Standardization of dosimetry practices for small and large animal irradiation in radiobiological studies

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[Funded by NIAID]

MAC-AAPM Annual Meeting
October 10-11, 2014
Georgetown University, Washington DC
Topics

• Introduction
• MCART RPC Overview
• MCART Sites
• RPC Objectives
• Achievements of RPC
• Looking Ahead
Introduction

- As a medical physicist we all follow a rigorous dosimetry standard to provide clinical physics services in cancer clinics all over the world.
- To follow and maintain a national dosimetry standard in these centers is a **given**.
- But it is not so in the field of radiobiology research centers. Even if these centers have good physics support there is no established national standard to follow and maintain.
Radiation Physics Core (RPC) Pre-History...

- The National Institute of Allergy and Infectious Diseases (NIAID) sponsored Medical Countermeasures Against Radiological Threats (MCART) Consortium in 2005 to conduct research on developing Medical Countermeasures (MCM) to treat the key sequelae of the acute radiation syndrome (ARS) and the delayed effects of acute radiation exposure (DEARE).
RPC : Pre-History...

• The development of MCMs against radiation syndrome requires well characterized and validated animal models.
• The animal research conducted in these laboratories utilize a variety of ionizing photon beams such as 250-320 kVp x-ray, Cs-137 photons, $^{60}$Co γ-ray, and 6MV x-ray.
• They also follow a variety of dose calculation schemes to conduct their experiments.
An important objective in the Consortium research activities is to measure a *Dose Response Relationship* (DRR) appropriate to their respective biological end points. A clear and unambiguous definition of the DRR is essential for the development of MCMs, and it is desirable that these DRRs are transferrable between centers.
But we have a **Challenge**...

A very sensitive relationship exists between

the Biological outcome – *the y-axis of the DRR*

and

the Delivered dose – *the x-axis of the DRR*
Let’s look at a DRR more closely...

Biological Outcome

Delivered Dose

- 60 day H-ARS
- 15 day GI-ARS

LD$_{50/50} = 7.45$ Gy [5.94, 7.69]
LD$_{50/15} = 11.33$ Gy [10.81, 11.75]
± 5% uncertainty at 8 Gy

Biological Outcome

Delivered Dose
± 10% uncertainty at 12 Gy
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Dosimetry at MCART sites involve

A variety of dosimetry protocols

- Task Group 51 of American Association of Physicists in Medicine (AAPM TG51) for megavoltage photon beams
- AAPM TG61 for medium energy X-Ray beam (40 to 400 KV)
- Institute of Physics and Engineering in Medicine and Biology (IPEMB) for X-Rays below 300 KV

- AAPM protocols are followed in USA and Canada
- IPEMB protocol is followed in Europe
NIAID funded MCART RPC

to Establish

• A Standardization of Dosimetry practices among MCART sites.
• A Quality Assurance Program and adherence to Standard Operating Procedures (SOPs)
• A Remote Dosimetry Monitoring Service to ensure compliance of Dosimetry Standard

and Evolve into a

Resource HUB for physics related information to radiobiology researchers
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Indianapolis, IN

JL SHEPHERD Cs-137 Irradiator

XRAD 320, Precision X-ray Inc.

TBI Pie shaped Platform

IUPUI

What matters. Where it matters.
Manchester, UK

STRAHL RS320

EPISTEM LTD.

Calibration at AIP

Lead boots for PBI

In-Air Calibration
GE LightSpeed CT Scanner

Varian ECLIPSE TPS

XRAD 320, Precision X-ray Inc.

Varian TrueBeam LINAC

TBI Rectangular Platform

WTLI Rectangular Platform

TBI Hexagonal Platform
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RPC Objectives

**Dosimetry Standard**

- A **nationwide recognized protocol** would be used for absolute dose calibration at a reference point
- Dosimetry equipment would have a valid **calibration traceable to NIST**
- It is recommended to have a **MDACC TLD** validation at new installation

**SOP driven Quality Assurance**

**Pre-Irradiation Output Check**

*IC response is verified against Expected Response prior to each irradiation to verify nominal output of the irradiator*

*(Expected Response is determined annually by liaison physicist)*
RPC Objectives

Measurement at Animal Irradiation Position

Rectangular Platform for Mice TBI

Rectangular Platform for Mice WTLI

Pin Point IC for AIP in WTLI
RPC Objectives

Remote Dosimetry Monitoring Service

• At some interval each center will receive **OSLD (nanoDots) embedded Mouse Phantoms** for each irradiator

• Each site will irradiate Mouse Phantoms using site beam following RPC provided **OSLD irradiation instruction**

• OSLDs returned from each site will be read at **RPC** using MicroStar II (Landauer) and issue a **certificate for compliance** of dosimetry standard
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• **Achievements of RPC**
• Looking Ahead
RPC Accomplishment: Dose Rate Equivalence

MCART desired dose rate range: 0.7 – 1.2 Gy/min

<table>
<thead>
<tr>
<th>Before RPC</th>
<th>After RPC</th>
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<tbody>
<tr>
<td><strong>Technique &amp;</strong></td>
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<td><strong>Dose Rate at AIP Level (Gy/min)</strong></td>
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<tr>
<td><strong>UMB-TRS : X-Ray</strong></td>
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<tr>
<td>320KV/12mA/2mmAl</td>
<td>300KV/10mA/2mmAl</td>
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<tr>
<td><strong>Rectangular Platform</strong></td>
<td><strong>Rectangular Platform</strong></td>
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<tr>
<td>TBI /PBI ~ 1.5-1.6 WTLI ~ 1.25</td>
<td>TBI /PBI ~ 1.1-1.2 WTLI ~ 0.95</td>
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<tr>
<td><strong>Pie Shaped HEX Platform</strong></td>
<td><strong>Pie Shaped HEX Platform</strong></td>
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<td>TBI /PBI ~ 1.7</td>
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## RPC Accomplishment: Dose Rate Equivalence

