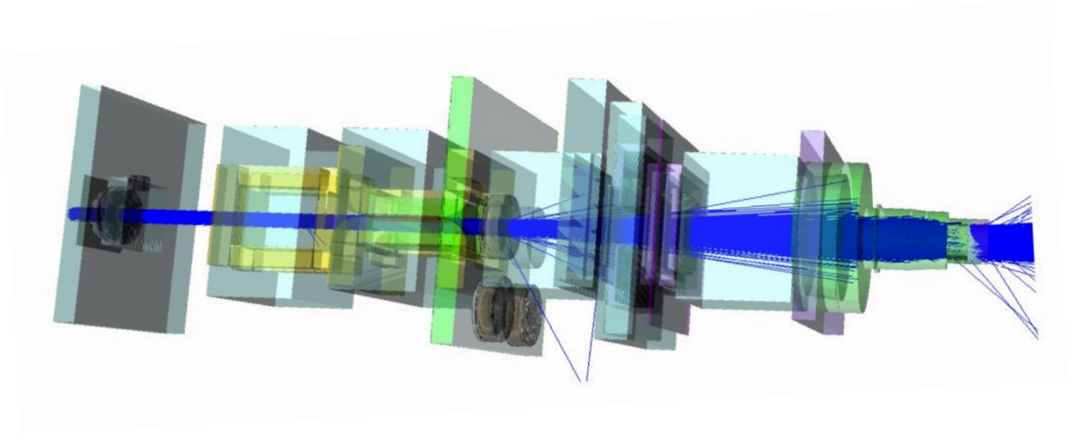
Monte Carlo simulations for research as well as clinical support in proton therapy



MASSACHUSETTS GENERAL HOSPITAL
RADIATION ONCOLOGY

HARVARD MEDICAL SCHOOL

Harald Paganetti PhD

Professor of Radiation Oncology, Harvard Medical School
Director of Physics Research, Massachusetts General Hospital, Department of Radiation Oncology

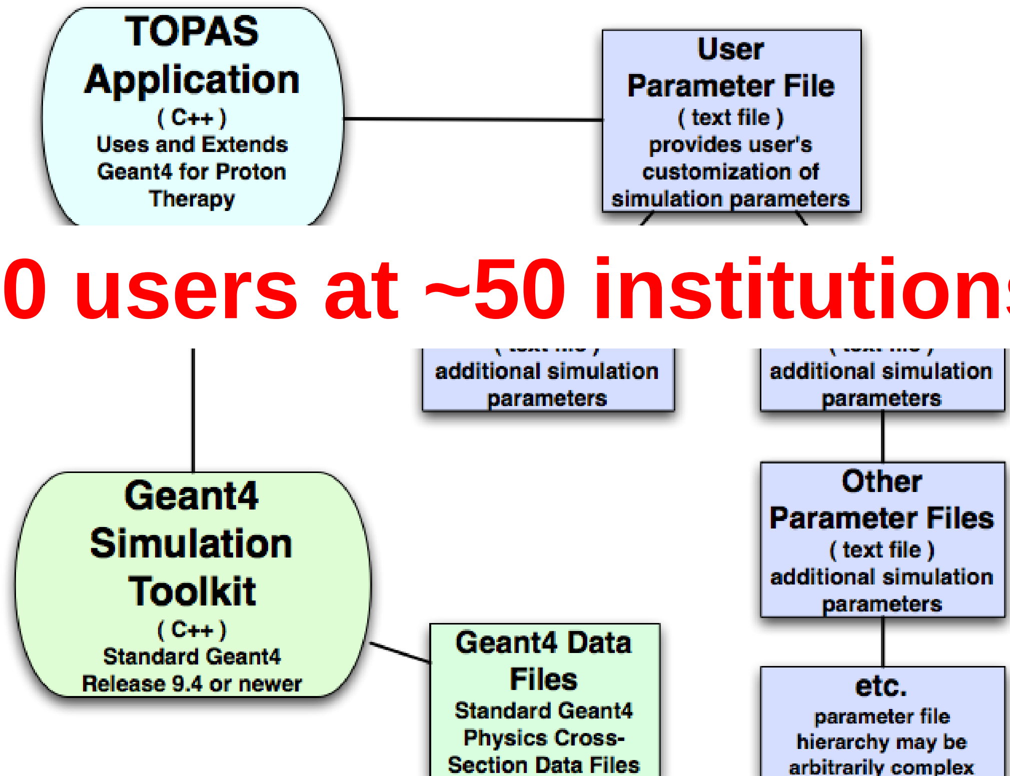
Monte Carlo tools

Versatile

Limited functionality

Tasks

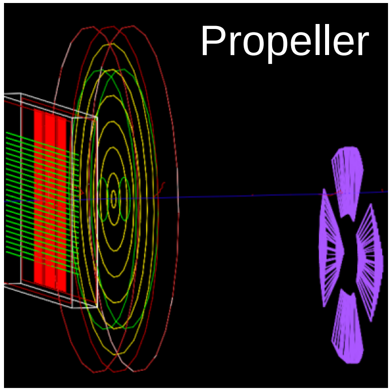
Tool for Particle Simulation

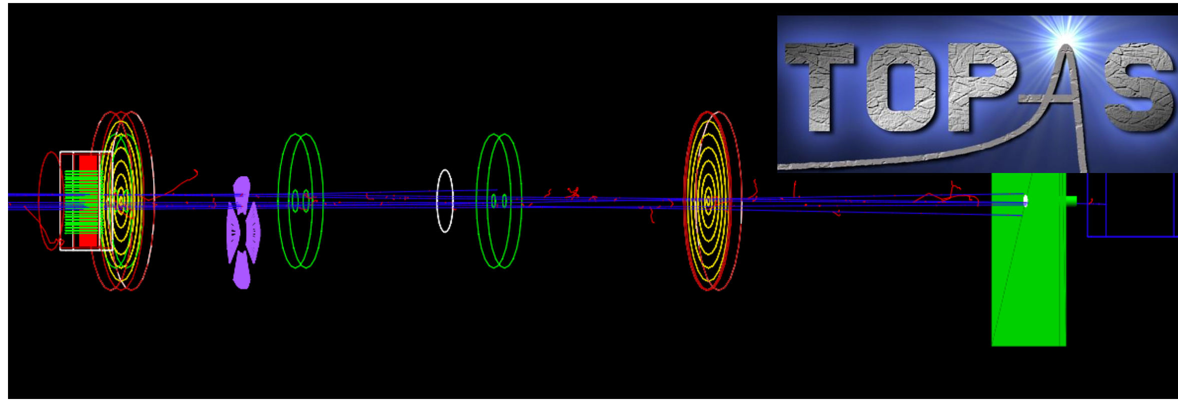


~150 users at ~50 institutions

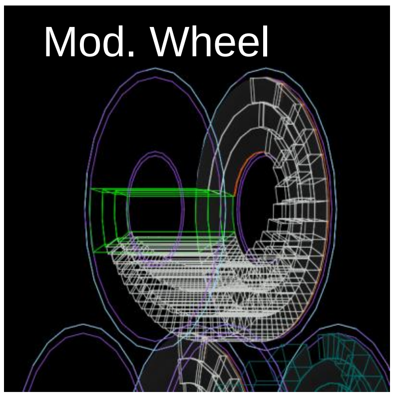
Perl J; Shin J; Schuemann S; Faddegon BA and Paganetti H: TOPAS - An innovative proton Monte Carlo platform for research and clinical applications. Medical Physics 2012 39: 6818-6837

