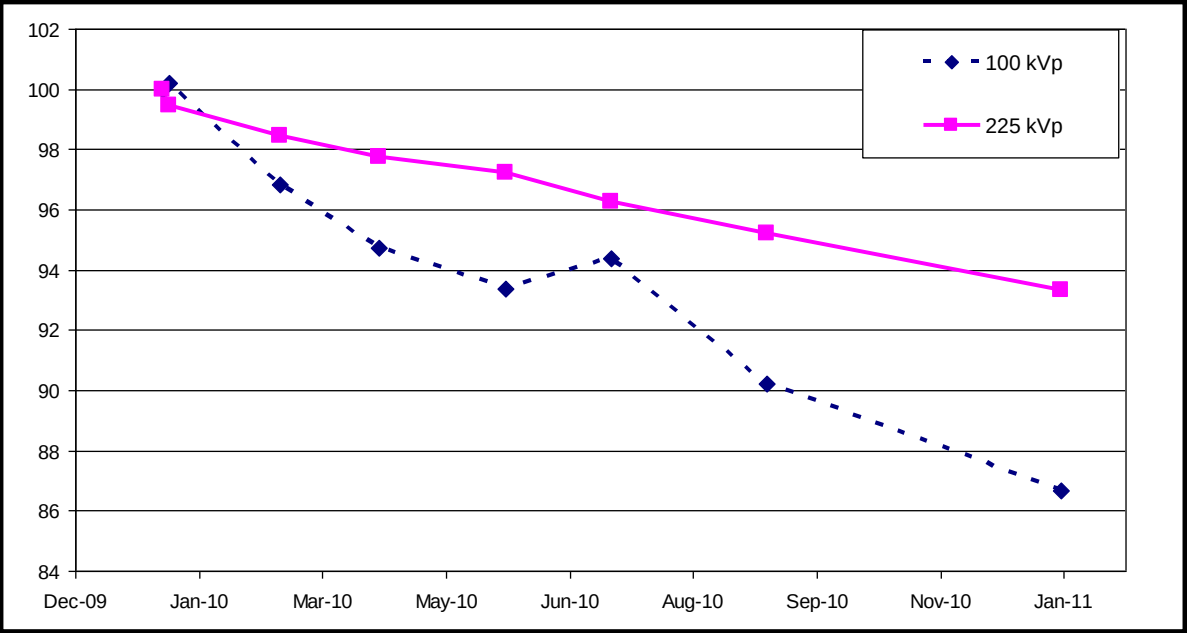
# Relative Dosimetry – percentage depth dose (PDD)

- Plane parallel chamber in small water tank
- Comparison with Monte-Carlo calculations using EGSnrc




*Chow et al, Med phys 37(10), 2010*

# System Output/Stability over time




- Tube output decreases over time

# System Use: Irradiations

| | |
|---|---|
| May - August 2008 | 301 |
| August - Dec 2008 | 276 |
| Jan - April 2009 | 93 |
| May - August 2009 | 314 |
| August - Dec 2009 | 485 |
| Jan - April 2010 | 665 |
| May - August 2010 | 535 |
| August - Dec 2010 | 403 |
| Jan – April 2011 | 395 |

Normal Tissue

- Lung
- Brain
- Liver
- Bone

Tumour Models

- Sub-cutaneous
- Brain
- Craniospinal
- Pelvis (prostate, cervix)
- Bone metastasis

Almost 3500 fractions of irradiation

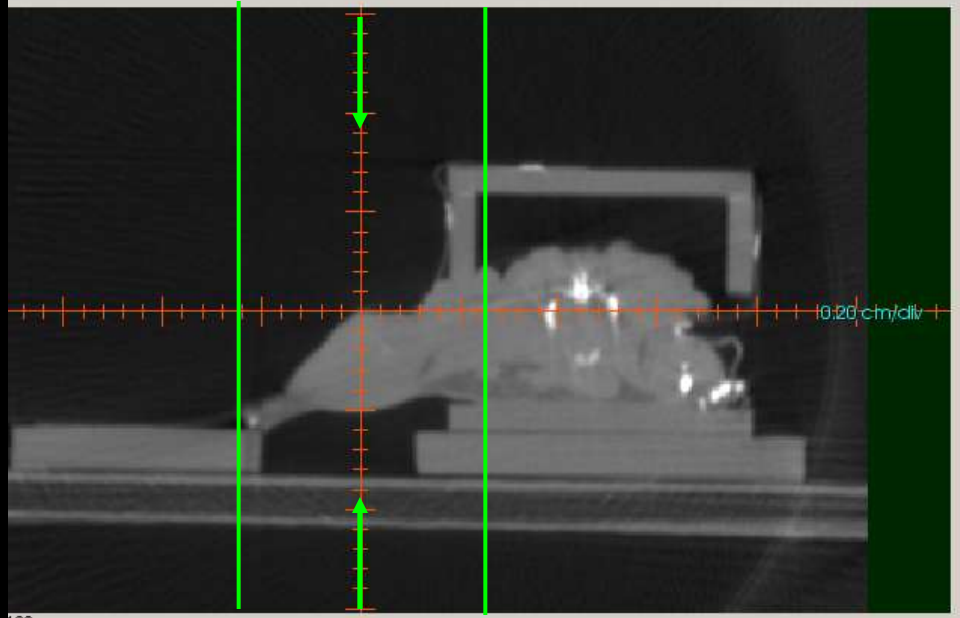
~ 100 irradiation/month (on average)

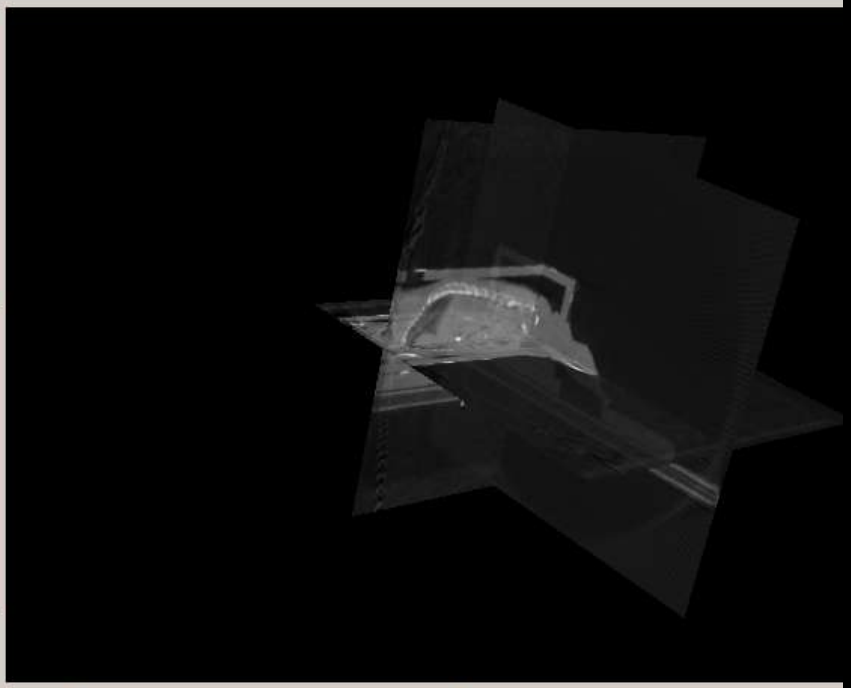
# Examples of Small Animal Irradiation

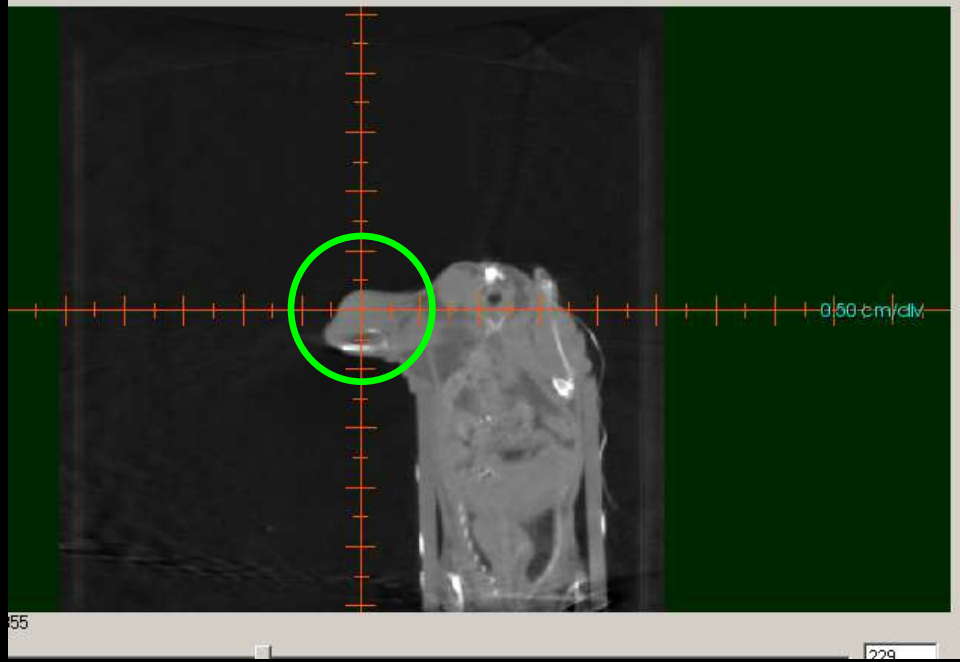
# Example 1 – Sub-cutaneous tumour

- Hind leg
- No-image guidance
- Standard field size for all animals (2-2.5 cm diameter)
- Parallel-opposed pair geometry
  - Prescribed to 5 mm depth
- Dosimetric sources of error
  - Tumor size
  - Scatter conditions

