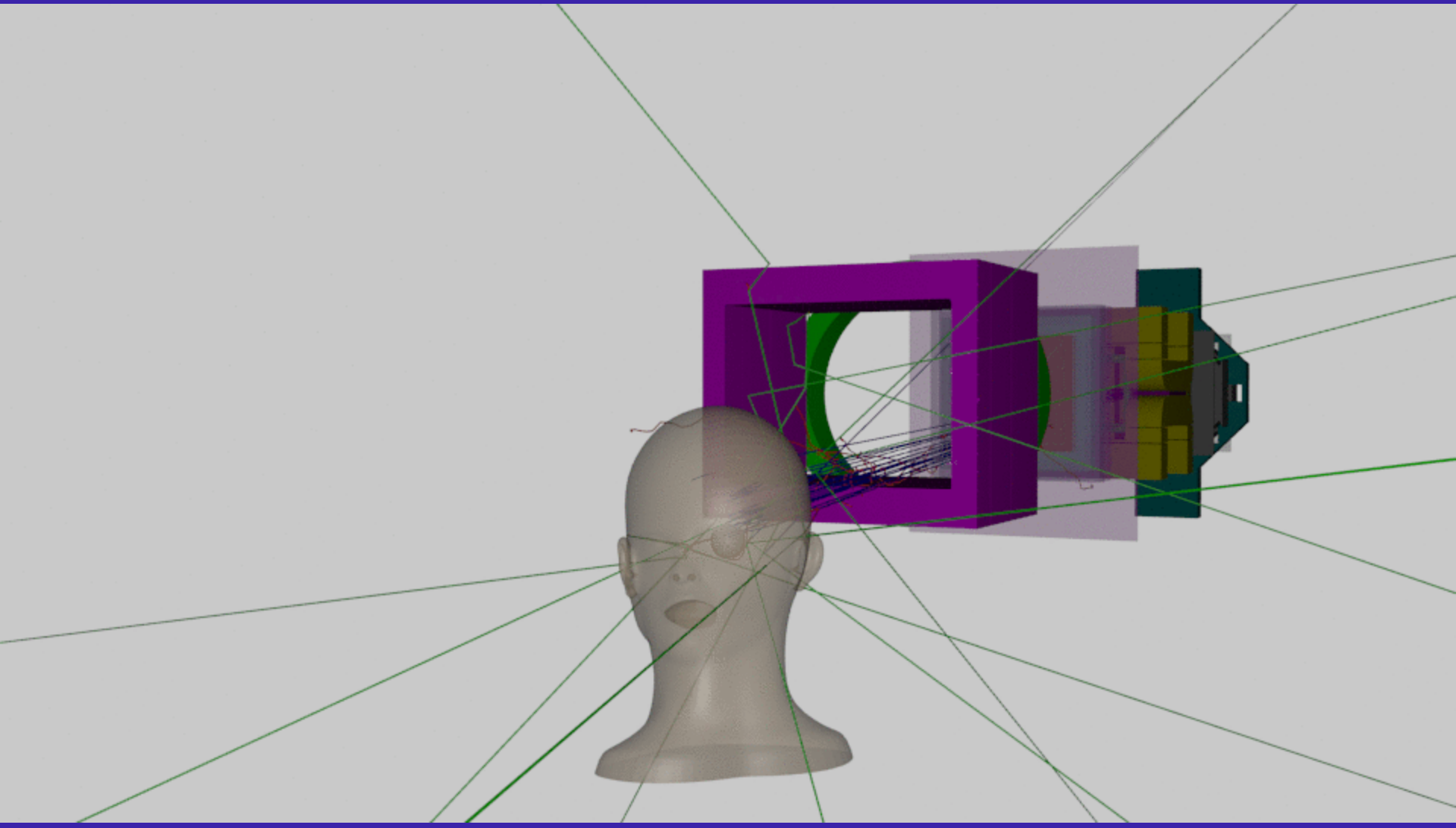
# *TOPAS (TOol for PArticle Simulation): An innovative Monte Carlo platform for research and clinical applications*

Bruce Faddegon* with Jose Ramos Mendez and Naoki Dominguez

*Professor in Residence,

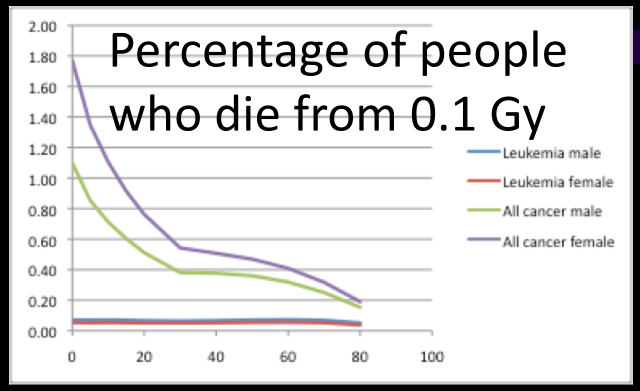
University of California San Francisco



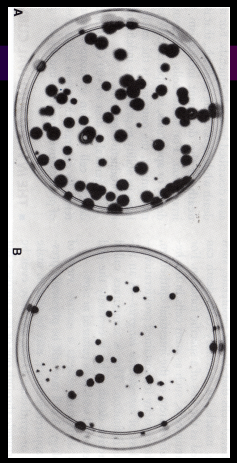
# *Outline*

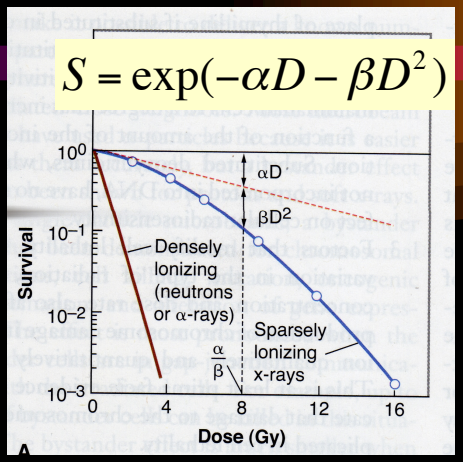
- Monte Carlo simulation in medicine
  - The A-B-C's
  - Introduction to Geant4 and TOPAS
- TOPAS for proton therapy
  - Radiotherapy physics with TOPAS
  - Radiation biology with TOPAS
- Extensions: TOPAS-nBio track structure and chemistry
- U24: TOPAS for all medical applications with all types of ionizing radiation

# *Monte Carlo in medicine: Applications*



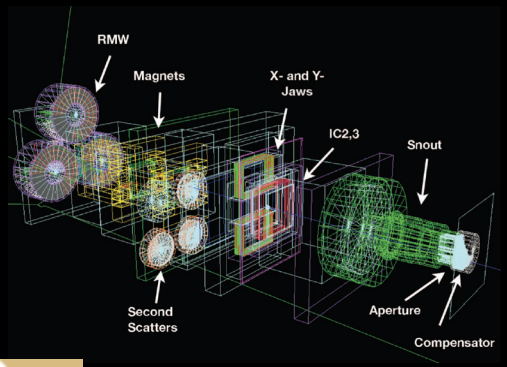

Radiation protection



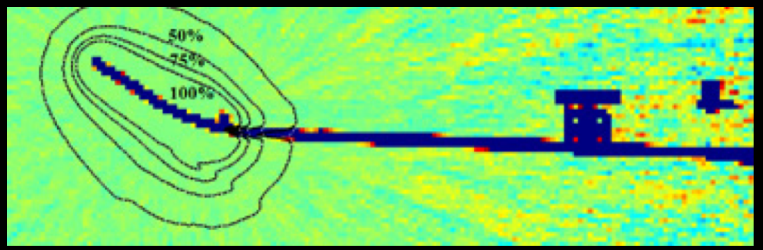



Radiobiology

Radiology




External beam radiation therapy




Brachytherapy

# *Monte Carlo in medicine: Benchmarks*

*Medical physics benchmarks for validation and regression testing of Geant4*

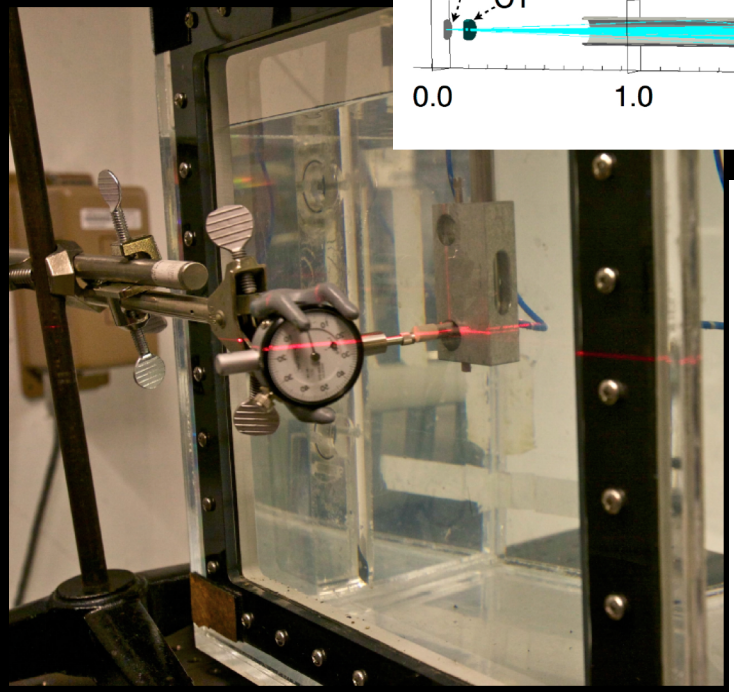
Geant4 Medical Simulation Benchmark Group: G4BSMG

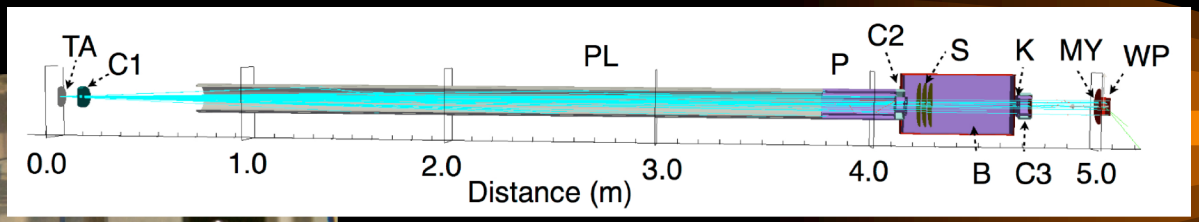
Bruce Faddegon, Pedro Arce, David Bolst, Dean Cutajar, Giacomo Cuttone, Jeremy Davis, Paolo Dondero, Andrea Dotti, Christian Fedon, Susanna Guatelli, Miguel Ant. Cortés Giraldo, Sebastien Incerti, Vladimir Ivanchenko, Mathieu Karamitros, Alfonso Mantero, José Manuel Quesada Molina, Luciano Pandola, Álvaro Perales, Jan Perrot, José Ramos-Méndez, Francesco Romano, Ioannis Sechopoulos