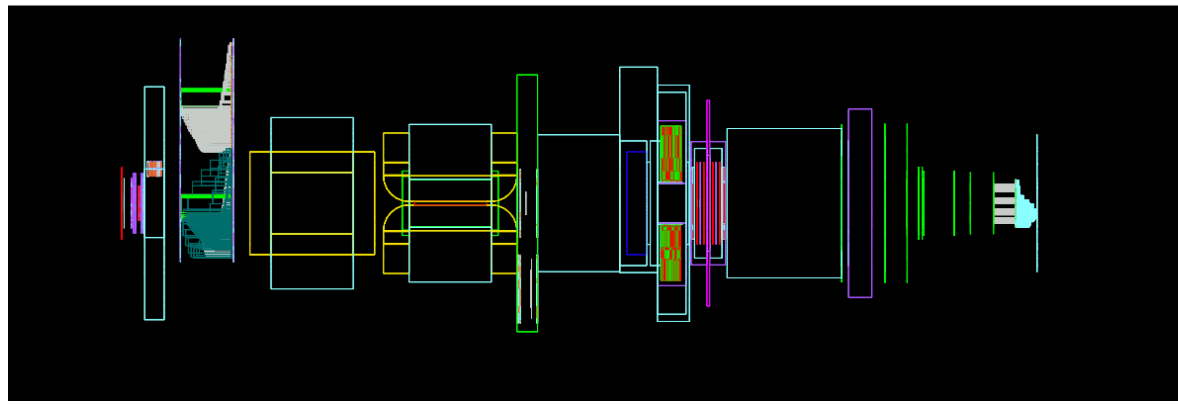
UC Davis eye treatment delivery system



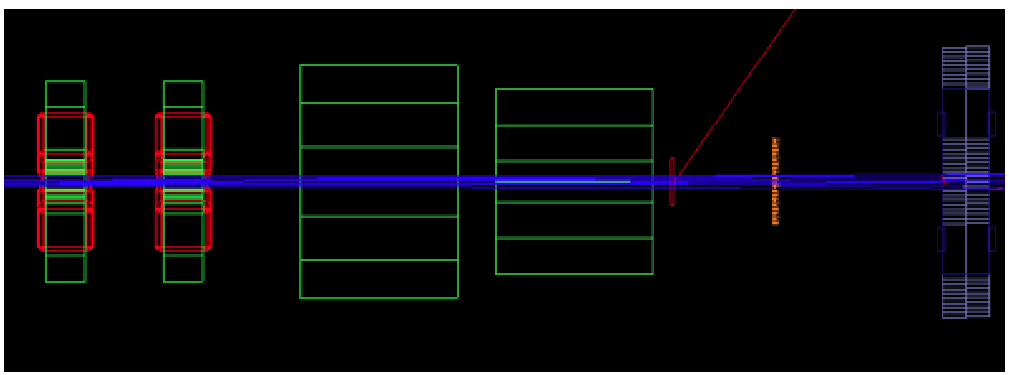


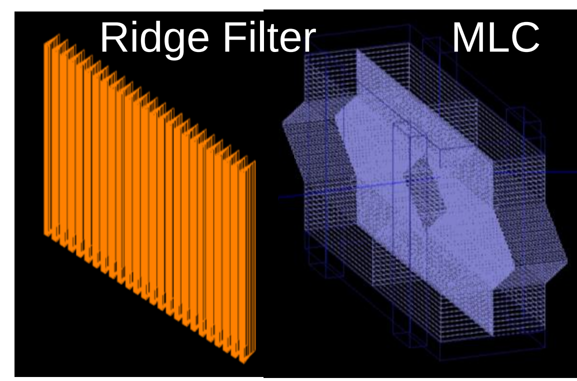
MGH gantry treatment delivery system





Samsung Medical Center





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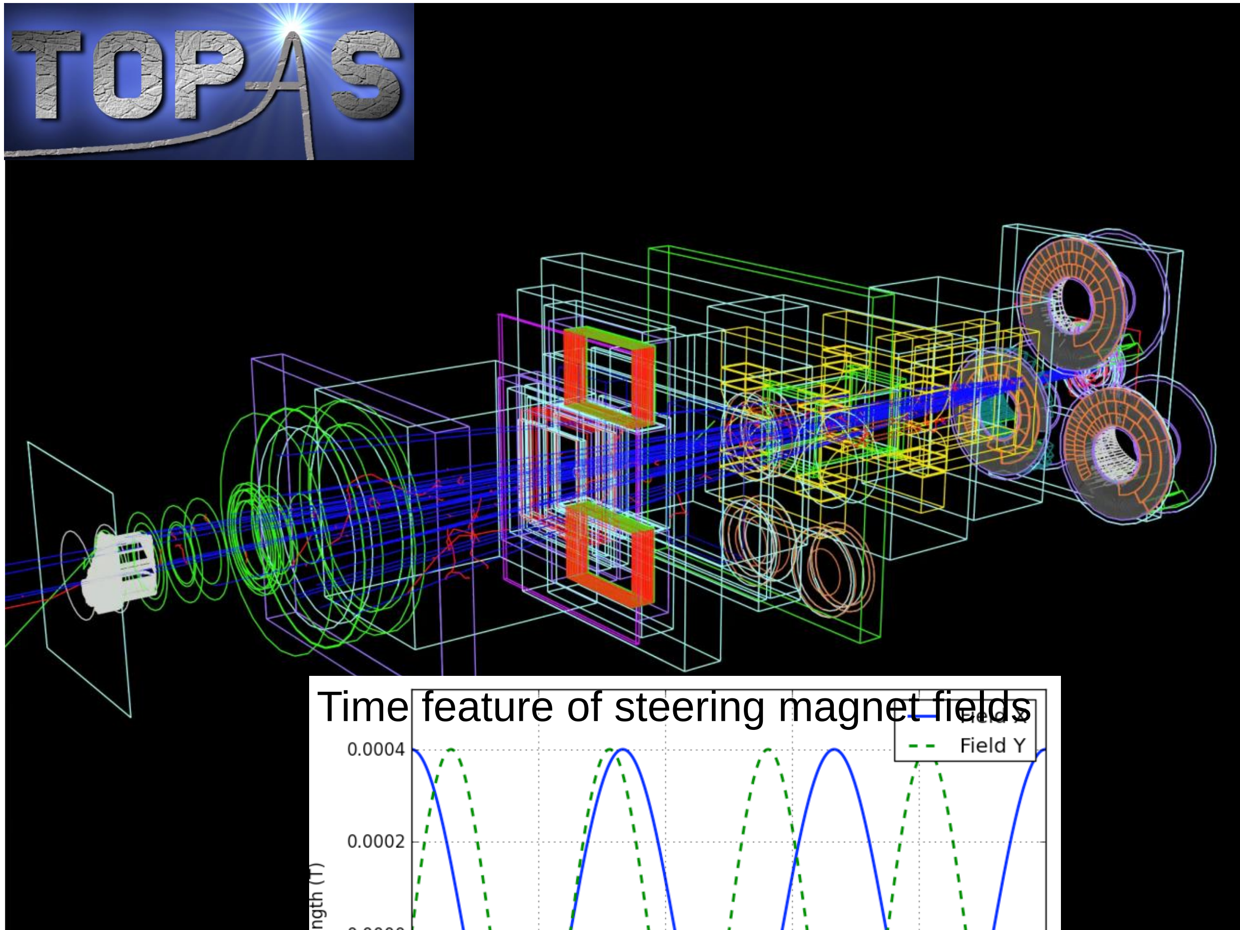
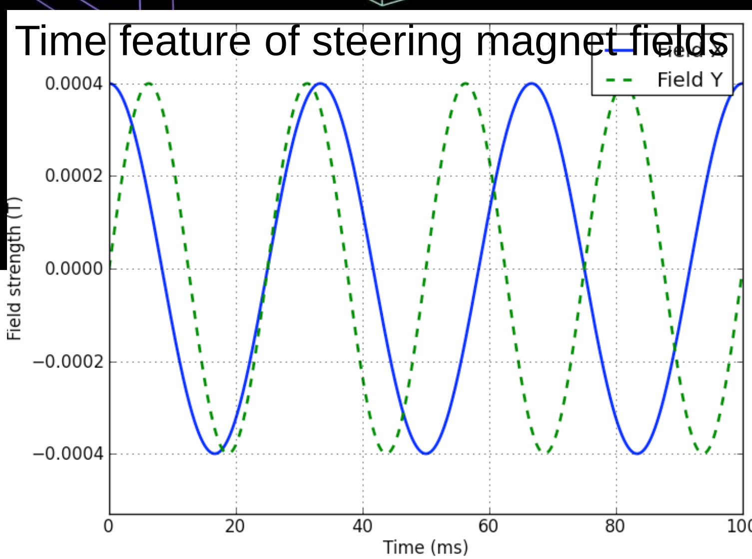
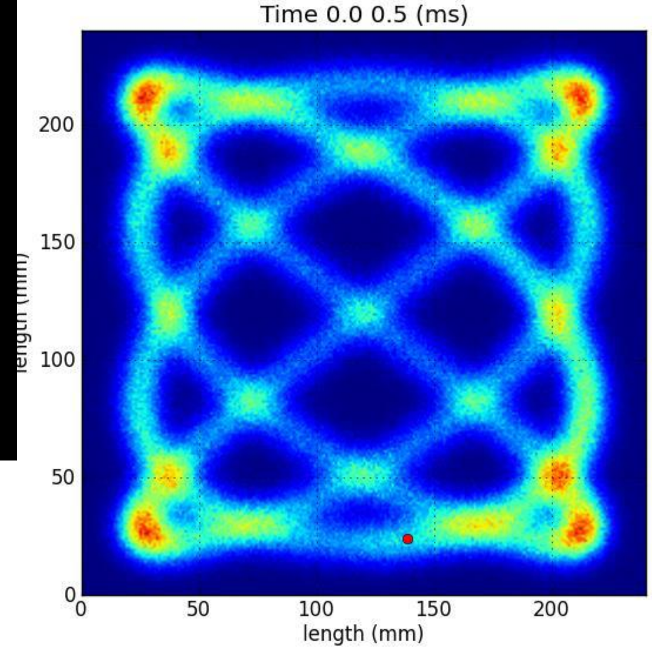


Time feature of steering magnet fields

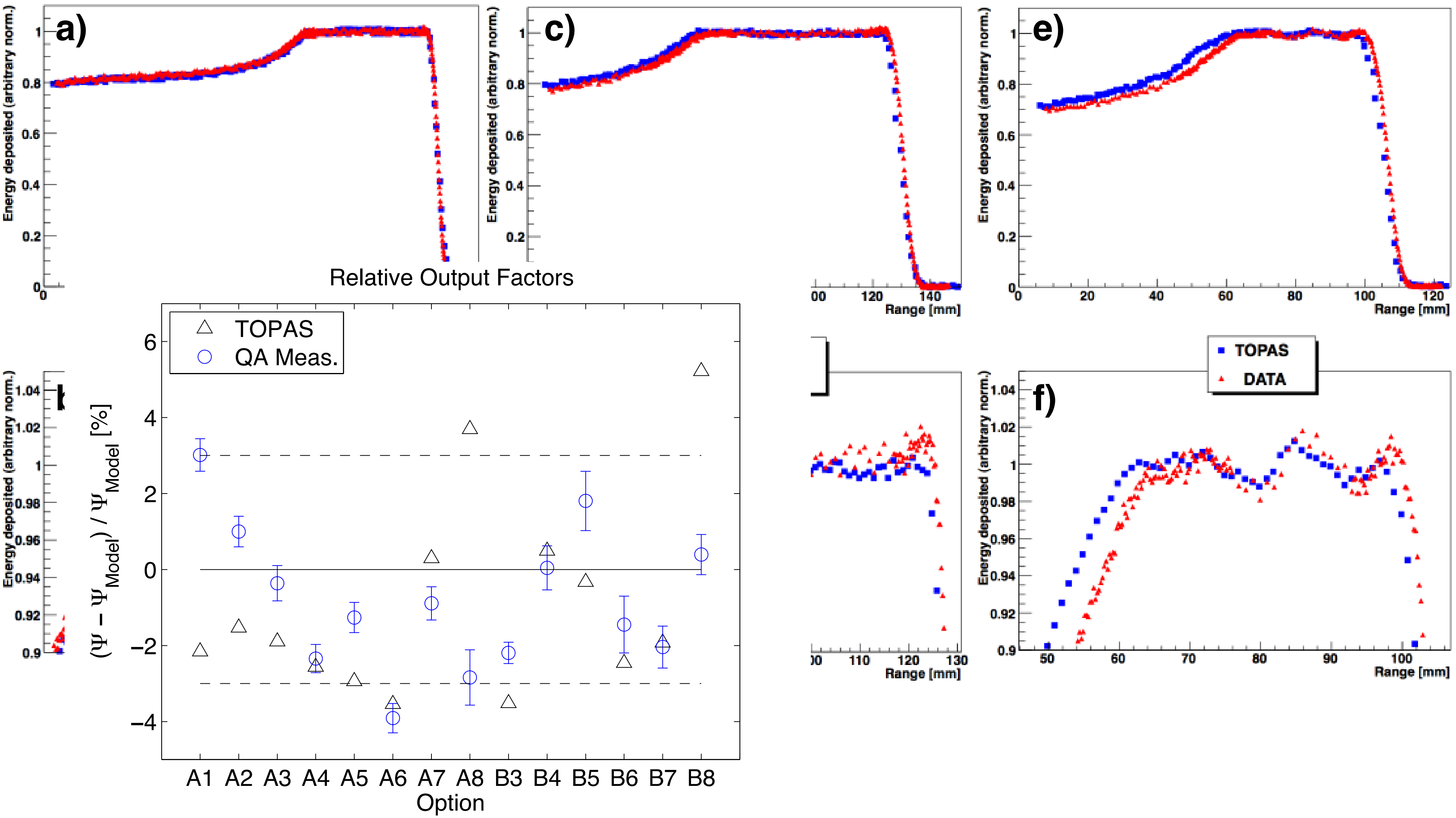


Points of every 0.5 ms



Shin J; Perl J; Schuemann S; Paganetti H and Faddegon BA: A modular method to handle multiple time-dependent quantities in Monte Carlo simulations. Physics in Medicine and Biology 2012 57: 3295-3308

Validation



Testa M; Schümann J; Lu H-M; Shin J; Faddegon B; Perl J and Paganetti H: Experimental validation of the TOPAS Monte Carlo system for proton therapy simulations. Medical Physics 2013 40: 121719

Monte Carlo tools

Versatile

Limited functionality

gPMC

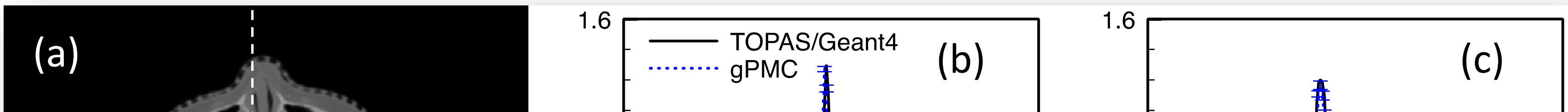
UT SOUTHWESTERN MEDICAL CENTER

MGH 1811

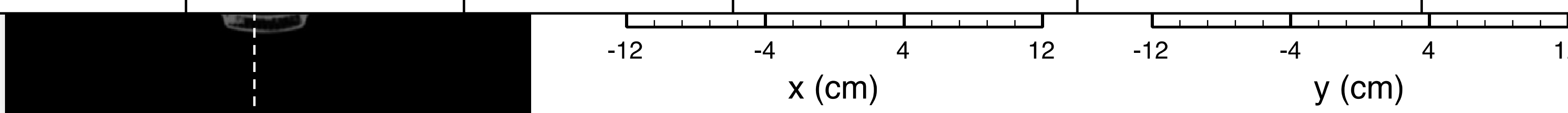
- Proton transport physics
  - Physics models

