Current Status of Radiobiology Dosimetry

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CIRMS
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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
  - DNA
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
- 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

Other Irradiators

- Linear accelerators

- “In-house x-ray irradiators”

Example from Princess Margaret Hospital in Toronto
Other Irradiators

- HDR Ir-192 based “microRT”

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%
Technical Challenges: A Specific Example

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

<table>
<thead>
<tr>
<th>Beam</th>
<th>kVp</th>
<th>Added Filtration</th>
<th>HVL1</th>
</tr>
</thead>
<tbody>
<tr>
<td>XRAD 320</td>
<td>320</td>
<td>2mm Al (Filter #1)</td>
<td>1 mm Cu (nominal)</td>
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</tbody>
</table>

- 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

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Nothing even close!
Spectra
NIST Beams

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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 had a conference in 2013

The Importance of Dosimetry Standardization in Radiobiology

Marc Desrosiers¹, Larry DeWerd², James Deye³, Patricia Lindsay⁴, Mark K. Murphy⁵, Michael Mitch⁶, Francesca Macchiarini⁷, Strahinja Stojadinovic⁸, and Helen Stone⁹
CIRMS Efforts

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

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

- “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”
UWMRRRC 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
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
  - Researchers using ion chambers, film, TLDs, OSLDs, plastics, etc.
  - Development of phantoms
  - Characterization of scatter conditions in cabinets
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 computed 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 C. 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 various agencies to codify 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 radiological 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 15.0 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 17.9 3D Dosimeters for Non-Standard External Beam Therapy Dosimetry - Lamy suggested adding Pressage and more description
A 18.0 Air-Kerma Standards for k-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