# Example 1 – Sub-q tumour

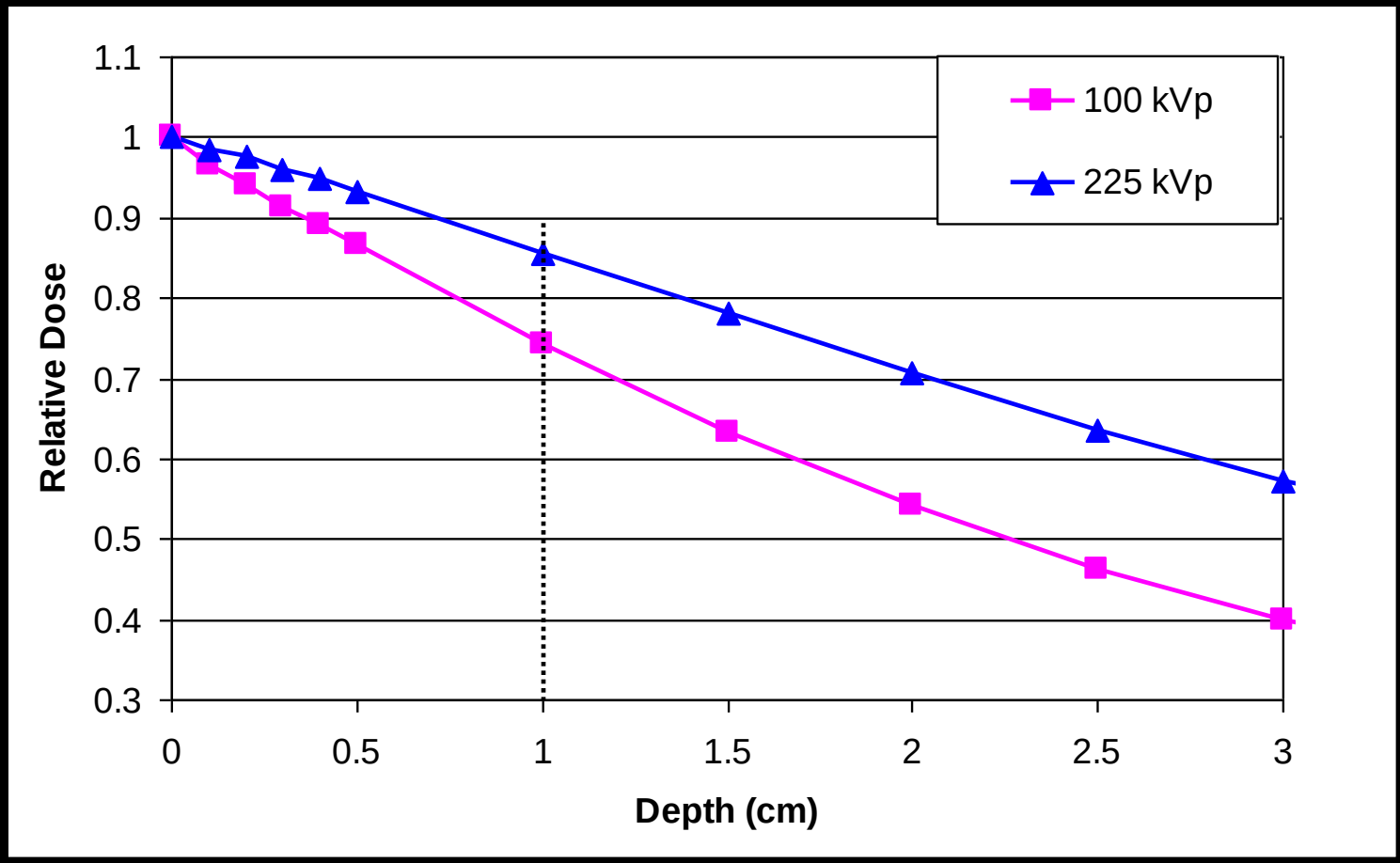


0.20 cm/div
160
241




0.50 cm/div
55
229


z
L
y
(507, 15) (5.03cm, -4.80cm) 0.013

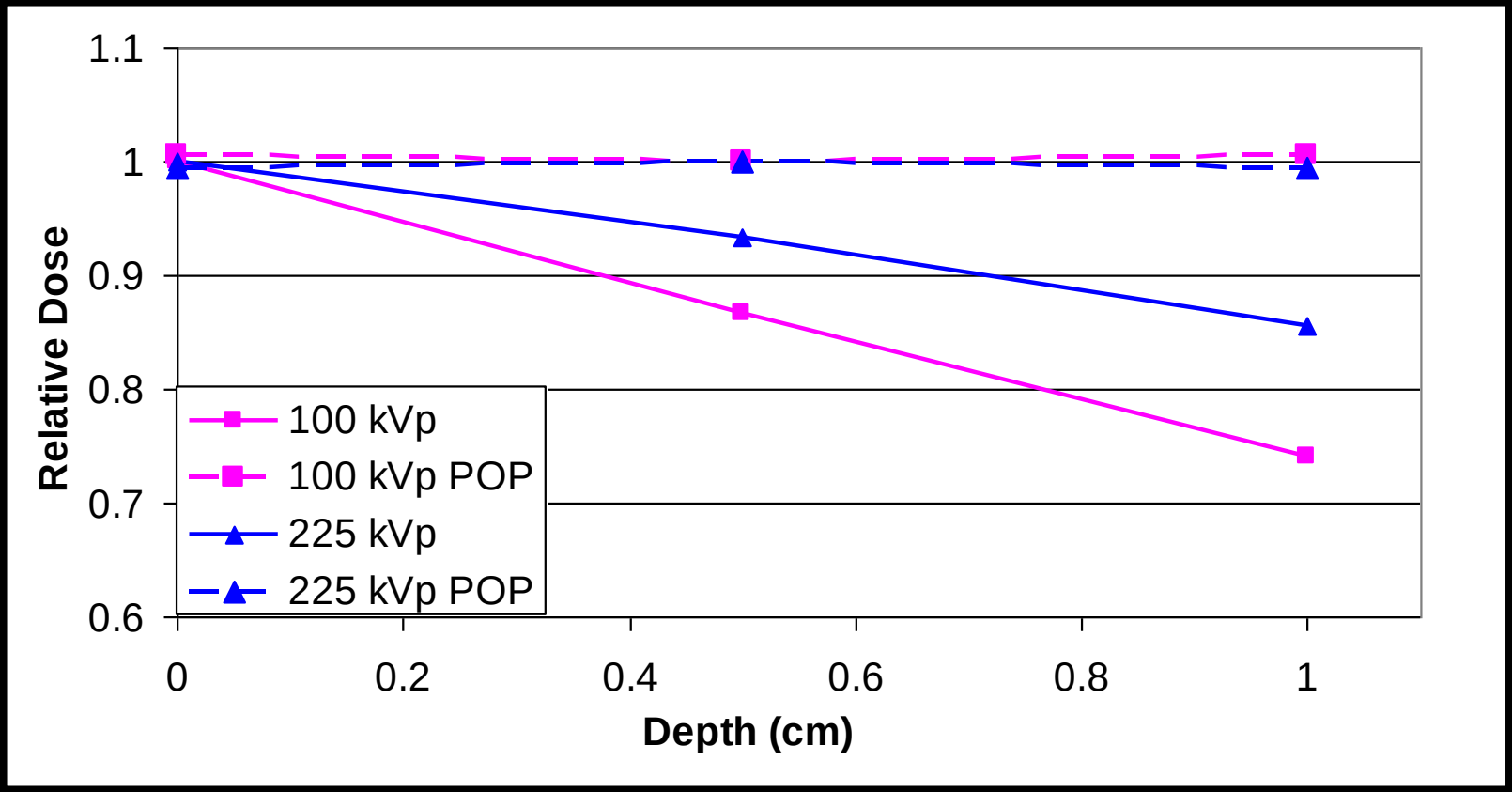
# Depth Dose – 2.5 cm field



# Single Field – inverse square

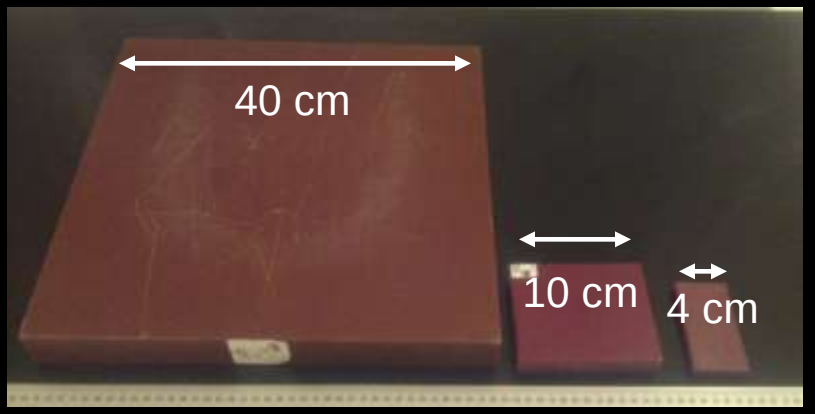
- Nominal 30 cm SSD
- Variation of 0.5 cm (30.5 cm SSD)
  - Dose decreases by 3.3%
- Variation of 1.0 cm (31 cm SSD)
  - Dose decreases by 6.8%

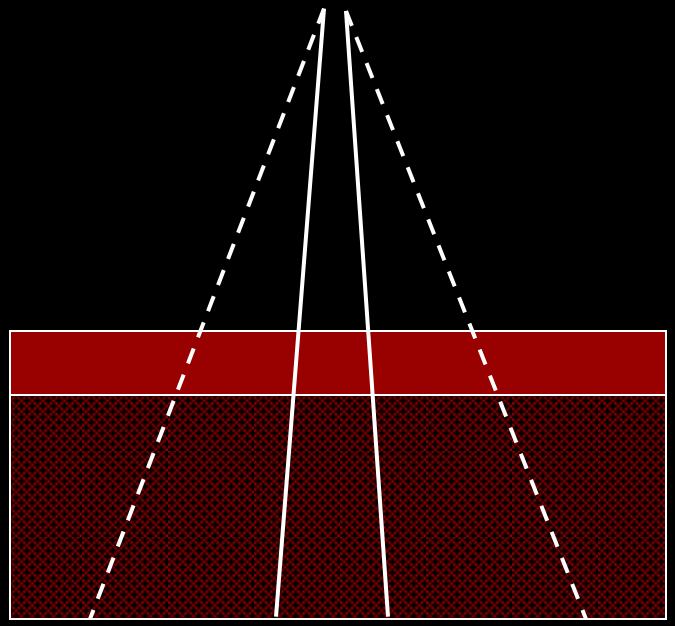
# Parallel Opposed Pair (POP) vs Single beam

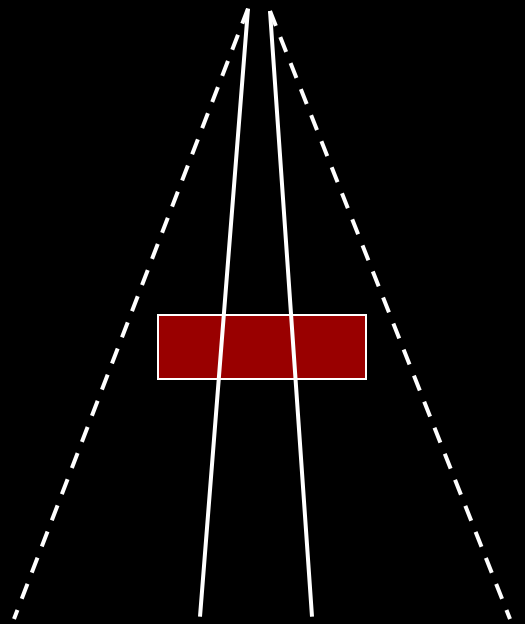