    Kawrakow, *Med Phys*, **27**, 485(2000), Fippel *et. al., Med Phys*, **31**, 2263 (2004), Penelope manual (2009), Geant4 physics manual (2011)
  - Multiple scattering and energy straggling
  - Nuclear interaction is handled by an empirical strategy

    Fippel *et. al.*, *Med Phys*, **31**, 2263(2004)



	Source Energy (MeV)	<σ/D> (%)	P_γ (1mm/1%)(%)	P_γ (2mm/2%)(%)	T (sec)
Inhomogeneous phantom	100	0.9	99.9	99.9	9.44
Patient	100	1.0	95.1	99.9	10.08



Jia X; Schuemann J; Paganetti H and Jiang SB: GPU-based fast Monte Carlo dose calculation for proton therapy. Physics in Medicine and Biology 2012 57: 7783-7798

Monte Carlo tools

Versatile

Limited functionality

Research

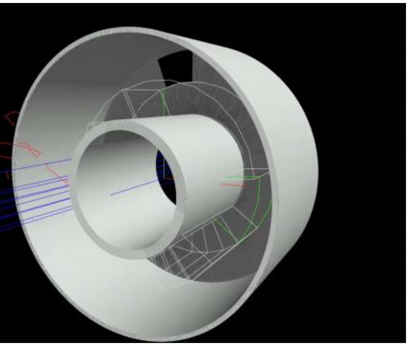
Tasks

Monte Carlo for Research

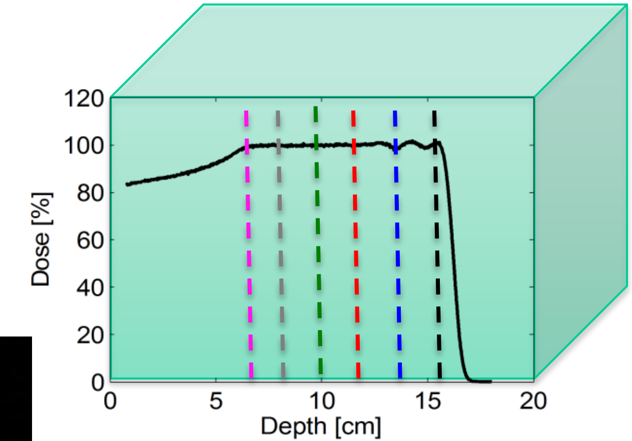
Example:

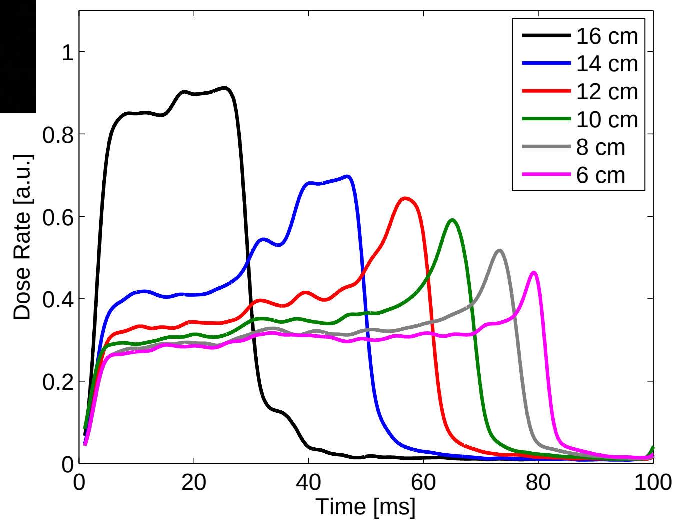
New concepts using prompt gamma range verification

Correlation of Prompt Gamma Rate Functions with position along an SOBP

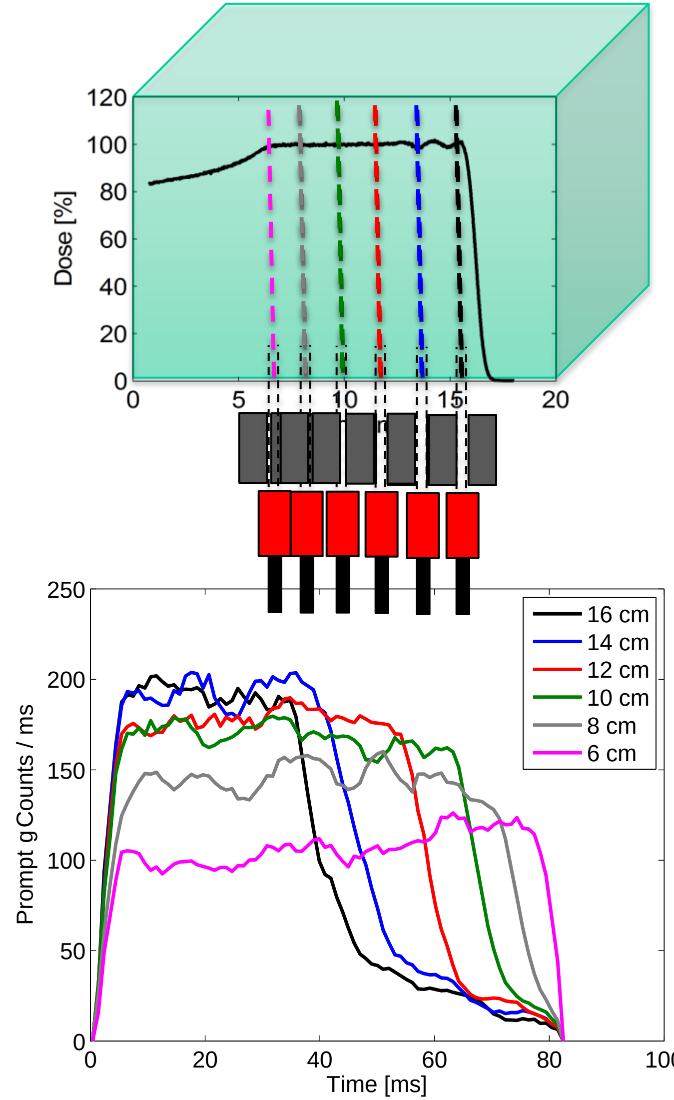


Dose Rate Functions: IC Measurements



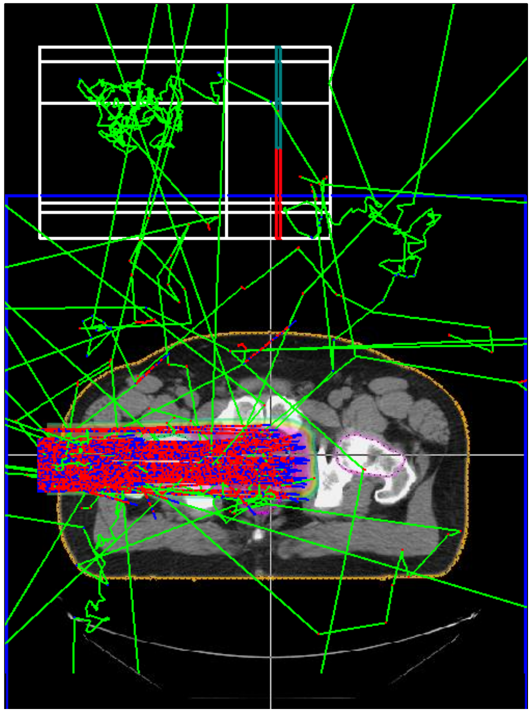


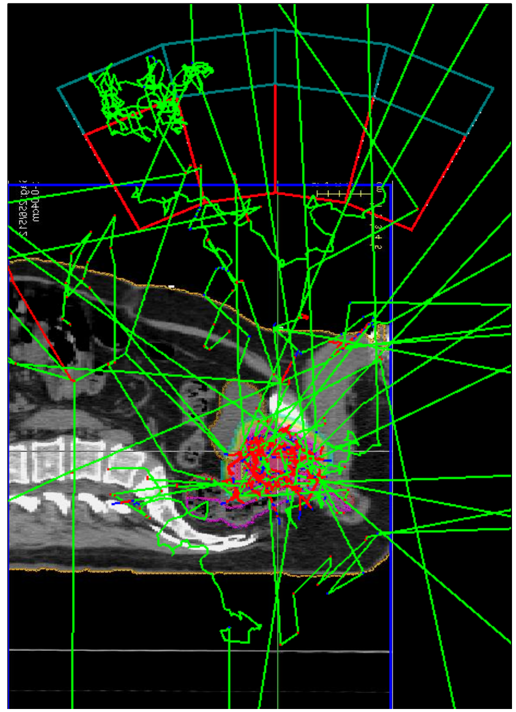
Prompt Gamma Rate Functions: TOPAS

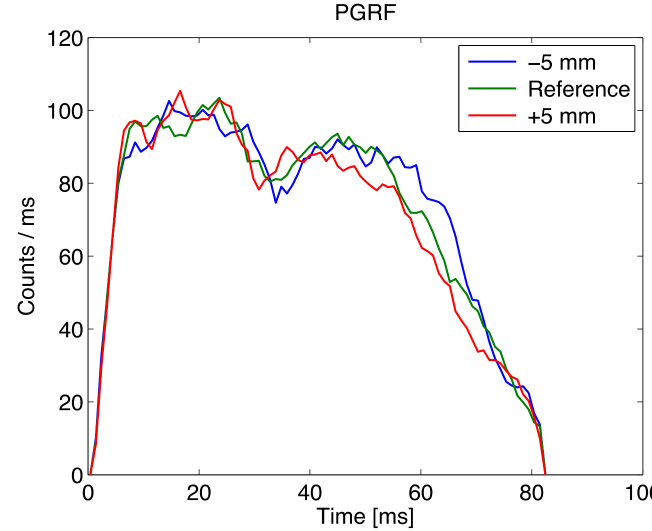


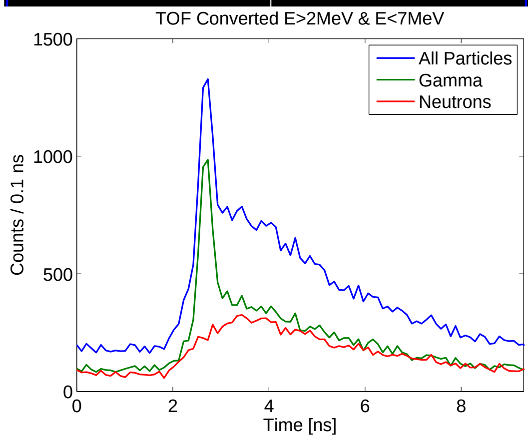
Testa; Min; Verburg; Schümann; Lu; Paganetti: Range verification in proton therapy based on the characteristic prompt-gamma time-patterns of passively modulated beams. Submitted