MCART desired dose rate range 0.7 – 1.2 Gy/min

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<tr>
<td><strong>IUPUI : X-Ray</strong></td>
<td></td>
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<tr>
<td>If used 320KV/12mA/2mmAl</td>
<td><strong>IUPUI : X-Ray</strong></td>
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<tr>
<td>Rectangular Platform</td>
<td>300KV/10mA/2mmAl</td>
</tr>
<tr>
<td>TBI /PBI Would have been</td>
<td>Rectangular Platform</td>
</tr>
<tr>
<td>~1.4-1.5</td>
<td>TBI /PBI ~ <strong>1.0-1.2</strong></td>
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<tr>
<td><strong>Technique &amp; Dose Rate (Gy/min)</strong></td>
<td>NO Change Necessary</td>
</tr>
<tr>
<td><strong>UMB-PRL:</strong></td>
<td></td>
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<tr>
<td>6MV X-Ray from LINAC</td>
<td></td>
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<tr>
<td>SSD 145 cm</td>
<td></td>
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<tr>
<td>Dose Rate at Mid-depth ~ 0.8</td>
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<tr>
<td><strong>EPISTEM:</strong> X-Ray</td>
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<tr>
<td>300KV/10mA/0.75mmCu</td>
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<tr>
<td>Dose Rate at AIP level ~ 0.81</td>
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<td><strong>IUPUI:</strong> Cs-137</td>
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<tr>
<td>Dose Rate at AIP level ~ 1.0</td>
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RPC Achievements

**Papers** published in Health Physics Journal

Kazi et al, “The MCART Radiation Physics Core: The Quest for Radiation Dosimetry Standardization”, Health Physics, 2014 Jan: 106; 97-105

(Response of letter to the editor "Dosimetric Consistency for Medical Countermeasures Research" by Zeman, GH)

**Posters** presented in Radiation Research Society meetings


14-A-279-RRS: Kazi et al, “Commissioning of XRAD320 irradiator for small animal studies”

**Oral Presentation** in Meeting organized by drug development company

April 28-29, 2014, University of Maryland School of Pharmacy, Baltimore, MD
RPC Achievements

Posters and Oral presentations at local meetings

Two posters at ‘Open House’ on June 21, 2013
Division of Translational Radiation Sciences, UMSOM, Baltimore

Oral presentation at MCART Summer ‘Data Fest’ on July 30, 2013
University of Maryland School of Pharmacy, Baltimore

Oral presentation at MCART Tissue Imaging Core meeting in October 3, 2013
University of Maryland School of Medicine, Baltimore, MD

Four oral presentations at the MCART annual meeting in March 18-19, 2014
Indiana University Purdue University, Indianapolis, IN

Colleen DesRosiers
David Mott
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Looking for answers

• Heterogeneity correction- how should it be introduced in radiobiological studies?

• What is the relationship between LET and RBE?

• How does HVL relate to Dose and RBE?

• Can we identify regions of biological changes and relate them to dose received in that region?

• Can we estimate delivered dose from portal film?
Heterogeneity and Dose

Left image: Red line is 1074 cGy prescribed to mid-depth using homogeneous anatomy - MU setting = 575 MU/field
Right image: Red line is 1074 cGy delivering 575 MU/field in Heterogeneous anatomy
DVH dose volume histogram
Plan Comparison

Lung V_{100} : 91%
Heterogeneity Correction Turned ON

Lung V_{100} : 95%
Heterogeneity Correction Turned OFF

% of Structure Volume
Dose in cGy
Dose to specific Organ

If it can be outlined - doses can be evaluated – Bone marrow, liver, kidneys heart & lung, small intestine, stomach
RBE vs LET for diverse processes such as Irreparable Lethal Dos, Potential Lethal Dose, DNA Double Strand Break etc.

LET range for beams used in MCART Studies
Up to ~ 5 cm depth, there is negligible difference in PDD for x-ray beams with HVL = 1.0 - 3.0 mmCu
Is it possible to connect radiobiologic effects to delivered dose?

• Overlay 3D dose distribution on follow up CT studies and if possible connect biological effects to radiation dose
  – A good deal of image analysis would be needed.

• Use inhomogeneity corrections in dose calculations to minimize uncertainty due to dose calculation inaccuracies

An intensive study is underway at RPC ...
Is it possible to estimate dose delivered from portal films?

A detail study is underway at RPC …
Conclusions

• RPC is here and making a difference
  • Made significant progress in equalizing X-Ray dose rate
  • Made an impact in radiobiology study by introducing portal imaging
  • Exploring possibility of identifying dose induced radiobiological effects
  • Exploring possibility of portal dosimetry

• Lot more to do ......
Thanks to the RPC Team!

Karl Prado  
Primary Dreamer

Abdul Kazi

Giovanni Lasio

Wei Lu

Mariana Guerrero

Colleen DesRosiers

Dave Mott

Charlotte Prado
Special Thanks to Tom and Professor Thomas J Macvittie
PI : MCART

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And Thank You all !!