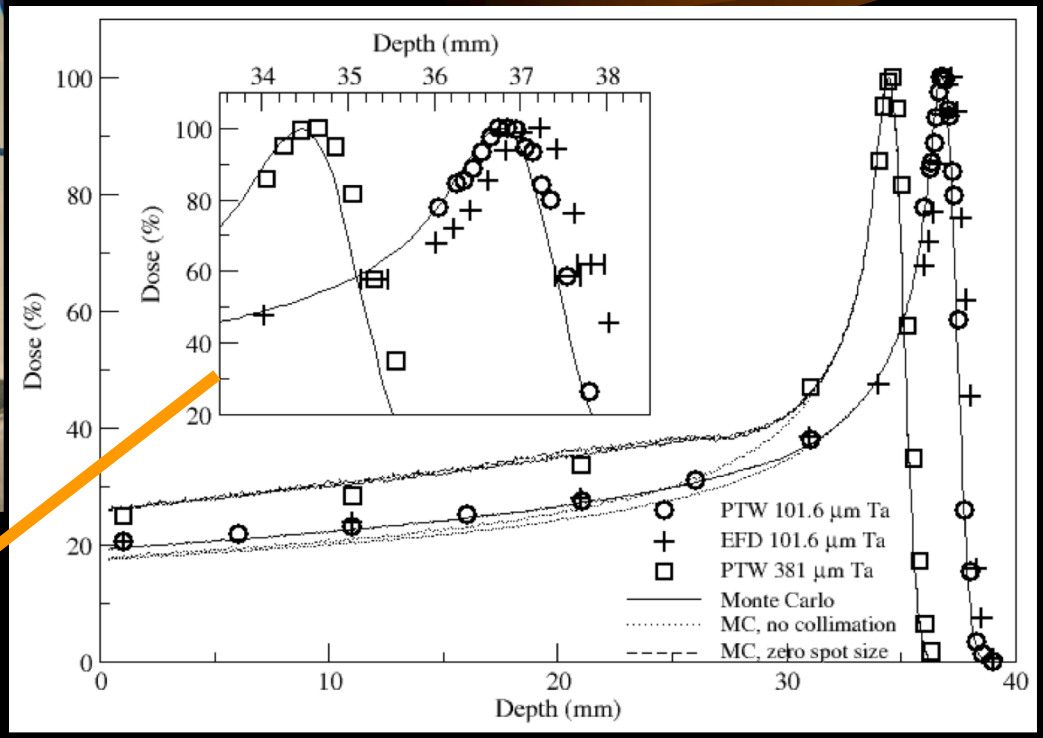
# *Geant4 Medical Simulation Benchmark Group: G4BSMG*

| Benchmark description | Responsibility |
|---|---|
| X-ray imaging | Sechopoulos |
| Bremsstrahlung from thick targets | Faddegon |
| Gamma attenuation | Guatelli, Davis, Pandola, Dondero Mantero |
| Electron stopping power | Ivanchenko |
| Electron backscatter | Dondero, Mantero |
| Electron forward scatter | Faddegon |
| Low energy isotropic electron kernels | Incerti, Karamitros, Perrot |
| Fano cavity | Arce |
| Brachytherapy validation | Guatelli and Cutajar |
| Proton Bragg curves | Faddegon and Ramos-Méndez |
| Neutron yield from protons | Ramos-Méndez |
| Light ion Bragg curves | Geraldo, Molina, Perales |
| Carbon-12 Bragg peak fragmentation | Bolst, Guatelli, Romano |

# *Proton benchmark measurement: Water stopping power*






I-value of water of 78 eV in simulation → 80-83 eV

B.A. Faddegon, J. Shin, C.M. Castenada, J Ramos-Mendez, I.K. Daftari, "Experimental depth dose curves of a 67.5 MeV proton beam for benchmarking and validation of Monte Carlo simulation," Med. Phys. 42(7):4199-4212, 2015

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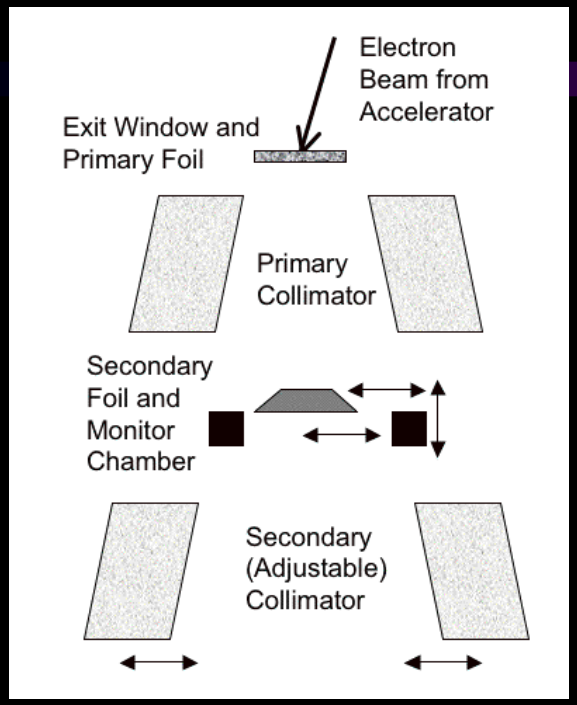
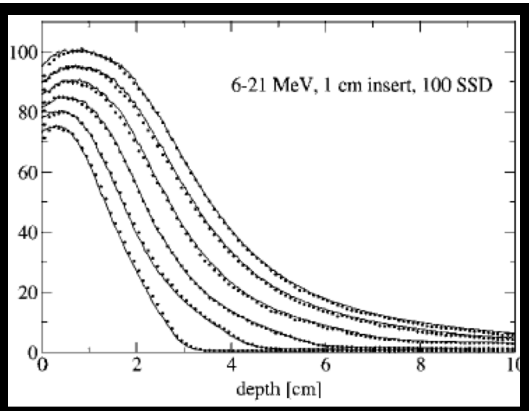
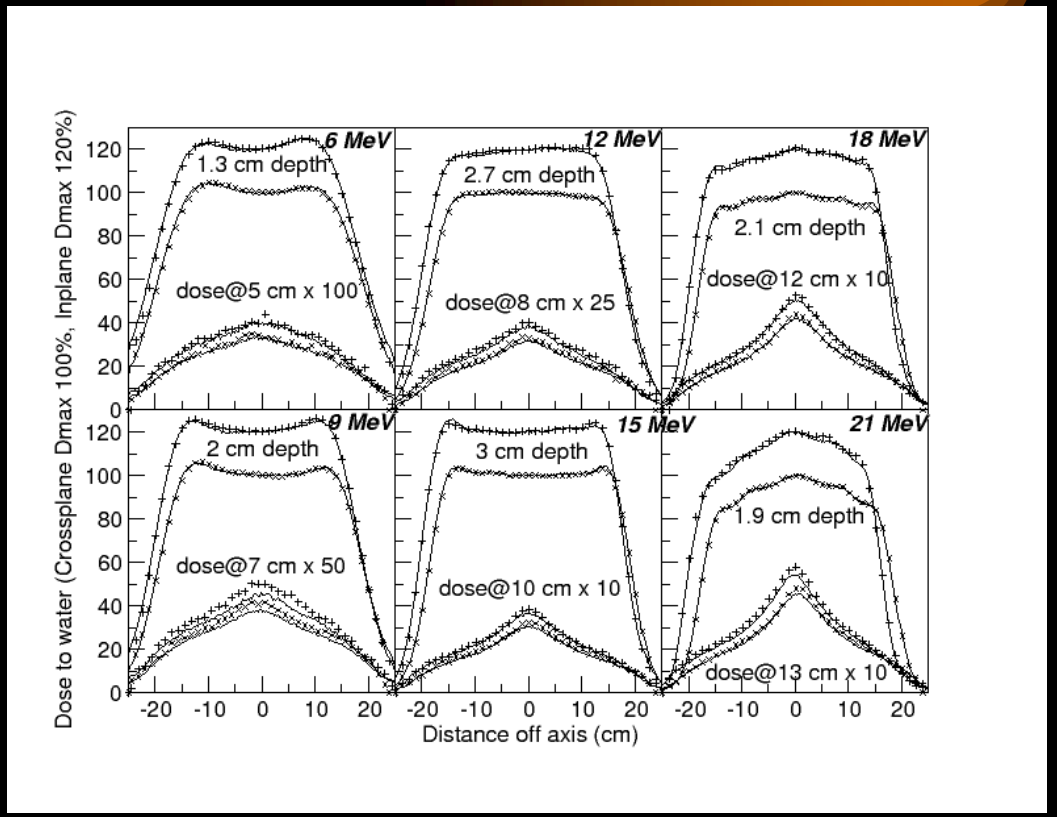
# Clinical electron beams



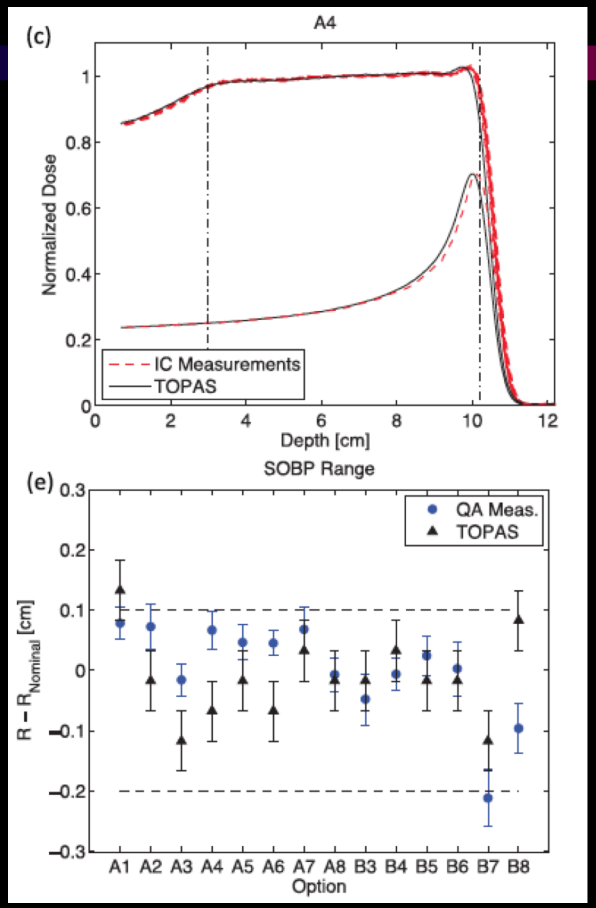



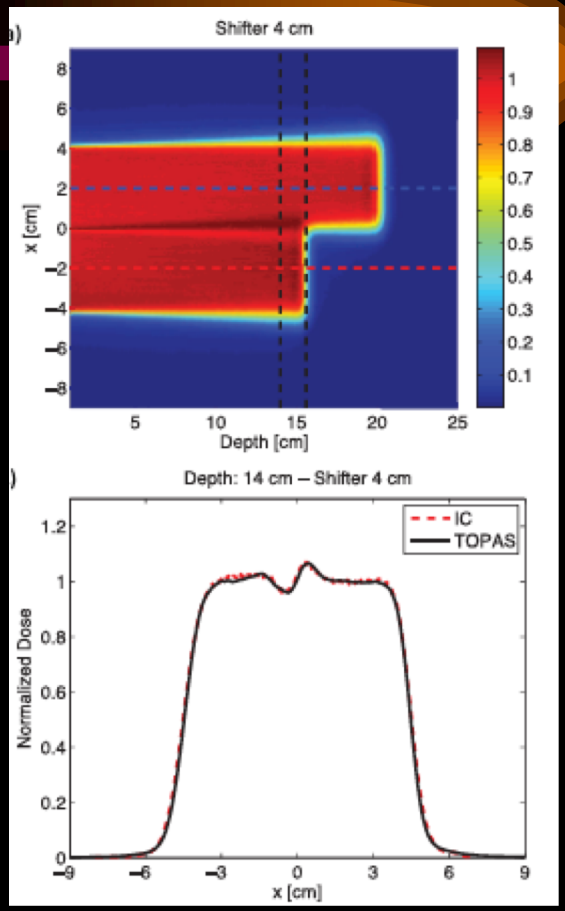




*Tuathan P O'Shea, Mark J Foley and Bruce A Faddegon, "Accounting for the fringe magnetic field from the bending magnet in a Monte Carlo accelerator treatment head simulation," Med. Phys. 38:3260-9, 2011*

# IBA double-scattering nozzle

| Option | Nominal settings for measurements of depth-dose curves | |
|---|---|---|
| | Range (cm) | Mod (cm) |
| A1 | 5.1 | 2.7 |
| A2 | 6.5 | 4.2 |
| A3 | 8.1 | 4.4 |
| A4 | 10.2 | 7.2 |
| A5 | 12.7 | 7.0 |
| A6 | 19.2 | 11.8 |
| A7 | 23.5 | 4.2 |
| A8 | 26.0 | 8.5 |
| B3 | 8.7 | 3.2 |
| B4 | 10.3 | 4.2 |
| B5 | 12.8 | 3.4 |
| B6 | 16.7 | 6.3 |
| B7 | 22.5 | 6.0 |
| B8 | 25.5 | 9 |




