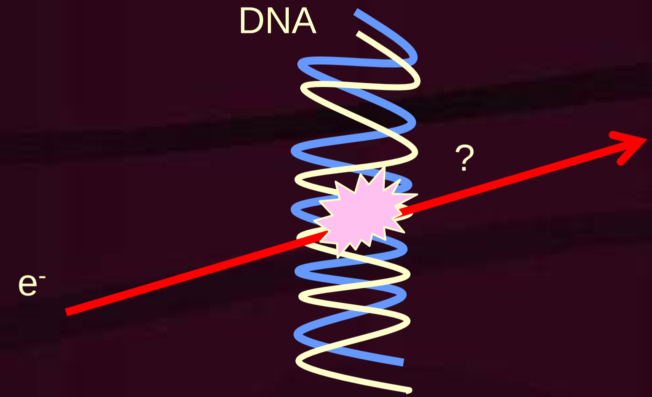

Current Status of Radiobiology Dosimetry

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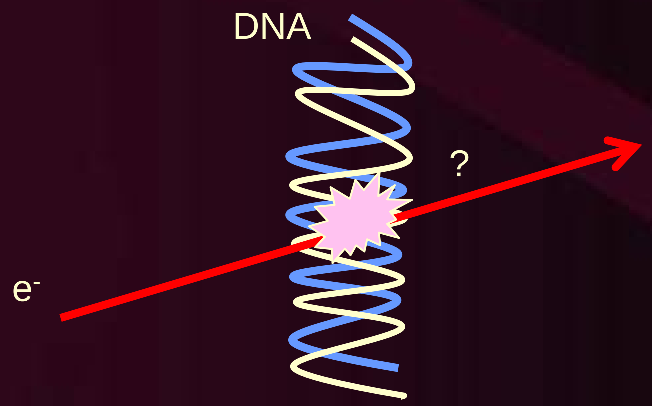
CIRMS
March 27, 2017

Objective of this Session

- Introduce the topic of radiobiology dosimetry
- Identify needs for standardization
- Provide results on some initial pursuits from the University of Wisconsin
- Kick start discussion for the next two speakers

Radiobiology Dosimetry Introduction

- Radiation Biology an active field of research for many years
- Primary goal is to study the effects of ionizing radiation on living things
- Has served as the fundamental basis for radiation therapy and radiation protection dosimetry
- Involves a wide variety of tools and techniques
  - Irradiators
  - subjects



Recent Advances

- Past few decades have seen rapid acceleration of the efficiency and accuracy of dose delivery technology in radiation oncology
  - Photons (RapidArc, VMAT, MRI-guided RT, tracking, gating, etc.)
  - Protons
  - Heavy Ions
  - Brachytherapy
- Concurrent rapid expansion in tools and knowledge on the biological target of irradiation, the cell's DNA.
  - Sequencing
  - Cell population counting
  - Small-animal imaging
  - Small-animal radiation delivery platforms
- Radionuclide-based irradiators falling out of favor due to regulatory restrictions

The Field

- Radiation Research Society (RRS) is the primary professional organization
  - Radiation Research Journal
  - Very little dosimetry research
- Radiobiology researchers are familiar with radiation dosimetry, but commonly do not involve medical physicists

The Field (cont.)

- American Association of Physicists in Medicine (AAPM)

From AAPM website, “What do Medical Physicists Do?”

“In cancer, they work primarily on issues involving radiation, such as the basic mechanisms of biological change after irradiation, the application of new high-energy machines to patient treatment, and the development of new techniques for precise measurement of radiation.”

So What's the Issue?

- Correlate doses of ionizing radiation with the effects on living things
- Irradiator geometries are vastly different from typical calibration conditions of NIST-traceable quantities
- Only the most advanced irradiators utilize computers to calculate the dose to complex geometries
- Very little in the area of dosimetry standardization
- Why?
  - Radiobiology researchers (and the rest of the community) are generally comfortable with larger uncertainties
  - Variety of irradiator configurations is vast
  - Medical physicists not involved
  - No dosimetry credentialing organization like the RTOG or IROC Houston
    - (MD Anderson RDS does provide orthovoltage independent output measurements)