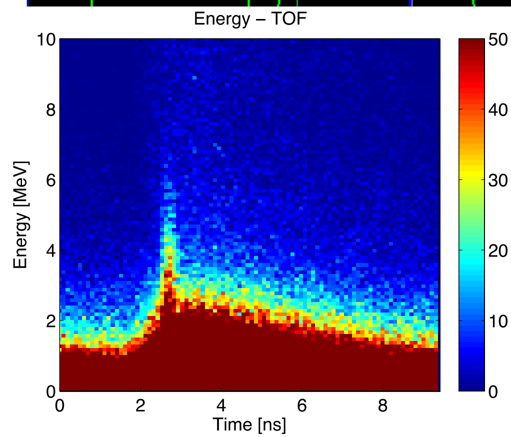
Application to a Prostate Patient











SOBP

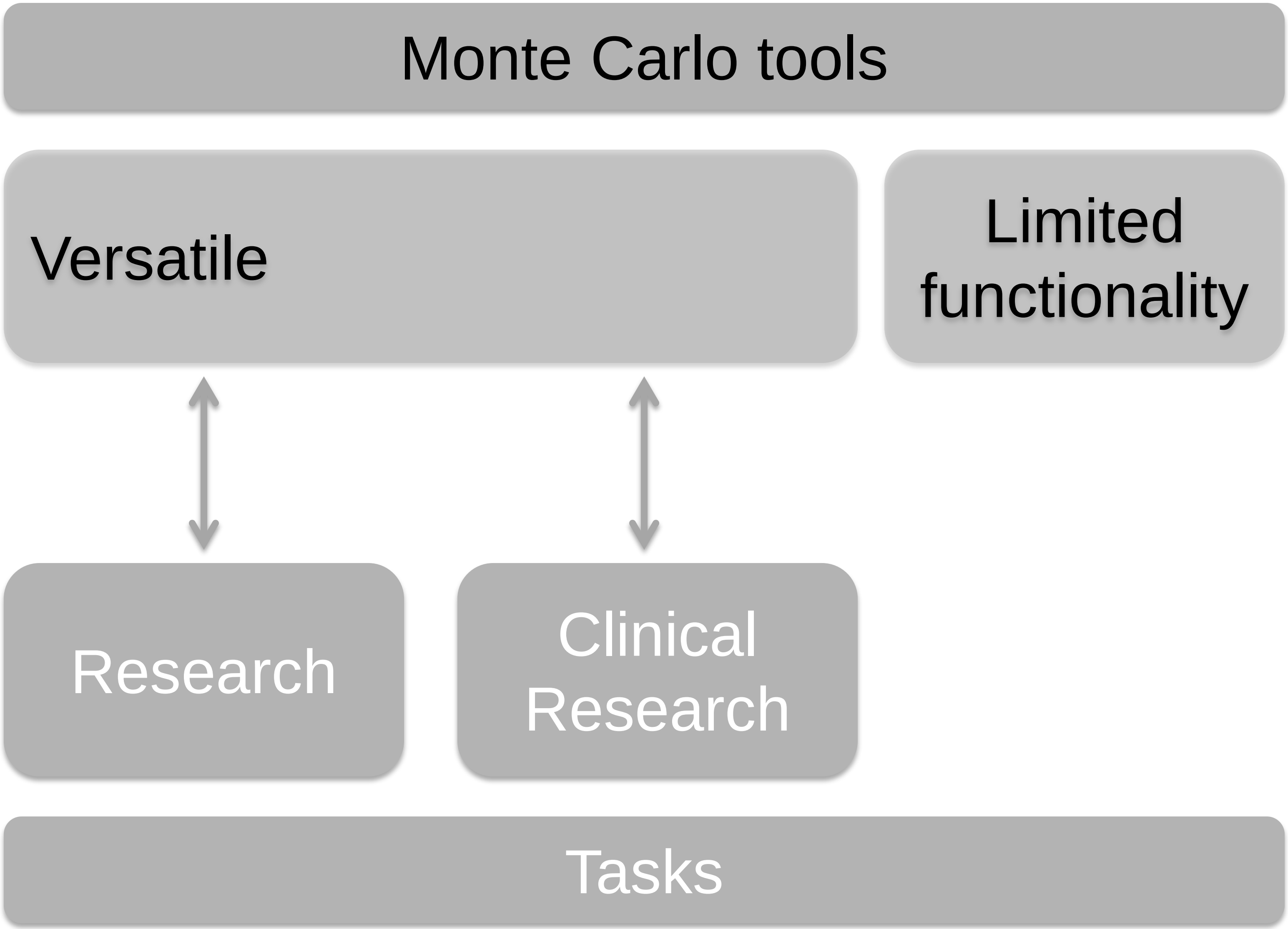
Range: 25.7 cm
Mod. Width: 8.5 cm
Dose: ~ 2.5 cGy

Testa; Min; Verburg; Schümann; Lu; Paganetti: Range verification in proton therapy based on the characteristic prompt-gamma time-patterns of passively modulated beams. Submitted

Example:
New concepts using prompt gamma range verification

- Prompt Gamma Ray Functions can be determined by MC-simulations.
- 2mm range verification is achievable in a water phantom for a dose of 2.5cGy.
- For a typical prostate tumor treatment a 4mm resolution in range is achievable for a dose of 15cGy.
- Energy and TOF-selection simplifies the detection design and is effective in discriminating the prompt-gamma signal from the background.

Testa; Min; Verburg; Schümann; Lu; Paganetti: Range verification in proton therapy based on the characteristic prompt-gamma time-patterns of passively modulated beams. Submitted


Monte Carlo tools
Versatile
Limited functionality
Research
Clinical Research
Tasks

Monte Carlo for Clinical Research

Example 1: Understanding the interplay effect when treating lung cancer with pencil beam scanning

Treatment planning (ASTROID)

↓

MCAUTO-4D

↓

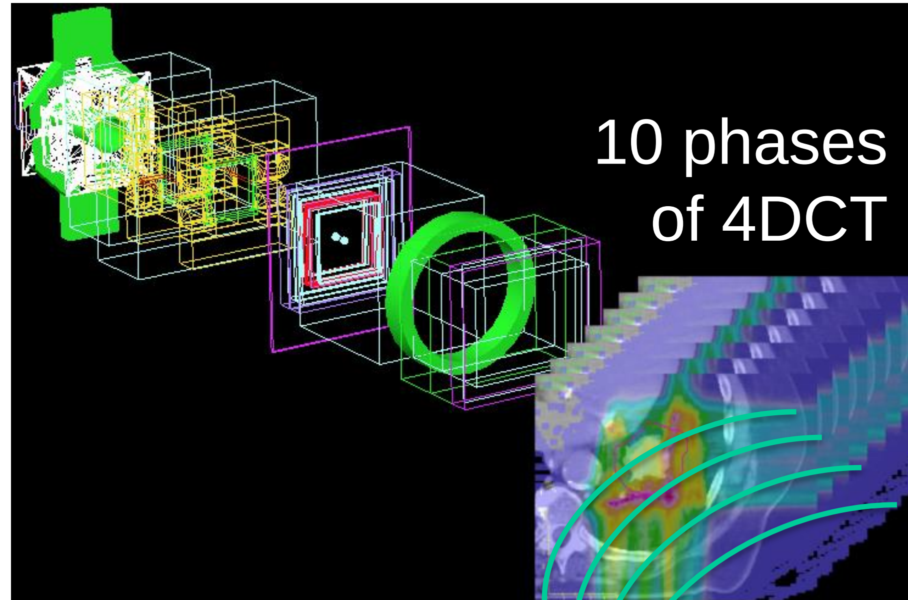
MC simulation on 10 4DCT phases

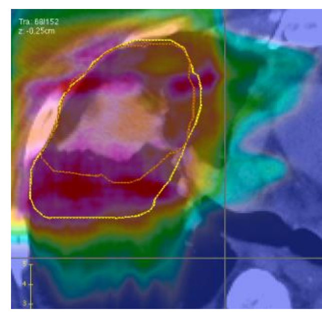
↓

plastimatch

↓

Dose distribution on reference phase (4D)





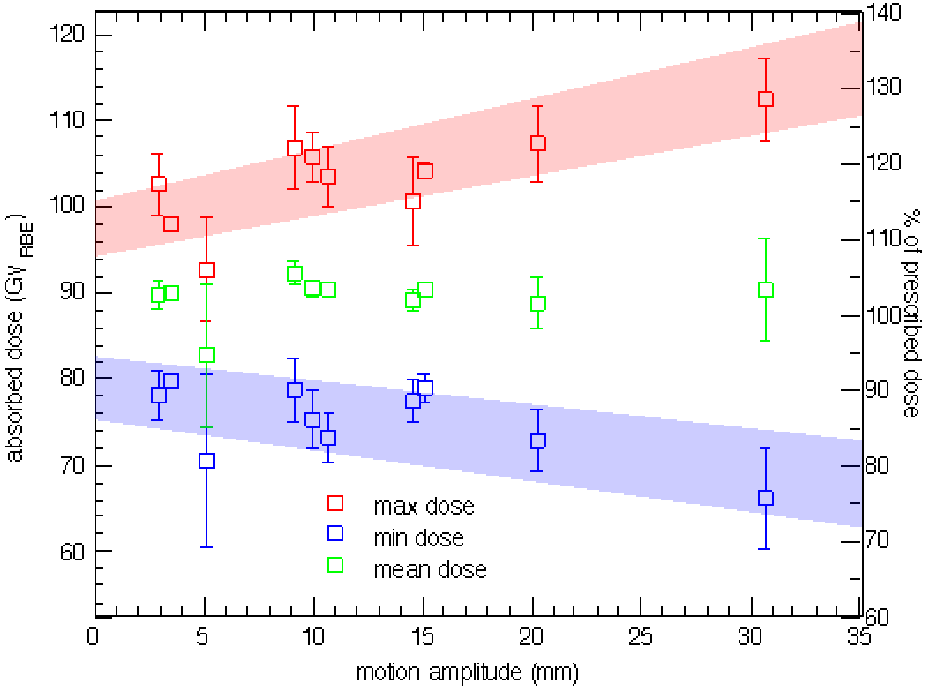
transform the resulting 10 dose distributions back to a reference phase (T_{50})

Grassberger; Dowdell; Shackleford; Sharp; Choi; Willers; Paganetti: Motion interplay as a function of patient parameters and spot size in spot scanning proton therapy for lung cancer. International Journal of Radiation Oncology, Biology, Physics 2013 86: 380-386

