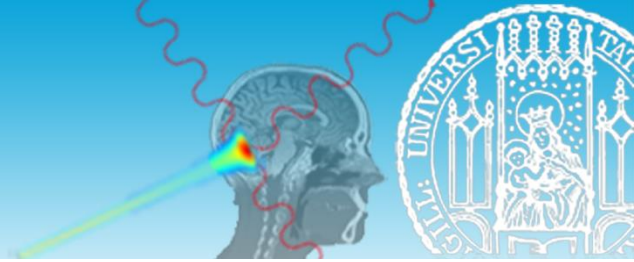
LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN



The role of Monte Carlo tools in prompt-gamma radiation monitoring research

Marco Pinto

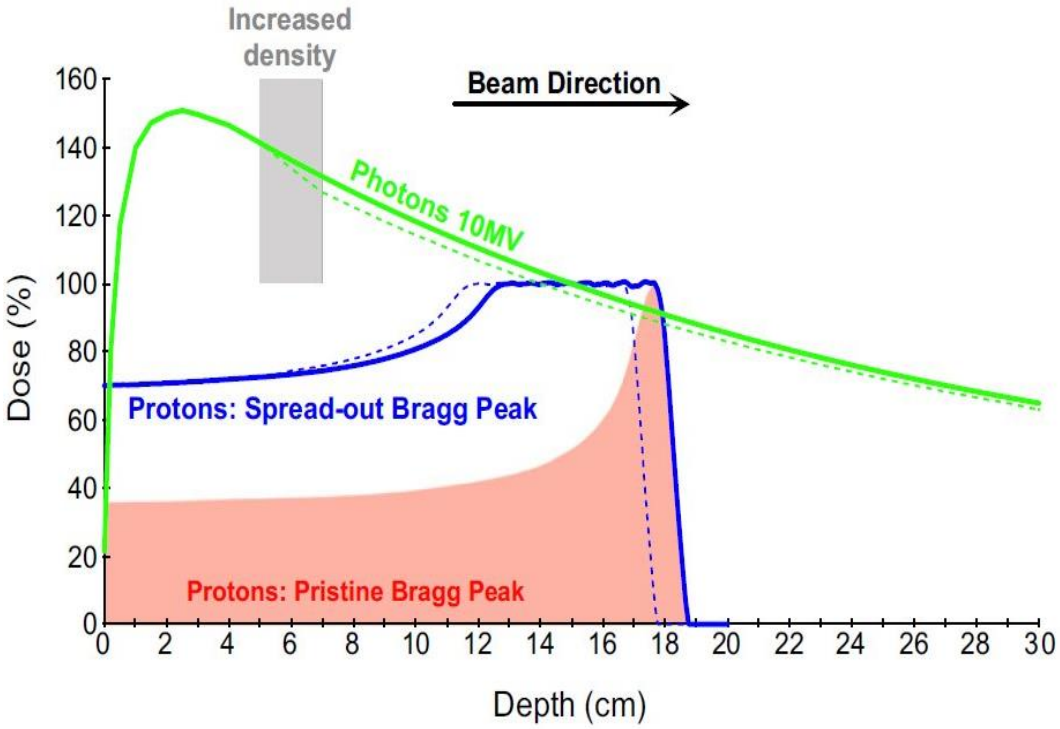
LMU Munich

YIWS: Prompt-gamma imaging in particle therapy

06.07.2023

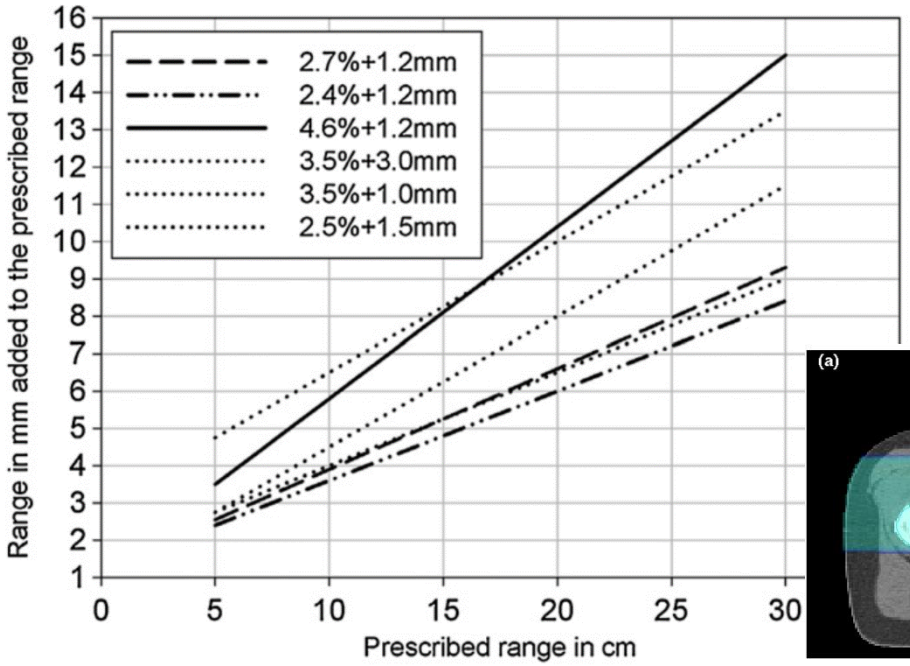
Proton beams: the promise and clinical challenge

"The advantage of protons is that they stop.
The disadvantage of protons is that we don't always know where."
(Prof. Dr. AJ Lomax, Center for Proton Radiation Therapy at PSI, Villigen, Switzerland)

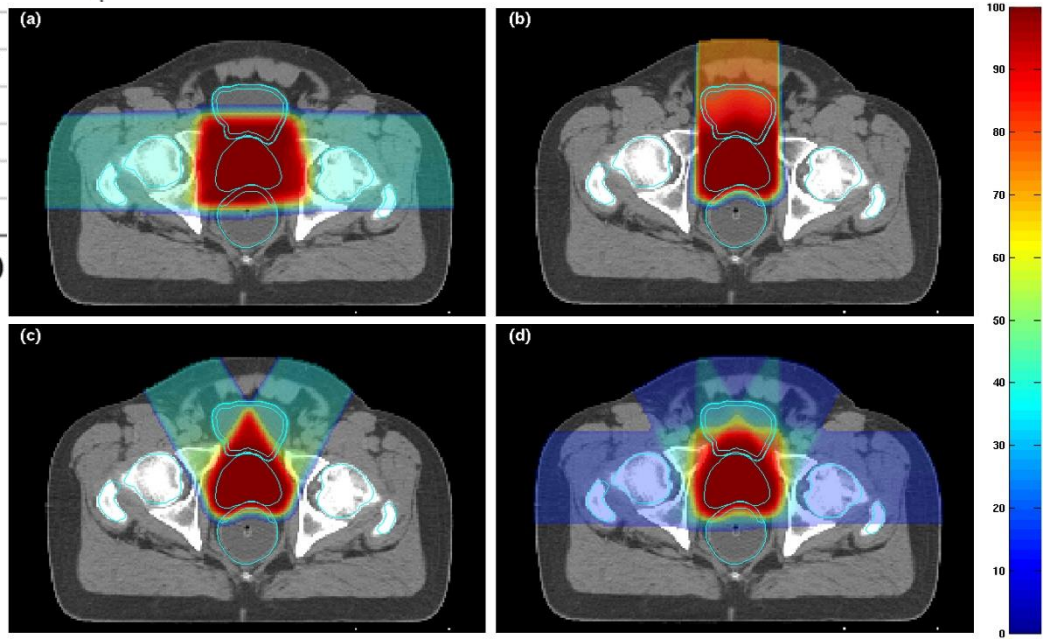


M. Engelsman et al, Seminars Rad. Onc. 2013

Proton beams: the promise and clinical challenge

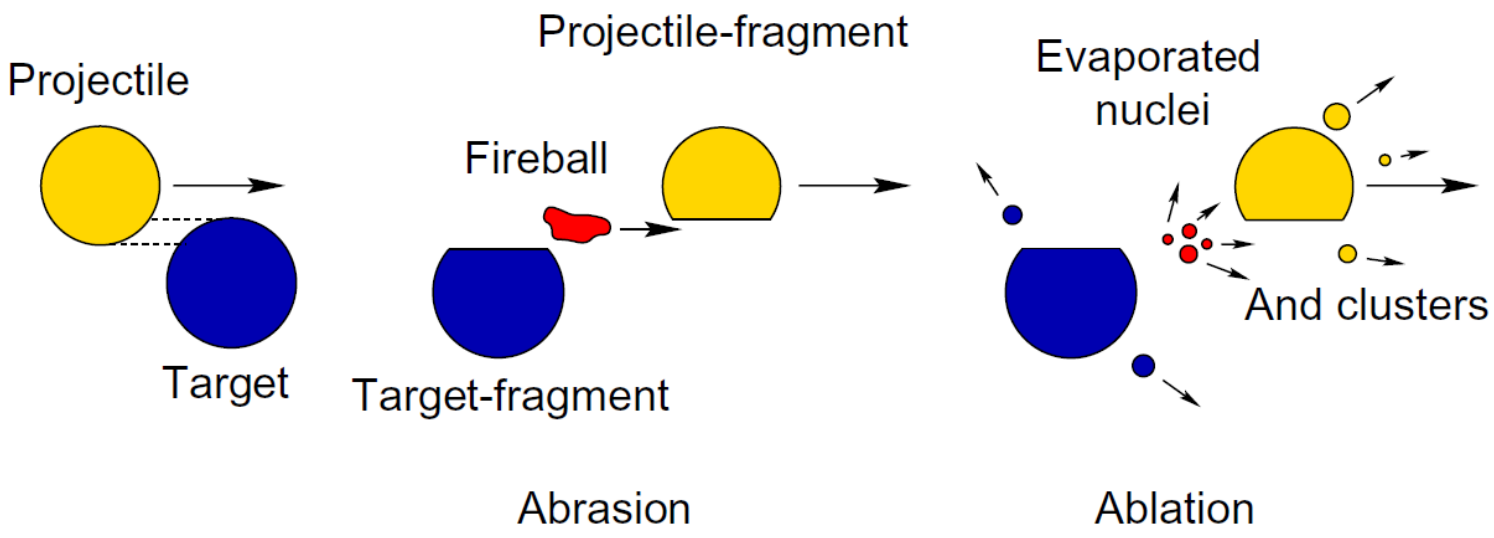


Paganetti, PMB, 2012



Tang et al., IJROBP, 2012

Exploiting nuclear reactions



Gunzert-Marx et al., New J. Phys., 2008

- Projectile-like and target-like fragments
  - ➢ **β+ emitters**, e.g. ^{11}C, ^{15}O
- Neutrons, light charged particles, **prompt γ-rays**

PG monitoring

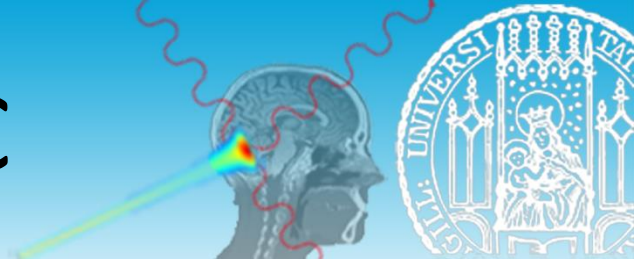
Verification of the proton beam position in the patient by the prompt gamma rays emission.

Y. Jongen and F. Stichelbaut, IBA

Several authors have studied the production of PET isotopes by therapeutic proton beams. The goal is to use a PET scanner to verify the location of the proton beam in the patient body immediately after the treatment. But, **when protons are stopped in the patient body, they produce also copious amounts of prompt gamma rays, which could be imaged** during the irradiation using a classical gamma camera. This would allow visualizing the proton energy deposition in the patient. **We have conducted Monte Carlo simulations of this problem using the GEANT Code. These simulations indicate that this method could offer a real potential in proton therapy treatment quality assurance.**

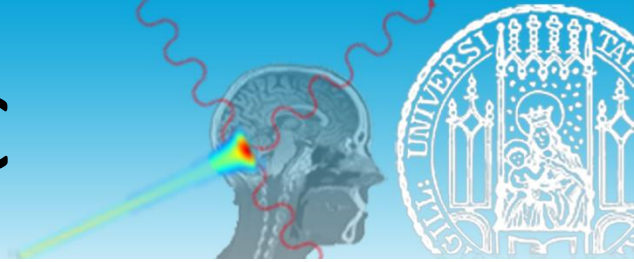
Book of Abstracts, PTCOG 39, California (USA), October 26-29 2003

The role of MC



- Monte Carlo tools are a very cost-effective approach to assess physical phenomena
- It allows to test hypothesis without the need for expensive experimental campaigns or building a device
- It can replace experiments when the MC application has been validated, e.g.:
  - Dosimetric data
  - Shielding calculations
  - Beamline modeling

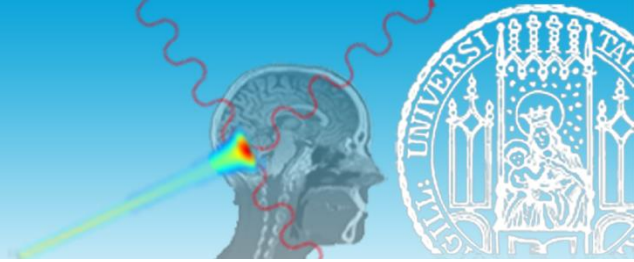
The role of MC



All models are wrong but some models are useful

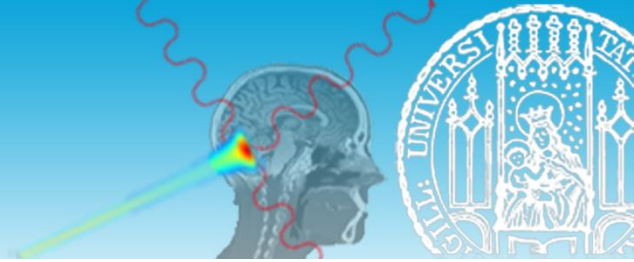
George Box

MC pitfalls



- MC tools rely on mathematical models that are an approximation of reality
- The models used may be initially developed having other applications in mind (e.g. high-energy physics)
- MC input data (e.g. cross sections) are often incomplete and/or of bad quality

MC pitfalls

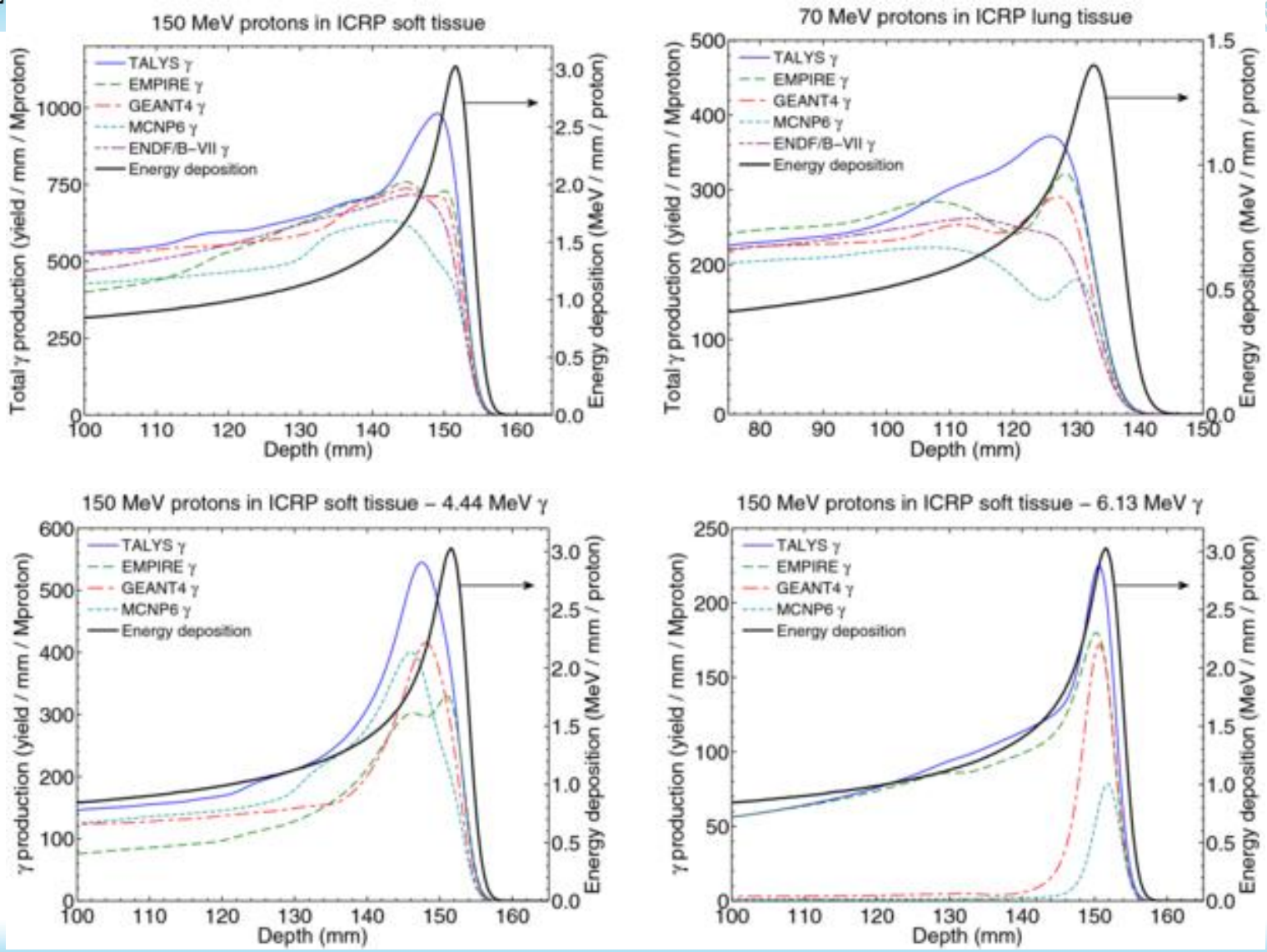


- Even if the models and input data are perfect, it is virtually impossible for the user to include all factors (e.g. geometry, material)

What to do then???