# Field Size and Scatter Conditions

# Scatter Conditions





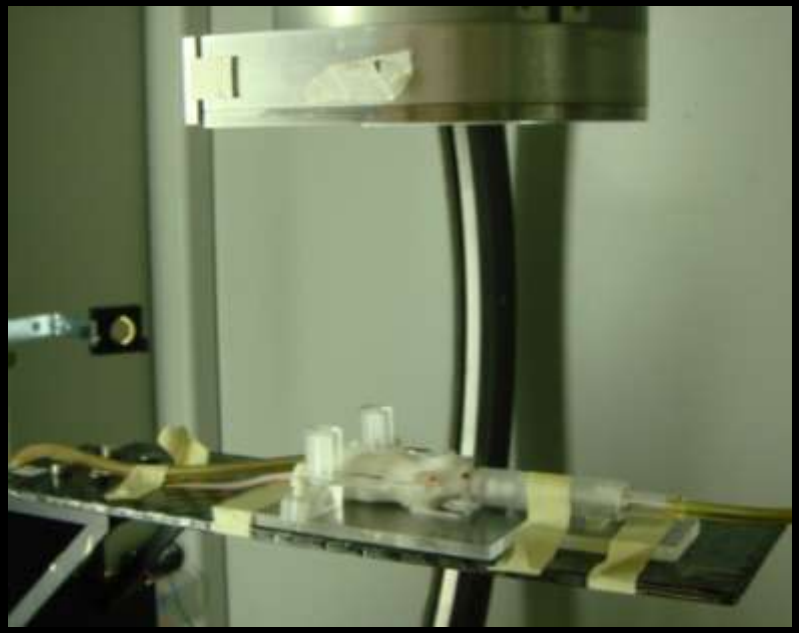
# Backscatter vs Field Size

From AAPM TG-61

| Field Size | 1 cm | 2 cm | 3 cm | 5 cm |
|---|---|---|---|---|
| 3 mm Al HVL | 1.063 | 1.120 | 1.164 | 1.221 |
| 1 mm Cu HVL | 1.044 | 1.096 | 1.139 | 1.211 |

# Example 2 – Focal Brain Irradiation

- 5 mm circular collimator
- Parallel-opposed pair geometry
  - Prescribed at 5mm depth
- Image-guided set-up
  - With multi-modality image fusion
- Sources of error
  - Tissue heterogeneity
  - Surface curvature