*M. Testa et al, "Experimental validation of the TOPAS Monte Carlo system for passive scattering proton therapy," Med Phys 40:121719 (2013)*

# *Monte Carlo simulation in medicine*

- An indispensible tool for Research, Development and Clinical Practice
- Has the accuracy needed for radiotherapy and radiology applications
  - x-rays
  - electrons
  - charged particles
- Serves as a benchmark for analytical calculations
- Complements measurement while providing exquisite detail

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# *Geant4*

- A toolkit for facilitating simulation of the transport of all types of ionizing particles using the Monte Carlo method
- Widely used and fully supported; e.g., see the Geant4 20th anniversary symposium (http://geant4.org/g420/)
  - Particle physics (SLAC, CERN, etc.)
  - Space (NASA, ESA, etc.)
  - Medicine (radiotherapy, radiology, radiation biology)
  - Material science
- Rapidly expanding use in medicine

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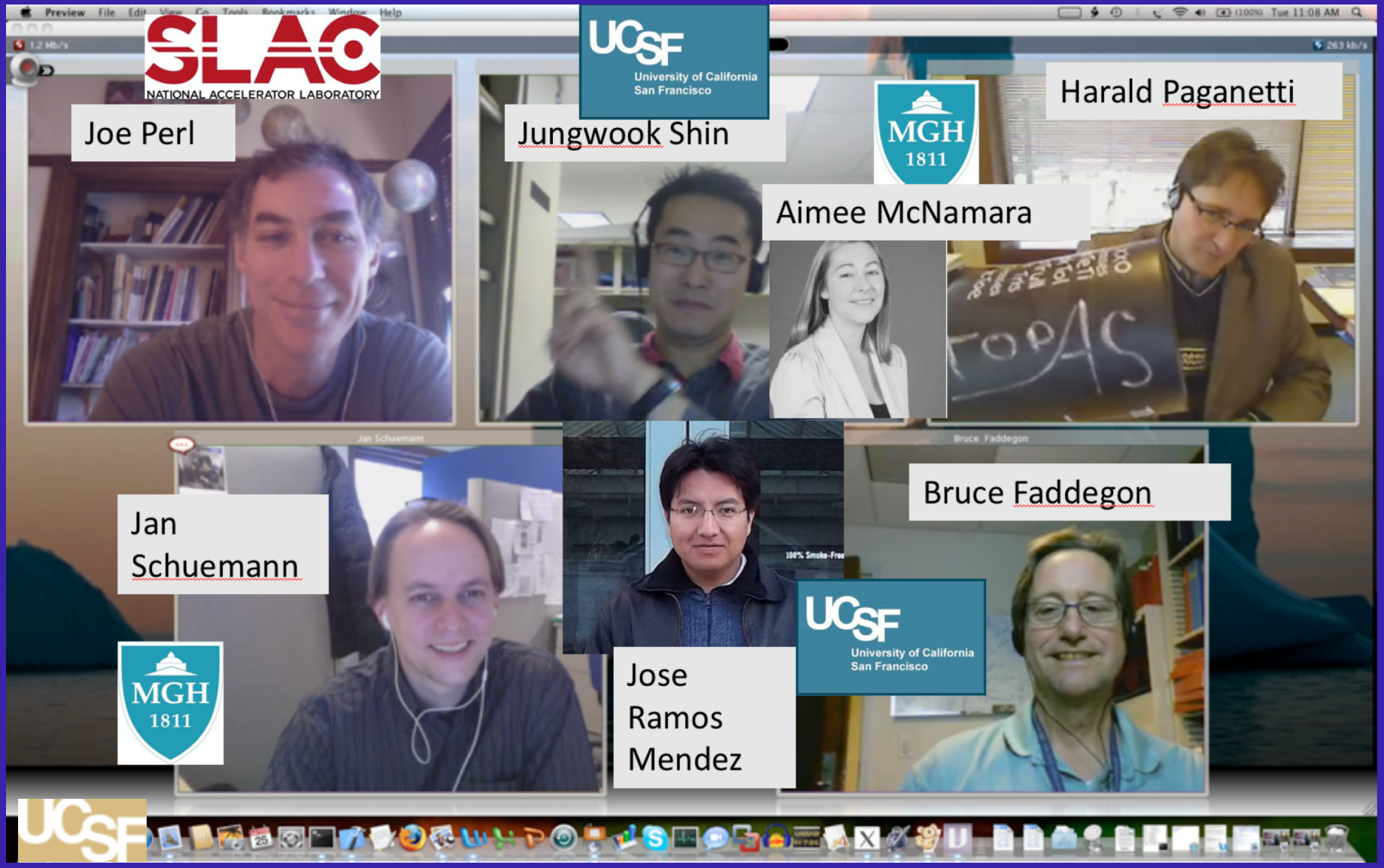
# TOPAS TOol for PArticle Simulaton: The Team



# *TOPAS:*
# *TOol for PArticle Simulation*



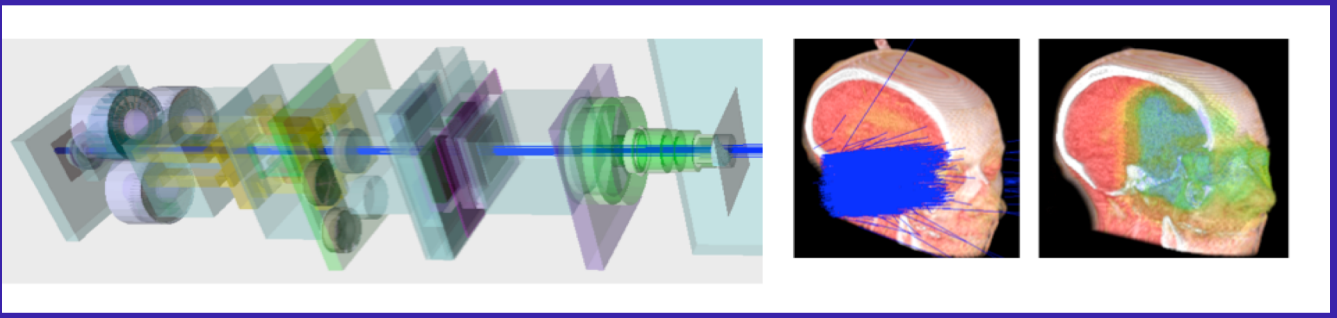

With TOPAS, a medical physicist can use Geant4 to study particle therapy without being an expert in Geant4 or computer programming.

Joseph Perl (SLAC)
Harald Paganetti (MGH)
Bruce Faddegon (UCSF)
Jan Schümann (MGH)
Jungwook Shin (UCSF)
Jose Ramos-Méndez (UCSF)
Aimee McNamara (MGH)

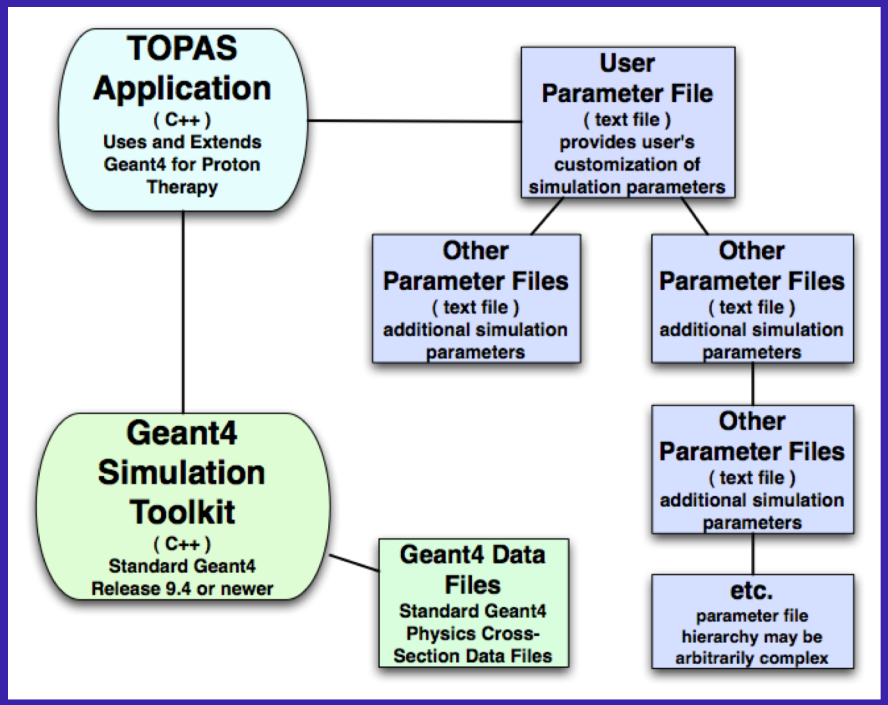
Perl et al, "TOPAS: An innovative proton Monte Carlo platform," Med. Phys. 39:6818, 2012

- Tri-university support from 2 NIH R01's over 7 years (2009-2016)
- Currently 290 users, 128 institutions, 24 countries
- TOPAS-nBio extension to TOPAS: Tri-university NIH R01 for 2015-2019
- A dozen peer-reviewed papers and counting
- General TOPAS paper (Perl et al, 2012) has 192 citations and counting

TOPAS



- Track any kind of particle through any kind of treatment head
- Import a patient
- Advanced graphics and scoring features
- Fully 4D




## Parameter Files

CHANGE PARAMETERS, NOT CODE!

s:Ge/BigBox/Material = "Air" # filling box with air

b:Ge/World/Invisible = "True"

i:Ge/Phantom2/NumberOfVoxelsX = 2

d:Ge/BigBox/HLX = 4. m

dv:Ge/RMWLexan_Brass/Angles= 4 69.11 92.29 111.04 126.02 deg

And simple ways to add, multiply, etc.:

Ge/Compensator/ZTrans =
Ge/Aperture/DistalEdge +
Ge/Compensator/HLZ mm

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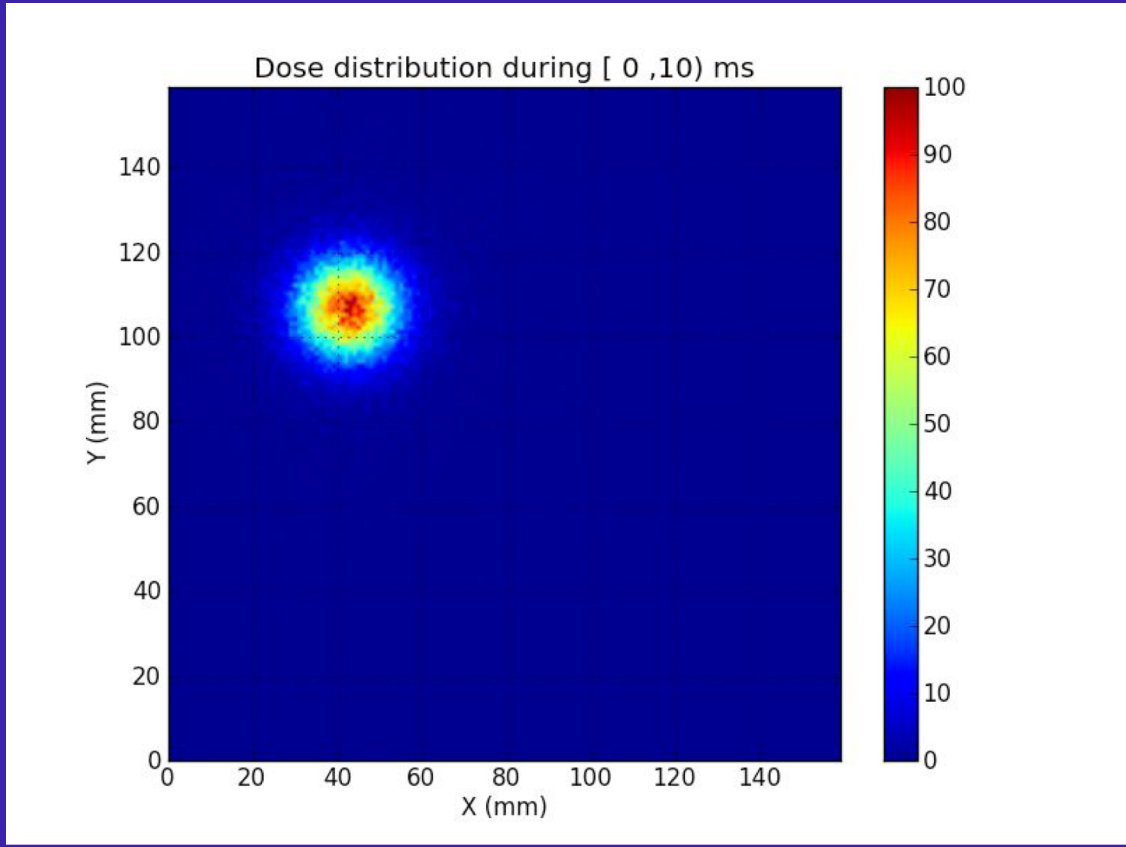
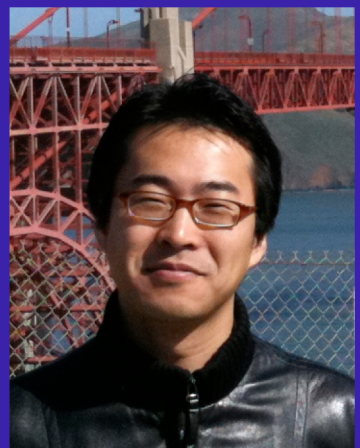
*J. Perl et al, "TOPAS: An innovative proton Monte Carlo platform," Med. Phys. 39:6818, 2012*