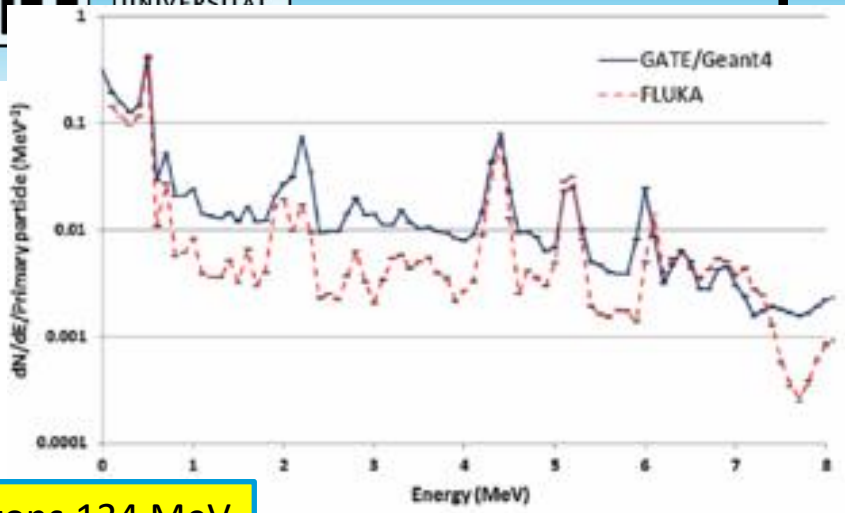
It depends on the application but **often it is more important to understand and to be aware of the limitations** than to enter into an endless loop of "improvements" (over-optimization)