The Early Irradiators

- Cs-137 cabinets

Duke University Cs-137 Mark I

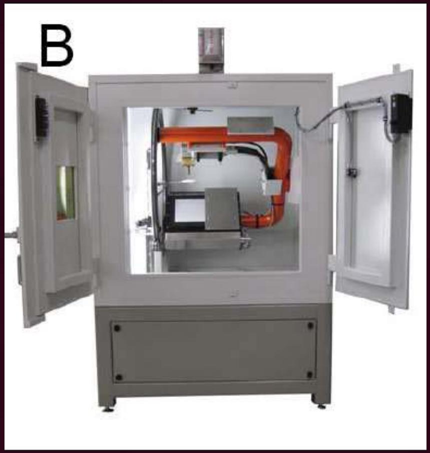
- Co-60 cell irradiators (MDS Nordion, Gammacell 220)

The More Modern Irradiators

- X-ray cabinet irradiators
  - Cabinets with shelving
- Examples
  - PXI X-RAD 320
  - Xstrahl RS320

High-Precision Conformal X-Ray Irradiators

- On-board imaging (CBCT, optical, etc.)
- Treatment planning systems
- Examples
  - PXI X-RAD SmART

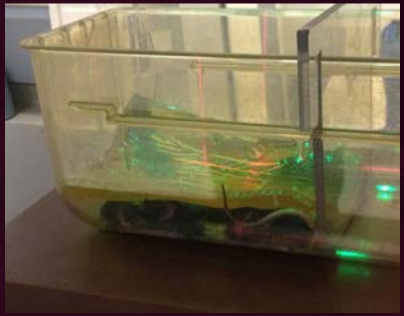


  - Xstrahl SAARP

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

Other Irradiators

- Linear accelerators

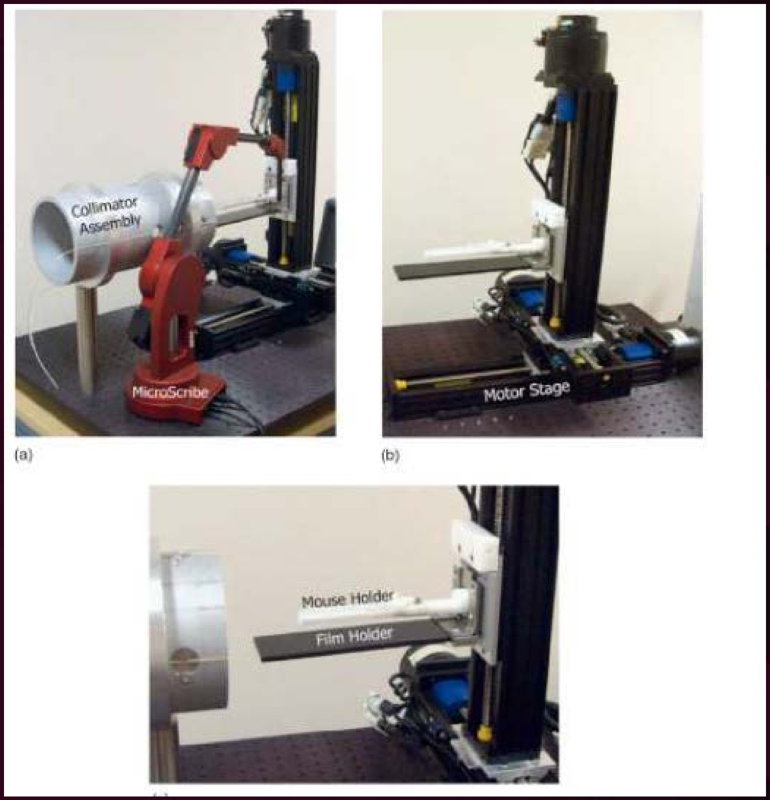


- "In-house x-ray irradiators"

Example from Princess Margaret Hospital in Toronto

Other Irradiators

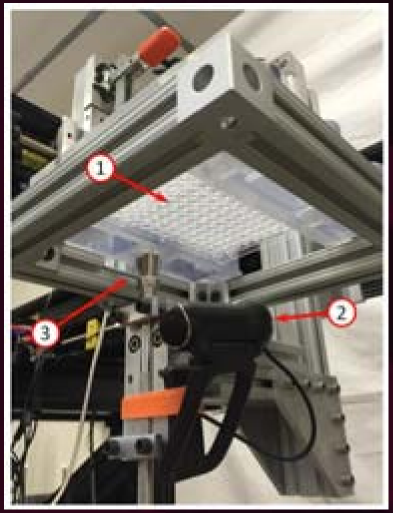
- HDR Ir-192 based “microRT”