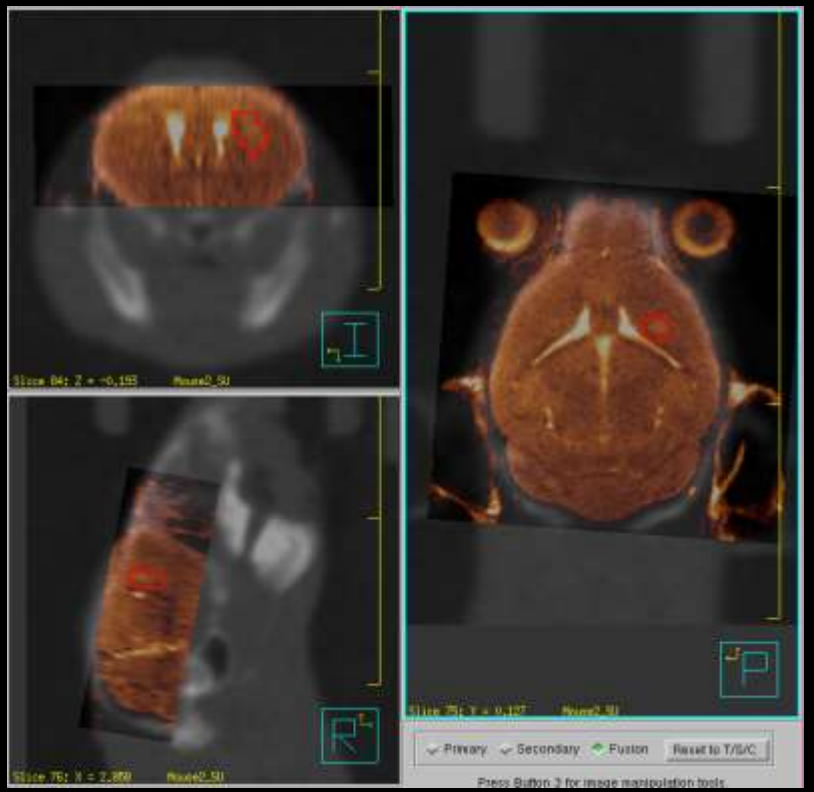


*Caroline Chung, MD*

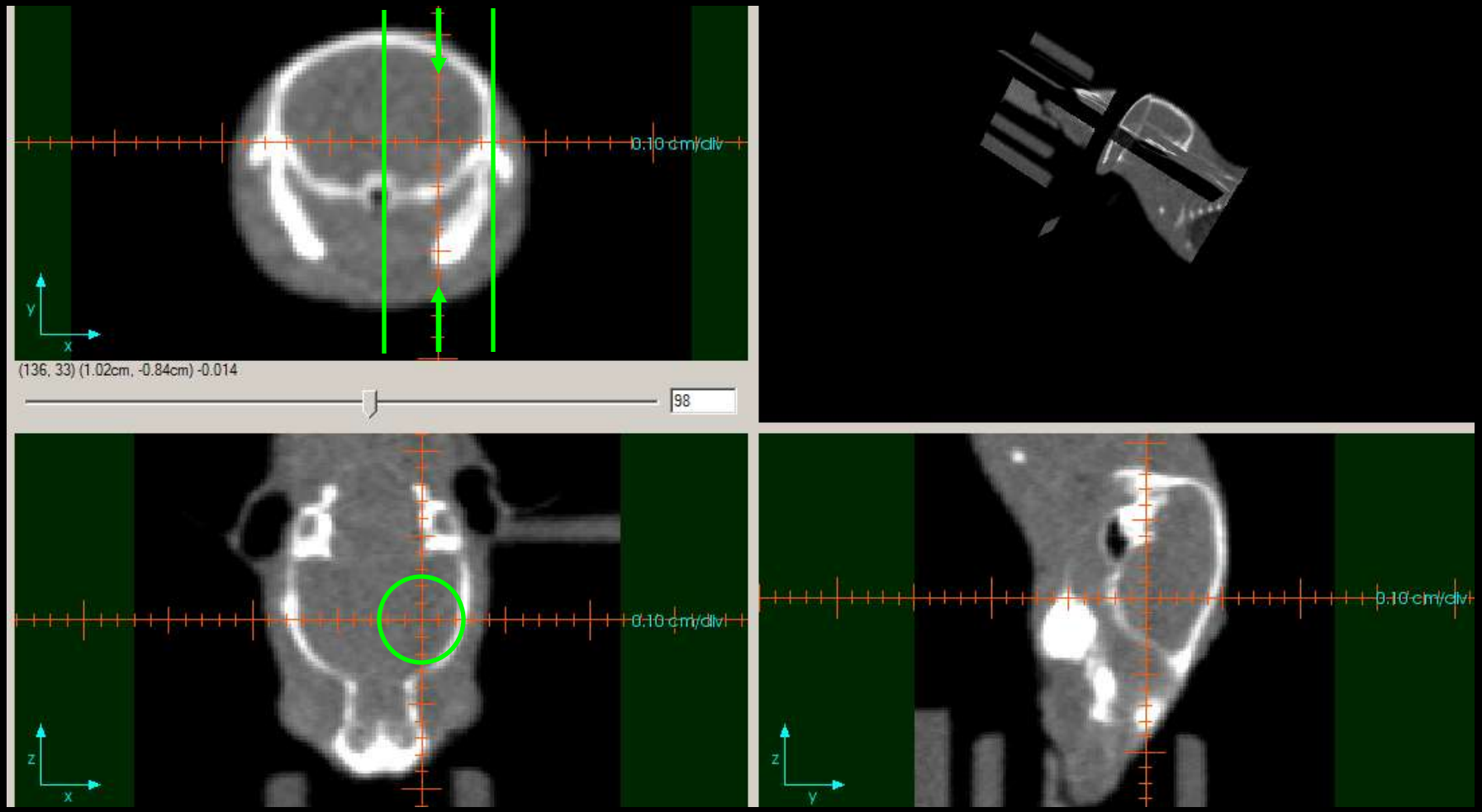
T1-Gad

T2


Primary
Secondary
Fusion
Reset to T/S/C
Press Button 3 for image manipulation tools.


Primary
Secondary
Fusion
Reset to T/S/C

# Example 2 – Focal Brain Irradiation

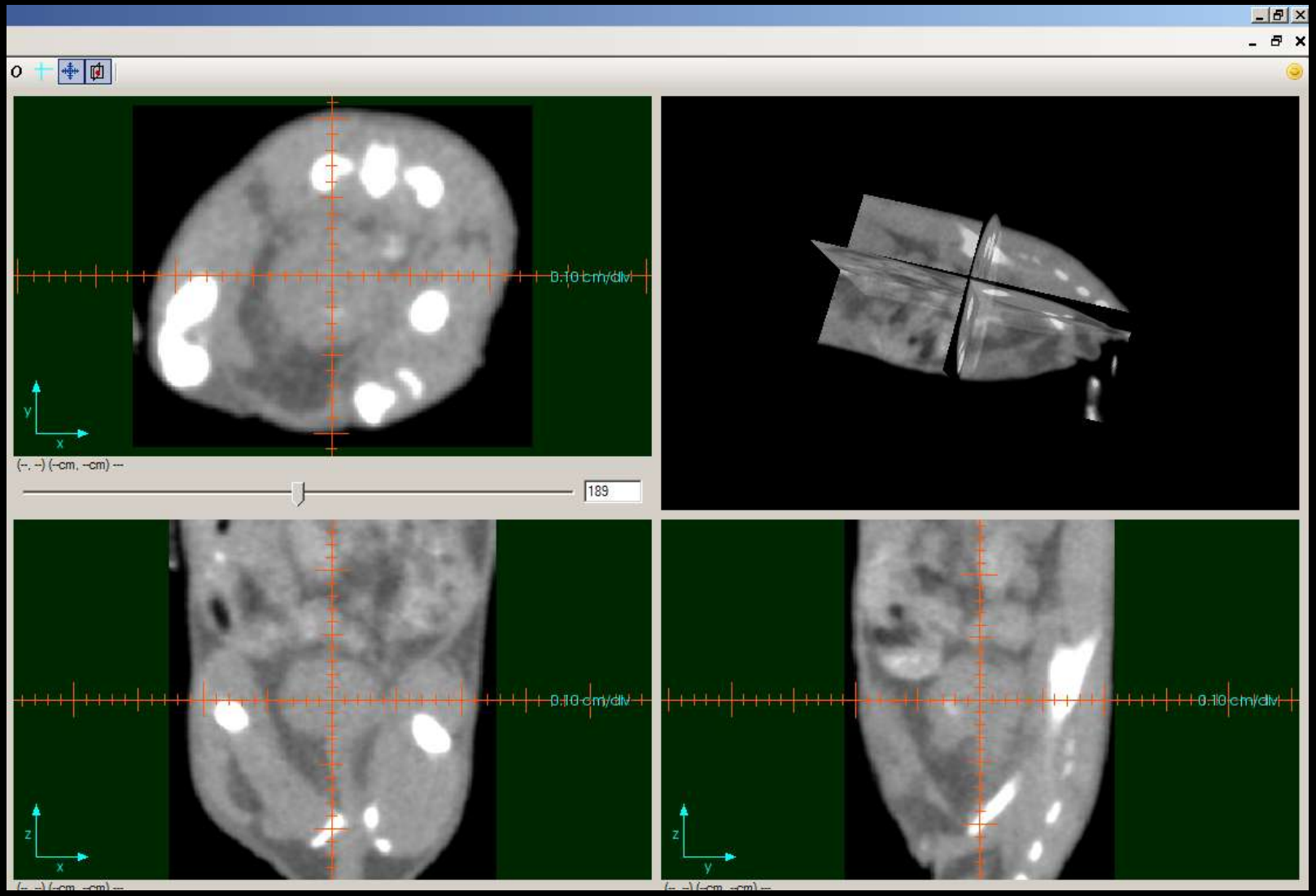


# Single Beam Dose Display

# Example 3 – Orthotopic soft-tissue irradiation

- 0.5 – 1.5 cm circular collimator
- Multi-beam geometry
  - Prescribed to the center of the tumor
- Image-guided set-up
  - With multi-modality image fusion
- Fractionated delivery
- Sources of error
  - Target localization and contouring
  - Set-up reproducibility