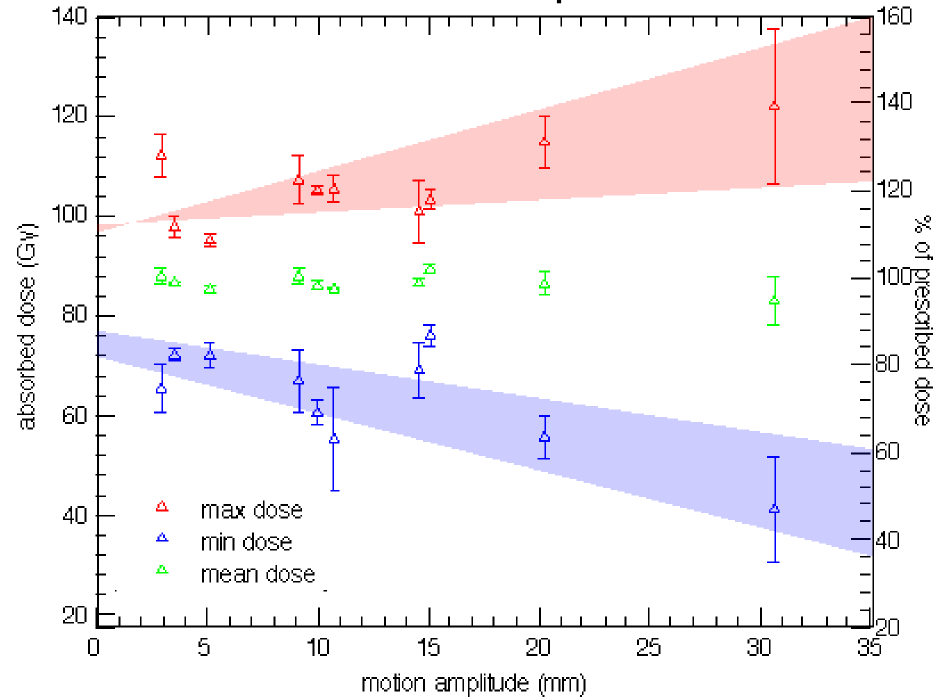
Results for single fraction delivery

attention: different scale

BigSpots



SmallSpots

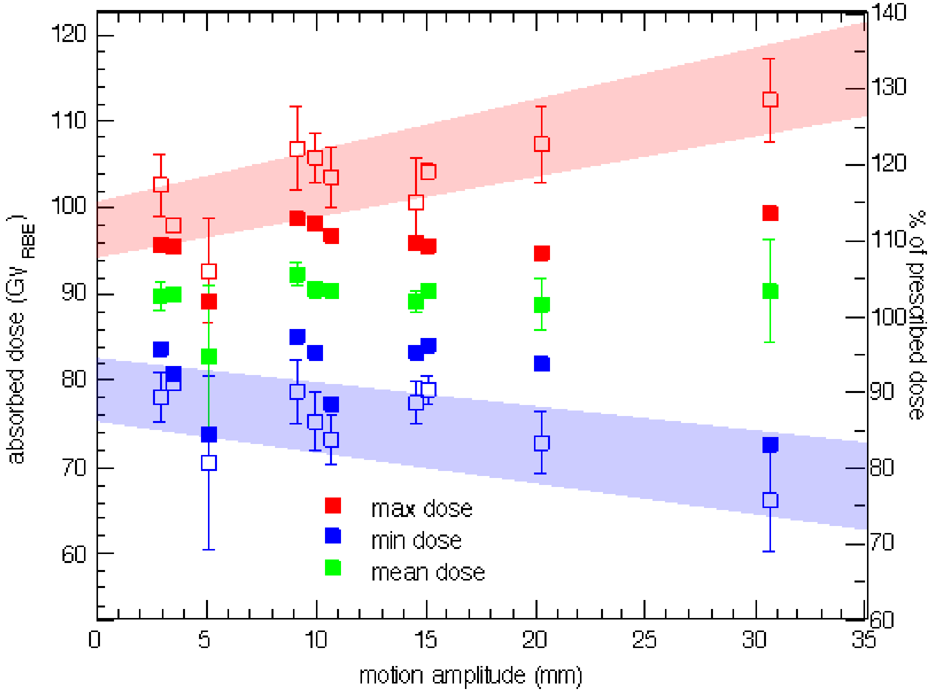


Grassberger; Dowdell; Shackleford; Sharp; Choi; Willers; Paganetti: Motion interplay as a function of patient parameters and spot size in spot scanning proton therapy for lung cancer. International Journal of Radiation Oncology, Biology, Physics 2013 86: 380-386

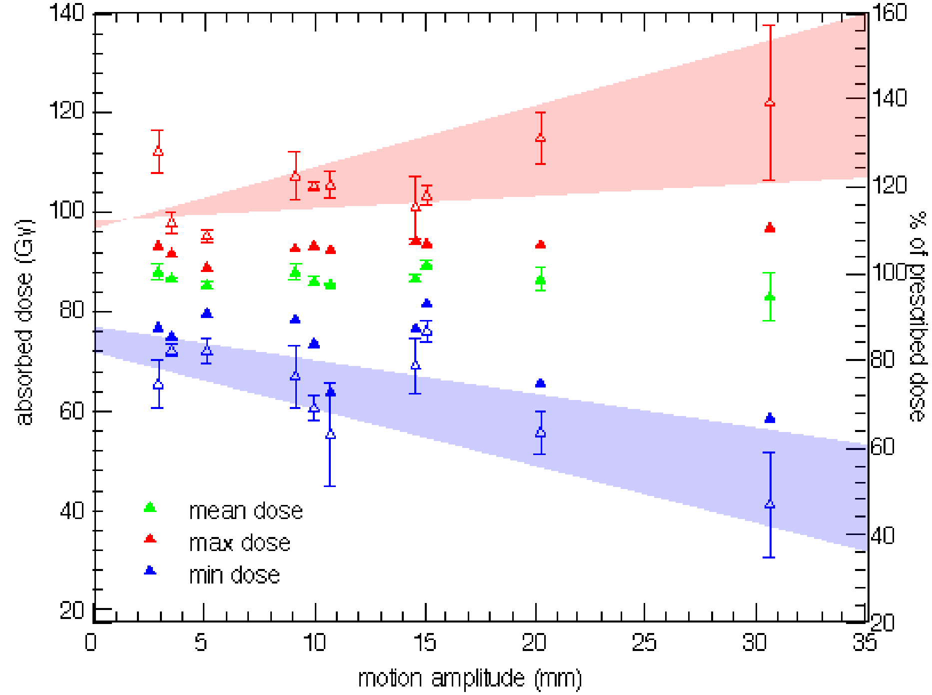
Results for 35 fraction delivery

attention: different scale

BigSpots



SmallSpots



Grassberger; Dowdell; Shackleford; Sharp; Choi; Willers; Paganetti: Motion interplay as a function of patient parameters and spot size in spot scanning proton therapy for lung cancer. International Journal of Radiation Oncology, Biology, Physics 2013 86: 380-386

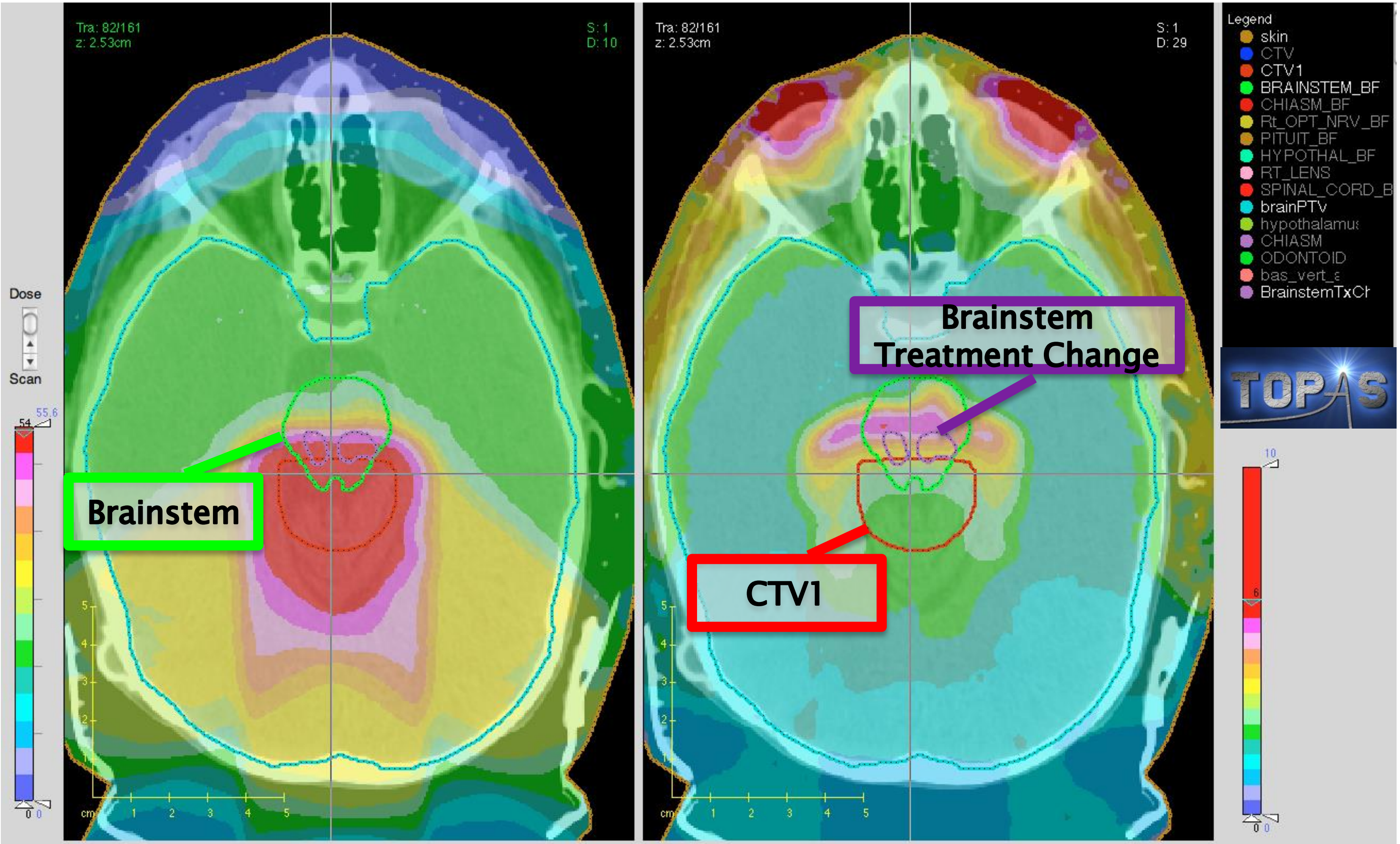
Example 1: Understanding the interplay effect when treating lung cancer with pencil beam scanning

- Local control is preserved using a large spot size and conventional fractionation, but not for SBRT
- Small spots appear to be generally more sensitive to interplay effects
- Up to 10% loss in 12-month local control even for 30 fractions using small spots
- Tumors with high amplitudes relative to their size show more significant interplay
- There is significant patient variability depending on tumor location and size

Grassberger; Dowdell; Shackleford; Sharp; Choi; Willers; Paganetti: Motion interplay as a function of patient parameters and spot size in spot scanning proton therapy for lung cancer. International Journal of Radiation Oncology, Biology, Physics 2013 86: 380-386