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

Other Irradiators

- UWMRRC High-throughput irradiator
  - 50 kVp Xoft Axxent source
  - Surface applicator
  - Source aiming "up" through the bottom of a cell plate
  - Developed with UW Professor Bryan Bednarz and his graduate student Tyler Fowler, PhD



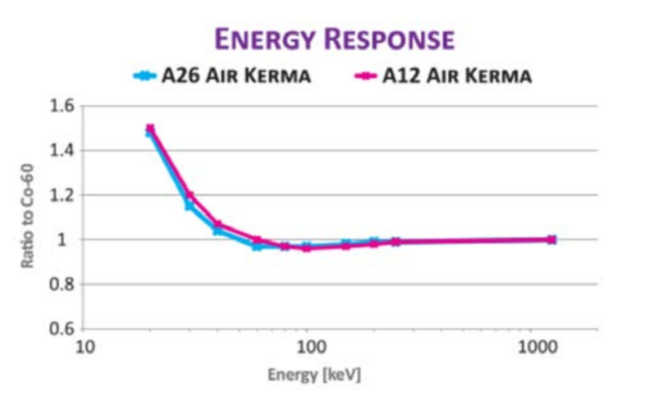
- Proton beam lines, carbon ion beams, neutron beams, nuclear reactors, many more…

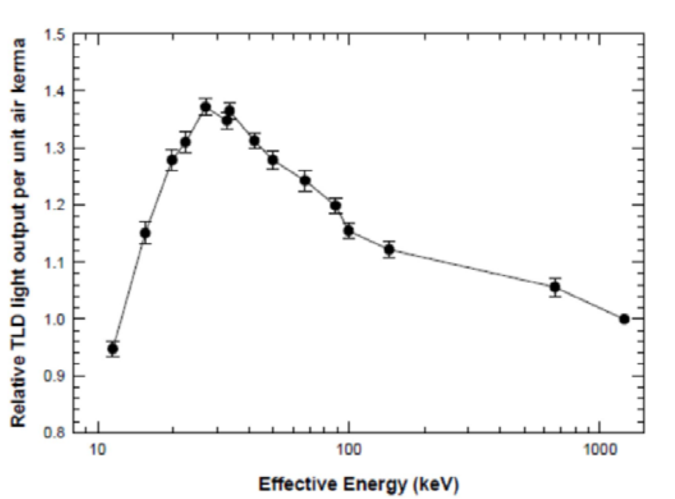
Technical Challenges

- Each experiment is unique geometry
  - Cell culture plates
  - Cell vials
  - Mice (different sizes)
  - Rats
  - Larger animals
- Conditions vary
  - Buildup
  - Scatter
  - Depth dose
  - Field uniformity
  - Field size

Technical Challenges

- Detectors have energy dependence!
- NIST-traceable dose to water standards do not exist for anything but Co-60
- AAPM TG51 works for linear accelerator platforms
- AAPM TG61 – “AAPM protocol for 40–300 kV x-ray beam dosimetry in radiotherapy and radiobiology”
  - Doesn’t account for individual experimental geometries (mice, cell plates, etc)
- ICRU 30 – Mostly fundamental physics including exposure to dose ratios (F factors), Bragg-Gray theory, and general recommendations. Published in 1979





Motivation?