# Time features

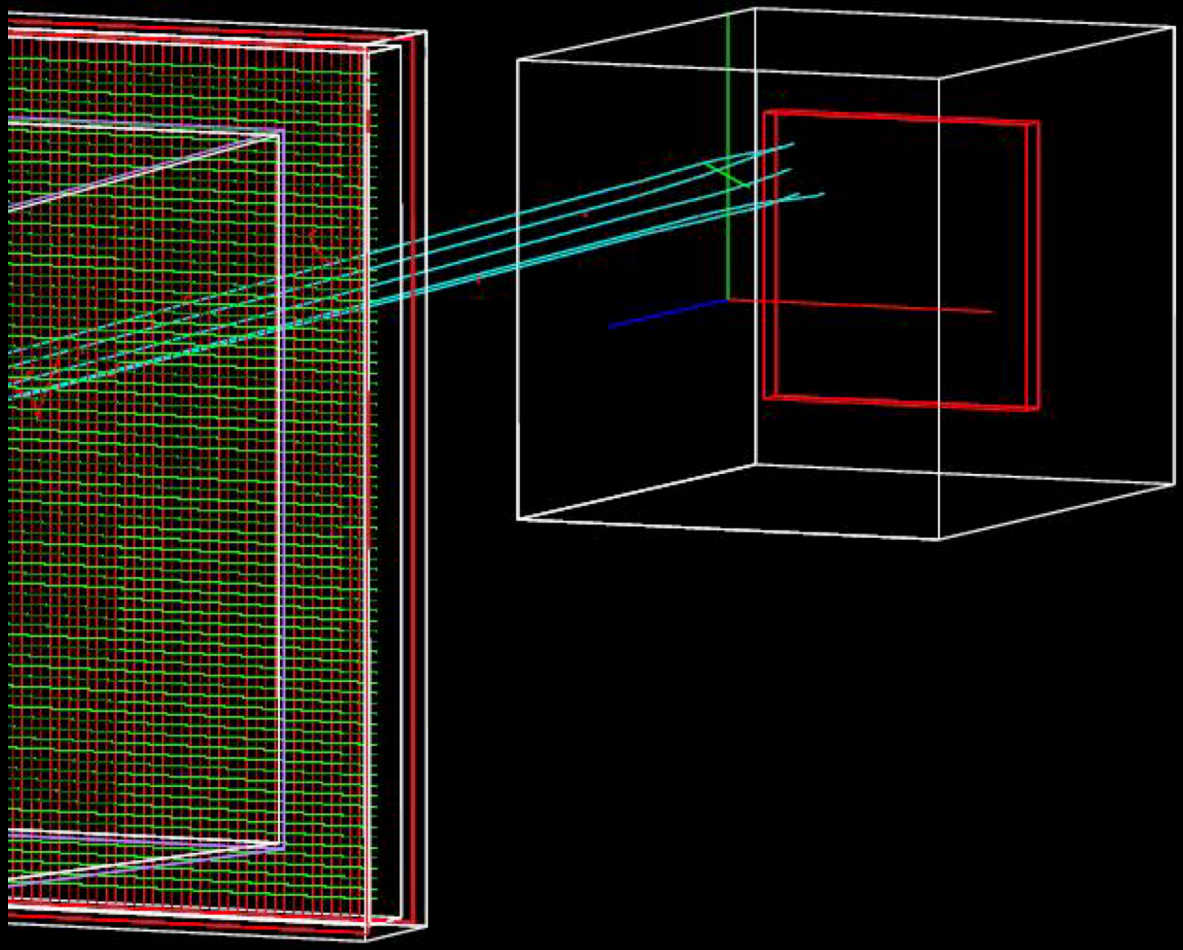



J Shin, J Perl, J Schümann, H Paganetti, and BA Faddegon, "A modular method to handle multiple time-dependent quantities in Monte Carlo simulations," Phys. Med. Biol., 57(11):3295-308, 2012