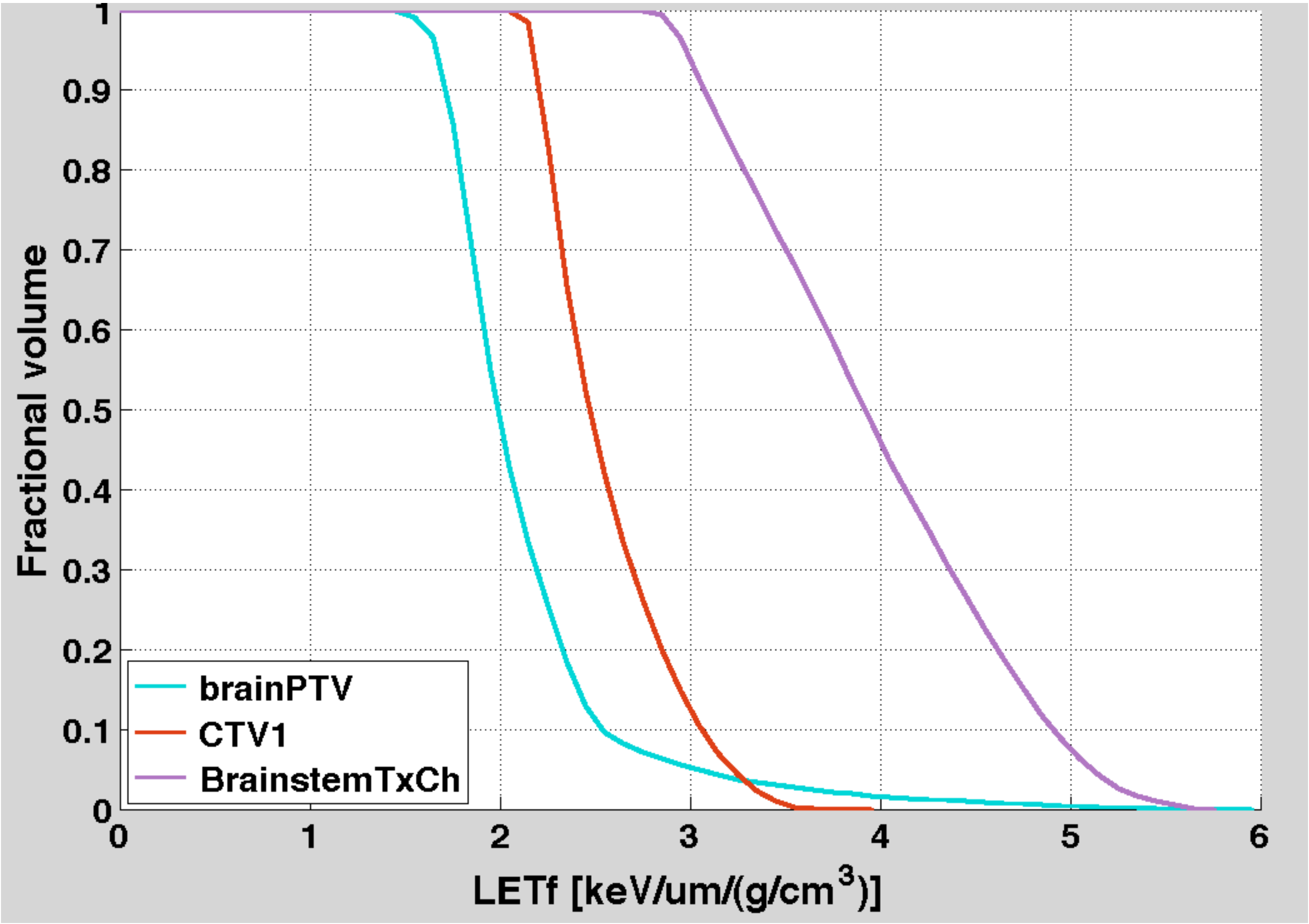
Monte Carlo for Clinical Research

Example 2: The use of LET information in proton therapy treatment planning



DOSE **LET**

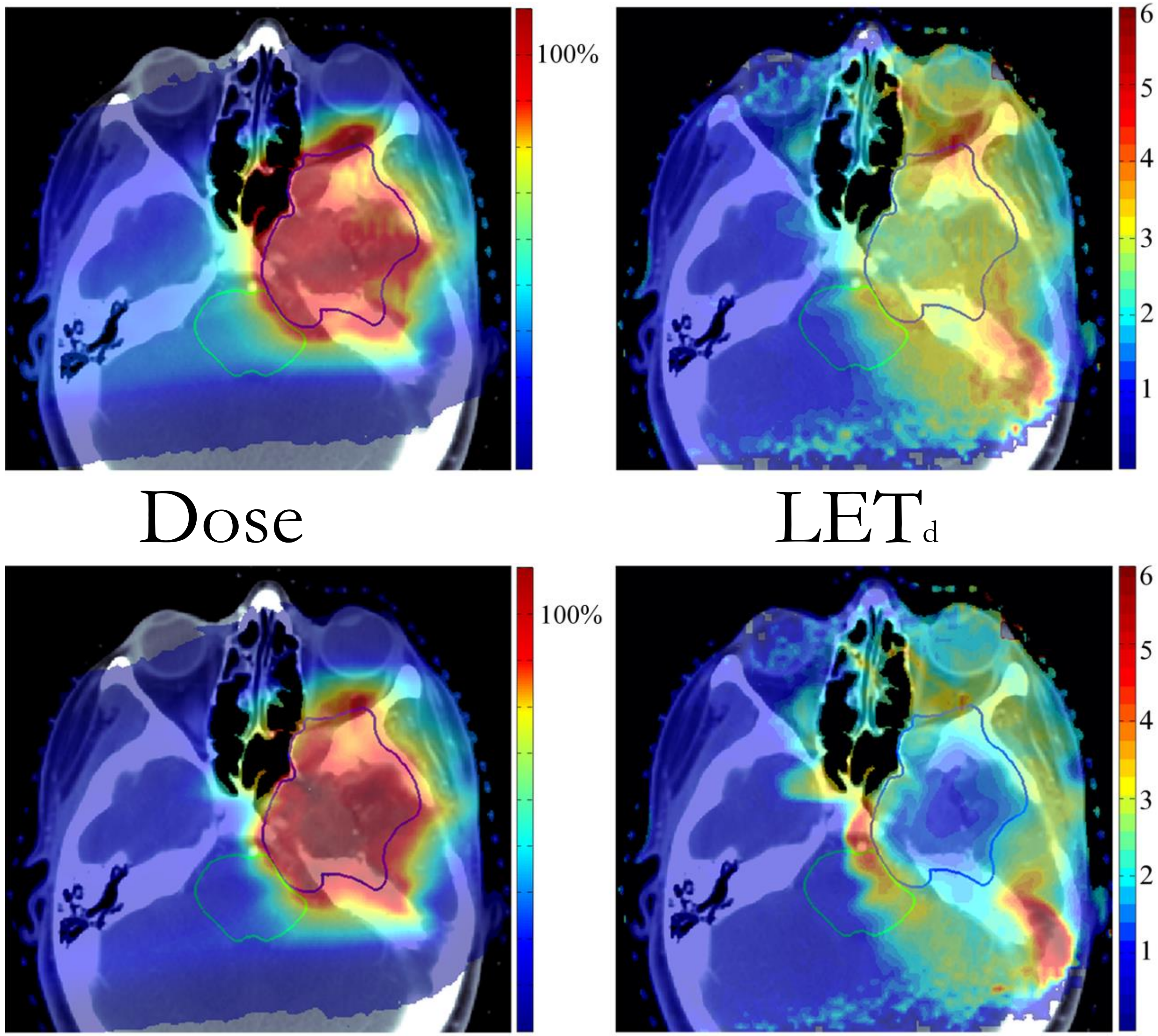
Sethi; Giantsoudi; Raiford; Rappalino; Caruso; Yock; Tarbell; Paganetti; MacDonald: Patterns of failure following proton therapy in medulloblastoma; LET distributions and RBE associations for relapses. International Journal of Radiation Oncology, Biology, Physics 2014 88: 655-663



Sethi; Giantsoudi; Raiford; Rappalino; Caruso; Yock; Tarbell; Paganetti; MacDonald: Patterns of failure following proton therapy in medulloblastoma; LET distributions and RBE associations for relapses. International Journal of Radiation Oncology, Biology, Physics 2014 88: 655-663

Intensity-modulated proton therapy (IMPT)

PLAN 1

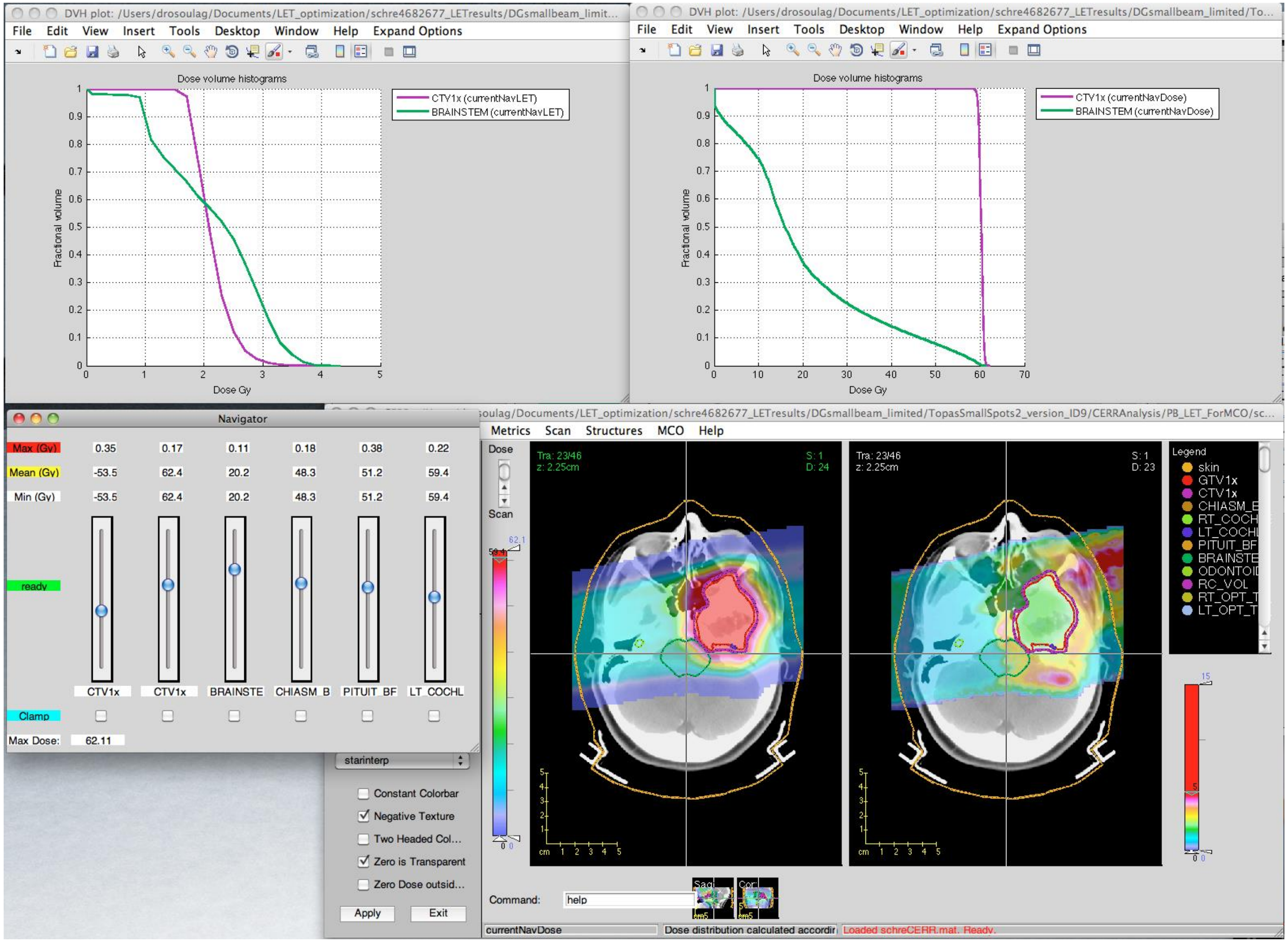


PLAN 2

Grassberger C; Trofimov A; Lomax A and Paganetti H: Variations in linear energy transfer within clinical proton therapy fields and the potential for biological treatment planning. International Journal of Radiation Oncology, Biology, Physics 2011 80: 1559-1566

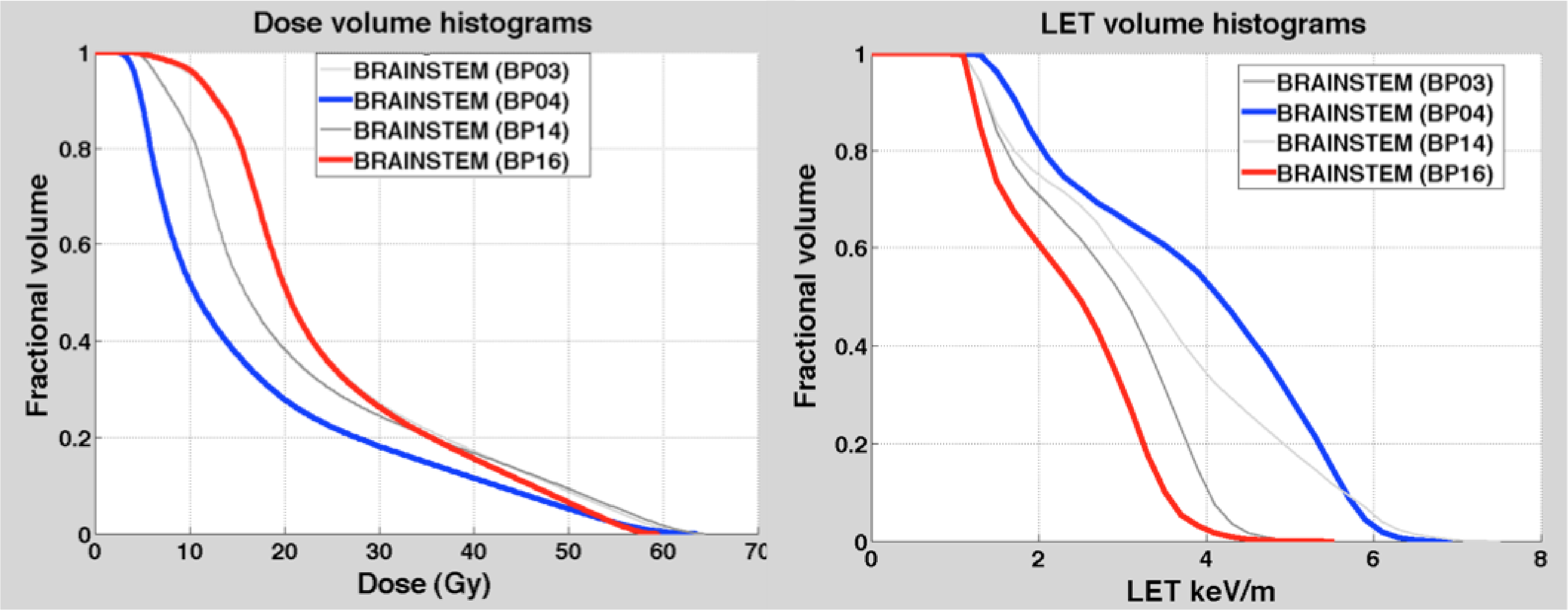
Biological dose optimization based on LET