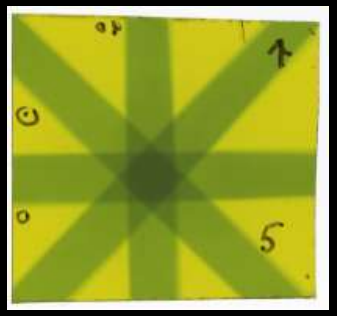
# Example 3 – Orthotopic soft-tissue irradiation

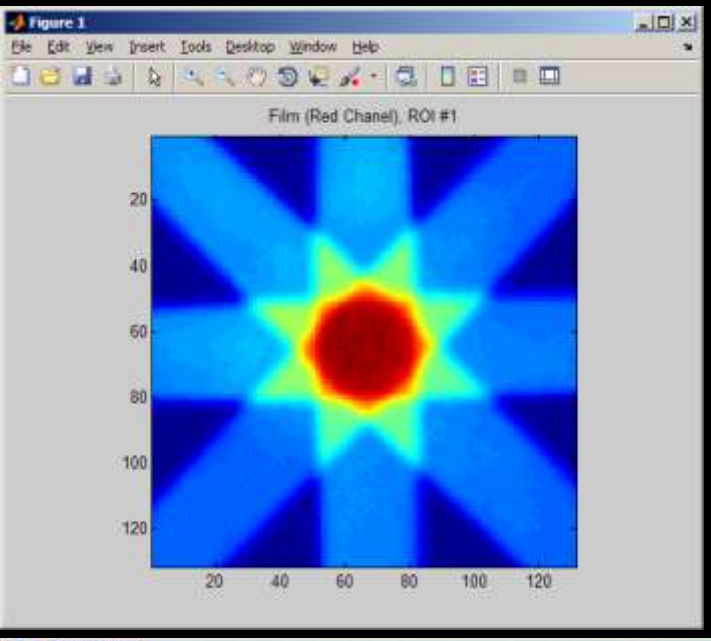


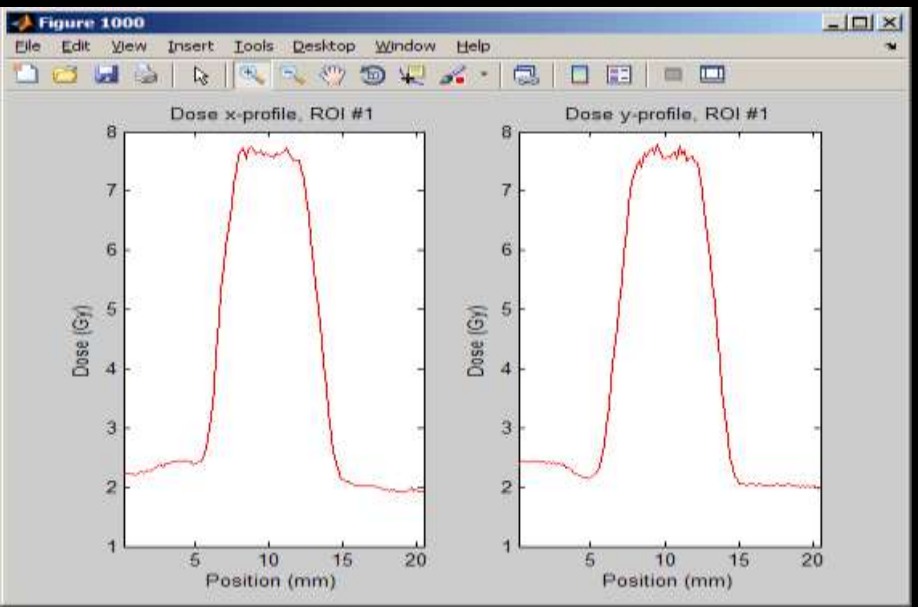

*Richard Hill, Naz Chaudary, Salomeh Jelveh*

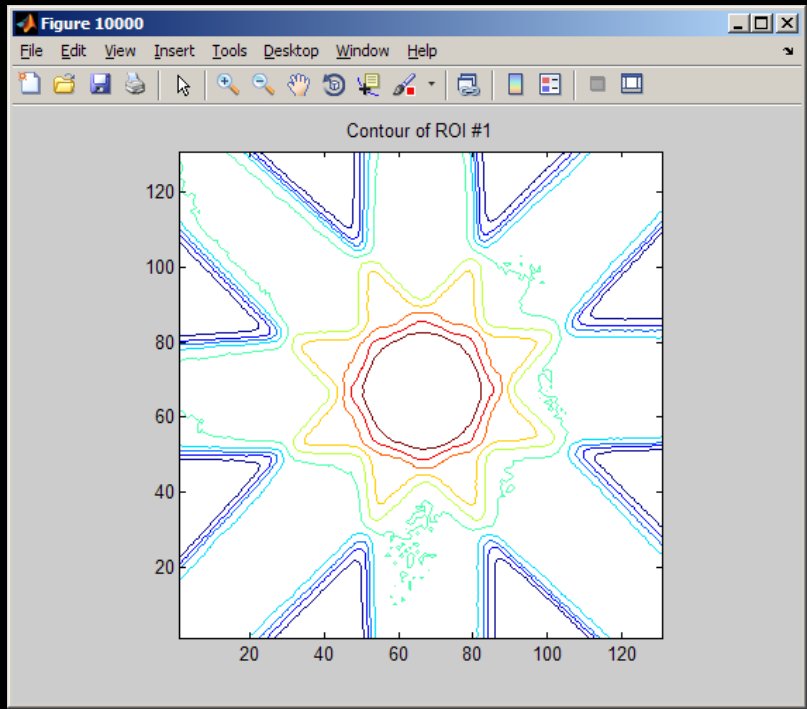
# Star Axial distribution, corrections ON