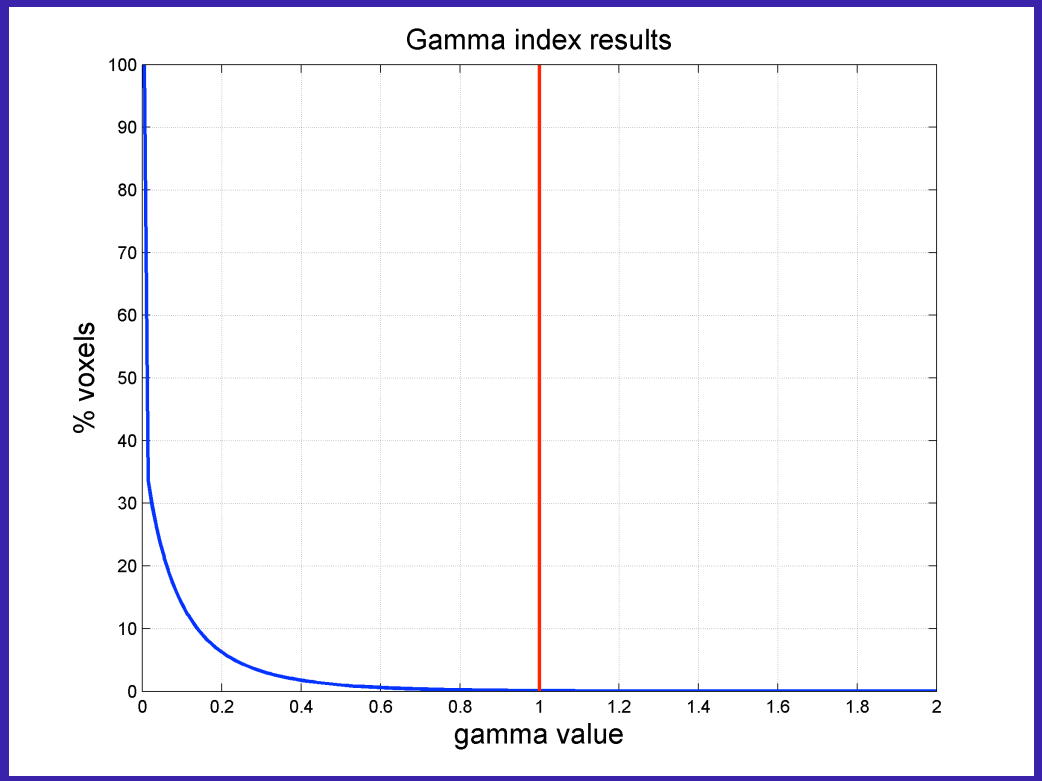
# Tracking a Moving Target

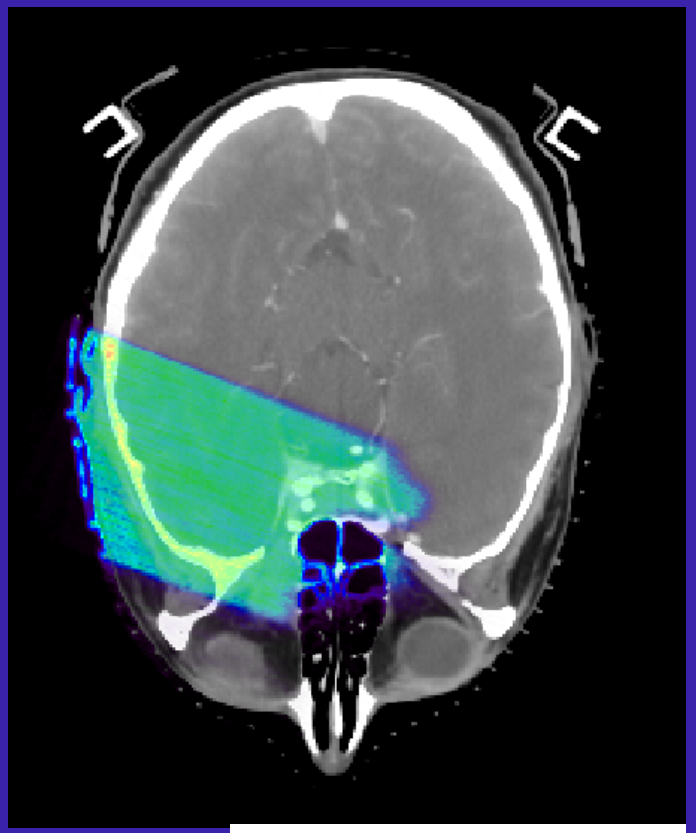
TOPAS



# Patient Dose Calculation

Energy Deposit
Gamma index for 2mm and 2%
TOPAS vs previous MGH Geant4

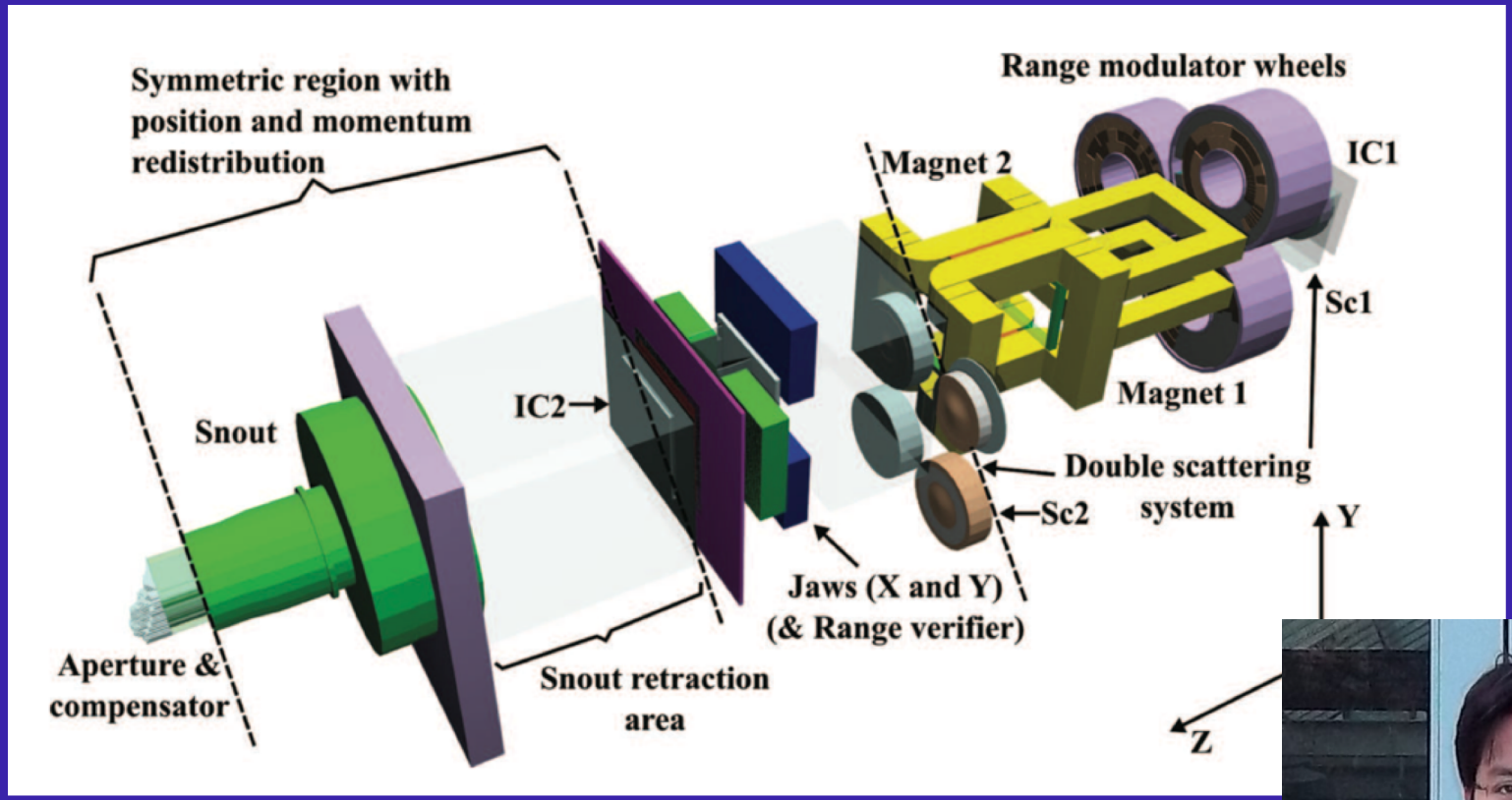


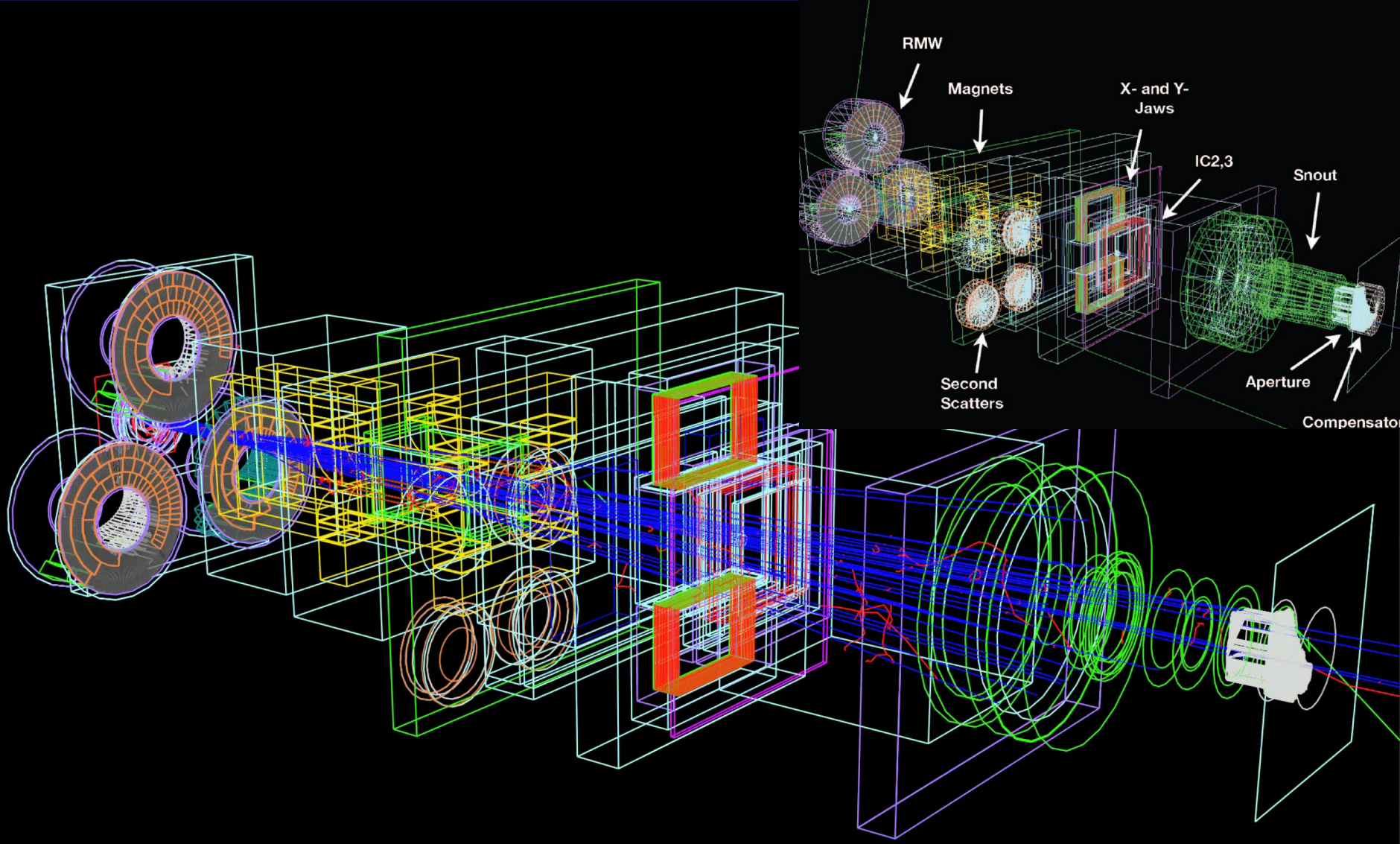
J. Schümann, H. Paganetti, J. Shin, B. Faddegon and J. Perl, "Efficient voxel navigation for proton therapy dose calculation in TOPAS and Geant4," Phys. Med. Biol., 57(11):3281-93, 2012

# Variance Reduction

Geometrical splitting with Russian Roulette




J.A. Ramos-Mendez, J. Perl, B. Faddegon, J. Schuemann, and H. Paganetti, "Geometrical splitting technique to improve the computational efficiency in Monte Carlo calculations for proton therapy," Med. Phys. 40(4):041718-1-10, 2013




IBA double-scattering nozzle at MGH

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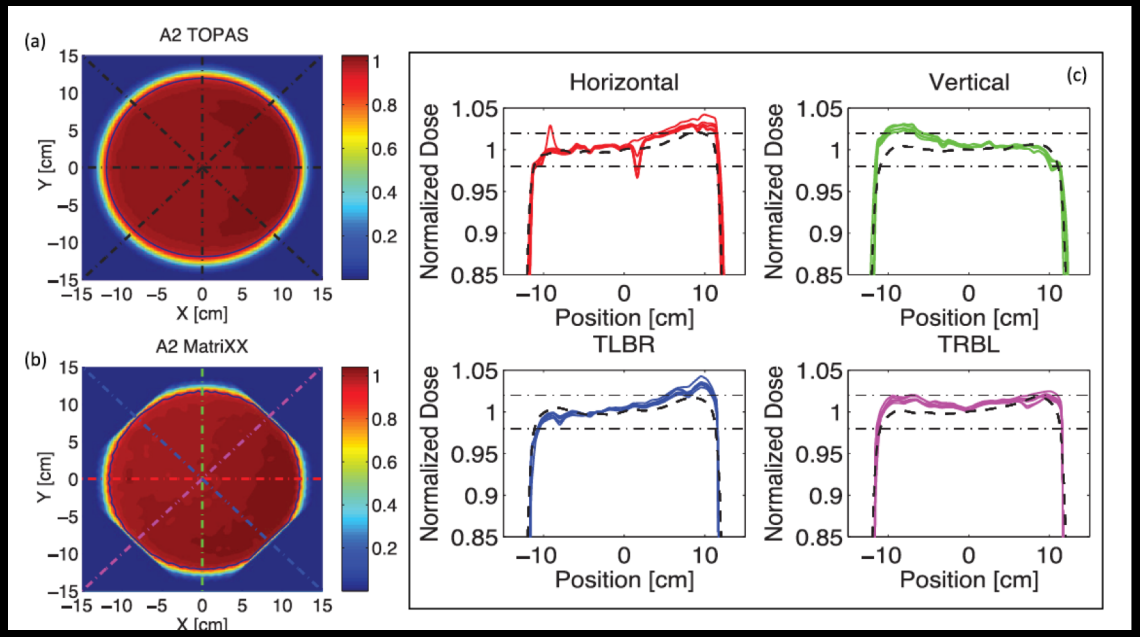
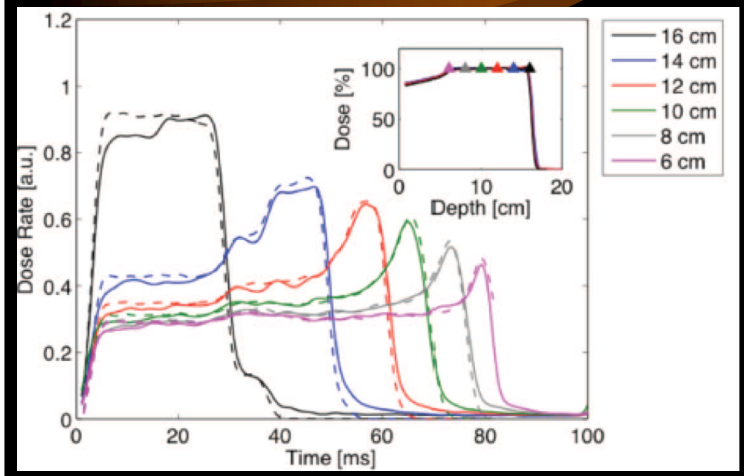
# *MGH Scattered Beam*




M. Testa, J. Schümann, H-M Lu, J. Shin, B. Faddegon, J. Perl, H. Paganetti, "Experimental validation of the TOPAS Monte Carlo system for passive scattering proton therapy", Med. Phys. 40(12):121719, 2013