LET-guided multi-criteria optimization (MCO)



Giantsoudi; Grassberger; Craft; Niemierko; Trofimov; Paganetti: Linear energy transfer (LET)-Guided Optimization in intensity modulated proton therapy (IMPT): feasibility study and clinical potential. Int J Radiat Oncol Biol Phys 2013 87: 216-222

LET-guided MCO

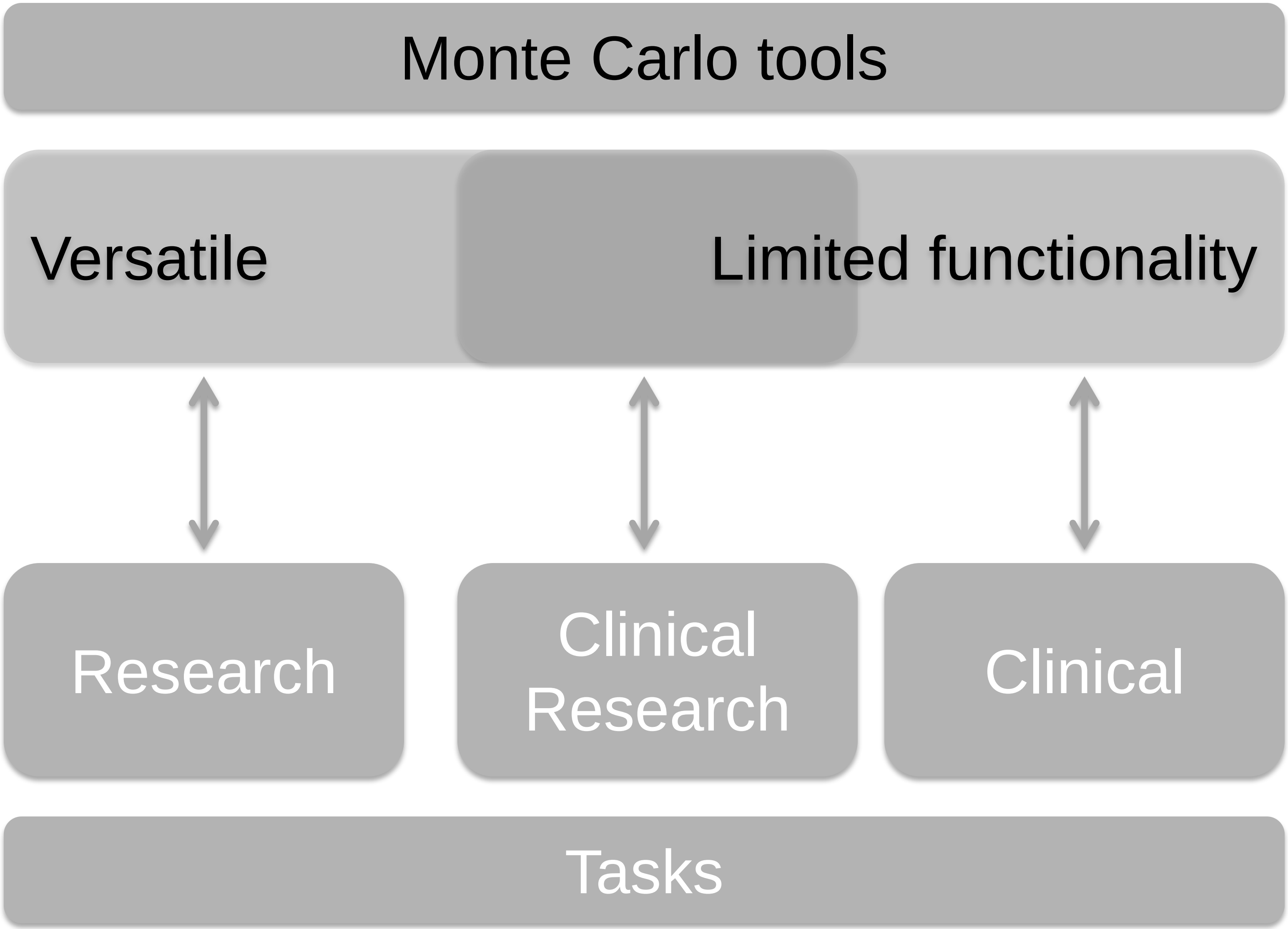


Giantsoudi; Grassberger; Craft; Niemierko; Trofimov; Paganetti: Linear energy transfer (LET)-Guided Optimization in intensity modulated proton therapy (IMPT): feasibility study and clinical potential. Int J Radiat Oncol Biol Phys 2013 87: 216-222

Example 2: The use of LET information in proton therapy treatment planning

- For doses and LET values relevant in proton therapy, one can assume a close to linear relationship between LET and RBE for a given α/β. LET information can potentially be used to understand unexpected side effects
- LET information can be used as additional parameter in treatment optimization

Giantsoudi; Grassberger; Craft; Niemierko; Trofimov; Paganetti: Linear energy transfer (LET)-Guided Optimization in intensity modulated proton therapy (IMPT): feasibility study and clinical potential. Int J Radiat Oncol Biol Phys 2013 87: 216-222



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RADIATION ONCOLOGY
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Uncertainties in predicting the beam range in patients

Source of range uncertainty in the patient	Range uncertainty
Independent of dose calculation:	
Measurement uncertainty in water for commissioning	± 0.3 mm
Compensator design	± 0.2 mm
Beam reproducibility	± 0.2 mm
Patient setup	± 0.7 mm
Dose calculation:	
Biology (always positive)	+ 0.8 %
CT imaging and calibration	± 0.5 %
CT conversion to tissue (excluding I-values)	± 0.5 %
CT grid size	± 0.3 %
Mean excitation energies (I-values) in tissue	± 1.5 %
Range degradation; complex inhomogeneities	- 0.7 %
Range degradation; local lateral inhomogeneities *	± 2.5 %
Total (excluding *)	**2.7% + 1.2 mm**
Total	**4.6% + 1.2 mm**

Typical

Worst case

H. Paganetti: Range uncertainties in proton beam therapy and the impact of Monte Carlo simulations. Phys. Med. Biol. 57: R99-R117 (2012)

Uncertainties in predicting the beam range in patients

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Independent of dose calculation:		
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Biology (always positive)	+ 0.8 %	
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CT conversion to tissue (excluding I-values)	± 0.5 %	± 0.2 %
CT grid size	± 0.3 %	
Mean excitation energies (I-values) in tissue	± 1.5 %	
Range degradation; complex inhomogeneities	- 0.7 %	± 0.1 %
Range degradation; local lateral inhomogeneities *	± 2.5 %	± 0.1 %
Total (excluding *)	**2.7% + 1.2 mm**	**2.4 % + 1.2 mm**
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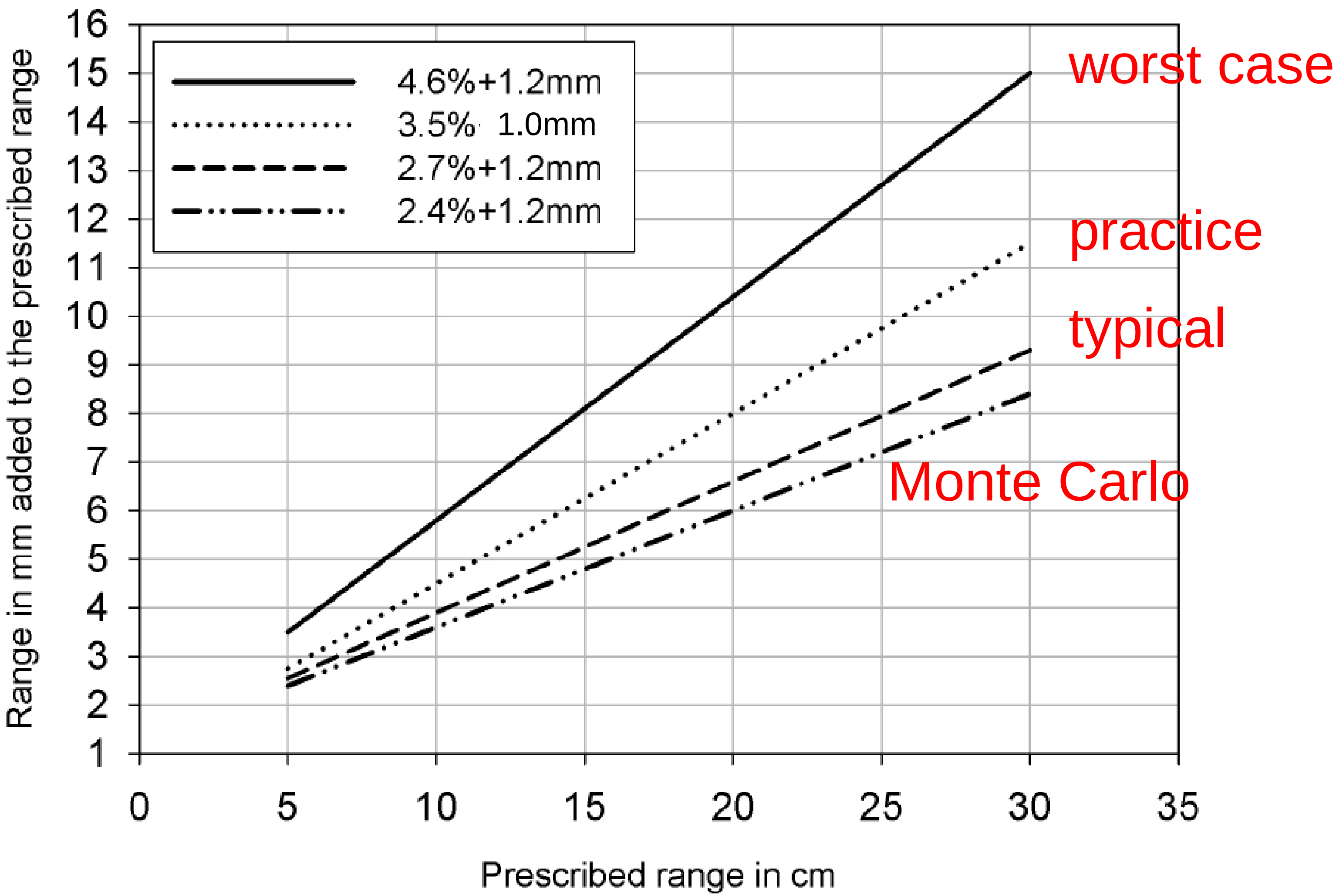
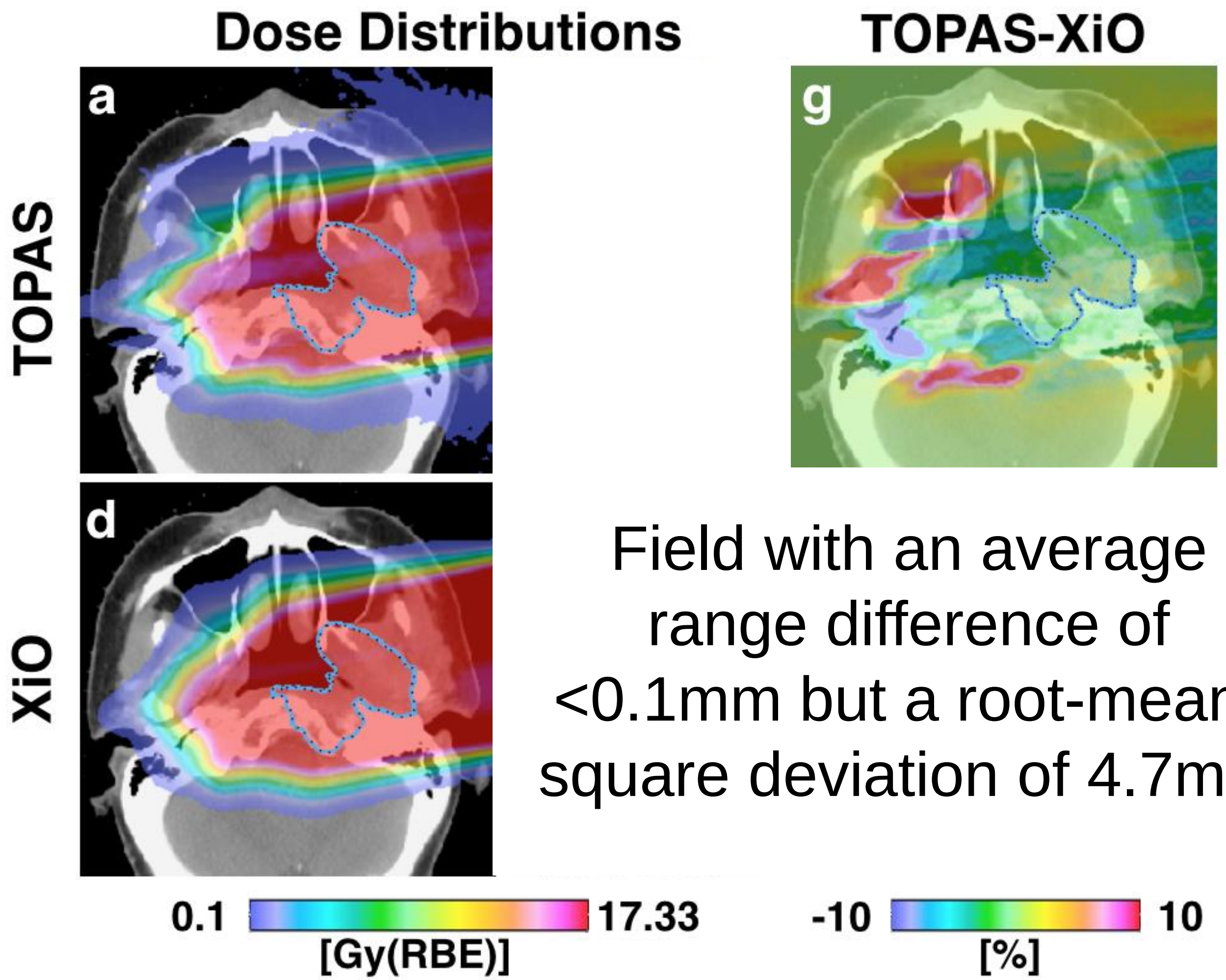
H. Paganetti: Range uncertainties in proton beam therapy and the impact of Monte Carlo simulations. Phys. Med. Biol. 57: R99-R117 (2012)