MC pitfalls

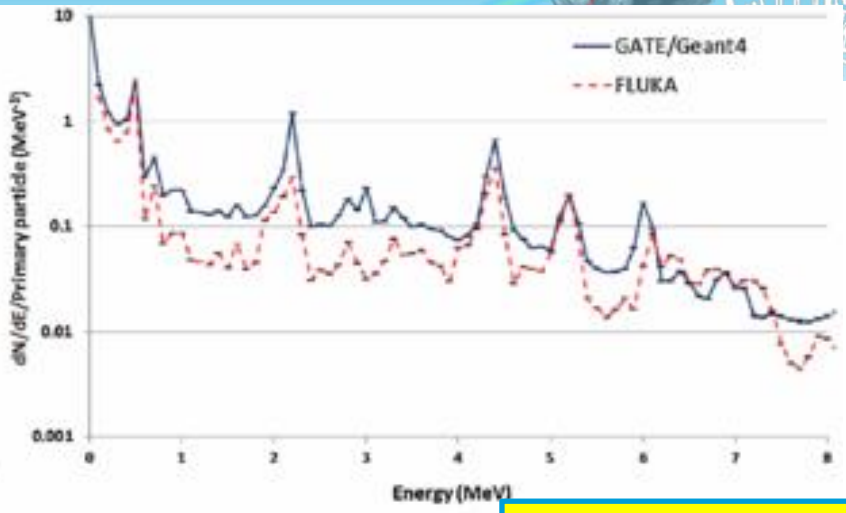


Verburg et al., PMB, 2012

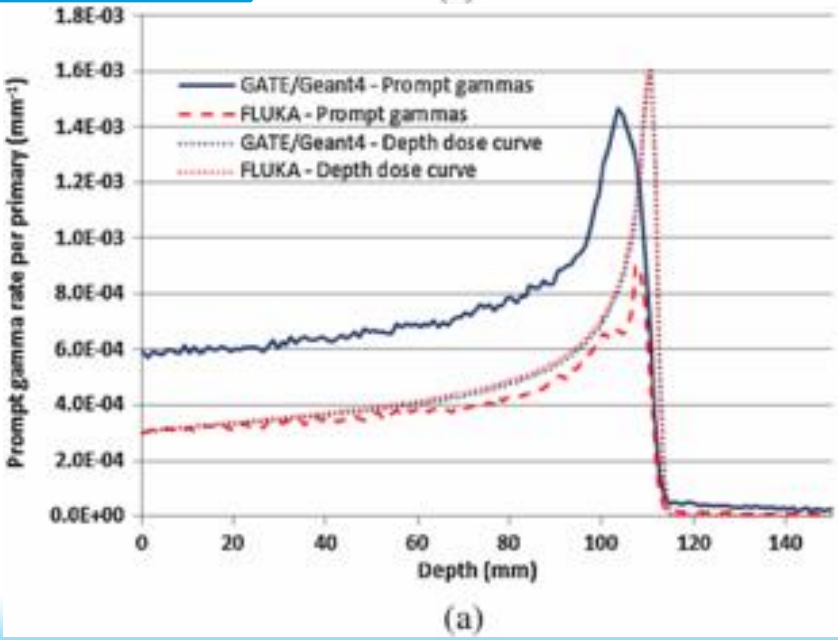
MC pitfalls

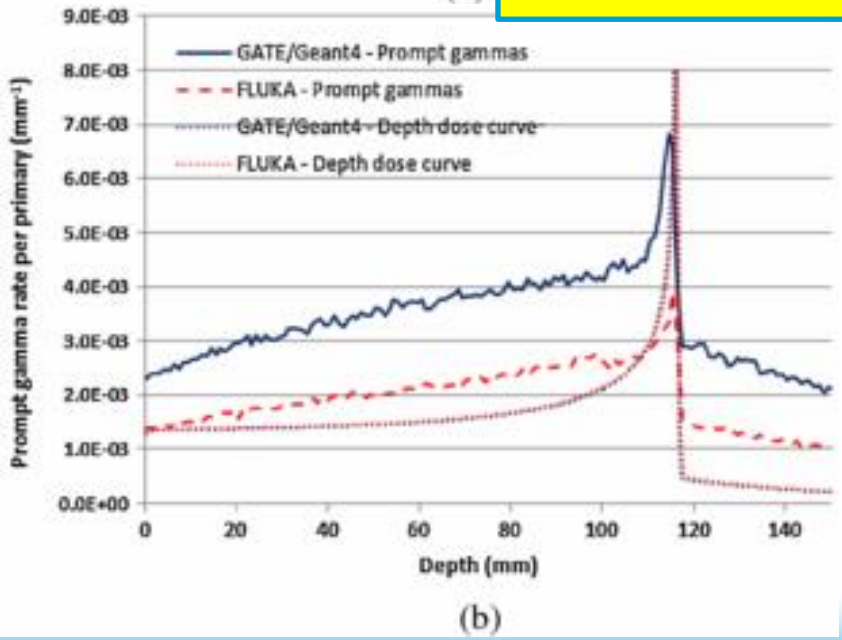


Protons 134 MeV



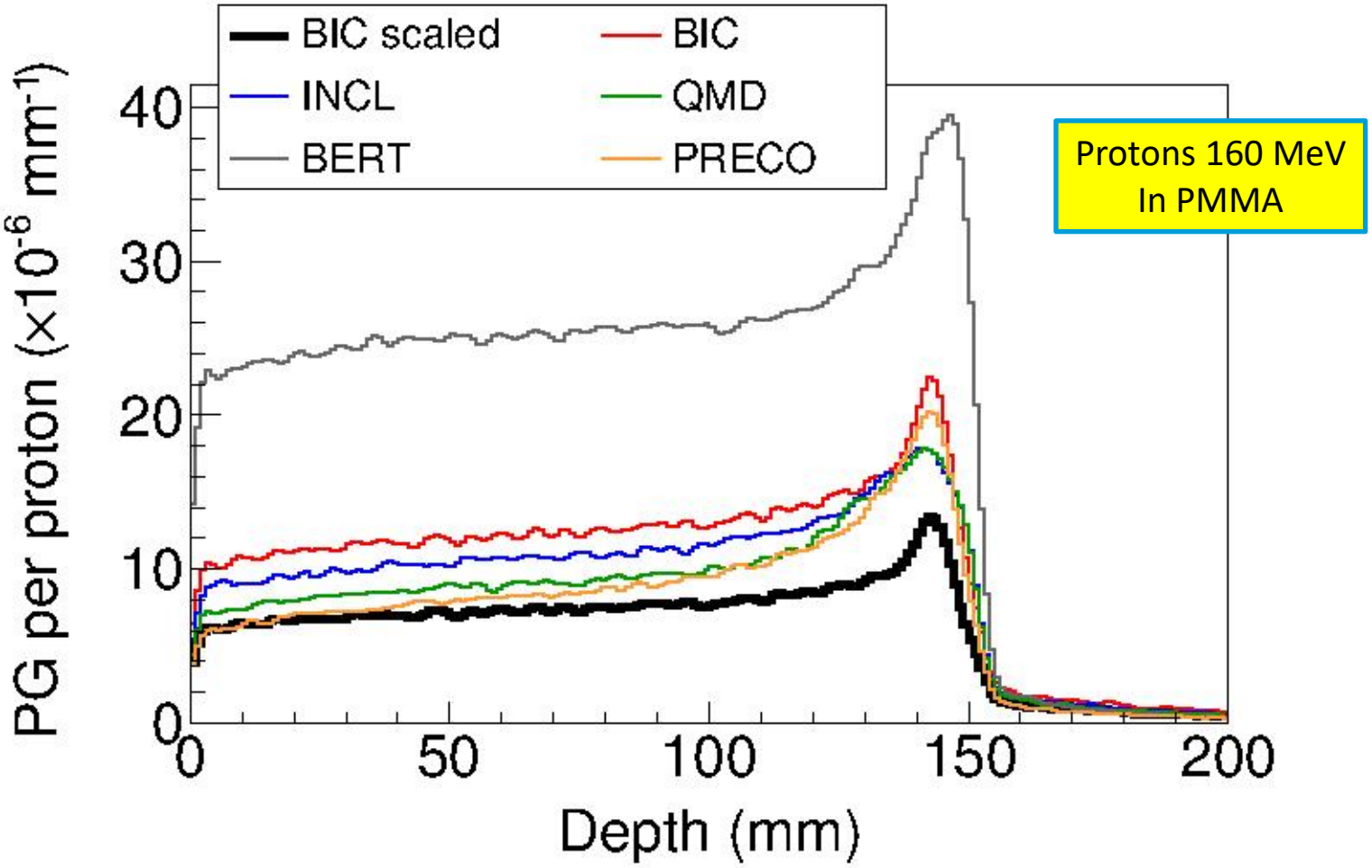
Carbon ions 260 MeV/u





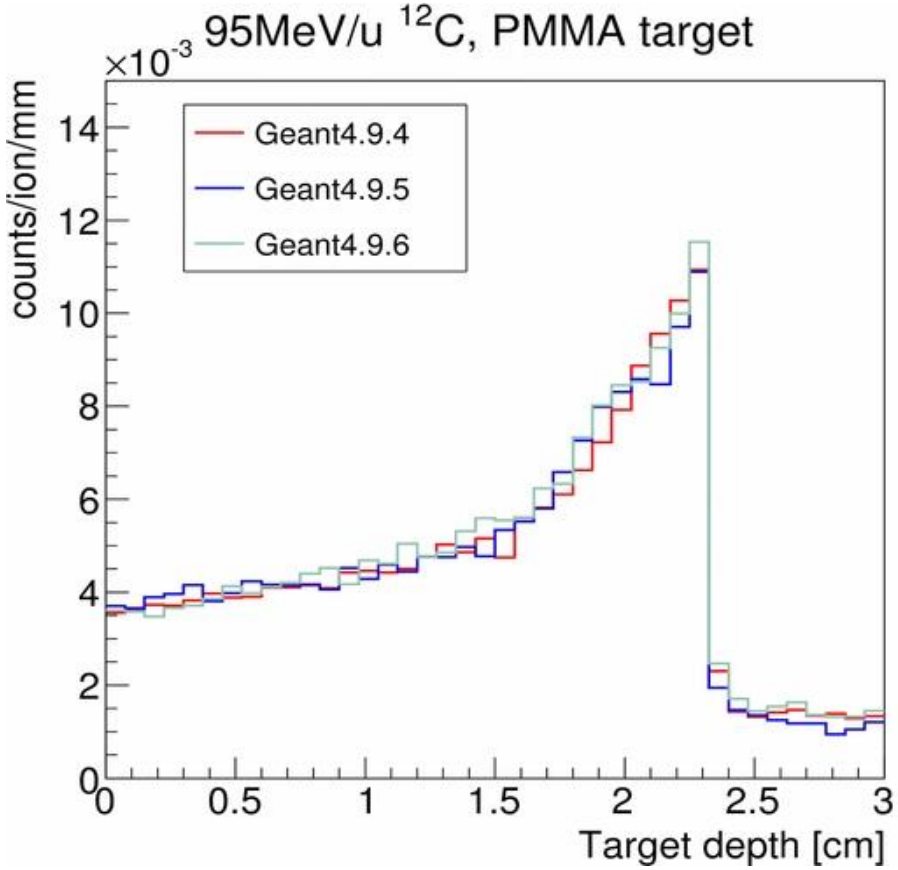
Robert et al., PMB, 2013

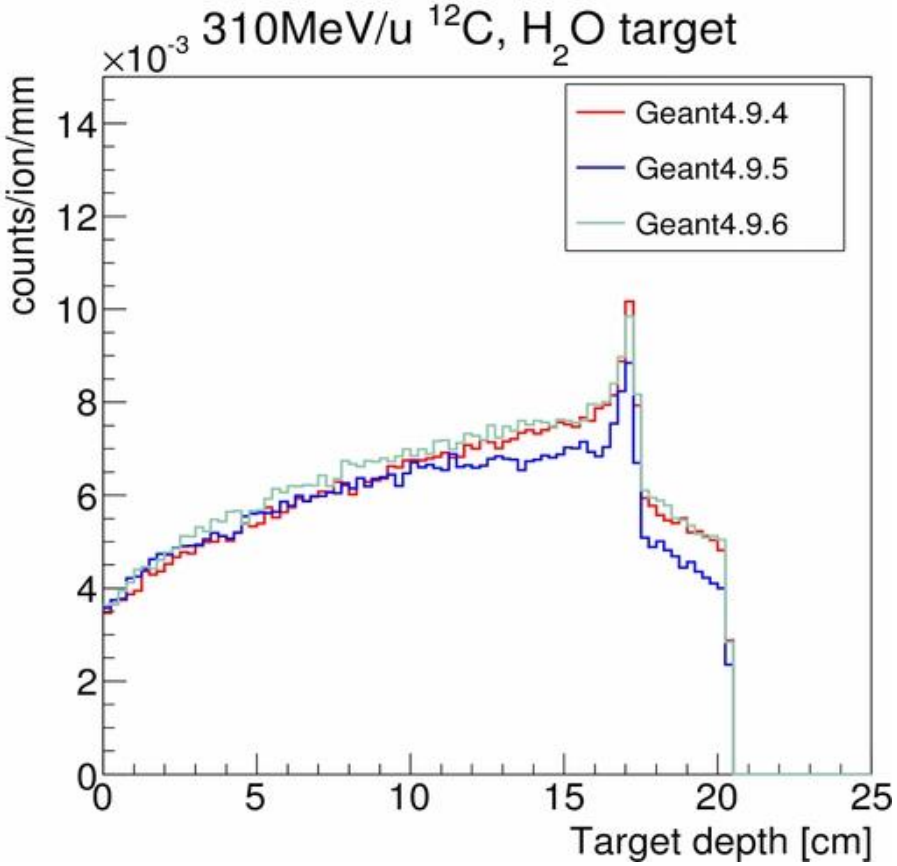
MC pitfalls



Pinto et al., Front. Oncol., 2016

MC pitfalls

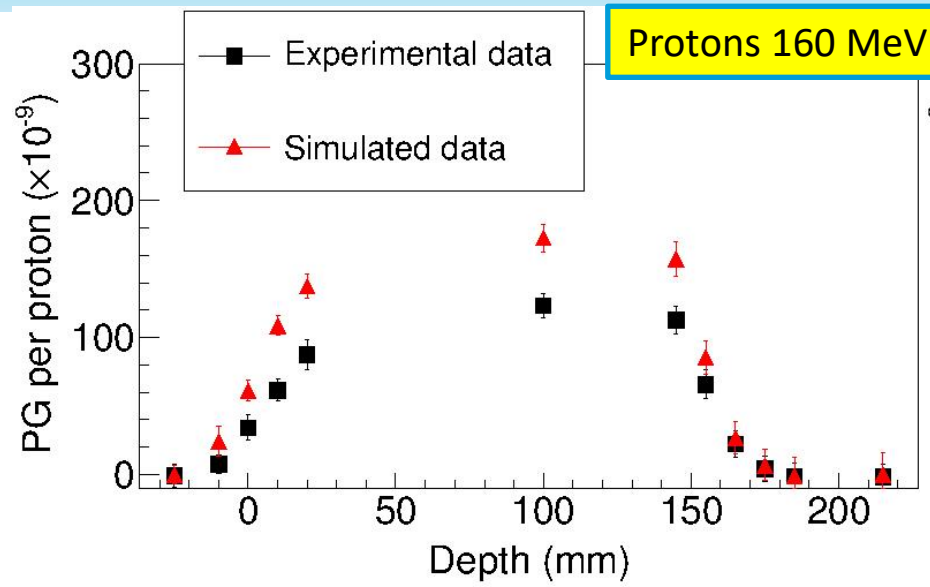


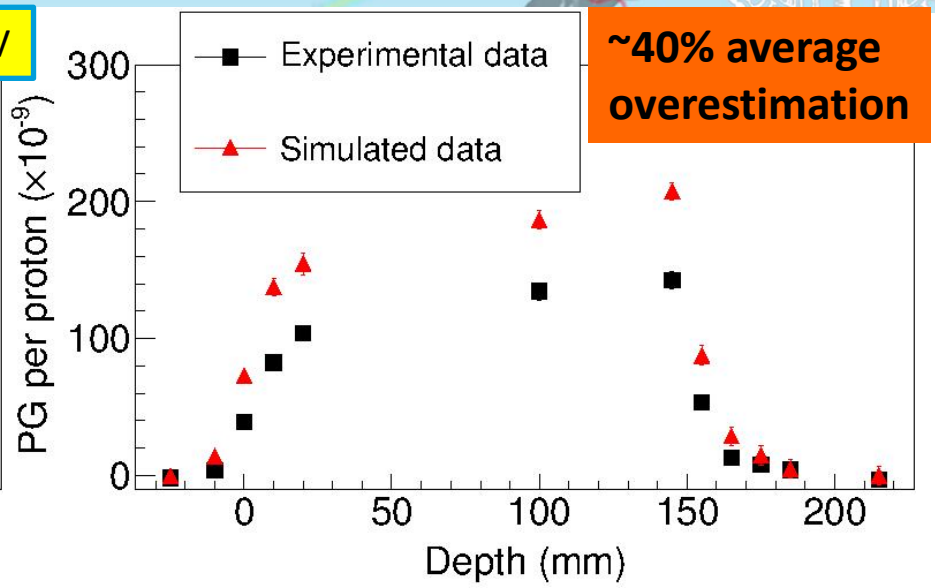


Dedes et al., PMB, 2014

MC pitfalls

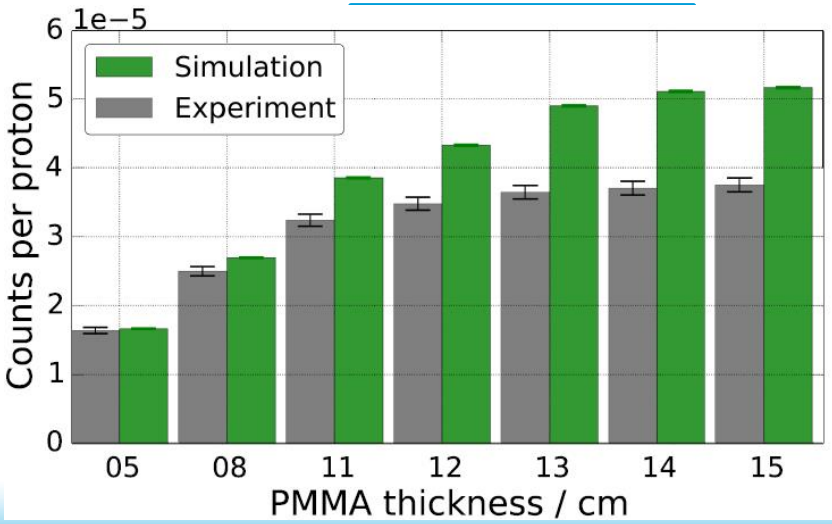
Protons 160 MeV

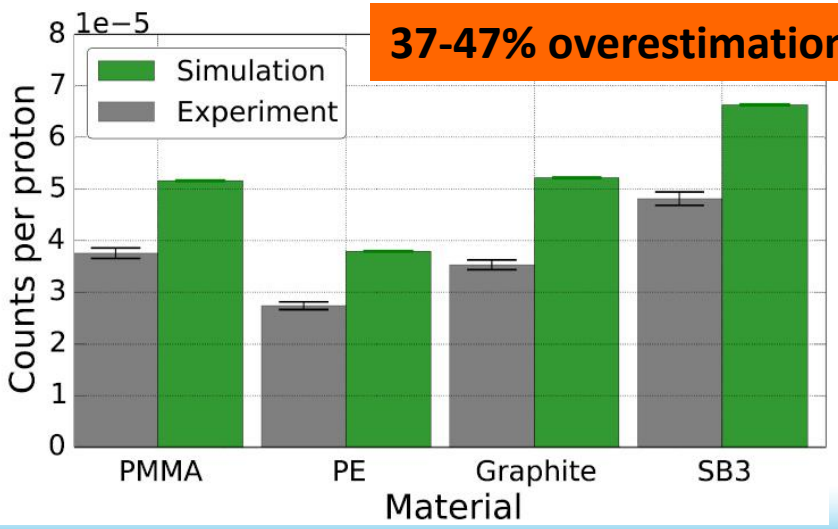




~40% average overestimation

Pinto et al., Front. Oncol., 2016

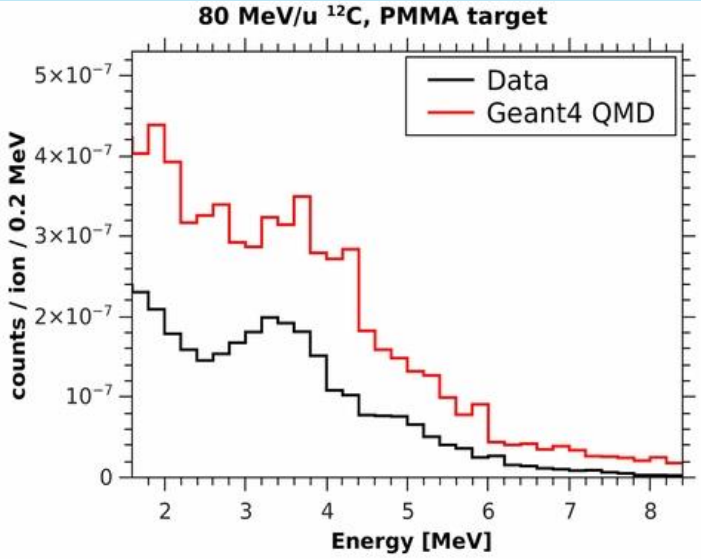


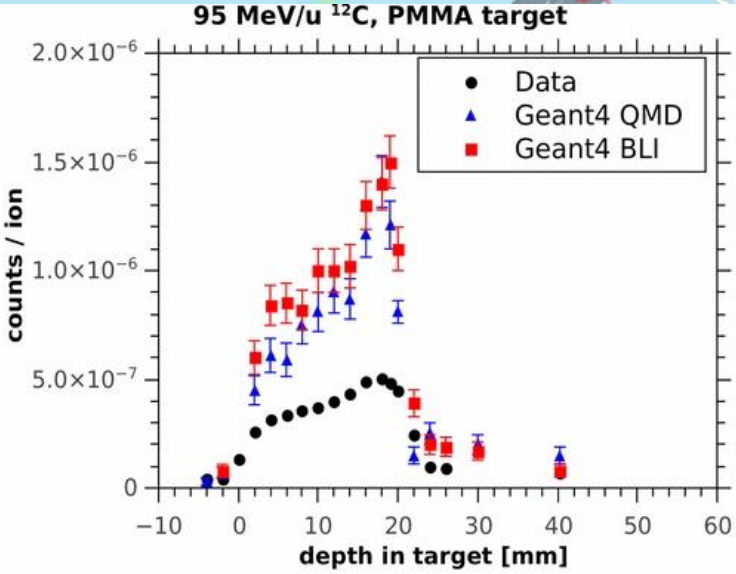


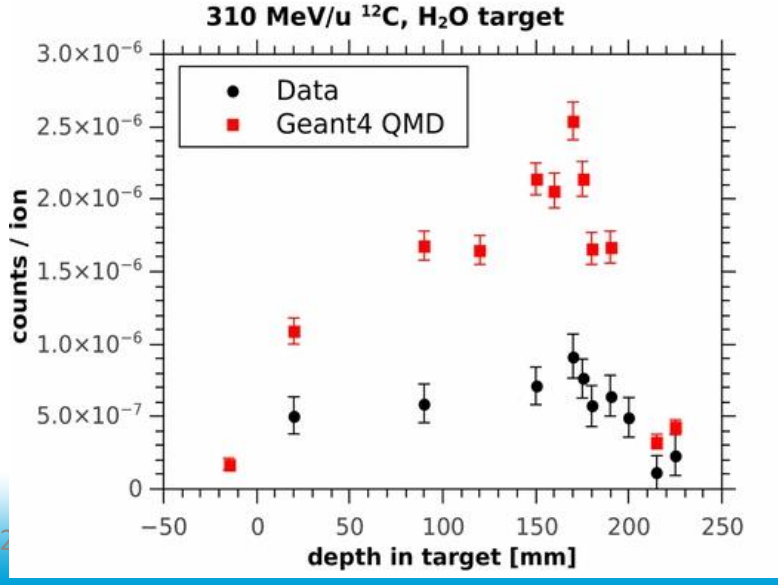
37-47% overestimation

Schumann et al., PMB, 2015

MC pitfalls





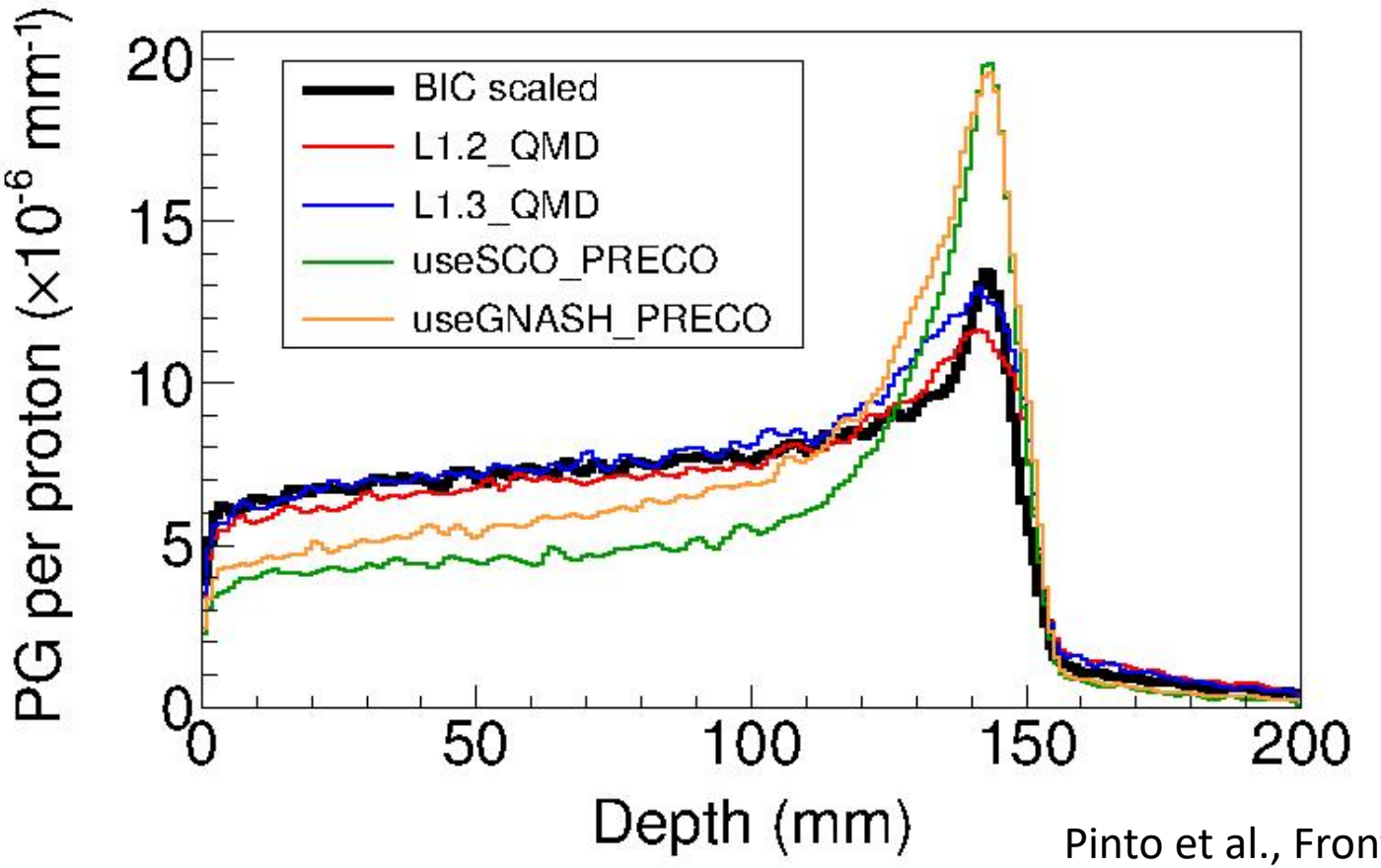


Carbon ions: difference factor 1.8-2.8

Dedes et al., PMB, 2014

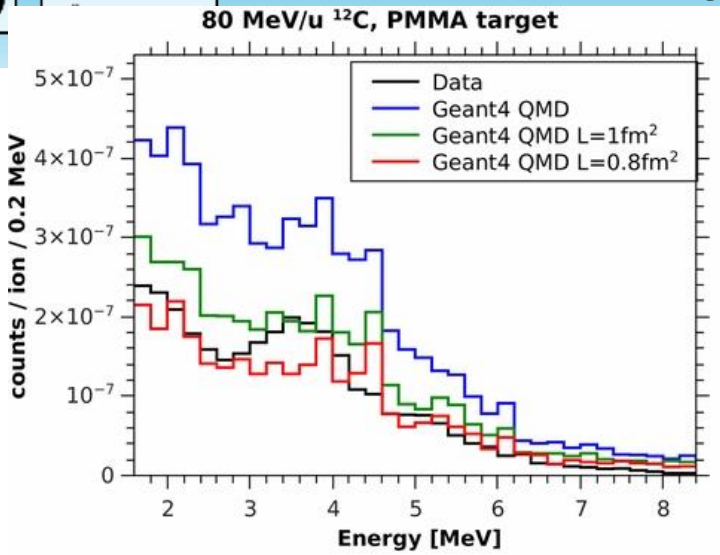
MC pitfalls

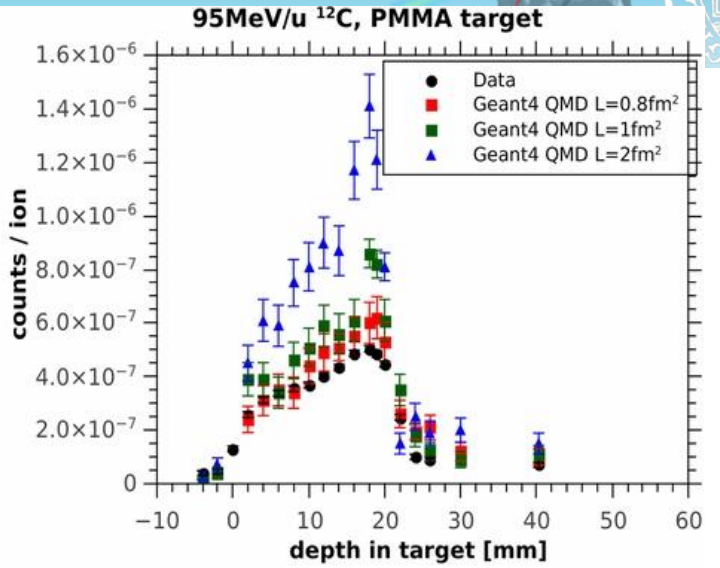
- Adapting the models and assessing their options