5 mm collimator

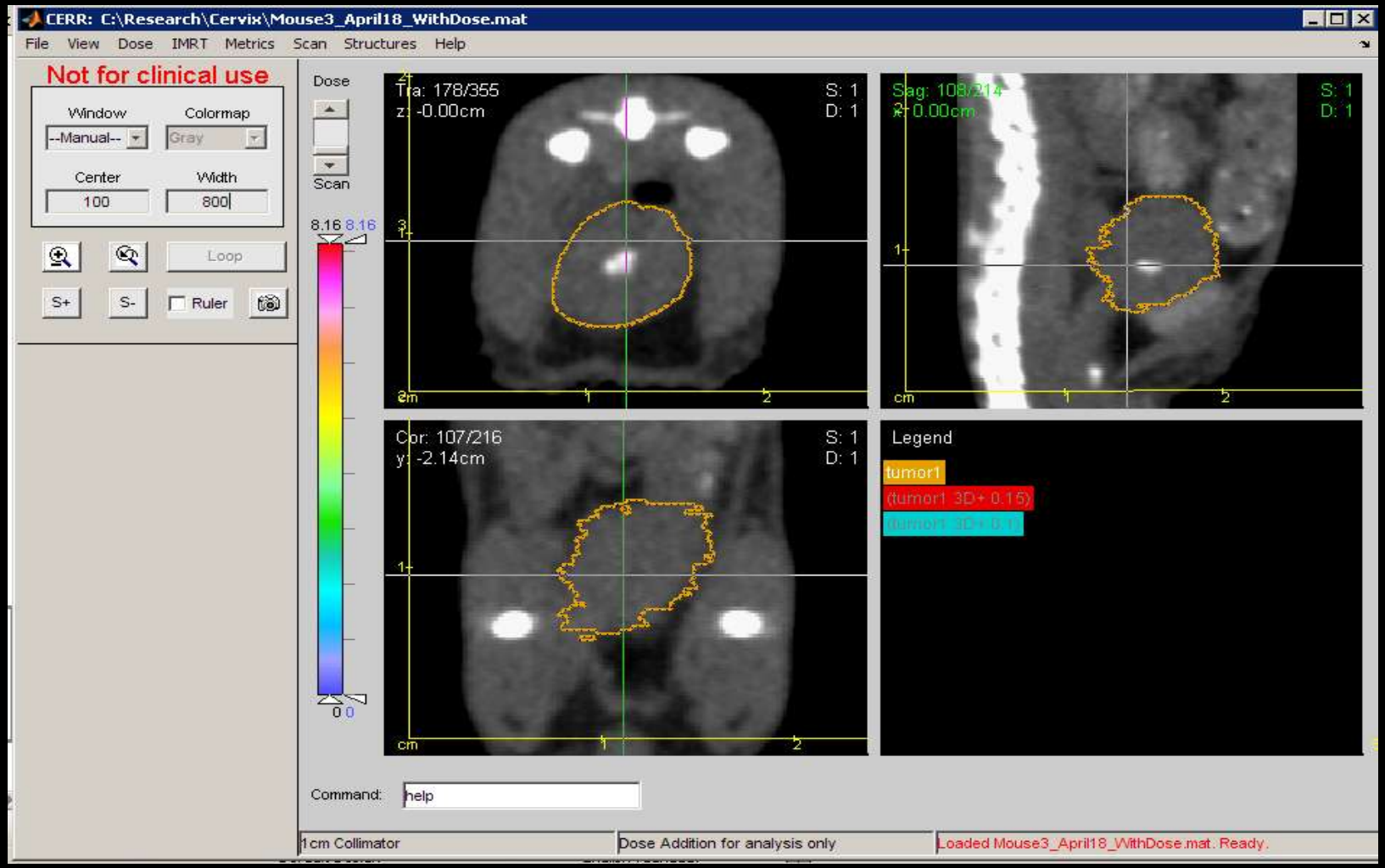




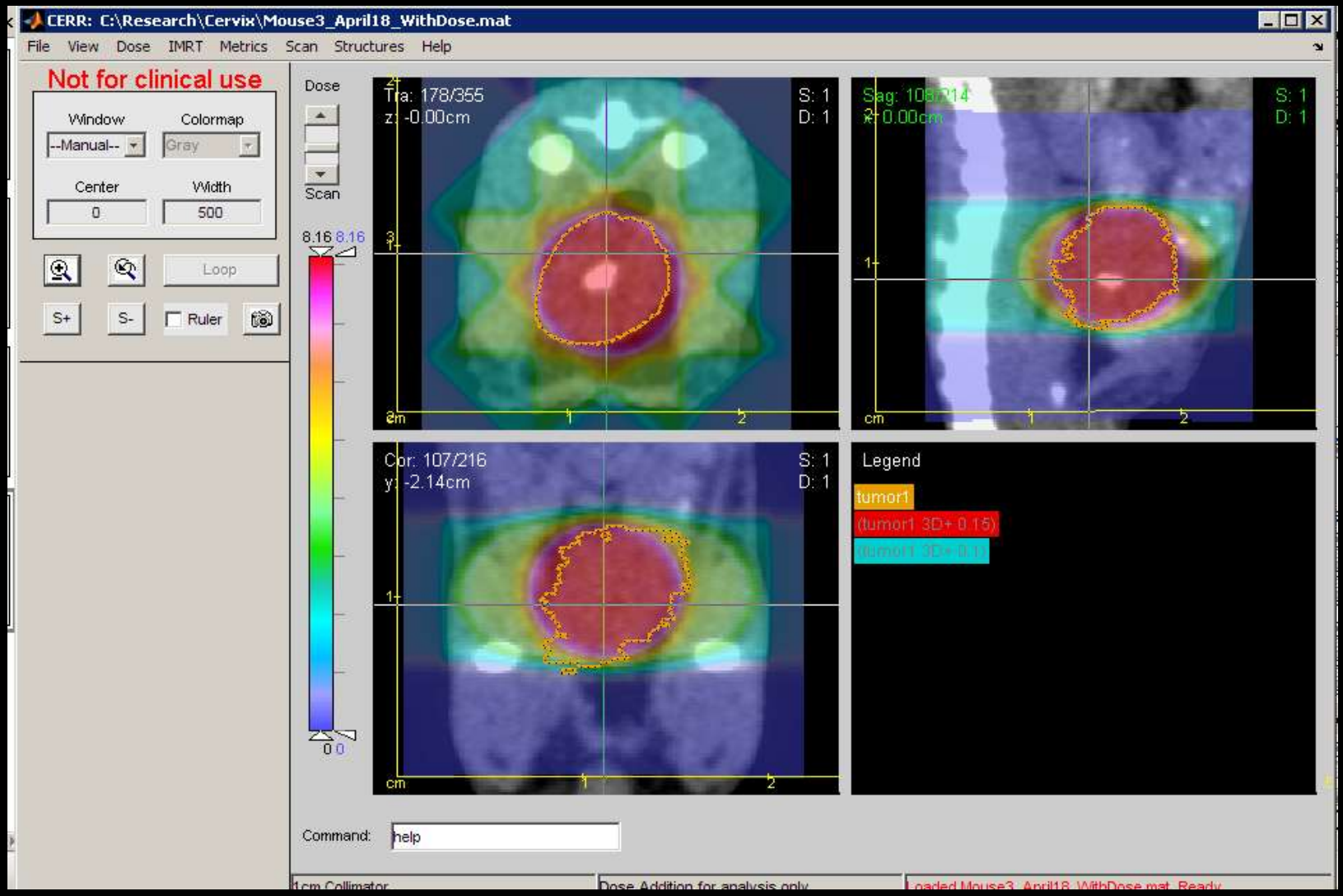



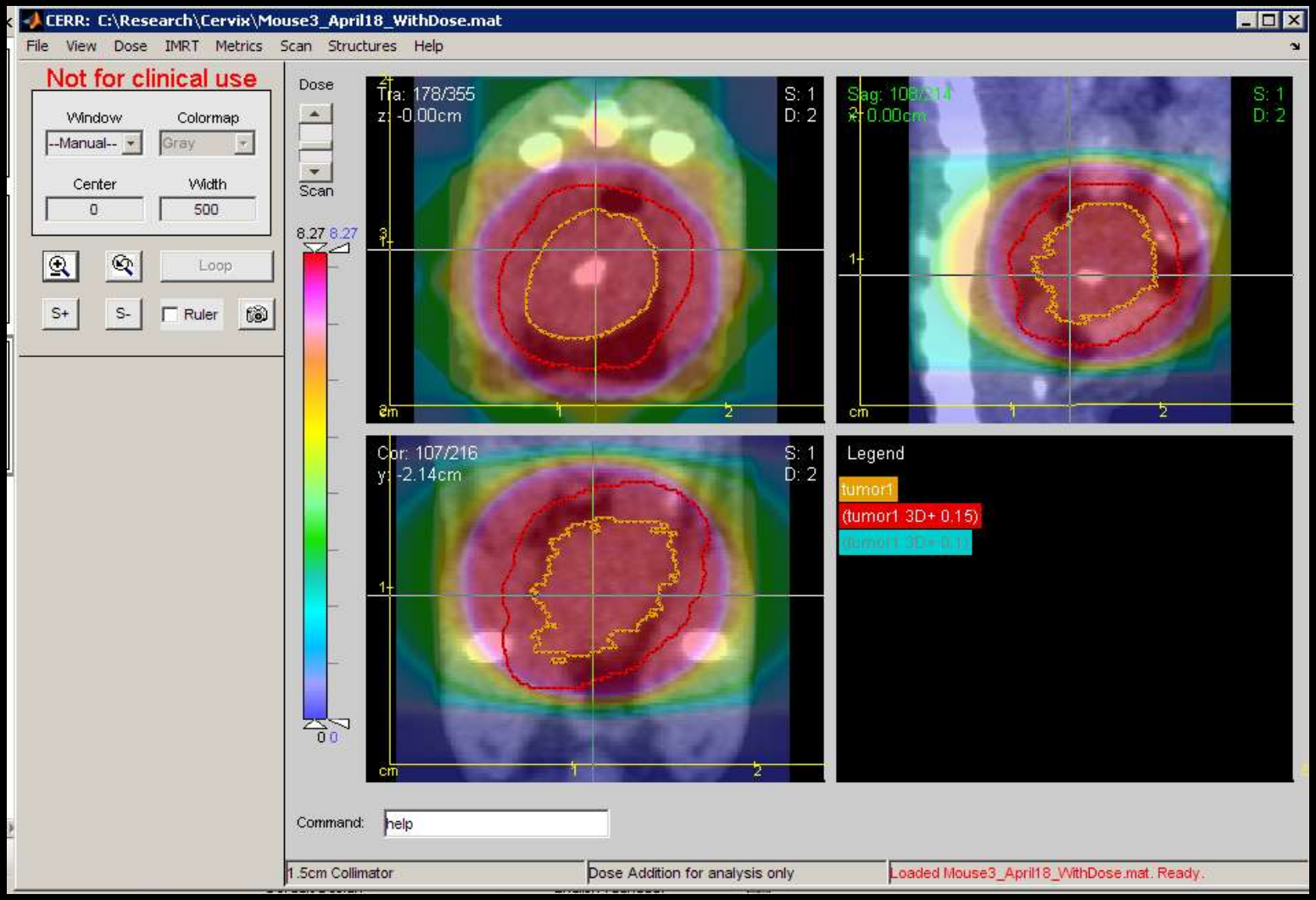
# Contouring of the tumor volume



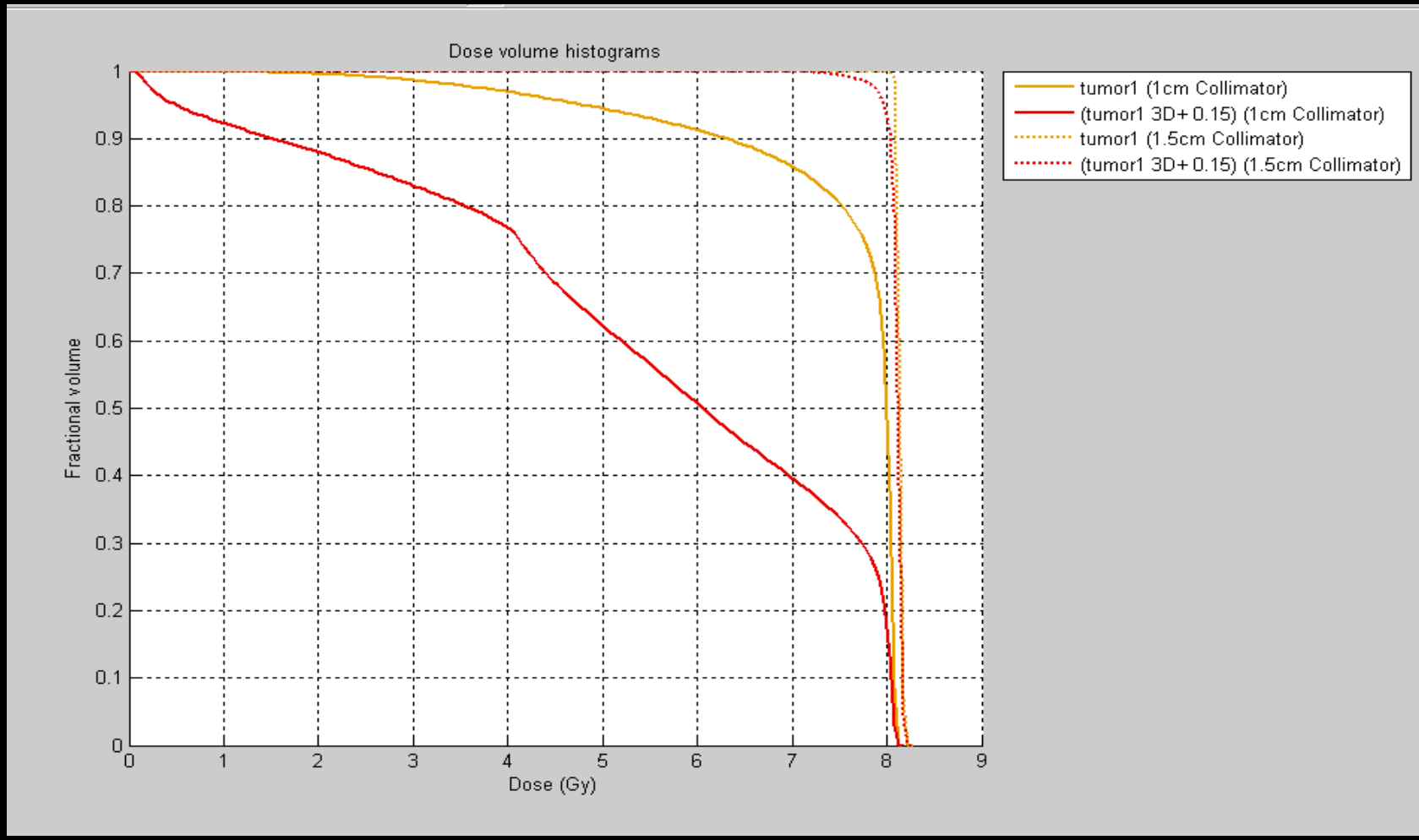
# 1 cm collimator



# 1.5 cm collimator



# 3D Dosimetric Evaluation



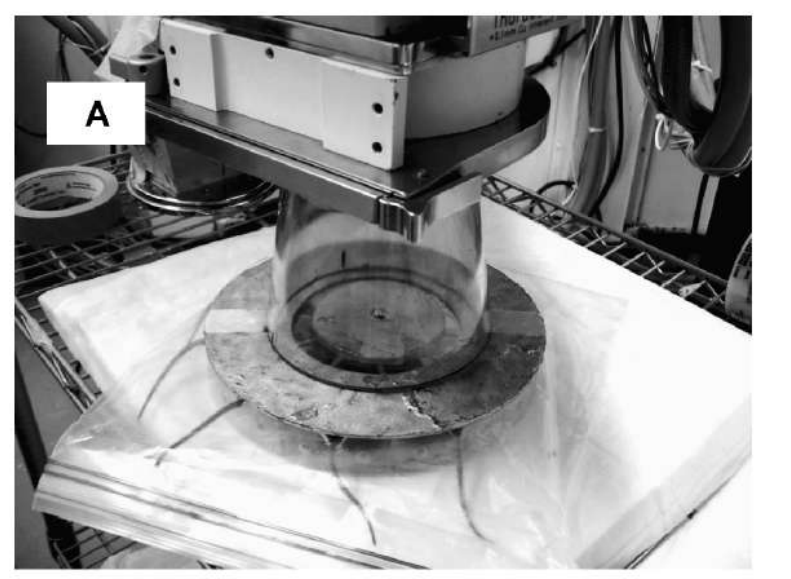
# Dosimetric Calculations and Validation

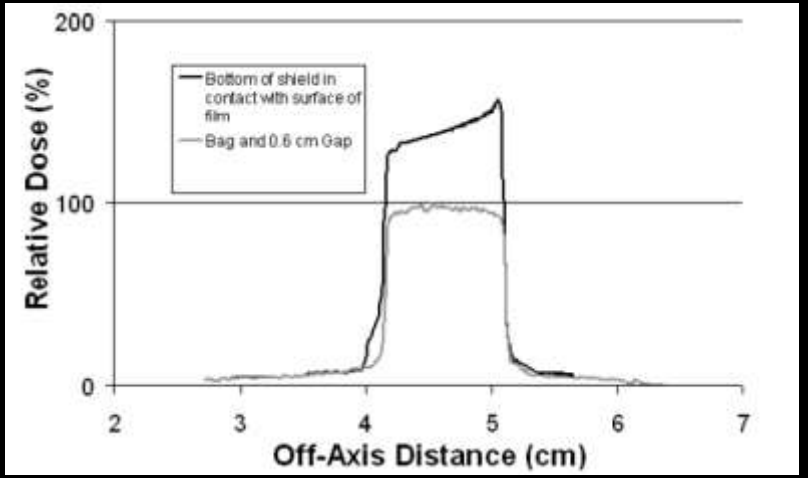
- Calculations
  - Treatment planning
  - Monte-Carlo Simulations
- Validation with Measurements
  - Custom Geometries
  - Biological end-points
    - γH2AX staining
  - In-vivo measurements
    - TLD, OSL,  Mosfets