- University of Wisconsin Medical Radiation Research Center performed a survey
  - Results showed doses measured were different than expected by up to 42%

Radiation Biology Irradiator Dose Verification Survey

Kurt H. Pedersen, Keith A. Kunugi, Clifford G. Hammer, Wesley S. Culberson and Larry A. DeWerd[1]

Department of Medical Physics, University of Wisconsin – Madison, School of Medicine and Public Health, Madison, Wisconsin

TABLE 11
Mouse Phantom Dose Results

Facility	Source	Average of measured dose: 1 Gy ADW	Average of measured dose: 4 Gy ADW	Average deviation (%)
1	^{137}Cs	1.12	4.41	11.2
2	^{137}Cs	1.09	4.32	8.7
3	^{137}Cs	1.06	4.12	3.9[a]
4	^{137}Cs	1.15	4.48	13.5
5	^{137}Cs	1.01	4.09	1.6
6	^{137}Cs	1.03	4.02	1.8
7	^{60}Co	1.02	4.08	1.8
8	X-ray 1	1.17	–	–12.4[b]
9	X-ray 2	0.838	3.39	–15.7
10	X-ray 3	0.580	2.07	–42.3
11	X-ray 4	0.986	3.99	–0.9
12	X-ray 5	0.826	3.51	–14.8

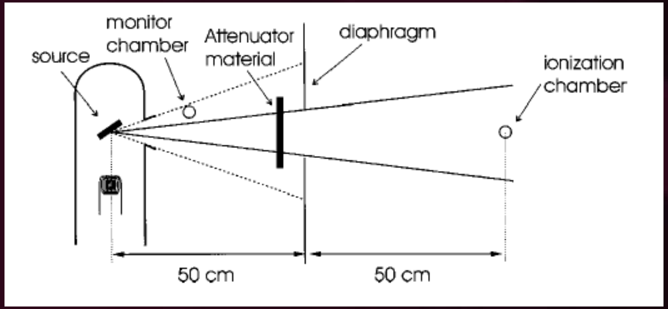
[a] Based on target doses of 1.009 and 4.008 Gy.
[b] Based on a target dose of 1.335 Gy.

Technical Challenges: A Specific Example

- PXI XRAD 320 is a popular x-ray irradiator
- Filter #1 yields ~3Gy/min, which is close to clinical RT dose rate

Beam	kVp	Added Filtration	HVL1
XRAD 320	320	2mm Al (Filter #1)	1 mm Cu (nominal)

- Difficult to measure HVLs in a cabinet (normally chamber placed at 100 cm SDD)



- Send chamber to an ADCL. Which beam do you choose?