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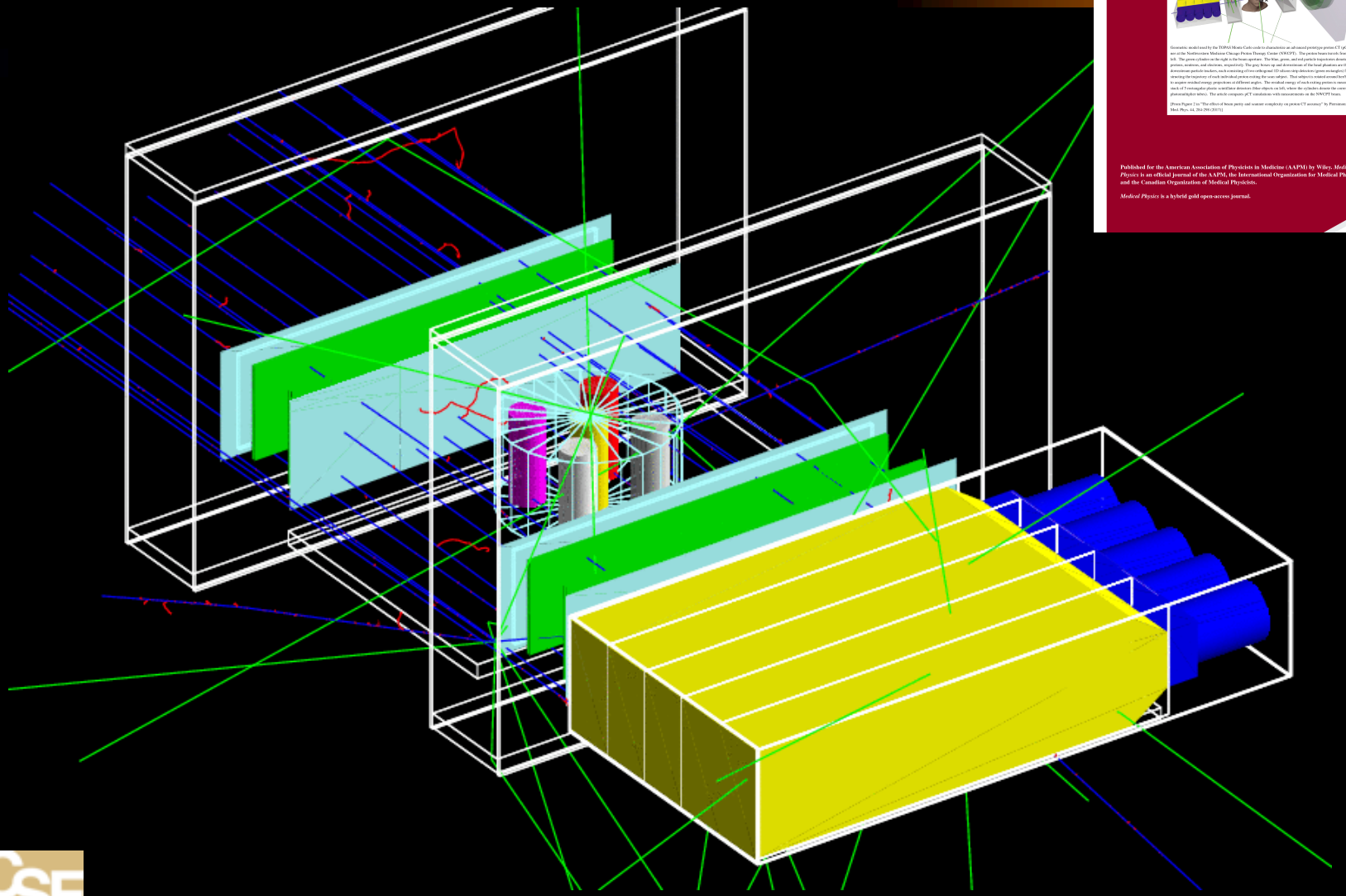
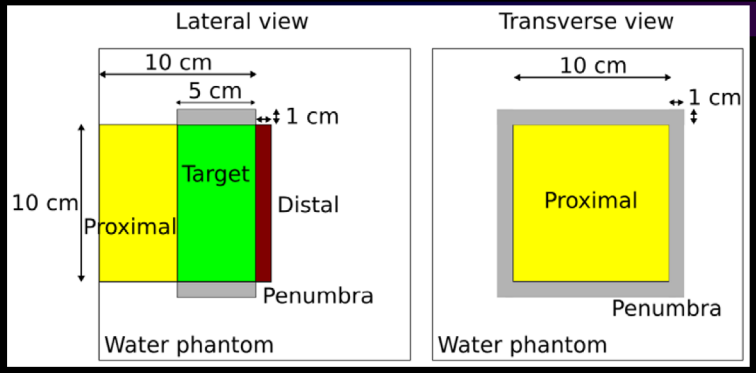
# *Particle CT: protons and helium*

# TOPAS for Organ Biology



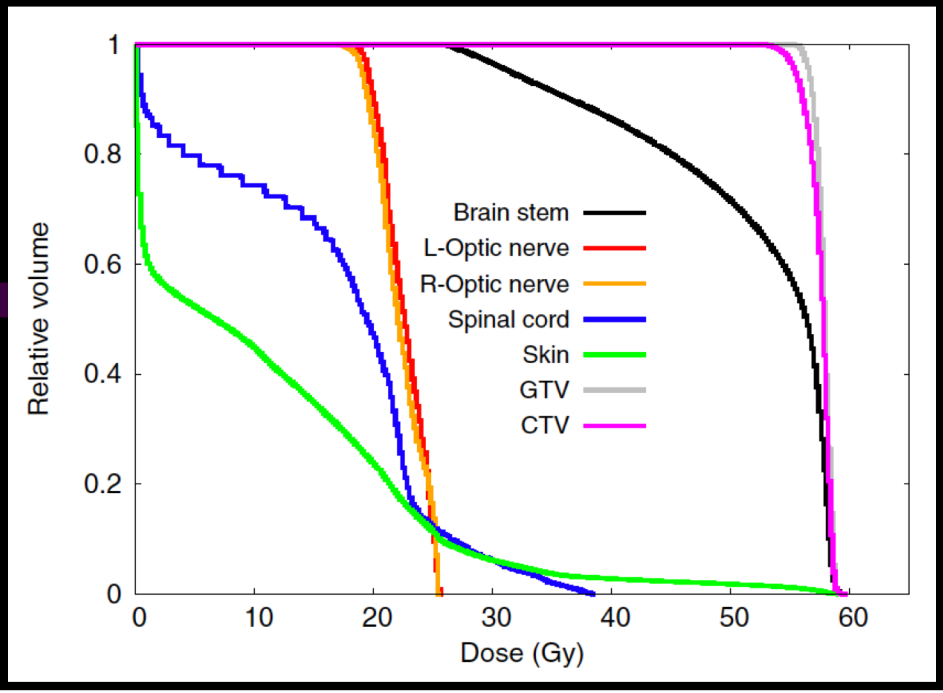




**Table 4.** NTCP, TCP and gEUD ($a = n = 1$) values per structure for proton therapy calculations.

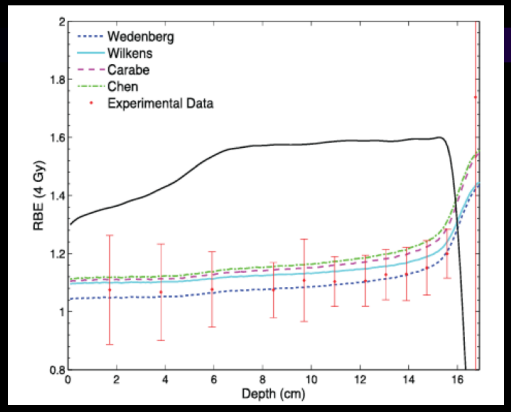
| Model | PTV | Proximal | Penumbra | Distal |
|---|---|---|---|---|
| S-Model | 46.88 (0.02) | 29.39 (0.01) | 1.15 (1.09) | 16.83 (0.28) |
| LKB with equation (4) | 44.91 (4.62) | 29.83 (2.36) | 0.04 (0.01) | 15.66 (2.20) |
| LKB without equation (4) | 47.72 (3.32) | 51.01 (2.19) | 0.48 (0.11) | 25.21 (2.32) |
| Niemierko | 45.31 (4.95) | 29.72 (3.02) | 0.32 (0.07) | 15.29 (2.40) |
| Critical volume | 50.62 (1.60) | 29.76 (0.78) | 0.12 (0.04) | 15.85 (1.99) |
| Critical element | 36.26 (0.01) | 32.23 (0.01) | 2.97 (1.09) | 4.78 (0.27) |
| Poisson (TCP) | 95.85 (0.01) | 78.73 (0.01) | Not applicable | Not applicable |
| $gEUD_{a=1}$(Gy) with equation (4) | 70.69 (1.21) | 53.95 (0.74) | 11.86 (0.30) | 24.46 (0.73) |
| $gEUD_{a=1}$ (Gy) without equation (4) | 72.63 (0.91) | 59.45 (0.61) | 14.92 (0.34) | 29.32 (0.74) |

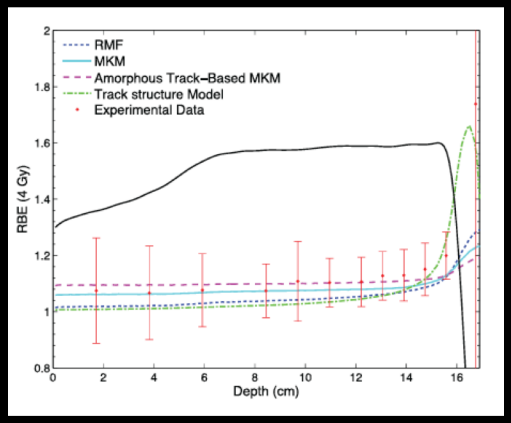
*Note:* A dose of 78 Gy in 39 fractions at the center of the SOBP. Statistical uncertainties in the parenthesis are only for the Monte Carlo calculation.

| | Brain stem | Optical nerve (left) | Optical nerve (right) | Spinal cord | Skin | CTV | GTV |
|---|---|---|---|---|---|---|---|
| S-Model | 12.30 | $1.0 \times 10^{-6}$ | $1.0 \times 10^{-6}$ | 0.0 | 0.048 | NA | NA |
| LKB with equation (4) | 9.27 | $7.17 \times 10^{-6}$ | $6.18 \times 10^{-6}$ | 0.02 | 0.004 | NA | NA |
| Niemierko | 12.10 | $5.0 \times 10^{-4}$ | $4.0 \times 10^{-4}$ | 0.06 | 0.159 | NA | NA |
| Critical volume | 6.92 | — | — | 0.17 | 0.015 | NA | NA |
| Critical element | 12.30 | $1.0 \times 10^{-6}$ | $1.0 \times 10^{-6}$ | 0.0 | 0.093 | NA | NA |
| $gEUD_{a=1}$ (Gy) | 49.30 | 16.88 | 16.58 | 12.31 | 8.211 | 57.41 | 57.74 |
| Poisson (TCP) | NA | NA | NA | NA | NA | 69.72 | 71.08 |

Ramos-Méndez, Jose; Perl, Joseph; Schuemann, Jan; Shin, Jungwook; Paganetti, Harald; Faddegon, Bruce, "A framework for implementation of organ effect models in TOPAS with benchmarks extended to proton therapy," Phys Med Biol. 60(13): 5037-5052, 2015

# *TOPAS for Cell Biology*

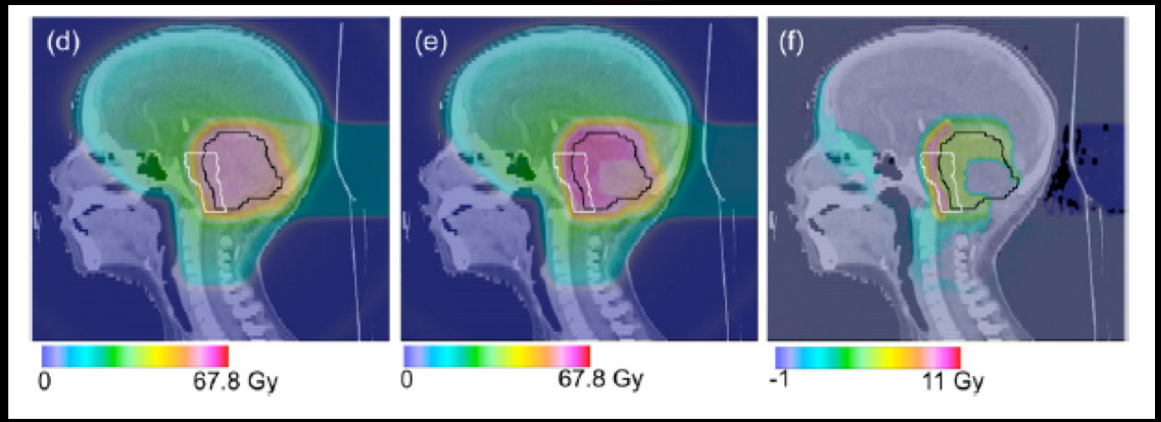



RBE=1.1

RBE of Wedenberg et al

Difference




Lisa Polster, Jan Schuemann, Ilaria Rinaldi, Lucas Burigo, Aimee Louise McNamara, Robert D Stewart, Andrea Attili, David J. Carlson, Alejandro Carabe-Fernadez, Bruce Faddegon, Joseph Perl, and Harald Paganetti, "Extension of TOPAS for the simulation of proton radiation on molecular and cellular endpoints," Phys Med Biol. 2015 Jun 10;60(13):5053-5070

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# *TOPAS-nBio extension to TOPAS*

- Track structure code (Geant4)
- Geant4-DNA for low energy physics and for chemistry
- Complex geometries of cells and cellular components
- Chemistry

Slides from Sebastien Incerti

Fully included in Geant4

# *Geant4-DNA from the Internet*

A unique web site for Geant4-DNA: http://geant4-dna.org

## The Geant4-DNA project

Extending the Geant4 Monte Carlo simulation toolkit for radiobiology

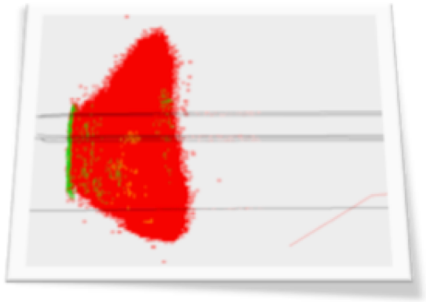
Geant4-DNA | Software | Physics | Chemistry | Examples & tutorials | Publications | Collaboration | Funding

Welcome to the Internet page of the **Geant4-DNA project**.