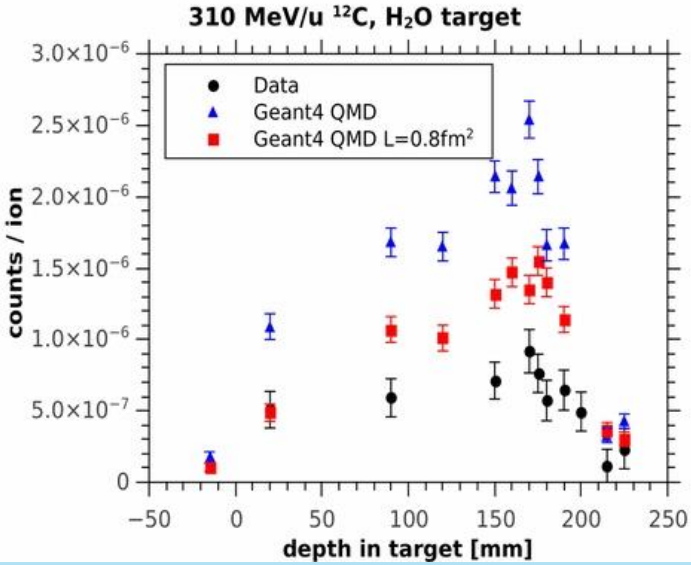
Pinto et al., Front. Oncol., 2016

MC pitfalls





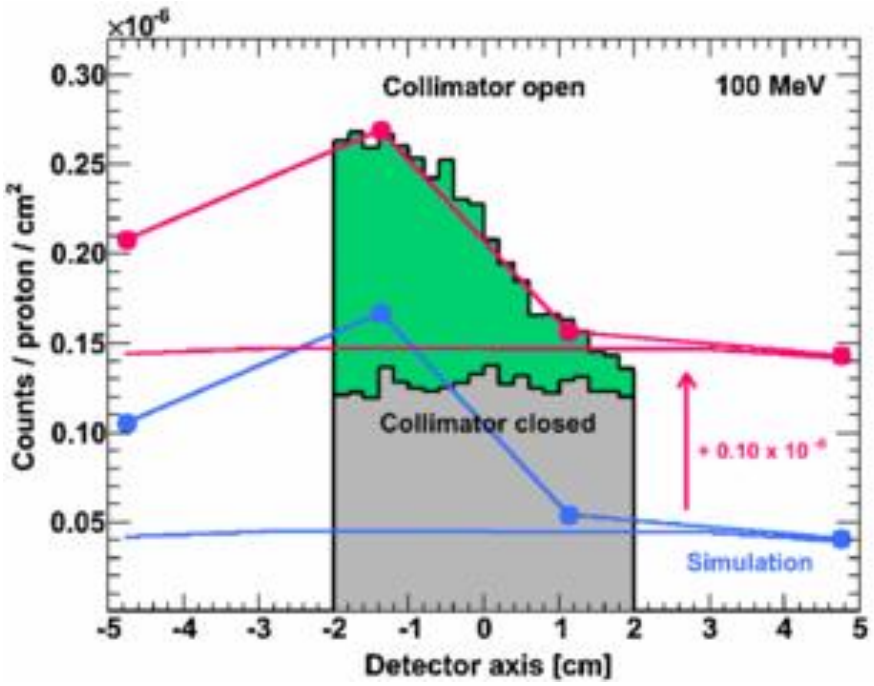
Tuning the models

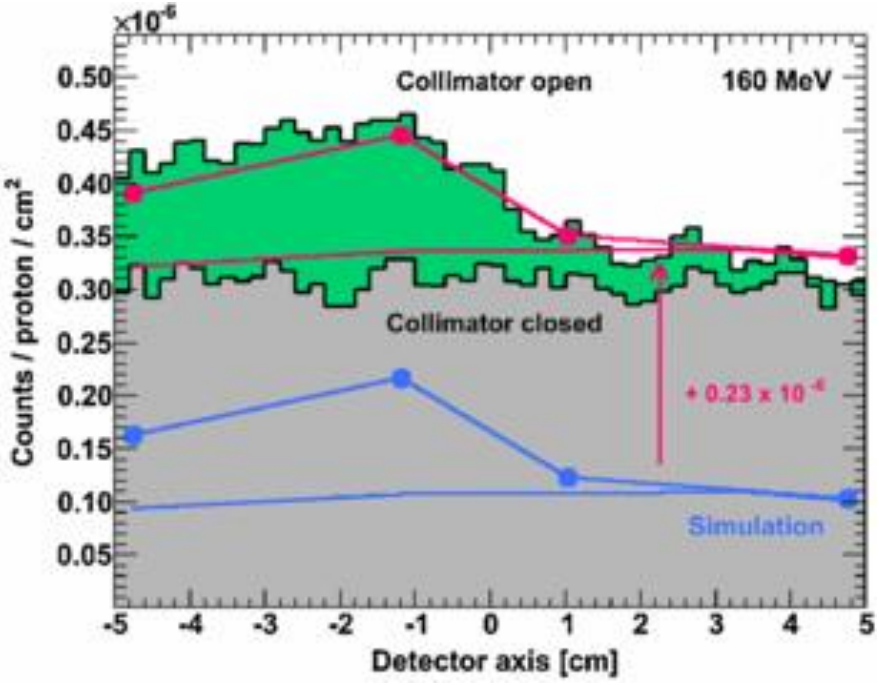


Dedes et al., PMB, 2014

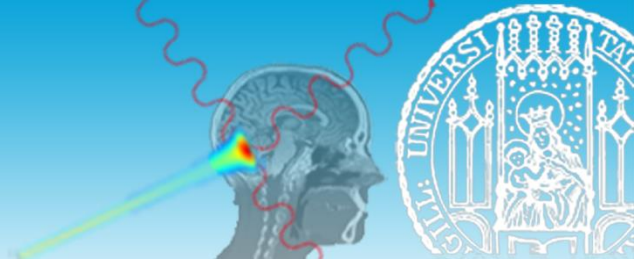
MC pitfalls

- It is virtually impossible to include all factors
  - **<u>One has to find ways to address such shortcomings</u>**



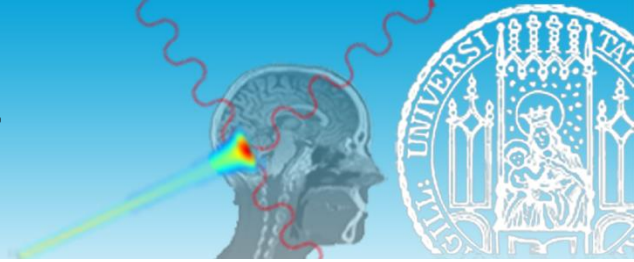


Smeets et al., PMB, 2012



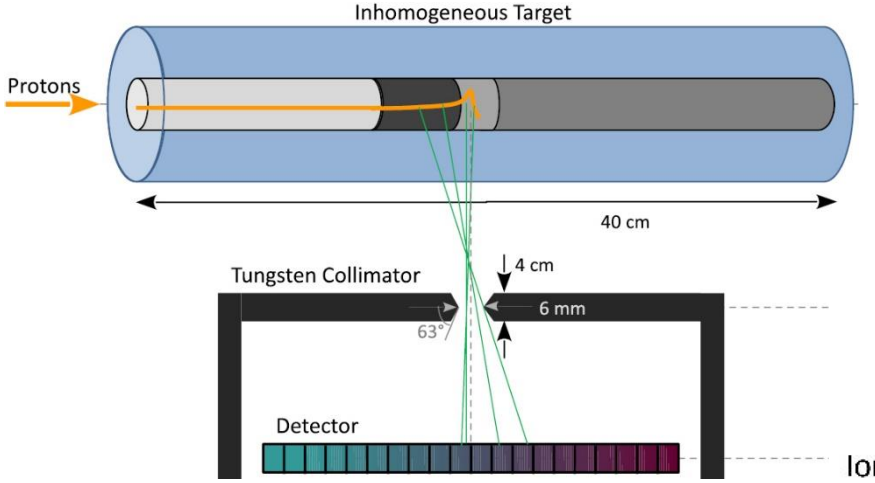
PG MONITORING

PG monitoring



- **Multi-slit collimated camera** (Min et al., Med. Phys., 2006; Testa et al., APL, 2007)
- **Knife-edge camera** (Bom et al., PMB, 2012; Smeets et al., PMB, 2012)
- **Single-slit collimated camera with energy information** (Verburg et al., PMB, 2013)
- **Single-slit collimated camera with time information** (passive delivery) (Testa et al., PMB, 2014)
- **Compton camera** (e.g. Peterson et al., PMB, 2010; Richard et al., IEEE TNS, 2011; Kormoll, NIM A, 2011)
- **Prompt-gamma timing** (Golnik et al., PMB, 2014)
- **Prompt-gamma peak integral** (Krimmer et al., APL, 2017)
- **Prompt gamma imaging combined with neutron detection** (Meric et al., Sci. Rep., 2023)

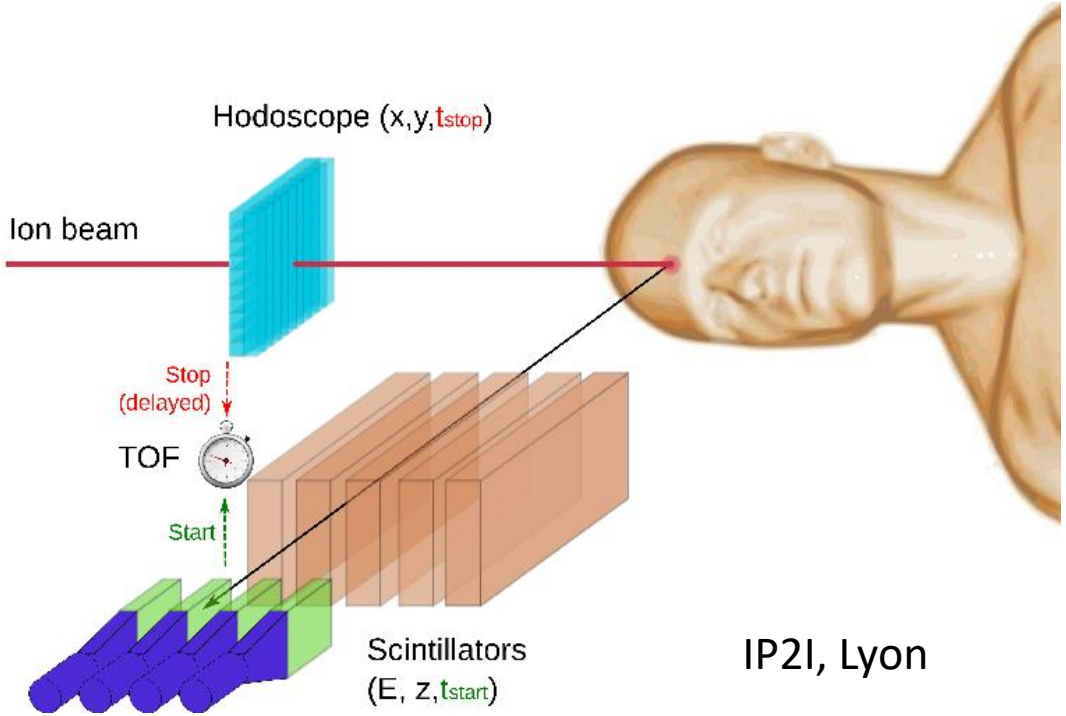
Knife-edge and multi-slit collimator



Priegnitz et al., Phys. Med. Biol., 2015

Richter et al., Radiother. Oncol., 2016

Passive/mechanical collimation



IP2I, Lyon

Knife-edge camera

LUDWIG-MAXIMILIANS-

medicalphysicsweb
RESEARCH • TECHNOLOGY • CLINICAL APPLICATIONS

Home | Opinion | Newsfeed | **Research** | Journals | Multimedia | Jobs | Buyer's guide | Events | Contact

LATEST NEWS ARTICLES
- Research briefs: medical imaging
- An alternative approach to small-field dosimetry
- Brain-penetrating nanoparticles restore neuron function
- CZT-based SPECT may predict cardiac outcomes
- Motion compensation improves cardiac PET

More news articles ▸

RELATED STORIES
- Ranging scheme may improve proton therapy
- Resolved gamma lines verify proton range
- Can prompt gammas monitor in real time?
- Proton therapy: how imaging can help

RELATED LINKS
- ICTR-PHE 2016
- Christian Richter
- OncoRay

SHARE THIS
- E-mail to a friend
- StumbleUpon
- Twitter

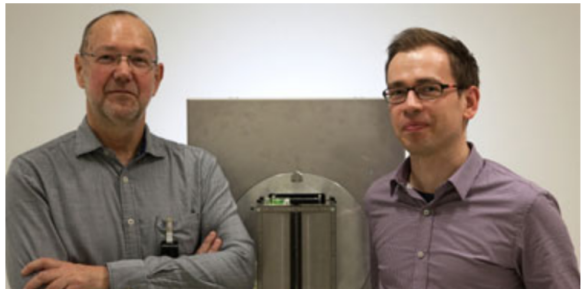
RESEARCH

Mar 2, 2016

Prompt gamma imaging goes clinical

Prompt gamma imaging is under development as a way to monitor proton therapy in real time, by detecting the gamma photons emitted when the therapeutic beam interacts with nuclei within the patient. At the recent International Conference on Translational Research in Radiation Oncology-Physics for Health in Europe (ICTR-PHE) in Geneva, Christian Richter reported on the first clinical application of prompt gamma imaging-based proton range verification.

The clinical study was performed at OncoRay in Dresden, using the first prototype of a knife-edge slit camera being developed by IBA. The camera works by directing the prompt gamma rays emitted during irradiation through a tungsten slit collimator, placed perpendicular to the beam. The prompt gammas are incident upon a segmented detector, creating a one-dimensional depth profile of the beam path. If the proton range changes, the prompt gammas pass through the slit at a slightly different angle and hit different detector segments, revealing any range shift.



PG imaging with passive delivery

medicalphysicsweb
RESEARCH • TECHNOLOGY • CLINICAL APPLICATIONS

Home | Opinion | Newsfeed | **Research** | Journals | Multimedia | Jobs | Buyer's guide | Events | Contact

LATEST NEWS ARTICLES
- Research briefs: medical imaging
- An alternative approach to small-field dosimetry
- Brain-penetrating nanoparticles restore neuron function
- CZT-based SPECT may predict cardiac outcomes
- Motion compensation improves cardiac PET

More news articles ▸

RELATED STORIES
- Prompt gamma imaging goes clinical
- Ranging scheme may improve proton therapy
- Resolved gamma lines verify proton range
- Can prompt gammas monitor in real time?

RELATED LINKS
- Radiation Oncology, University of Pennsylvania
- IBA
- Kevin Teo
- Radiation Oncology, UCSF

RESTRICTED LINKS
- Int. J. Radiat. Oncol. Biol.

RESEARCH

May 30, 2017

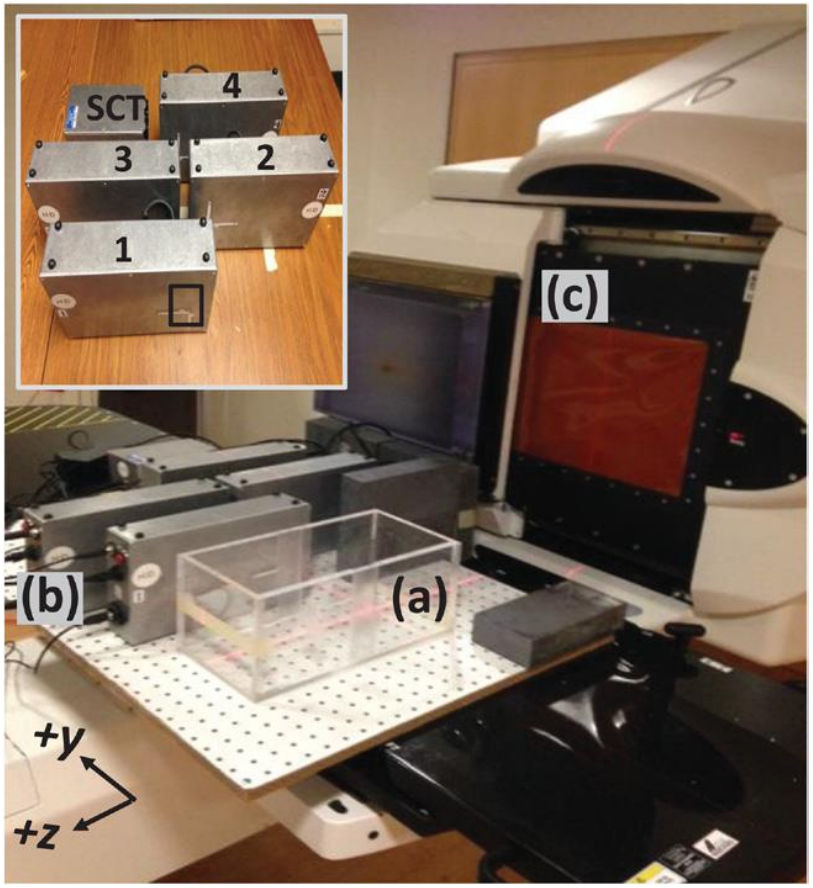
First clinical prompt gamma imaging of PBS protons

Proton therapy offers superior dosimetric properties to photon therapy, but there is uncertainty as to the exact location where protons stop during treatment. Such uncertainties, which can arise from patient misalignment, organ motion, anatomical changes or conversion of CT Hounsfield units to proton stopping power, are accounted for by adding a distal margin to the treatment plan, resulting in additional dose to healthy tissue.

To reduce margins, researchers are developing methods for *in vivo* proton range verification. Two approaches - PET imaging of positron emitters generated in the patient and MR imaging of radiation-induced tissue changes - have been demonstrated clinically. Now, researchers from the University of Pennsylvania and IBA have reported the first clinical use of prompt gamma imaging (PGI) for range verification in pencil-beam scanned (PBS) proton therapy (*Int. J. Radiat. Oncol. Biol. Phys.* doi: 10.1016/j.ijrobp.2017.04.027).

