Spatial Mapping of the RBE of Scanned Particle Beams

AAPM 2016

David Grosshans M.D., Ph.D.

MDAnderson Cancer Center Proton Therapy Making Cancer History*

Background

- · Clinical Radiation Oncology
 - Proton Therapy
 - Brain (adults and children)
 - Base of skull
- Scientific
 - Neuroscience (not physics)
 - & now "particle" biology



MD Anderson Cancer Center Proton Therapy Making Cancer History"

Motivation to explore RBE





Goals for today...

- Biologic assays used to define RBE

 Limitations and new directions
- · Emphasize the need for involvement of physicists
 - Experimental design, setup, data analysis, reporting, grants etc.
- "Radiobiology from a clinician's perspective"

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Making Cancer History"	

What is RBE?

- A comparison of two radiation types using whatever measure you want.
 - -Typically cell kill (clonogenic survival)
 - Measured with established (but NOT standardized) techniques



Clonogenic survival assays



Limitations of clonogenic survival?





Can only be performed in cell lines which can grow in culture

Limitations of clonogenic survival?





· V79 cells

CHO cells Often in non-patient derived cells lines

Limitations of clonogenic survival?



Time and labor intensive.....

What is the RBE for proton therapy?



Paganetti 2003

What does RBE depend on?

- dose
- alpha/beta
- end point
- BIOLOGY
- LET



Liu...Willers IJROBP 2015

Mid SOBP....





Liu...Willers IJROBP 2015

What can we control....

• RBE (and LET) increases with depth



Along the SOBP....

- · How do we all deal with this with PSPT?
 - No single beams (except prostate)
 - Select angles
 - Don't end in critical structure



What about IMPT?





A PSPT Beam

An IMPT Beam

This is a real opportunity

We need more and better data (for models)



High-through put clonogenic assays



We must think about the physics!



Disclosures....

	 Lawrence Bronk 	 Steven Lin
	 Fada Guan 	 Erik Sulman
	 Uwe Titt 	 Kathy Mason
	 Radhe Mohan 	 Ray Meyn
	 Dragan Mirkovic 	 Jeff Dinh
HUR EL	 Chris Peeler 	
A A A A A A A A A A A A A A A A A A A	 Darshana Patel 	 <u>Funding:</u>
	 Wenhua Cao 	 NCI
ST	 Michael Gillin 	• R21
J-	 Ron Zhu 	• U19
	 Falk Poenisch 	 CPRIT
	 Narayan Sahoo 	

"The Jig"



Drs. Guan & Titt





"IMPT in a dish"









Models....

What do all models attempt to describe?
 A: Cell kill

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10 LET [keV/μm]



.....

Carbon???



Comparison of protons vs. carbon





Protons vs. Protons



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Other cancer cell models



GSC23 response



What about normal tissues?





What is necrosis?

- Not just cell kill
 - An active spreading process involving multiple cell types
- We are forcing models of clonogenic survival onto a complex process....

Normal tissues – "Rat brain organoids"



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Normal tissues – "Rat brain organoids"



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Normal tissues - "organoids"



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Mapping Biologic Effect



Animals....



Dr. Poenisch

Patients!!!

Voxel-Level Analysis of Adverse Treatment Response in Pediatric Patients Treated for Ependymoma with Passive Scattering Proton Therapy

CPeeler^{1,2}, D Mirkovic¹, U Titt¹, D Grosshans¹, R Mohan¹, (1) The University of Texas MD Anderson Cancer Center, Houston, TX, (2) The University of Texas Graduate School of Biomedical Sciences at Houston, Houston, TX

Presentations WE+FG-202-9 (Wednesday, August 3, 2016) 1:45 PM - 3:45 PM Room: 202



Pediatric ependymoma cohort





Critical issues

- Particle therapy is different - "It's not just dose"
- Clonogenic survival – Is still the "gold" standard
- "Biology" makes correlations with physical factors challenging

We do understand the physics

- Technology is changing rapidly
 IMPT...
- If we believe RBE (or LET) matters...
 This can (<u>and should</u>) be incorporated with IMPT.
 - What models to use for treatment planning?
 - Are we ready to use this clinically?
- · Heavy ions may have even more benefits

Needs to be more collaboration

- Physics is essential, especially for particles
 - Experimental design
 - MC based design
 - Minimization of uncertainties
 - Accurate data
 - Dose
 - LET
 - Team science

The Team!

	•	Lawrence Bronk	•
	•	Fada Guan	•
	•	Uwe Titt	•
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