Uncertainties in predicting the beam range in patients



H. Paganetti: Range uncertainties in proton beam therapy and the impact of Monte Carlo simulations. Phys. Med. Biol. 57: R99-R117 (2012)

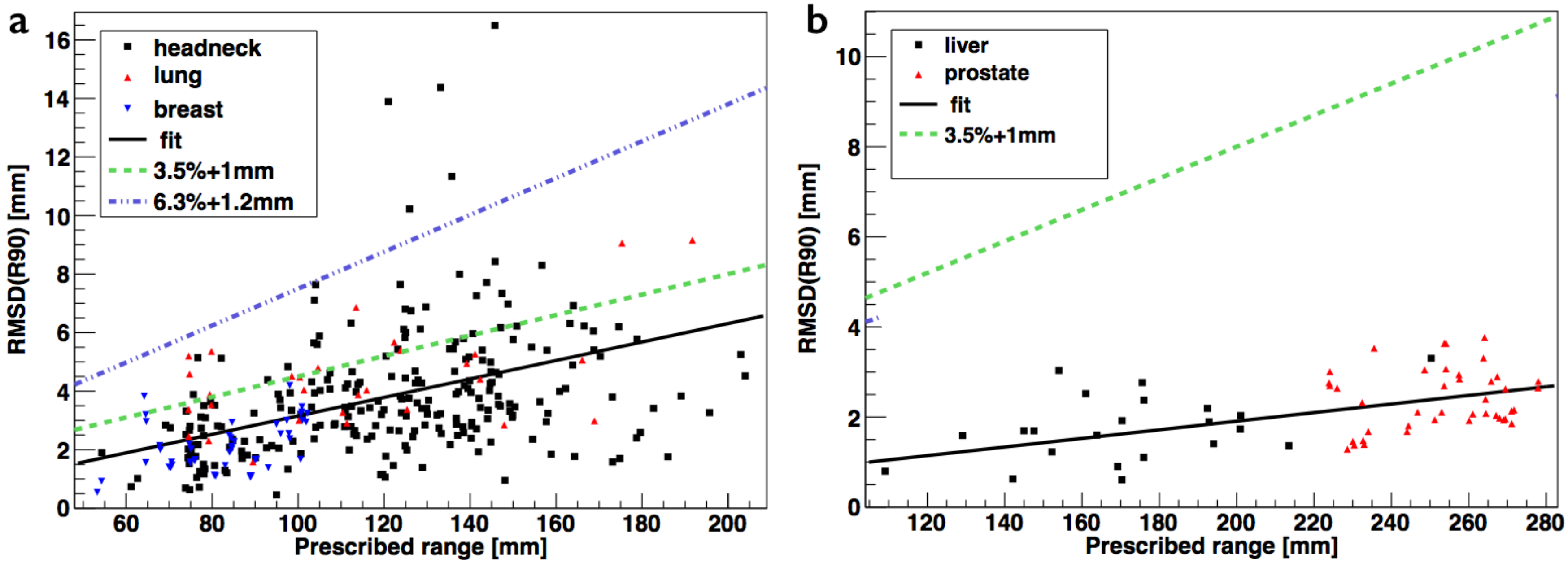
Range differences between analytical and Monte Carlo based dose calculation analyzed by comparing distal dose surfaces in patients



Field with an average range difference of <0.1mm but a root-mean-square deviation of 4.7mm

Schuemann, Dowdell, Min, Paganetti: Site-specific range uncertainties caused by dose calculation algorithms for proton therapy: Phys. Med. Biol. submitted

Estimation of range uncertainties by performing MC dose calculation on 508 fields



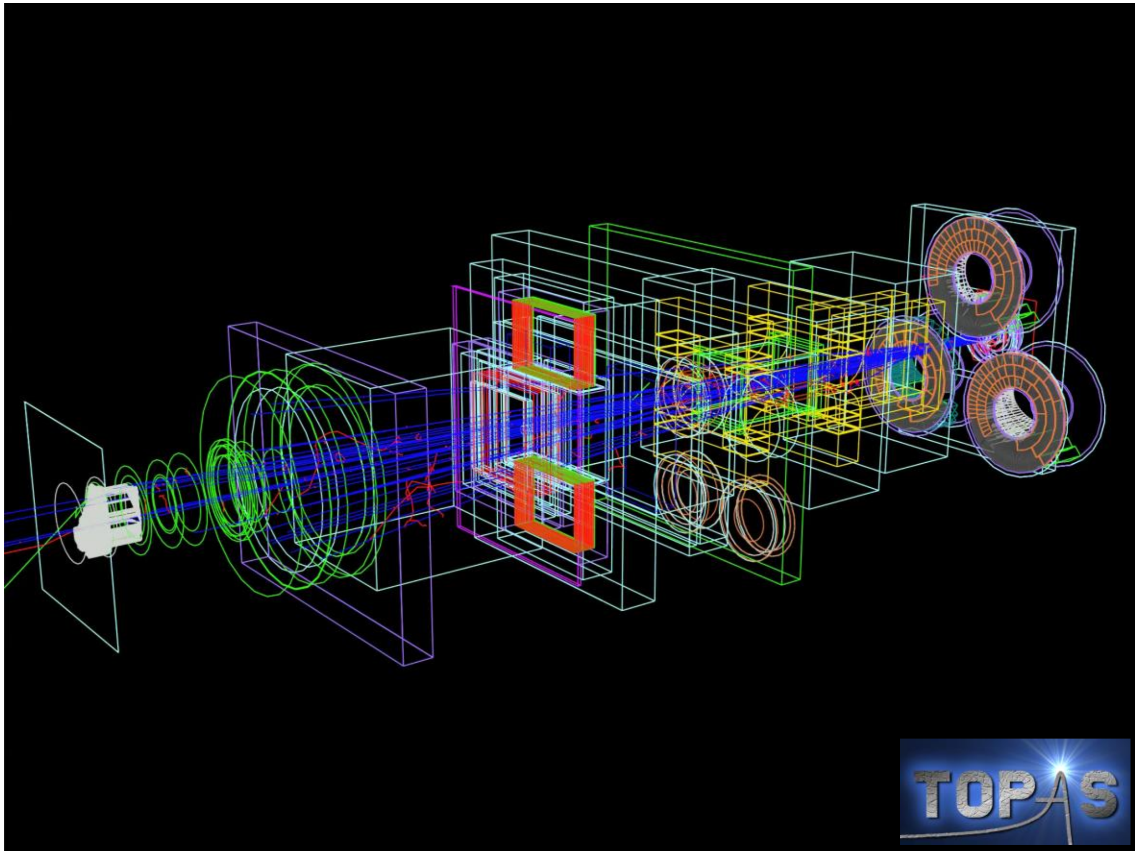
includes uncertainties from sources other than dose calculation

Schuemann, Dowdell, Min, Paganetti: Site-specific range uncertainties caused by dose calculation algorithms for proton therapy: Phys. Med. Biol. submitted

Monte Carlo for Clinical Use

- Monte Carlo in routine dose calculation has the potential to reduce treatment margins
- Monte Carlo can be used to revise current margins and better understand uncertainties due to dose calculation

MGH Radiation Oncology
Physics Research team



Funding by the NCI

- P01 CA021239-31
  "Proton Therapy Research"
- R01 CA111590-05
  "Four-dimensional Monte Carlo dose calculation"
- R01 CA140735-05
  "TOPAS. Fast and easy to use Monte Carlo system for proton therapy"
- Federal Share on C06 CA059267
  "Accurate Monte Carlo Dose Calculation for Proton Therapy Patients"
- MGH ECOR
  "Biologically Optimized Treatment Planning for Proton Beam Therapy"