PG imaging with active delivery

Compton cameras

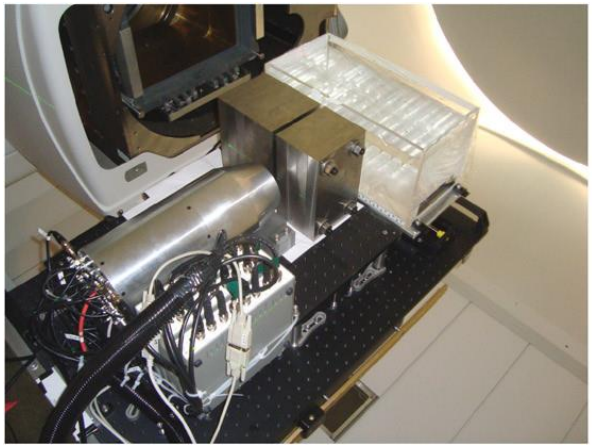


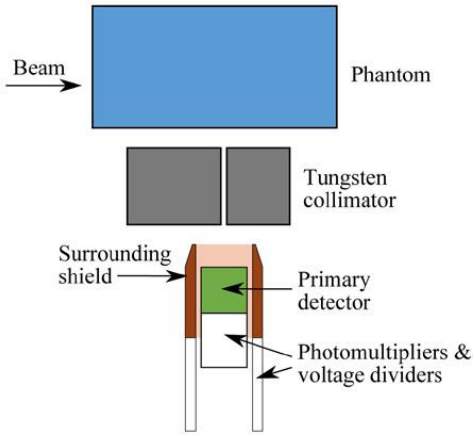
Polf et al., Phys. Med. Biol., 2015

Electronic collimation

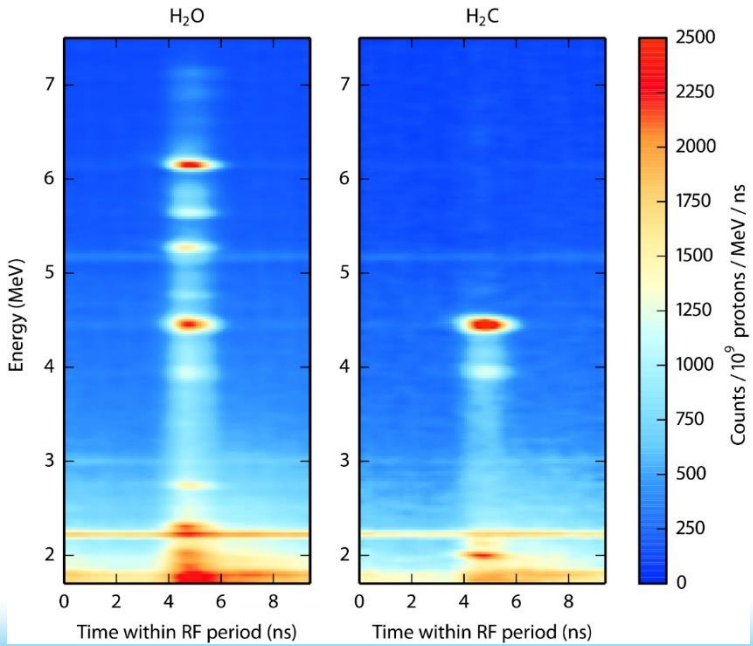
Solevi et al., Phys. Med. Biol., 2016

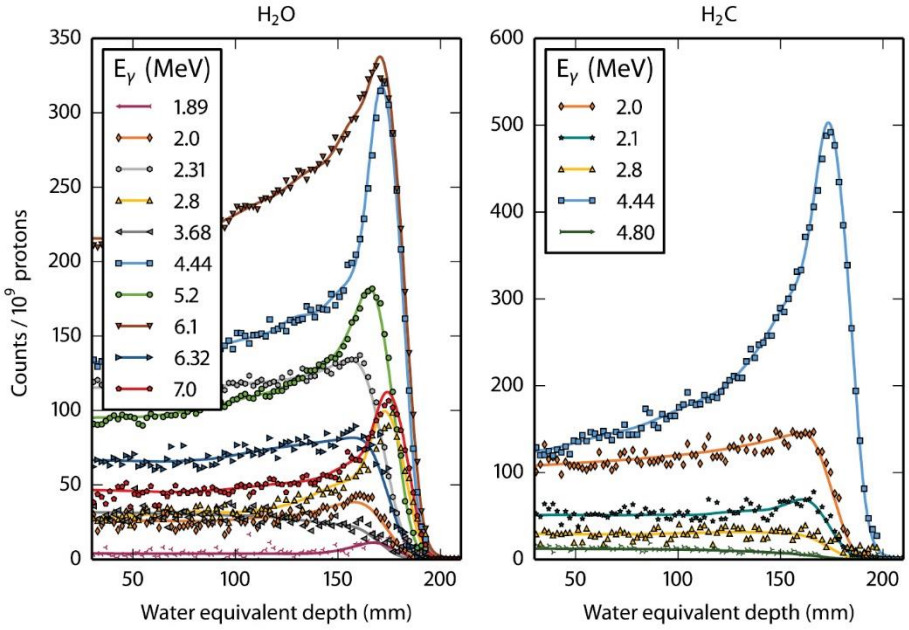
PG spectroscopy





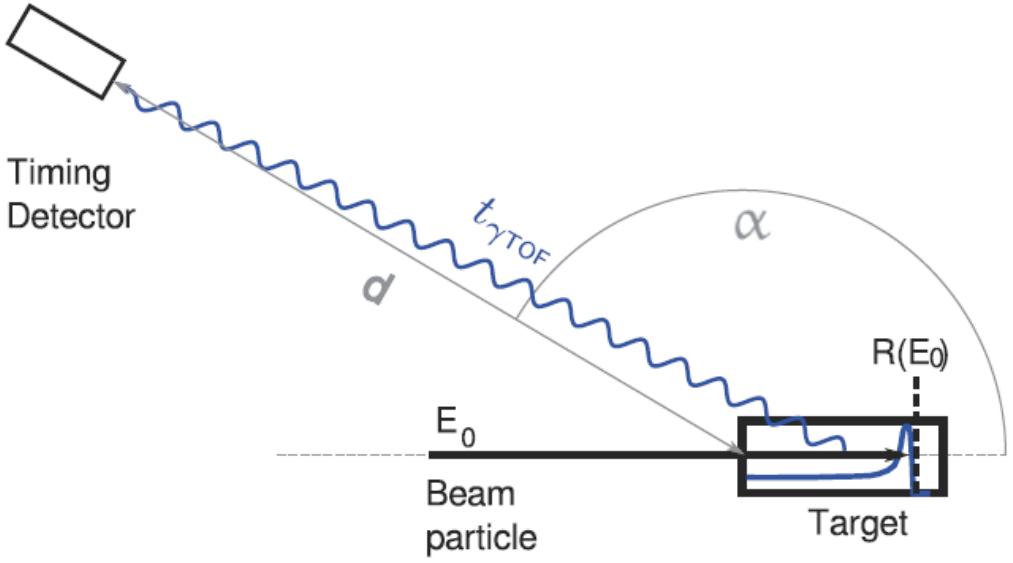
Verburg and Seco, Phys. Med. Biol., 2014

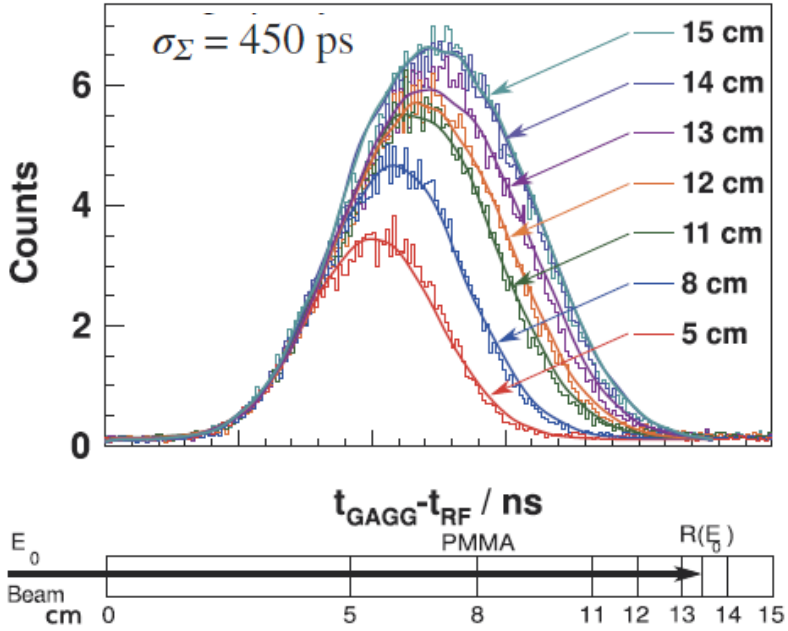




PG timing

PG timing: range monitoring concept relying on time spectroscopy without need of collimation

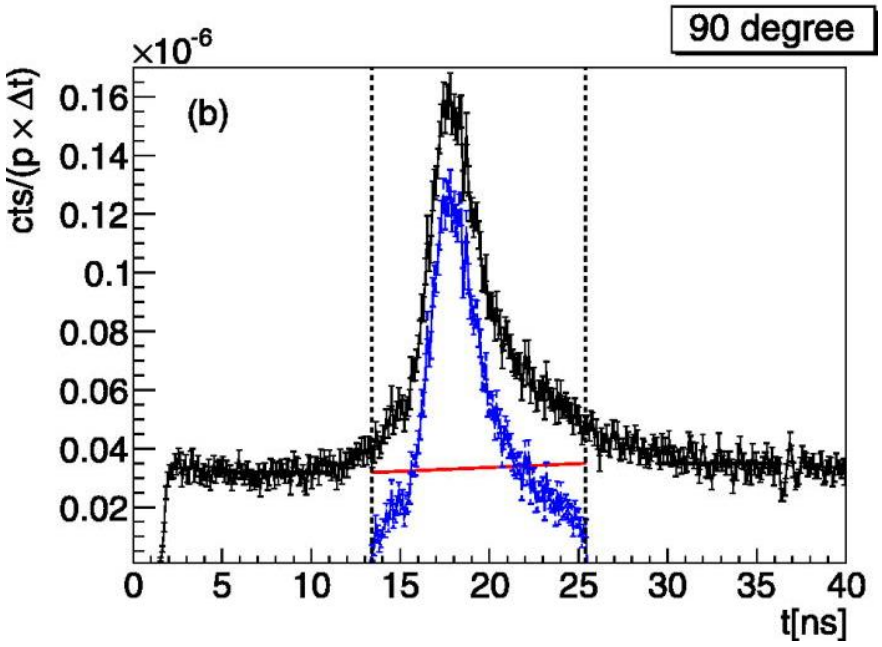


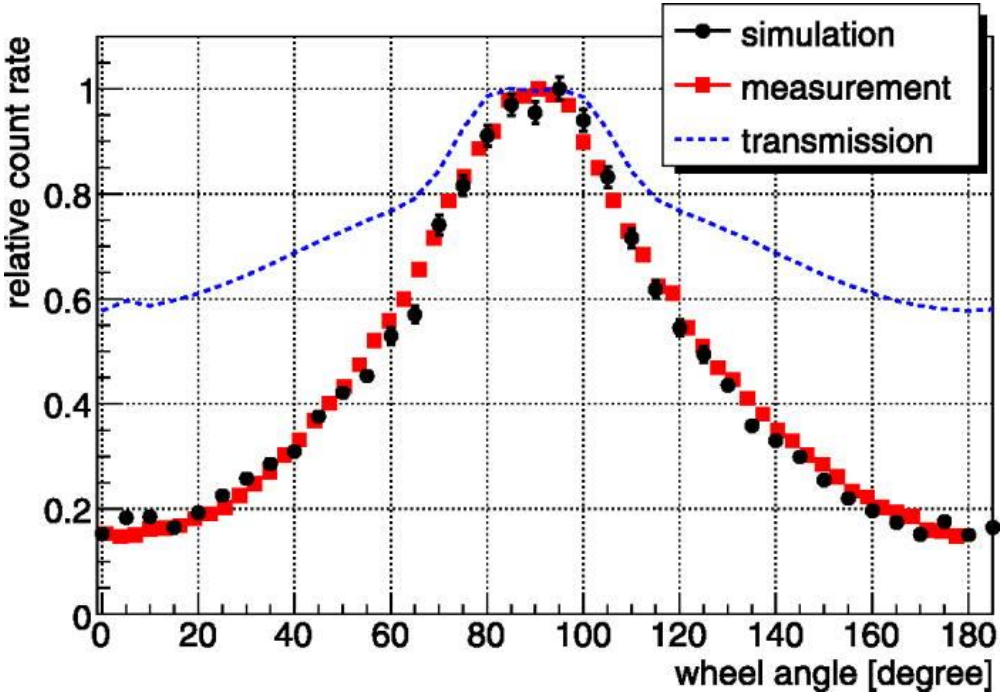


Golnik et al., Phys. Med. Biol., 2014

PG peak integral

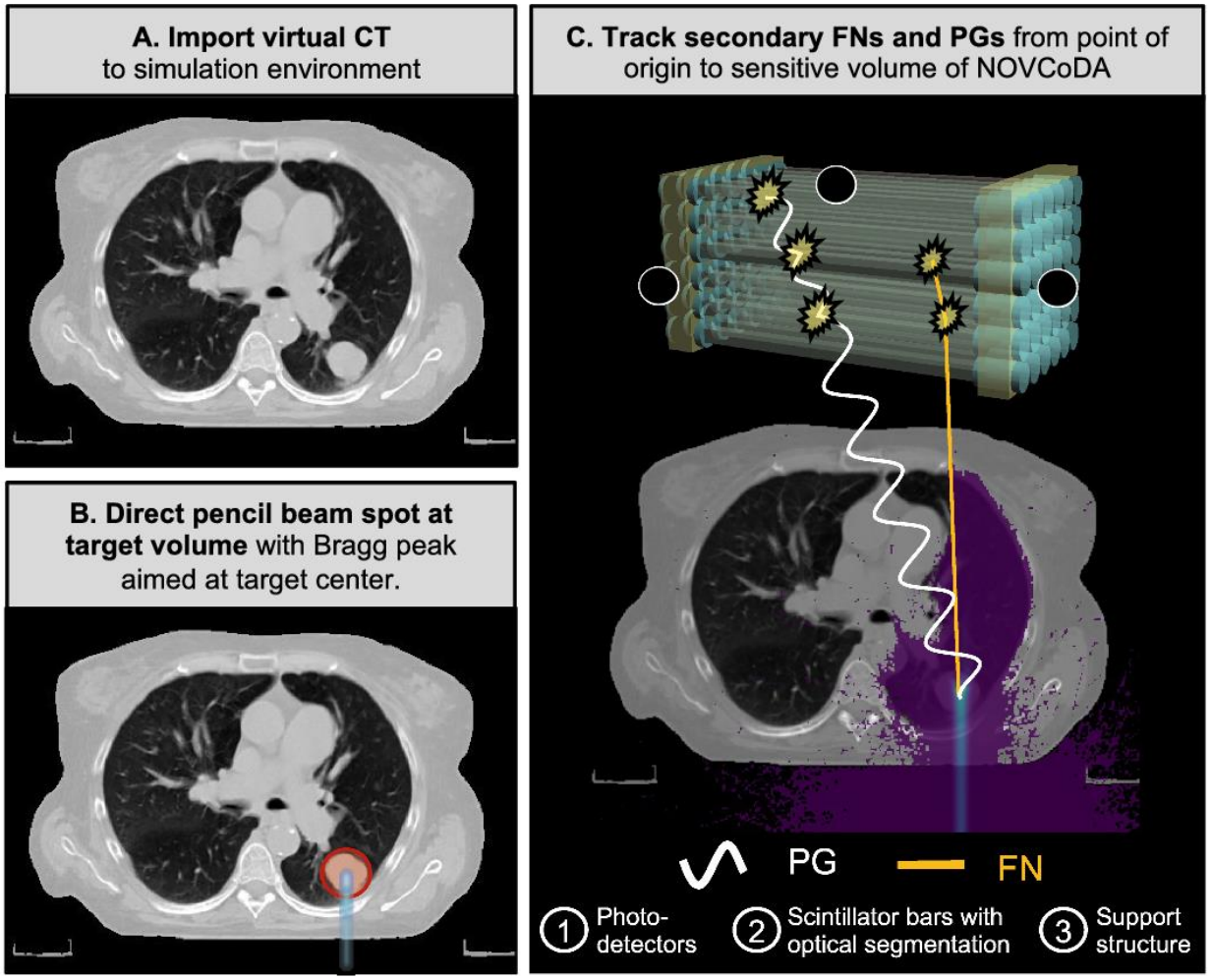
- Uncollimated detector
- Integral of the PG TOF peak