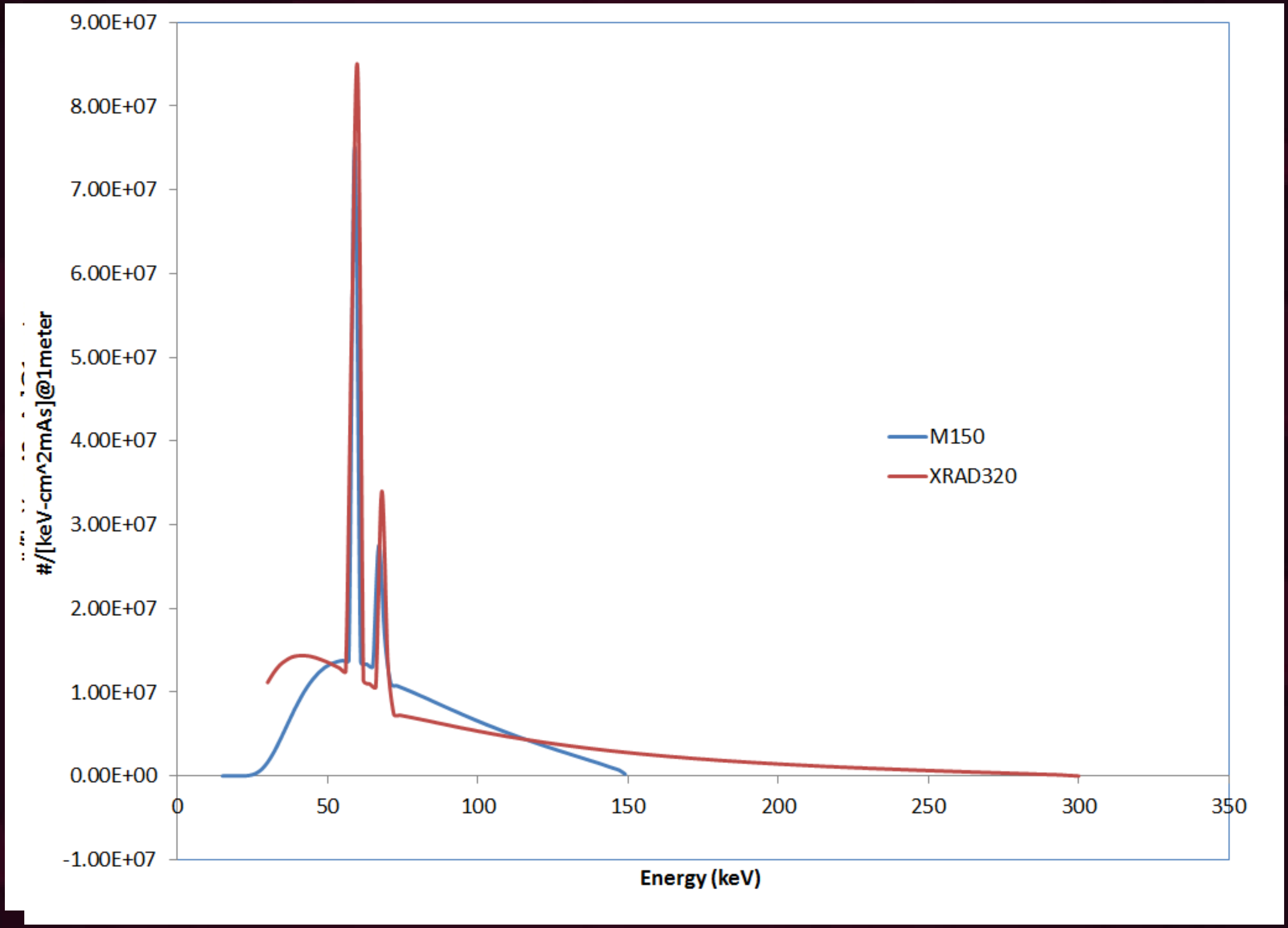
UWADCL Beams

Beam	kVp	Added Filtration	HVL1
XRAD 320	320	2mm Al (Filter #1)	1 mm Cu (nominal)

Tungsten Anode X-Ray Beam Qualities					
Beam Code	Added Filter (mm Al or Cu)	HVL 1 (mm Al)	HVL 1 (mm Cu)	HC (Al)	Air Kerma Rate (mGy/sec)
UW30-L	0.25 Al	0.228		60	2.308
UW40-L	0.48 Al	0.530		61	2.002
UW50-L	0.41 Al	0.789		61	2.845
UW80-L	1.16 Al	1.80		59	3.588
UW100-L	1.75 Al	2.81		59	3.910
UW20-M	0.15 Al	0.146		80	1.014
UW30-M	0.40 Al	0.351		65	1.319
UW40-M	0.79 Al	0.742		68	1.315
UW50-M	1.08 Al	1.04		66	2.020
UW60-M	1.50 Al	1.65		67	1.796
UW80-M	2.75 Al	3.00		68	1.821
UW100-M	4.77 Al	4.98		72	1.822
UW120-M	3.0 Al + 0.10 Cu	6.77		75	2.365
UW150-M	2.83 Al + 0.28 Cu	10.1	0.657	87	2.173
UW200-M	1.00 Al + 1.01 Cu	14.8	1.63	95	1.930
UW250-M	1.96 Al + 2.36 Cu	18.3	3.15	98	1.633

Nothing even close!

Spectra



9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
#/[keV-cm^2mAs]@1meter
0
50
100
150
200
250
300
350
Energy (keV)
M150
XRAD320

NIST Beams

Beam	kVp	Added Filtration	HVL1
XRAD 320	320	2mm Al (Filter #1)	1 mm Cu (nominal)

Beam code[a]	Additional filtration[b]				Half-value layer[c] (HVL)	
	Al (mm)	Cu (mm)	Sn (mm)	Pb (mm)	Al (mm)	Cu (mm
X-Ray Beam Qualities						
L10	0				0.037	
L15	0				0.059	
L20	0				0.070	
L30	0.3				0.23	
L40	0.53				0.52	
L50	0.71				0.79	
L80	1.45				1.81	
L100	1.98				2.80	

Beam code	Additional filtration (mm)[a]				First HVL[b]	
	Al	Cu	Sn	Pb	Al (mm)	Cu (mm)
HK10					0.042	
HK20	0.15				0.128	
HK30	0.52				0.408	
HK60	3.19					0.079
HK100	3.90	0.15				0.298
HK200		1.15				1.669
HK250		1.60				2.463
HK280		3.06				3.493
HK300		2.51				3.474

Still nothing close!