  - Transit Dosimetry
    - Flat-panel detector/Film

# Dose Calculations and Treatment Planning

- Hand calculations of the dose at isocenter based on tabulated data (current method)
- Pencil beam/ray tracing based method
- Superposition-convolution
  - Valid for kilovoltage energies?
- Monte Carlo
  - Image data-sets may be as large as 1024x1024x1024 voxels
- Small field dosimetry and dose calculations

# Surface dose enhancement



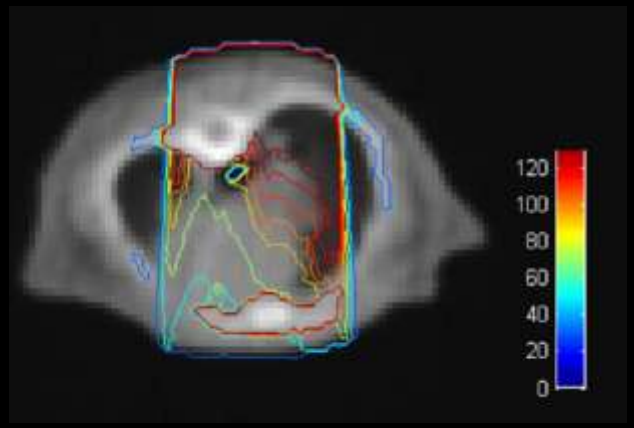

Arndt et al, Radiation Research 175: 784-789 (2011) *Dosimetric Calibration and Characterization for Experimental Mouse Thoracic Irradiation Using Orthovoltage X Rays*