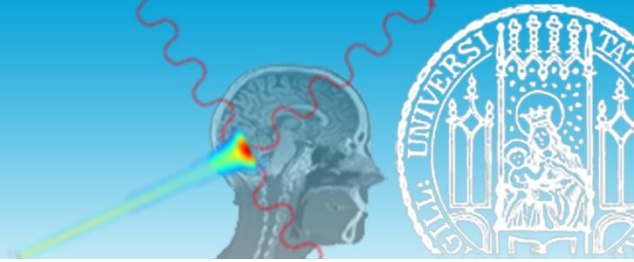


Krimmer et al., APL, 2017

PG + neutron imaging

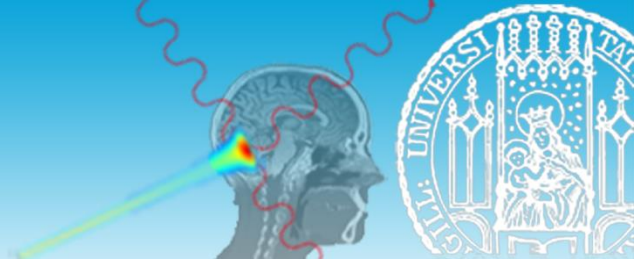


Adapted from Meric et al., Sci. Rep., 2023



EXAMPLES OF MC APPLICATION IN PG MONITORING

Examples MC

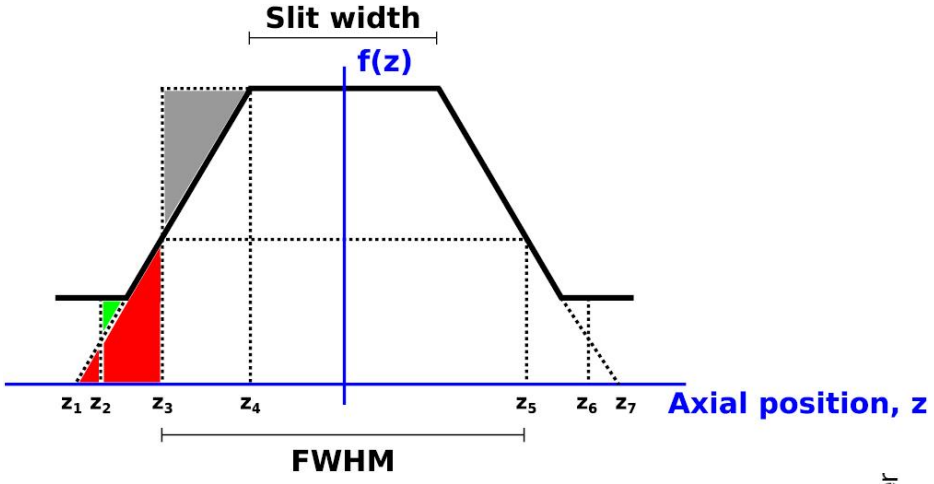


- All PG monitoring approaches shown before have used MC simulations extensively

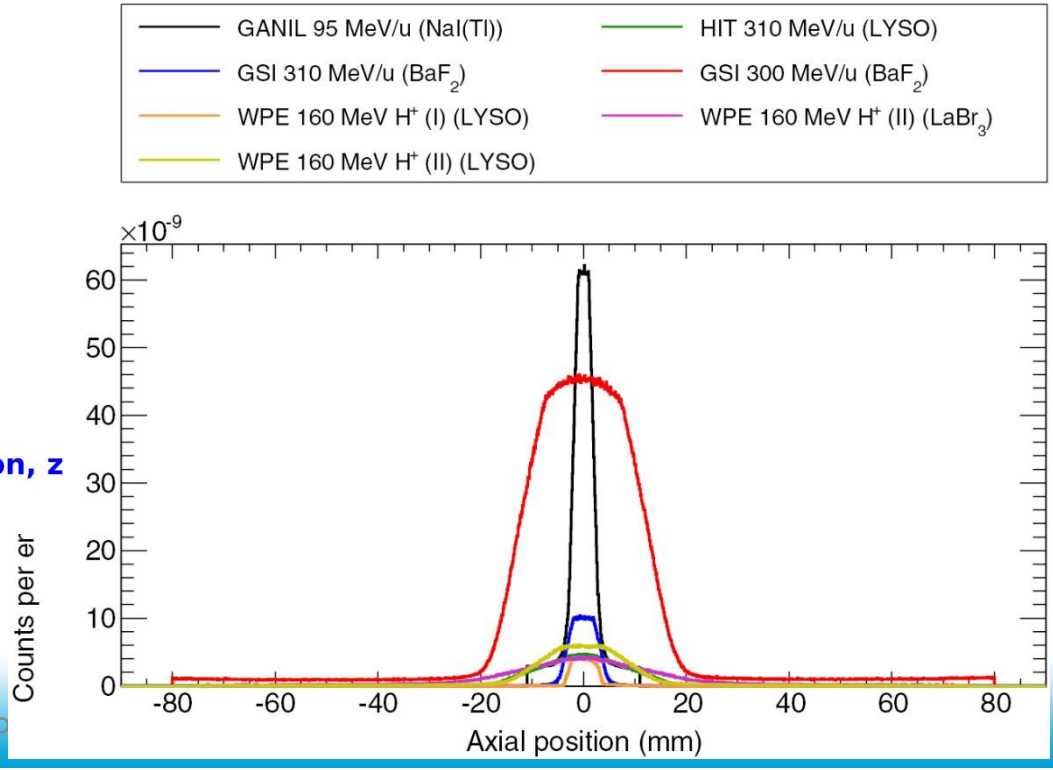
- The application of MC will be shown for some use cases

Fundamental science

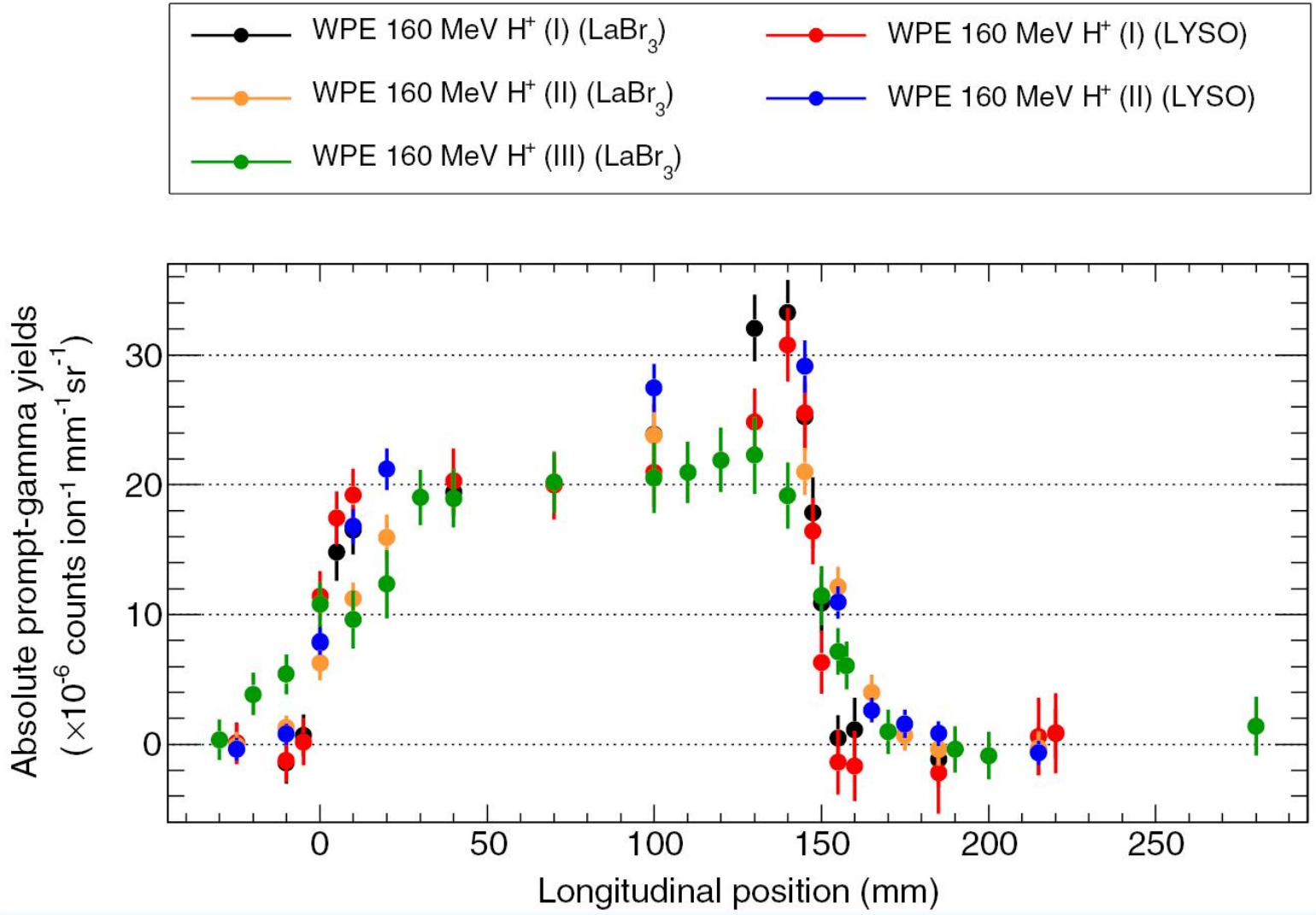
- **Absolute yields and cross section experiments**
  - Even though MC tools have issues to model PG yields, they can still be used, for example, to estimate corrections (e.g. solid angle, FOV, detection rate)