From AAPM TG61

- “It is generally considered to be insufficient to use only tube potential or HVL to specify a beam.”
- “The chamber shall be calibrated at a beam quality sufficiently close to the user’s beam quality in terms of *both* the tube potential *and* HVL to ensure the validity of the calibration factor in the clinical situation”

NIST Efforts

- NIST had a conference in 2013

Volume 118 (2013) http://dx.doi.org/10.6028/jres.118.021
Journal of Research of the National Institute of Standards and Technology

The Importance of Dosimetry Standardization in Radiobiology

Marc Desrosiers[1], Larry DeWerd[2], James Deye[3], Patricia Lindsay[4], Mark K. Murphy[5], Michael Mitch[1], Francesca Macchiarini[6], Strahinja Stojadinovic[7], and Helen Stone[3]

CIRMS Efforts

- Two years ago we had a CIRMS breakout session dedicated to radiobiology standardization

Medical Applications Session III Radiation Biology, "Research, Devices & Dosimetry"

- **Jim Deye**, NIH/NCI (retired)
  Dose is More than a Number: The Growing Need for "Radiobiology Dosimetry Standards"
- **Kurt Pedersen**, University of Wisconsin, Department of Medical Physics
  Output Verification of Radiobiological Irradiators
- **Bryan Bednarz**, University of Wisconsin, Department of Medical Physics
  Novel High-throughput Irradiators for In Vitro Radiation Sensitivity Bioassays

NCI Efforts

- NCI requiring NIST-traceable dosimetry on U01 grants, PAR posted Feb 23, 2016

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Cancer Institute (NCI)
Funding Opportunity Title	Cooperative Agreement to Develop Targeted Agents for Use with Systemic Agents Plus Radiotherapy (U01)
Activity Code	U01 Research Project – Cooperative Agreements

- “Ensuring accuracy and consistency of irradiation protocols through NIST-traceable dosimetry testing and on-going validation, and detailed, translatable reporting of irradiation set-up details (standard operating procedures) for both *in vitro* and *in vivo* studies;”

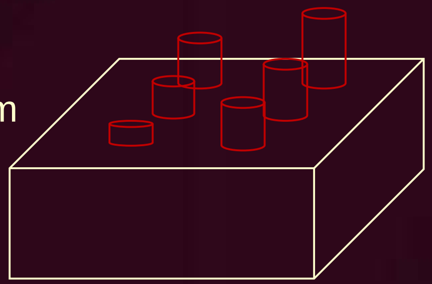
AAPM Efforts

- Working Group on Conformal Small Animal Irradiation Devices
  - Under the Biological Effects SC – TPC – Science Council
  - Magdalena Bazalova-Carter is the Workgroup Chair
  - "To generally promote research ideas and opportunities related to small animal conformal irradiation"
  - Dosimetry is not in their Charge
  - Also working on funding strategies for "foundational issues" including "phantom, QA"

UWMRRC Efforts

- Goal is to set up independent dosimetry services for radiobiology researchers
- Remote dosimetry services will be TLD based
- Several phantoms available (mice, cell plates and cell vials)
- A film-based attenuation phantom will help determine calibration / correction factors for TLDs
- Preliminary measurements are complete showing feasibility

Attenuation phantom



UWMRRC Efforts – Mice

- Novel mouse models of anal cancer
- Irradiation with Xoft eBT source

UWMRRC Efforts - Mice

- Four groups of mice
  - Control
  - chemo alone (BEZ235)
  - Chemo + RT (with mitomycin C and 5FU)
- Anal tumors treated daily for five days with 2 Gy prescribed to 5 mm depth.
- eBT dosimetry NIST traceable with low uncertainties
- Well-type ionization chamber used for source output checks daily
- Tumor growth rates measured and compared

Various Other Research Efforts

- Many research projects
  - 2016 AAPM Farrington Daniels Award
    - Steven Bache et al. “Investigating the accuracy of microstereotactic-body-radiotherapy utilizing anatomically accurate 3D printed rodent-morphic dosimeters” Medical Physics 2015
  - Researchers using ion chambers, film, TLDs, OSLDs, plastics, etc.
  - Development of phantoms