The Geant4 Monte Carlo simulation toolkit is being extended with processes for the **modeling of early biological damages induced by ionising radiation at the DNA scale**. Such developments are on-going in the framework of the Geant4-DNA project, originally initiated by the European Space Agency/ESTEC.

**On-going** developments include

- **Physics** processes in liquid water and other biological materials
- **Physico-chemistry** and **chemistry** processes for water radiolysis
- Molecular **geometries**
- Quantification of **damage** (such as single-strand, double-strand breaks, ...)



Recent posts

Check-out our new movie in the **Chemistry** section !

The last Geant4 release (10.0+P01) is available for download, see our **Software** section.

A new advanced example, dnageometry, is available, see our **Examples & tutorials** section.

PhD theses by the Geant4-DNA collaboration are listed in the **Publications** section.

© The Geant4-DNA collaboration - **Contact us**

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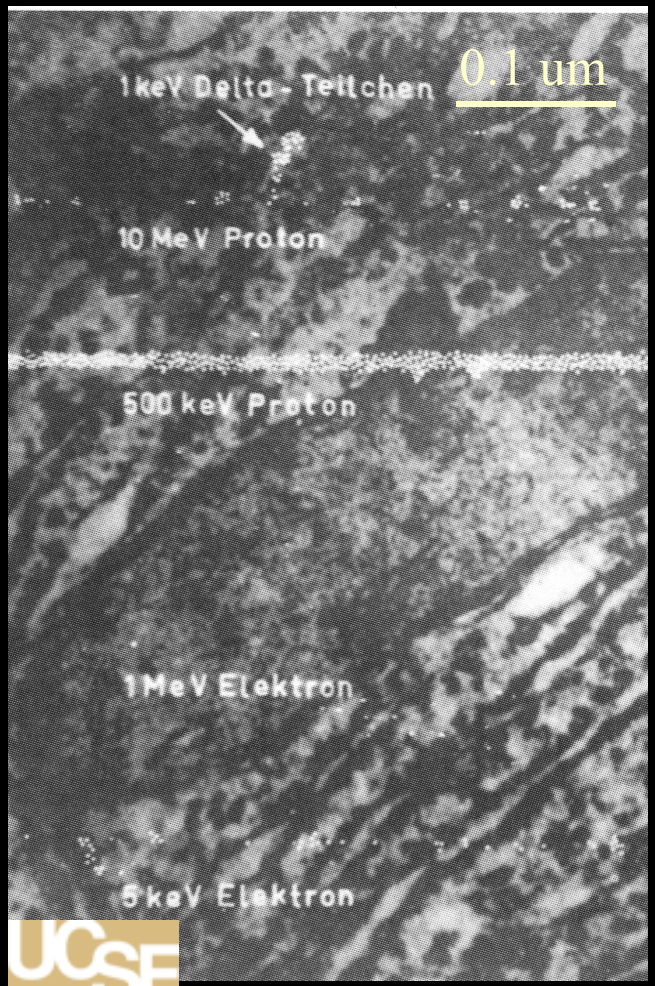
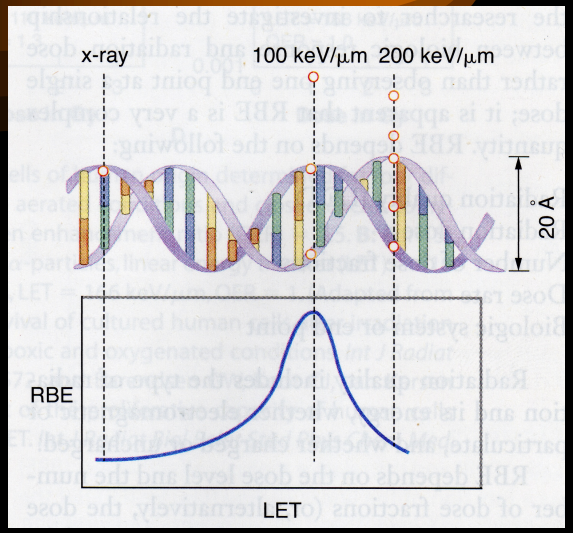
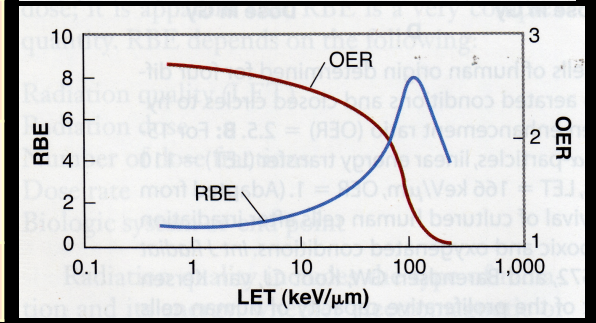
# *Linear energy transfer and relative biological effect*



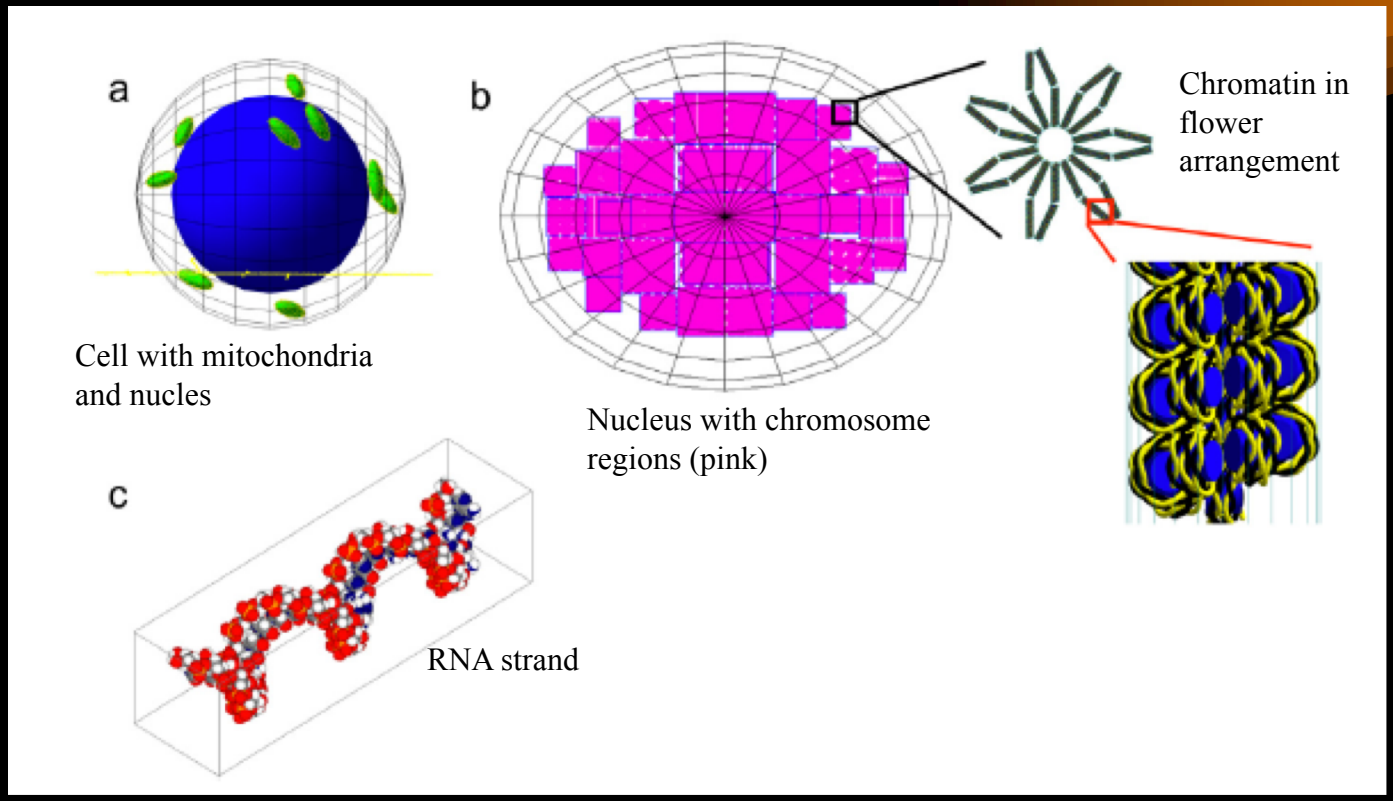

| Radiation | LET (keV/um) |
|---|---|
| $^{60}$Co | 0.2 |
| 250 kV x-rays | 2.0 |
| 10 MeV protons | 4.7 |
| 150 MeV protons | 0.5 |
| 14 MeV neutrons | 12-100 |
| 2.5 MeV alphas | 166 |
| 2 GeV Fe ions | 1000 |



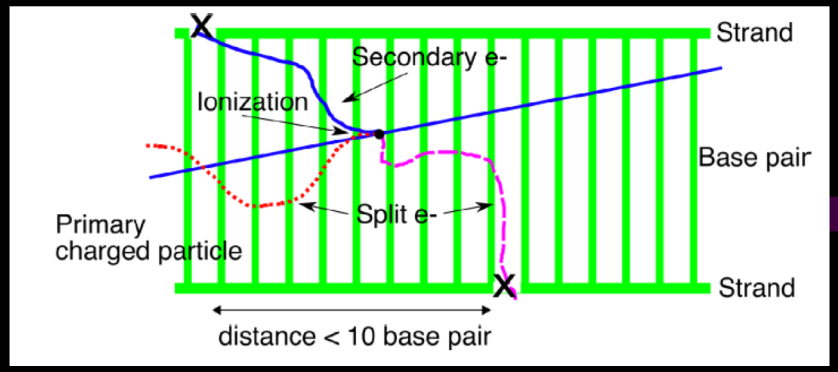

$RBE = D_{xray}/D_{particle}$ for same survival

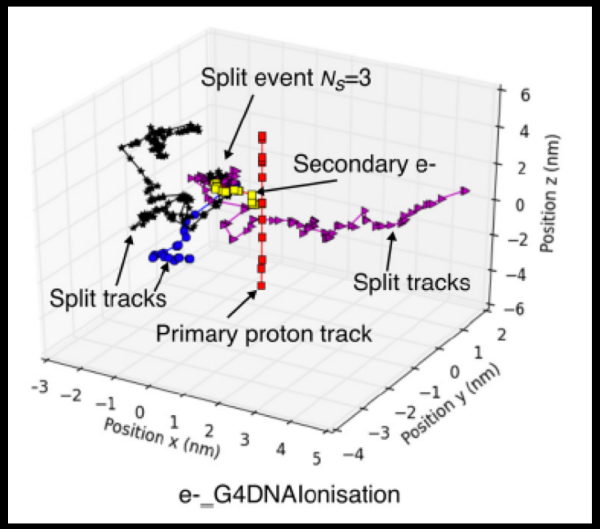
# *TOPAS-nBio complex geometry*

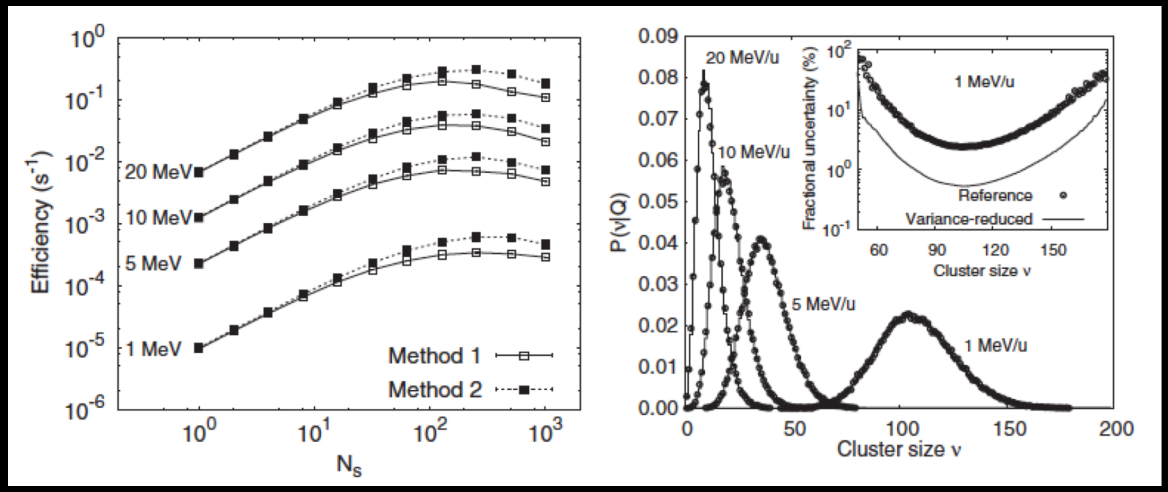



Aimee McNamara, Robert Turner, Joseph Perl, Jose Ramos Mendez, Pierluigi Piersimoni, Harald Paganetti, Kathryn Held, Bruce Faddegon and Jan Schuemann, "Validation of the radiobiology toolkit TOPAS-nBio in simple DNA geometries," Physica Medica 33:207-215, 2017