Pinto et al., PMB, 2014



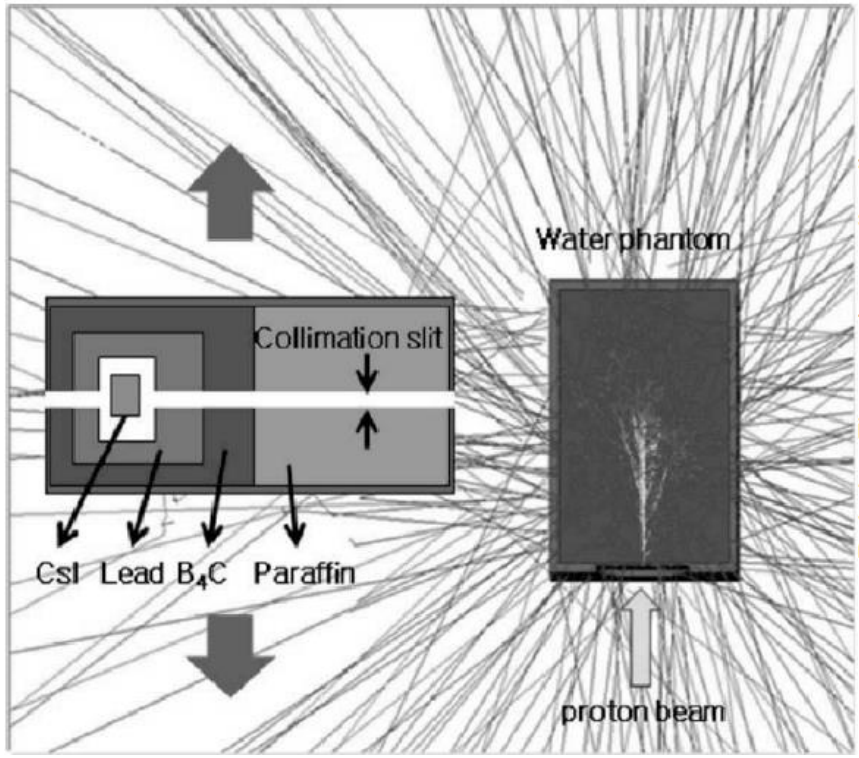
Fundamental science

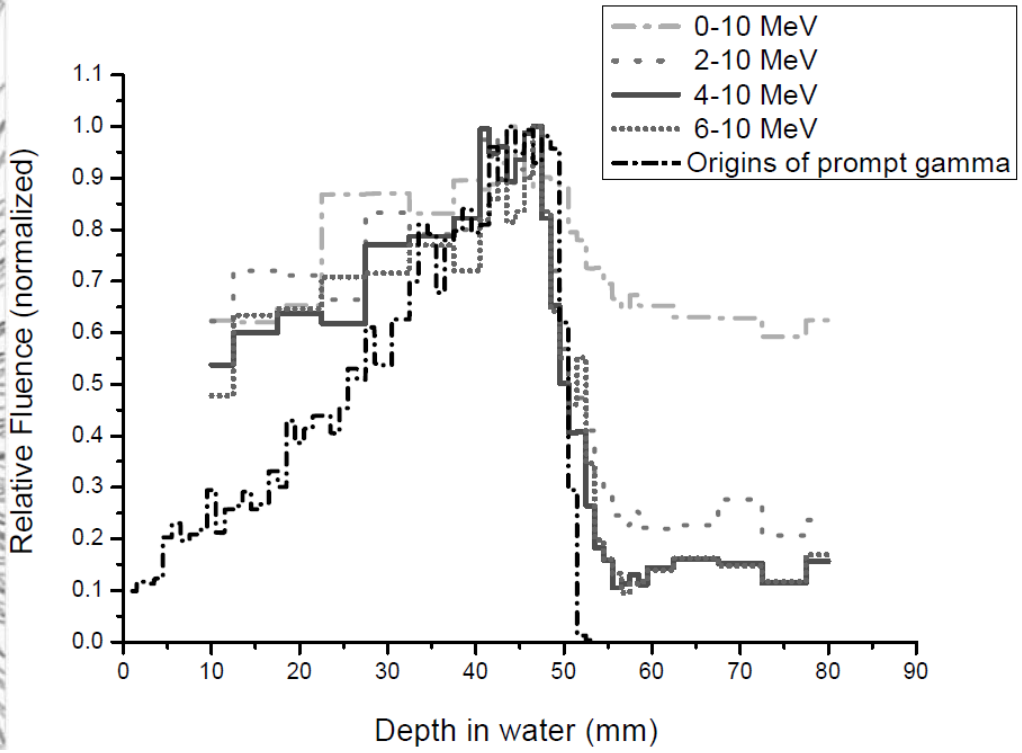


Pinto et al., PMB, 2014

PG camera optimization

- **Energy thresholds optimization**

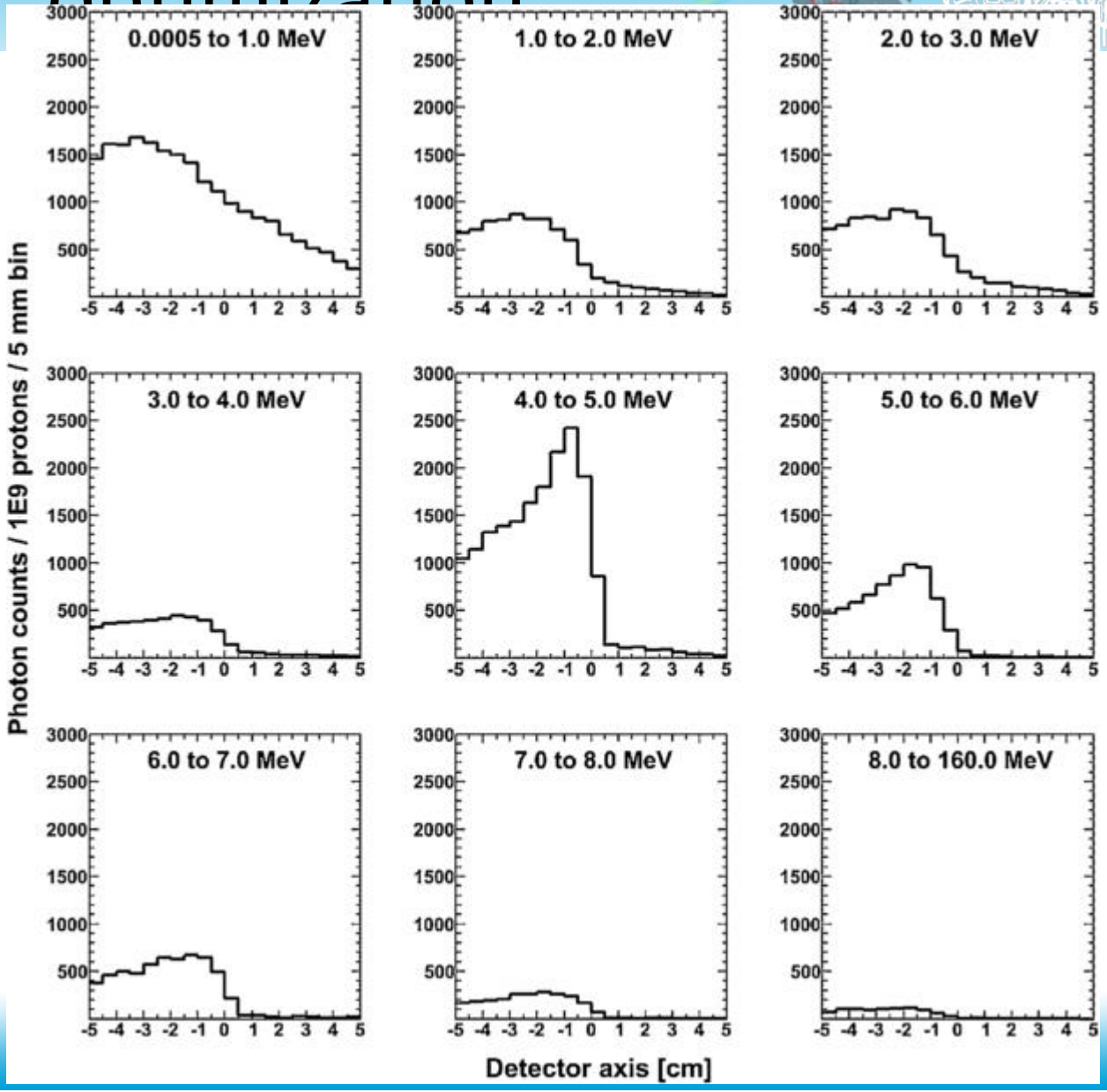




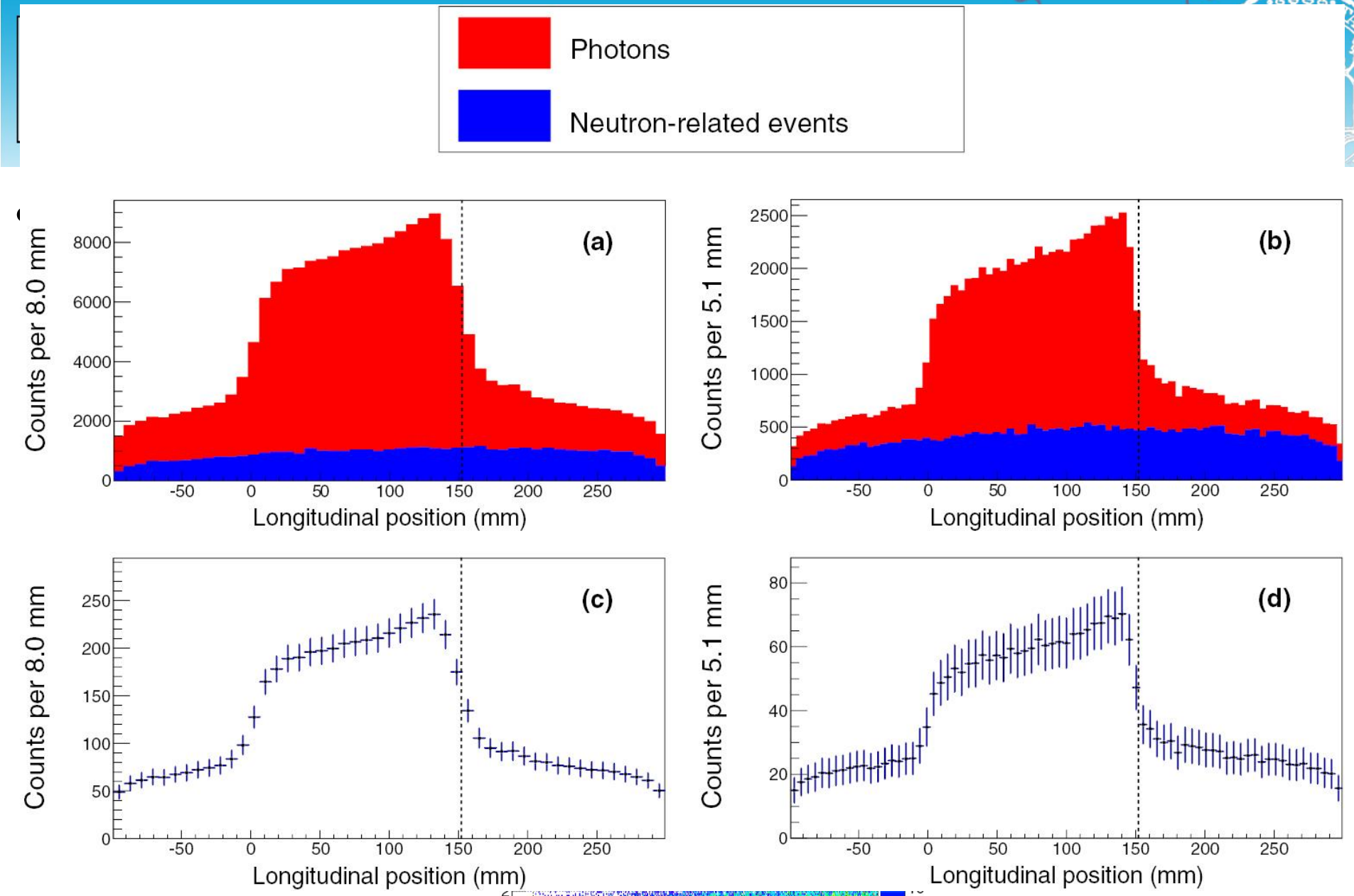
Min et al., Journal of Nuclear Science and Technology, 2008

PG camera optimization

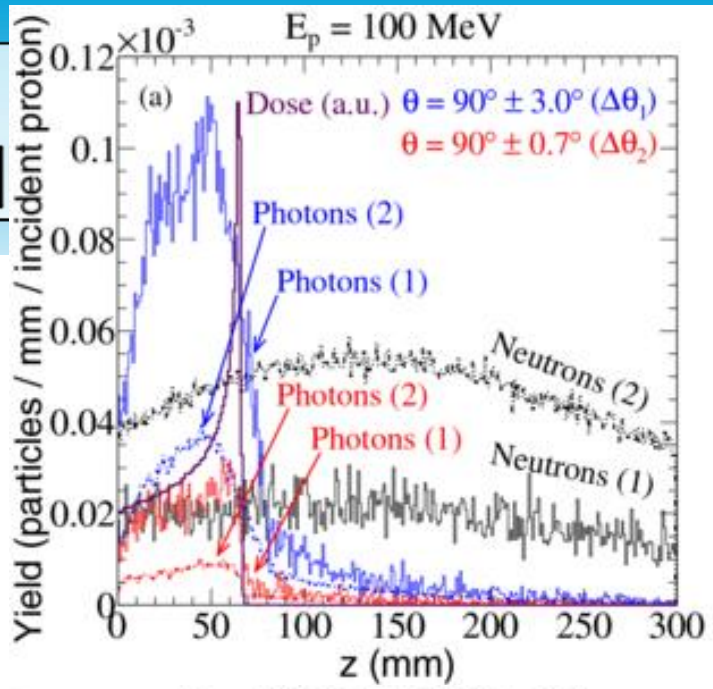
- **Energy thresholds optimization**

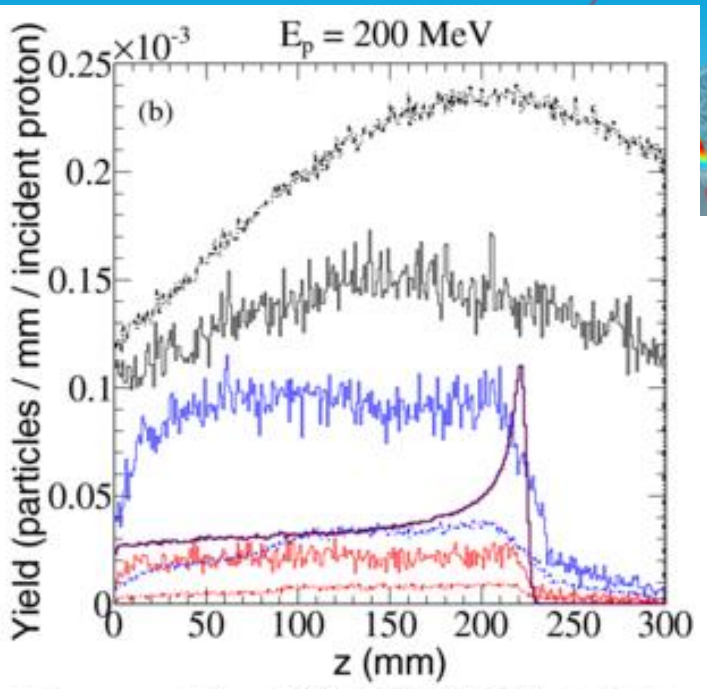


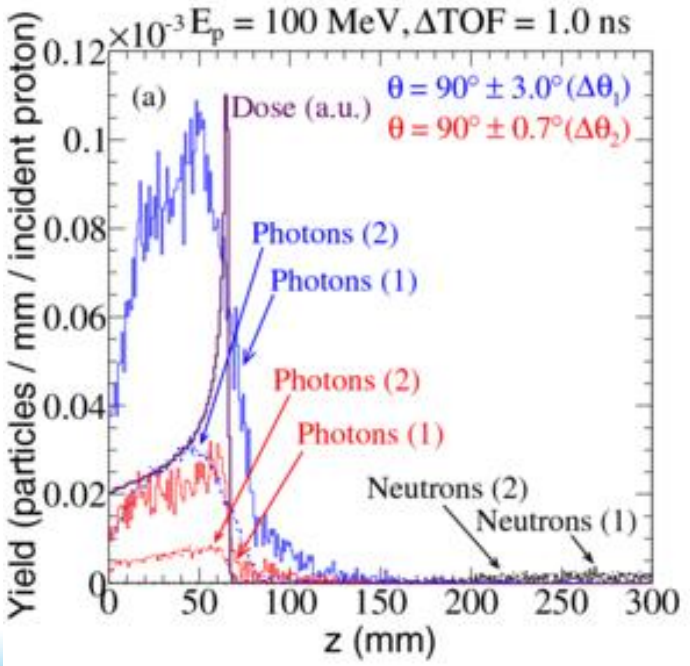
Smeets et al., PMB, 2012

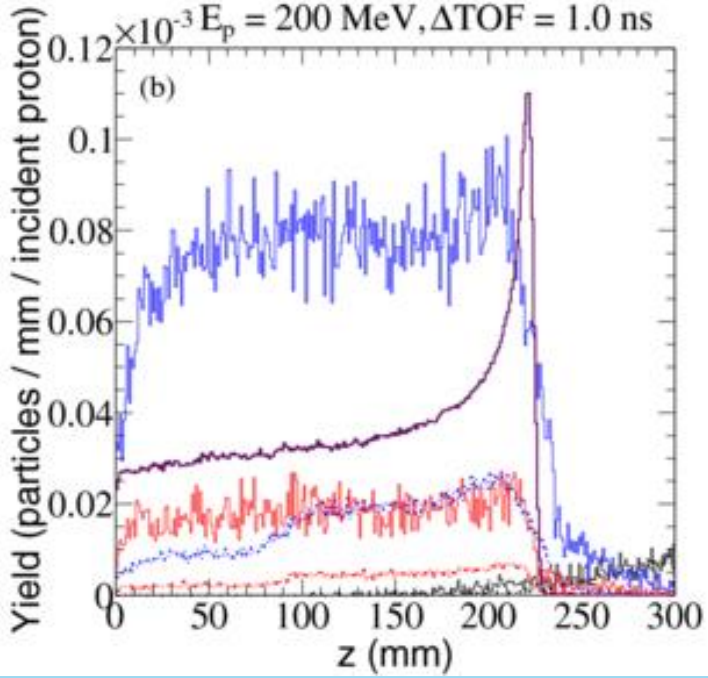


Pinto et al., PMB, 2014







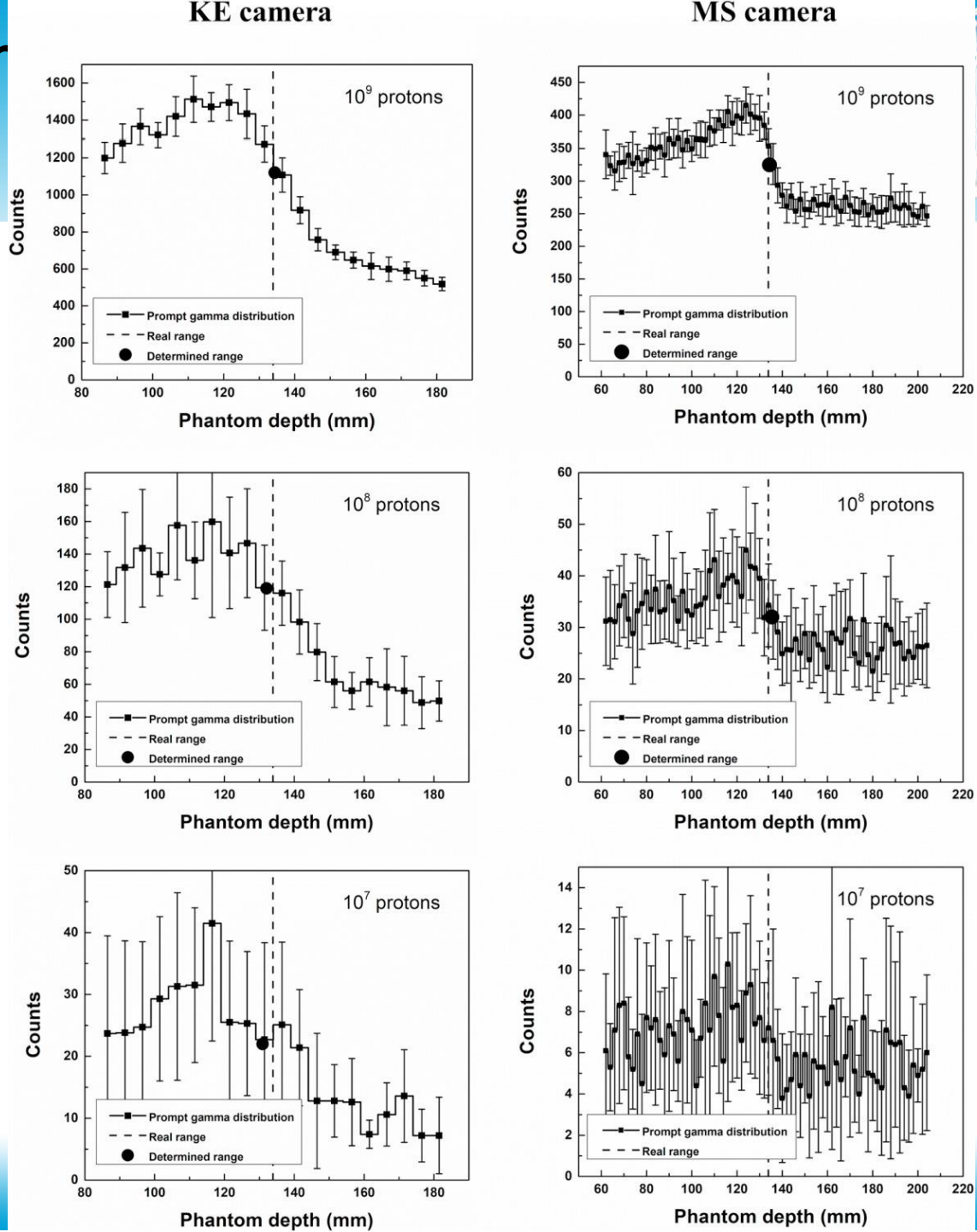


(1) Geant4
(2) MCNPX

Biegun et al., PMB, 2012

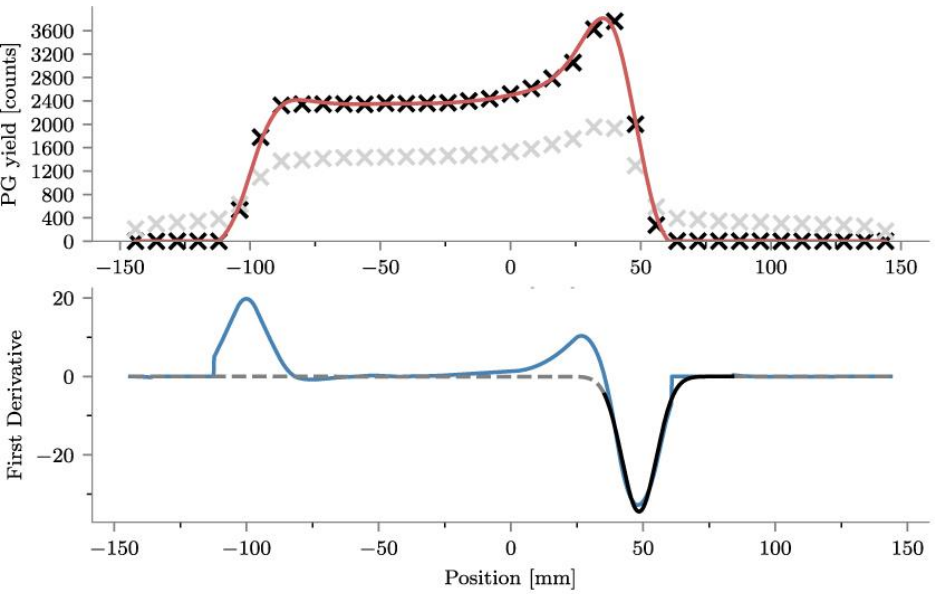
Com

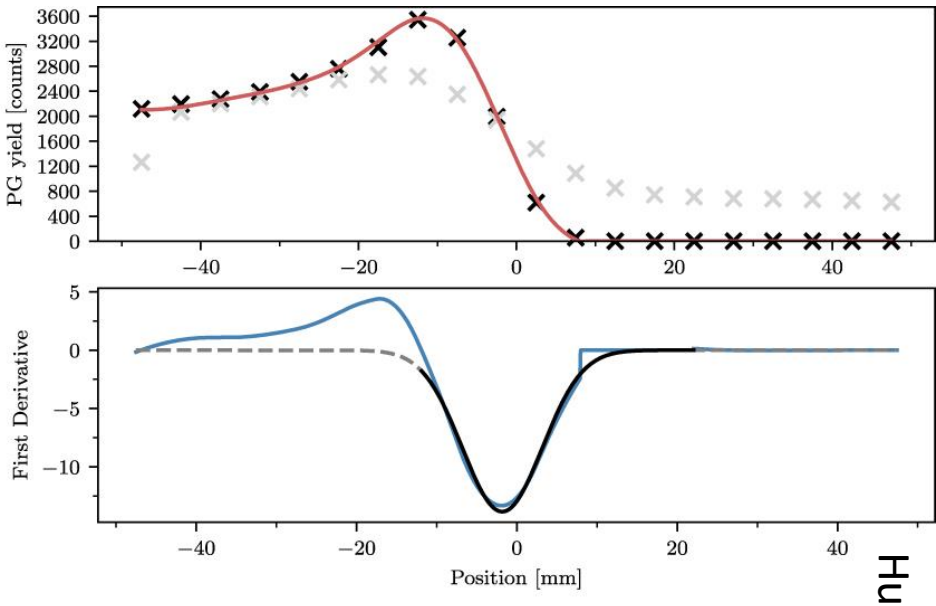
- **Comparison between PG cameras**



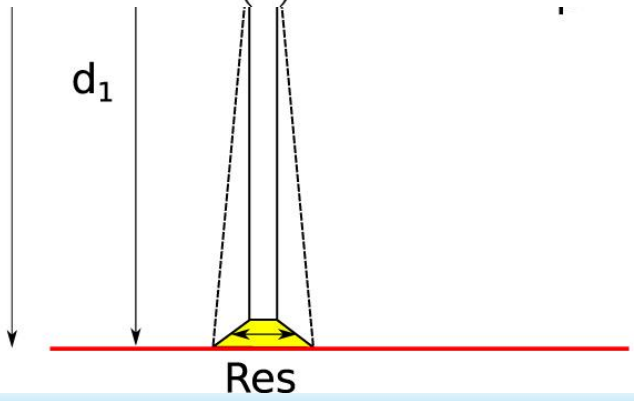
Park et al., Nuclear Engineering and Technology, 2019