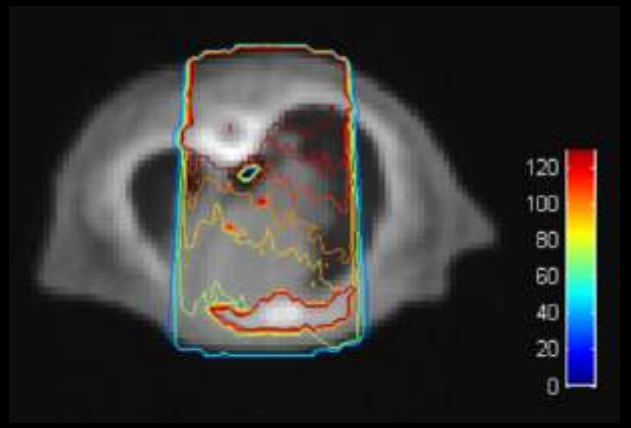
# Monte Carlo Results

100 kVp

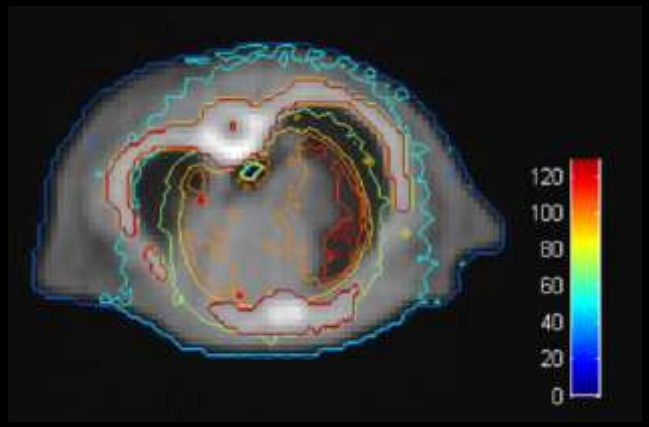
225 kVp

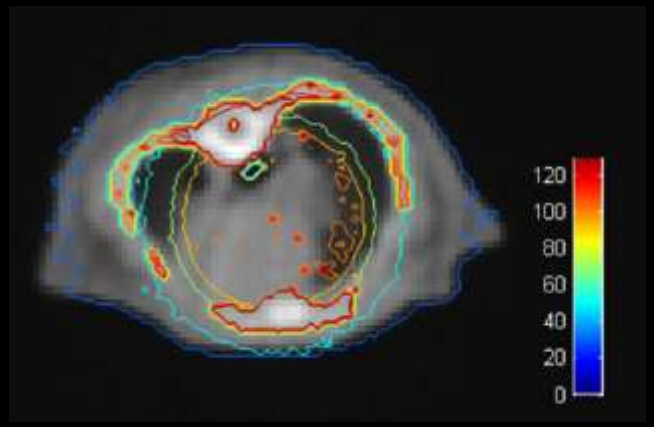
Single beam



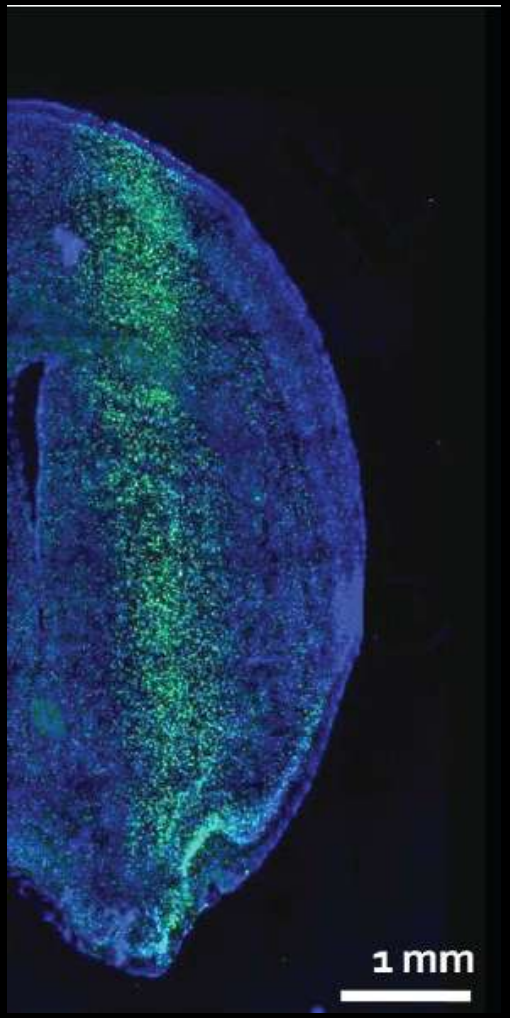

360 arc

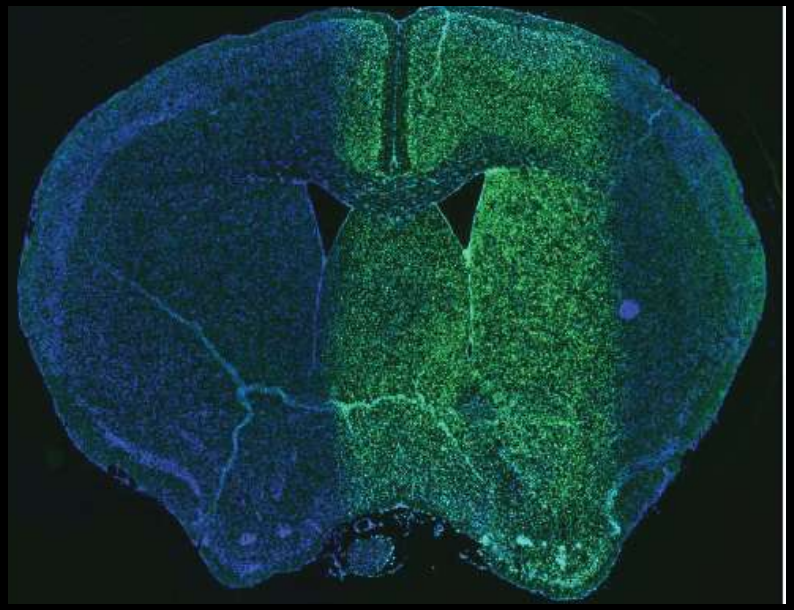



*Chow et al, Med phys 37(10), 2010*

# γ-H2AX

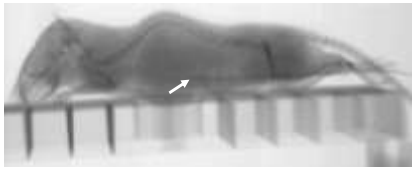


Ford et al, Rad Research 175: 774-783 (2011), *Localized CT-Guided Irradiation Inhibits Neurogenesis in Specific Regions of the Adult Mouse Brain*

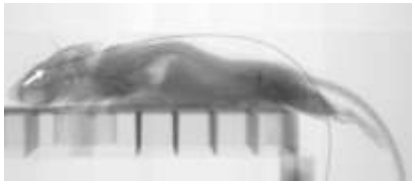
# “Mouse-fet” project at the Dana-Farber Cancer Institute

- MOSFETs surgically implanted in organs of interest in newly expired mice
- Irradiated with 220 kVp, 13 mA, 0.15 Cu, 5x5 mm, from above (PA) only
- Compared calculated dose with measured dose
- Results indicate effect of homogenous assumption in 2D planning
- overall, no more that 6% difference for any site



Pancreas

Left Kidney



Brain

Liver

Prostate

Left Lung

Ngwa, Korideck, Chin, Makrigiorgos, and Berbeco, “MOSFET assessment of radiation dose delivered to mice using the Small Animal Radiation Research Platform (SARRP)”. Radiation Research. *In Press*

# Dosimetric and Image-Guidance Intercomparison

AAPM Working Group on Conformal Small Animal Irradiation

- Members from ~15 different institutions
- Intercomparison of dosimetry and image-guidance capabilities across member institutions
- Will look at small (1-5mm) and moderate (1-2cm) fields
- Using EBT-2 Film and solid water phantoms

# Summary

- Systems for image-guided animal allow individualized treatments for specific animals/animal models
- Extensive characterization of the dosimetric (and mechanical and imaging) properties of the system are necessary
- Dosimetric sources of error include
  - Irradiation geometry
  - Scatter conditions
  - Tissue heterogeneities
  - Target identification
  - Set-up reproducibility