# TOPAS-nBio
# Track structure

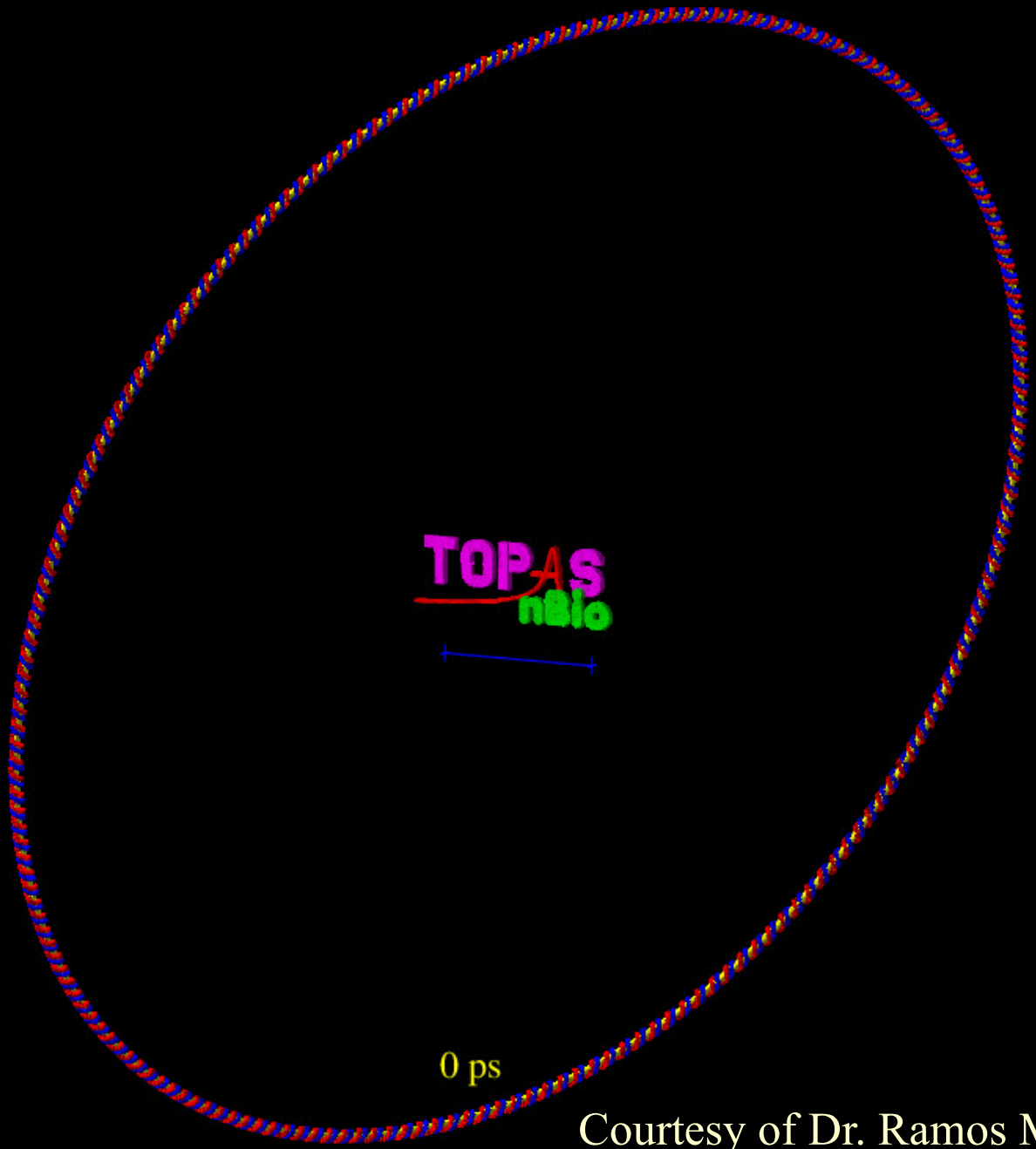



José Ramos-Méndez, Jan Schuemann, Sebastien Incerti, Harald Paganetti, Reinhard Schulte and Bruce Faddegon, "Flagged uniform particle splitting for variance reduction in proton and carbon iontrack-structure simulations," Phy Med Biol 62: 5908-5925, 2017

UCSF




Courtesy of Dr. Ramos Mendez

# *TOPAS U24*

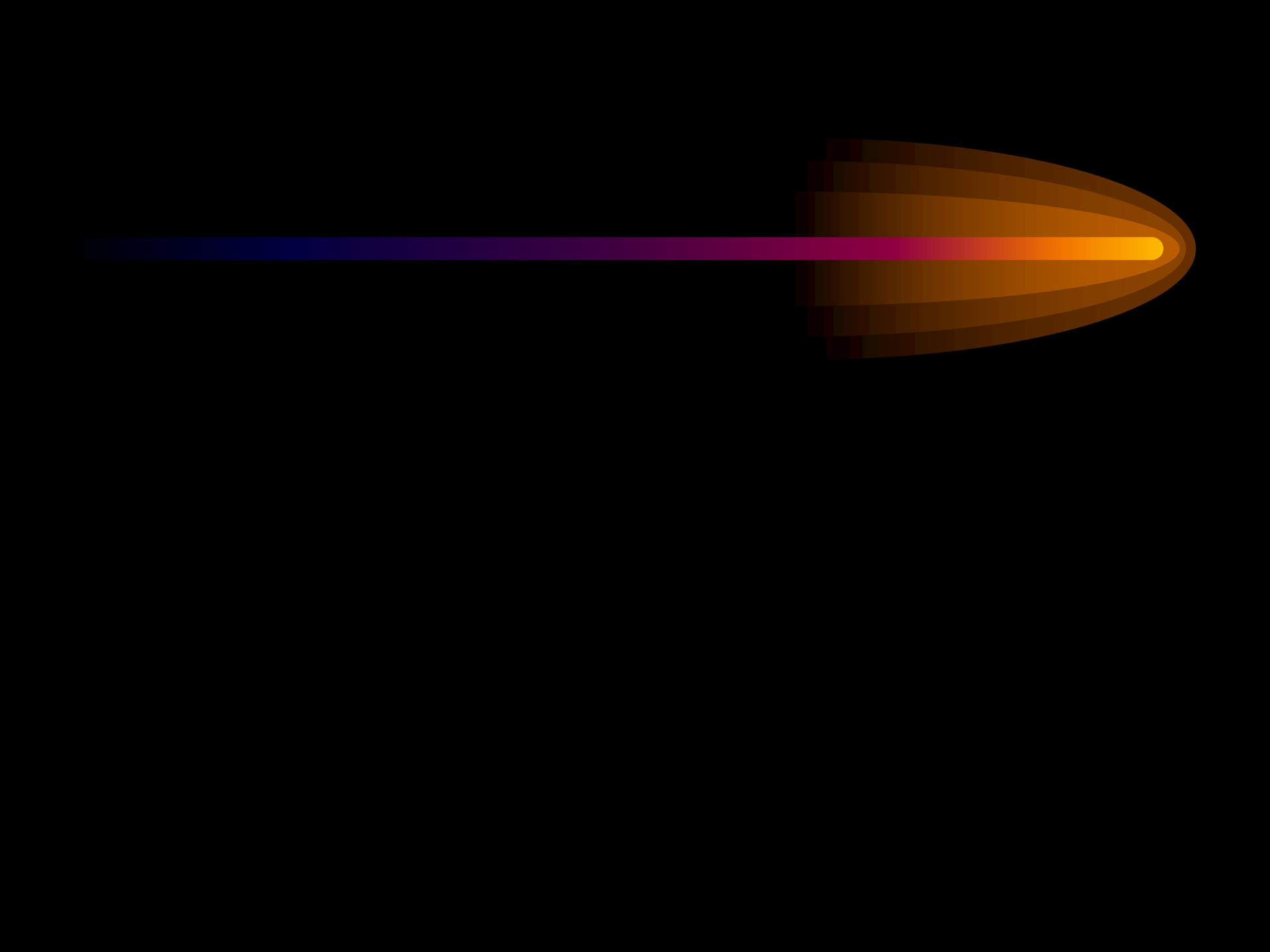
- Advanced simulation accessible for all medical applications of ionizing radiation
- Specific Aims
  1. **Enhance the TOPAS Environment for User-Friendly Interactive Modeling and Simulation**
  2. **Extend TOPAS Capabilities for Translational and Clinical Applications**
  3. **Maintain TOPAS for all User Communities**
  4. **Disseminate TOPAS with Full Participation in ITCR Program Activities**

UCSF

# *TOPAS/TOPAS-nBio consortium*

- UCSF: Bruce Faddegon, Jose Ramos Mendez, Jungwook Shin (now at MGH)
- MGH: Harald Paganetti, Jan Schuemann, Aimee McNamara
- SLAC: Joseph Perl





# *Enhance the TOPAS Environment for User-Friendly Interactive Modeling and Simulation*

- Expand support for multi-processor, cluster, cloud and grid environments
- Improve I/O compatibility with other medical physics standards, tools, databases and file-sharing resources, automate interfacing between treatment planning systems and TOPAS, improve CAD support
- Improve computational speed through improvements to physics algorithms, variance reduction, bridging to external GPU MC libraries, improved math libraries and automated decision of simulation completion
- Continuously improve the Graphical User Interface including and expand options for 3D and 4D graphics export

# *Extend TOPAS Capabilities for Translational and Clinical Applications*

- TOPAS for Radiotherapy:
  Expand library of components, simplify setup of complex therapy simulations, QA and shielding calculations
- TOPAS for Biology:
  Expand and enhance biological modeling capabilities, extend to pre-clinical research
- TOPAS for Imaging with Detector System Developments:
  In-room PET including time of flight, prompt gamma, proton CT and standard in-room imaging
- TOPAS for Patient and Phantom Simulations:
  Incorporate NURB-segmented, digital human phantoms covering the range of age, gender and size, and
  expand existing 4D CT handling to incorporate deformation vectors

## *Maintain TOPAS for all User Communities*

- Respond to changes in underlying software packages and operating systems
- Expand automated regression testing system for quality control, incorporating key x-ray and electron benchmarks

# *Disseminate TOPAS with Full Participation in ITCR Program Activities*

- Disseminate TOPAS through workshops and web site with the whole TOPAS source code released the final year
- Provide user support through online user forum, web-based training and twice-yearly in-person training courses, adapted in the final year to include in depth training in the TOPAS source code, including the intricate core
- Develop TOPAS through Collaboration:
  Maintain depository for users to exchange customizations and extensions, and
  Collaborate with users on high value projects to address key user needs identified post-award
- Incorporate the highest level of ITCR compatibility, including moving TOPAS to open source