  - Characterization of scatter conditions in cabinets

CIRMS Needs Report

Needs Report

Executive Summary
Policy Recommendations
Metrology Needs
- Medical Applications
- Homeland Security
- Industrial Applications and Materials Effects
- Computational Needs
Sponsors
About Us

Tools
What links here
Related changes
Special pages
Printable version
Permanent link
Page information

Navigation

Page | Discussion | Read | View source | View history | Search

Medical Applications

The CIRMS Medical Applications subcommittee deals with diagnostic and therapeutic uses of ionizing radiation, whether isotope or accelerator sourced radiation. New topics of interest involve the growing use of proton beam therapy for more targeted cancer treatment and a need for enhanced dosimetry systems to quantify exposure levels in computerized tomography scans (CT scans). An introduction to the overall areas of interest in the medical area in the use of ionizing radiation can be found in (Appendix D). This was taken from the fourth "Needs Report" of December 2004. More complete details on all of the MPD's generated by the CIRMS Medical Applications subcommittee can be found in PDF form in prior "Needs Reports" which are accessible on the CIRMS web site: www.cirms.org [1].

CIRMS has been very effective in the Medical Applications area by drawing together professionals from the academic and medical communities, from the US FDA's Center for Devices and Radiological Health (CDRH), and by involvement of the National Institutes of Health, in particular the National Cancer Institute, and of inter-agency groups such as the Biomedical Advanced Research and Development Authority (BARDA). One of CIRMS early success stories (MPD A.1.0 - National Air-Kerma Standards for Mammography) was the organization's ability to pull together of various agencies to cofund a needed radiation target facility at NIST so that air-kerma measurements for mammography equipment could be calibrated.

NIST, through the guidance of the CIRMS Medical Applications subcommittee, has also established radioactivity standards for nuclear medicine (MPD A.2.3) and for determining the absorbed dose-to-water for photon external beam radiation therapy (MPD A.4.1 - Absorbed-Dose-to-Water Standards for Photon External Beam Radiation Therapy). National standards for the air-kerma measurements of diagnostic X-ray beams (MPD A.5.0 - Air Kerma National Standards for Diagnostic X-ray Beams) and for the air kerma strength of photons emitted by brachytherapy sources (MPD A.6.0 - National Air Kerma Strength Standards for Photon Brachytherapy Sources) have also been established. NIST has obtained equipment, such as a medical linear accelerator, to facilitate these activities. Below is a list of the completed Measurement Program Descriptions prepared by the CIRMS Medical Applications subcommittee. One or two page descriptions of the active MPDs follow. These present the objectives, some background information and needs in each active area.

Medical Applications - Active Measurement Program Descriptions (MPD's)

----High Priority----

A.19.0 Standardization in Radiobiology

A.9.0 Dosimetry for Proton Beam Therapy

A.15.0 Standards for Small Fields in External Beam Therapy

---Medium Priority---

A.8.1 Liquid Based and Micro-Brachytherapy Sources

A.13.0 Enhanced Dosimetry Systems for CT Scans

A.14.0 Cone-Beam CT Dosimetry in Radiation Therapy - maybe this can be combined into A.13.0

A.16.0 Absorbed Dose to Water Standards for Megavoltage Therapy Beams - (Modify for dissemination)

A.17.0 3D Dosimeters for Non-Standard External Beam Therapy Dosimetry - Larry suggested adding Presage and more description

A.18.0 Air Kerma Standards for Ir-192 and Electronic Brachytherapy Sources - (Updating)

A.20.0 Absorbed Dose to Water Standards for Low-Energy X-ray Beams - (Updating)

CIRMS Needs Report (cont)

Action Items:

1 – With cooperation between NIST, AAPM, AACR, and the NIH, standard measurement techniques need to be established through the use of standard operating procedures (SOPs) and dosimetry equipment validation. The measurement techniques must include NIST-traceability and appropriate primary standard development / utilization.

Resource Requirements:

1 – Undetermined dollar amount - Partnerships between NIST, AAPM, AACR, and the medical community are essential in this area.

The Discussion

- What next?

Questions