Comparison between PG cameras

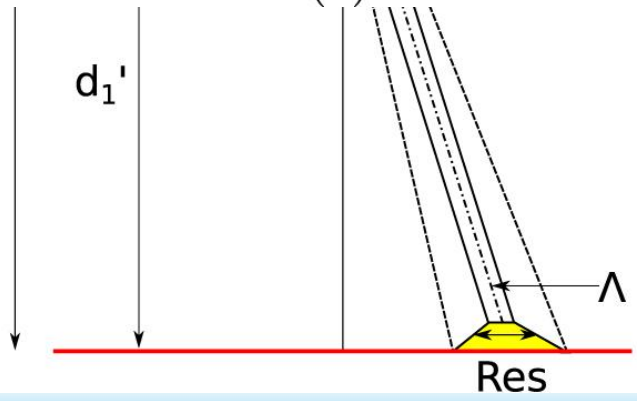




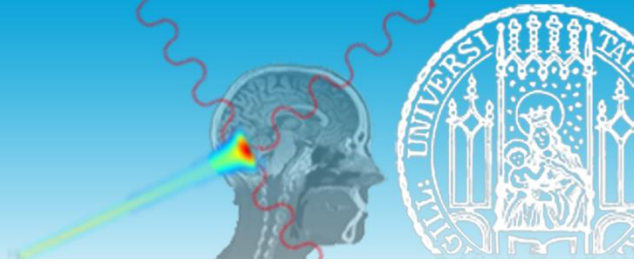
(a) MPS



(b) KES



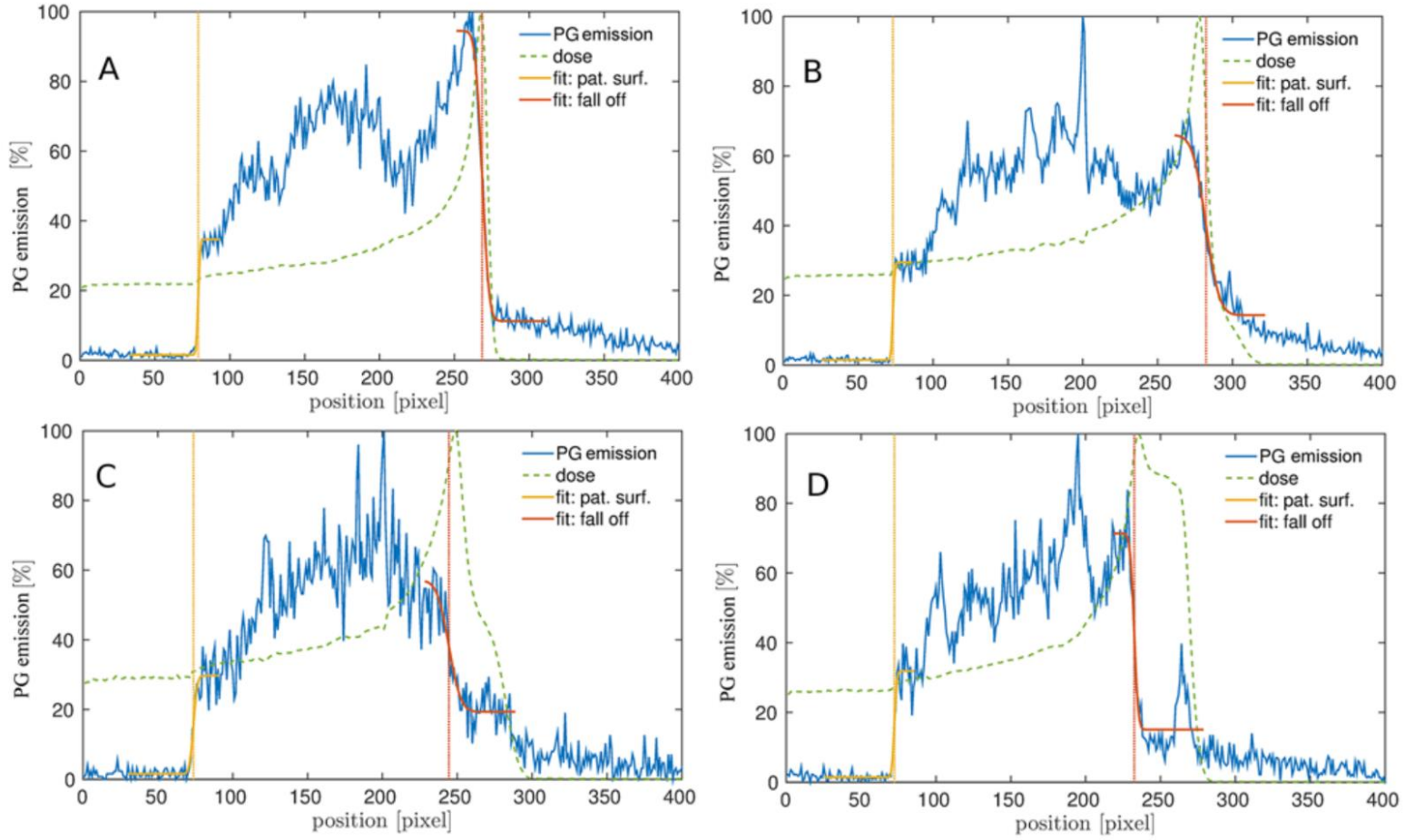
Huisman et al., PMB, 2023



BEYOND JUST MC

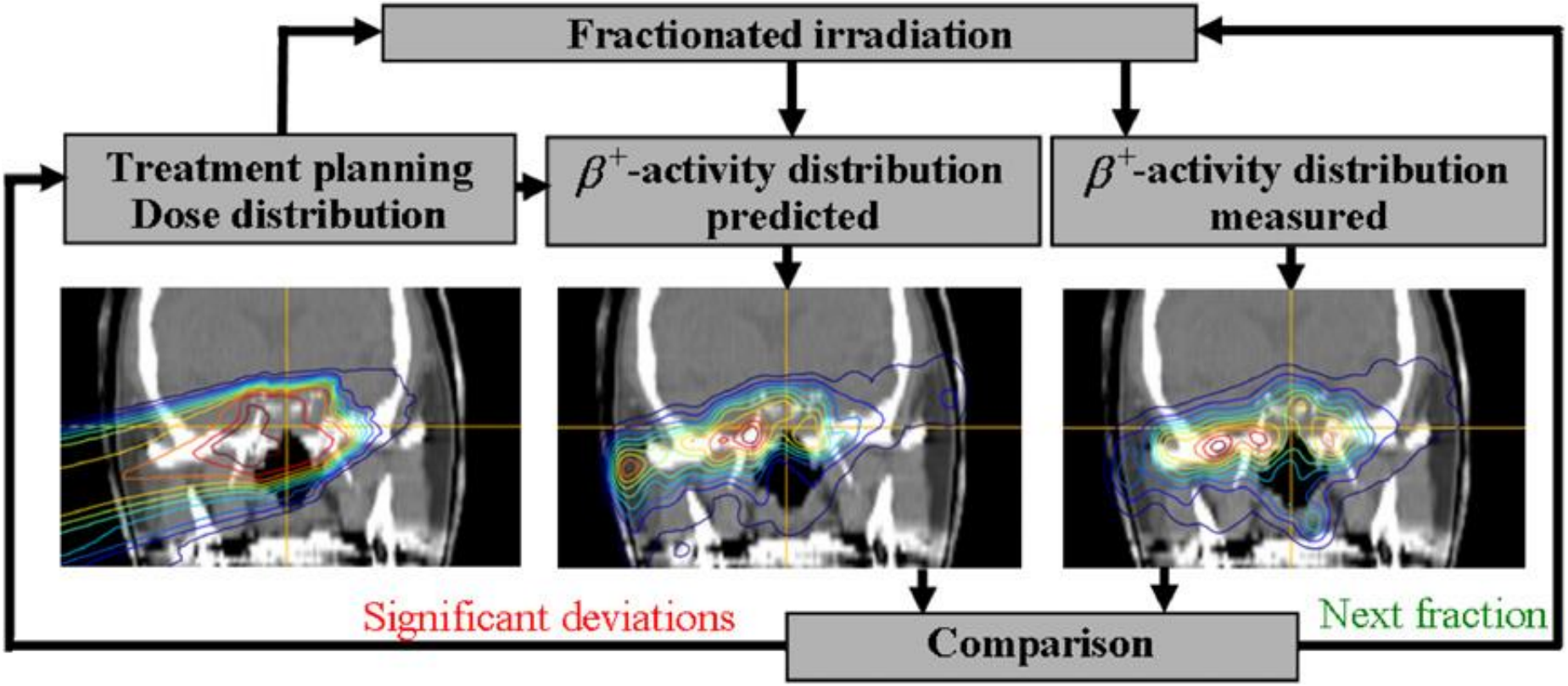
Beyond just MC

!!! PET/PG distribution ≠ dose distribution !!!



Schmid et al., PMB, 2015

Beyond just MC

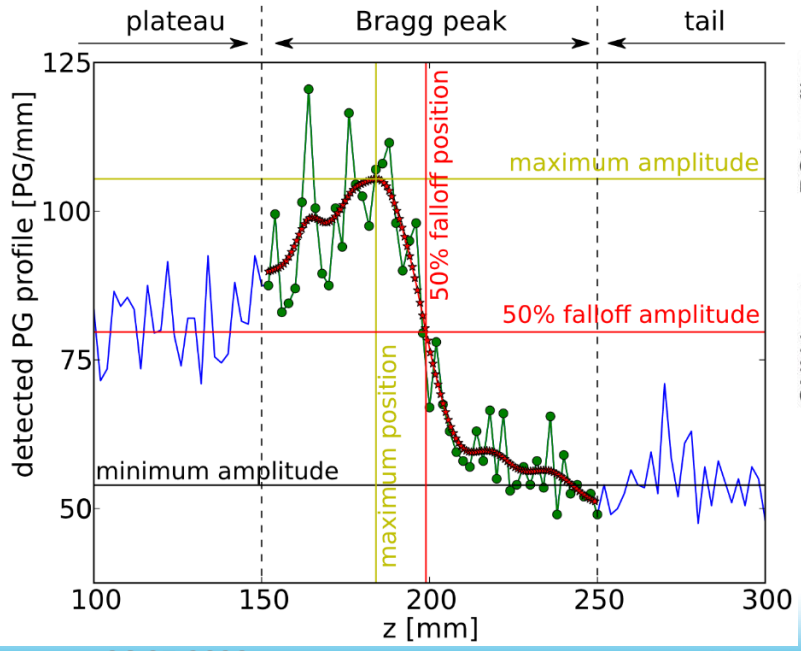


Shakirin et al., PMB, 2011

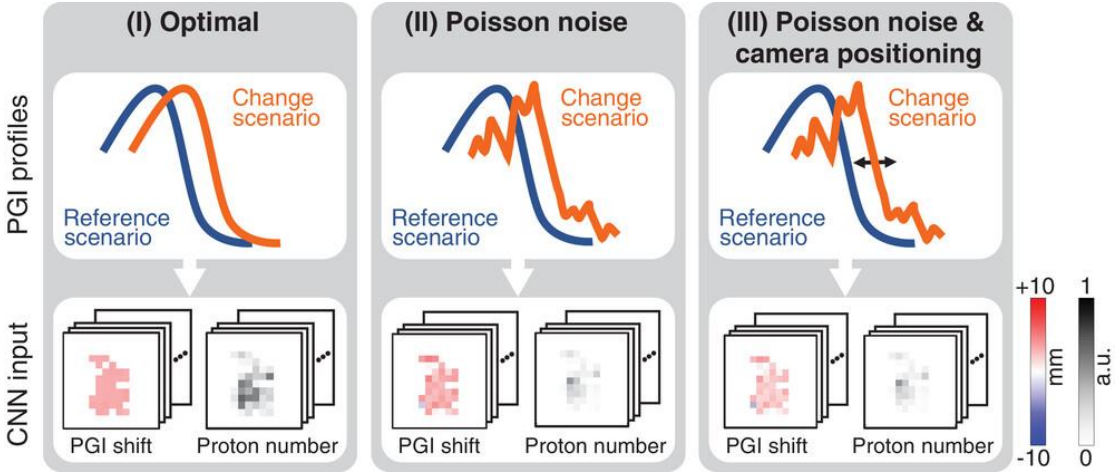
Beyond just MC

Prediction

- Make the comparison
- Develop methods for better comparison
- Develop and train algorithms for automatic shift detection and classification

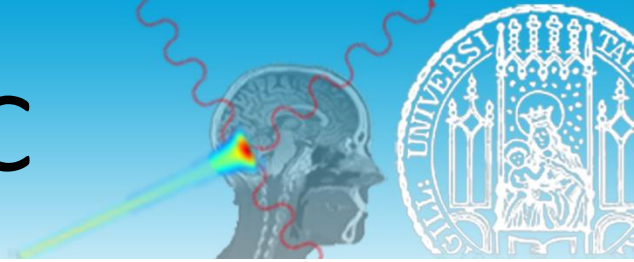


Gueth et al, PMB, 2013



Pietsch et al, Med. Phys., 2022

Beyond just MC



Prediction usually estimated with Monte Carlo simulations

!!! PROBLEM !!!

- Assuming $5x10^6$ protons per spot
- Assuming 1000 spots
- Assuming one has enough statistics with 1% of the protons per spot
- 150 MeV protons ≈ 0.943 ms/proton (computer-dependent)

13 hours per patient

Beyond just MC: Filtering approach

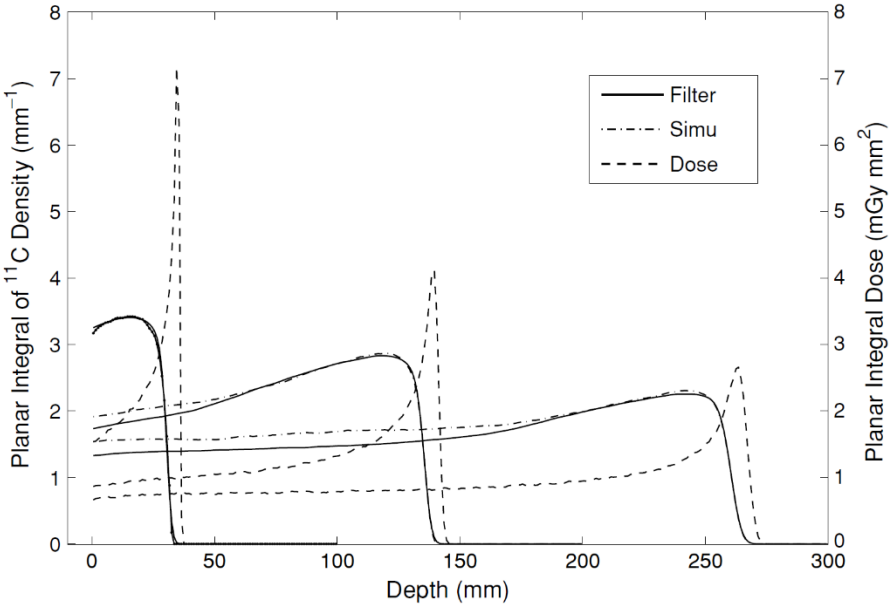
A filtering approach based on Gaussian–powerlaw convolutions for local PET verification of proton radiotherapy

Katia Parodi and Thomas Bortfeld

Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, 30 Fruit Street, Boston, MA 02114, USA

E-mail: kparodi@partners.org and tbortfeld@partners.org

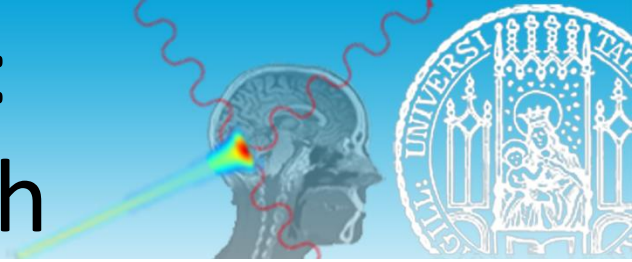
Received 19 August 2005, in final form 18 January 2006
Published 30 March 2006
Online at stacks.iop.org/PMB/51/1991



$$P(z) = (f * D)(z)$$

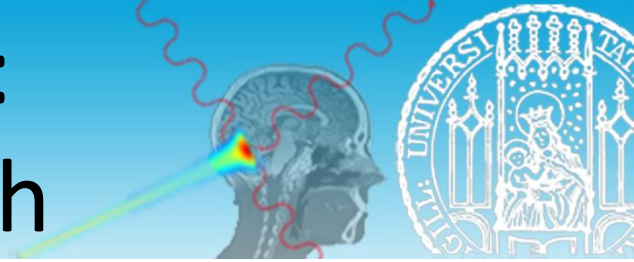
P(z): laterally integrated PE
f(z): the filter function
D(z): laterally integrated physical dose

Beyond just MC: Filtering approach



- Since 2006 several studies have been published using the filtering approach
- Those studies used mostly in-house solutions
- Implementation of the filtering approach in a research version of the commercial TPS RayStation
- Development of the filtering approach relying on MC data

Beyond just MC: Filtering approach

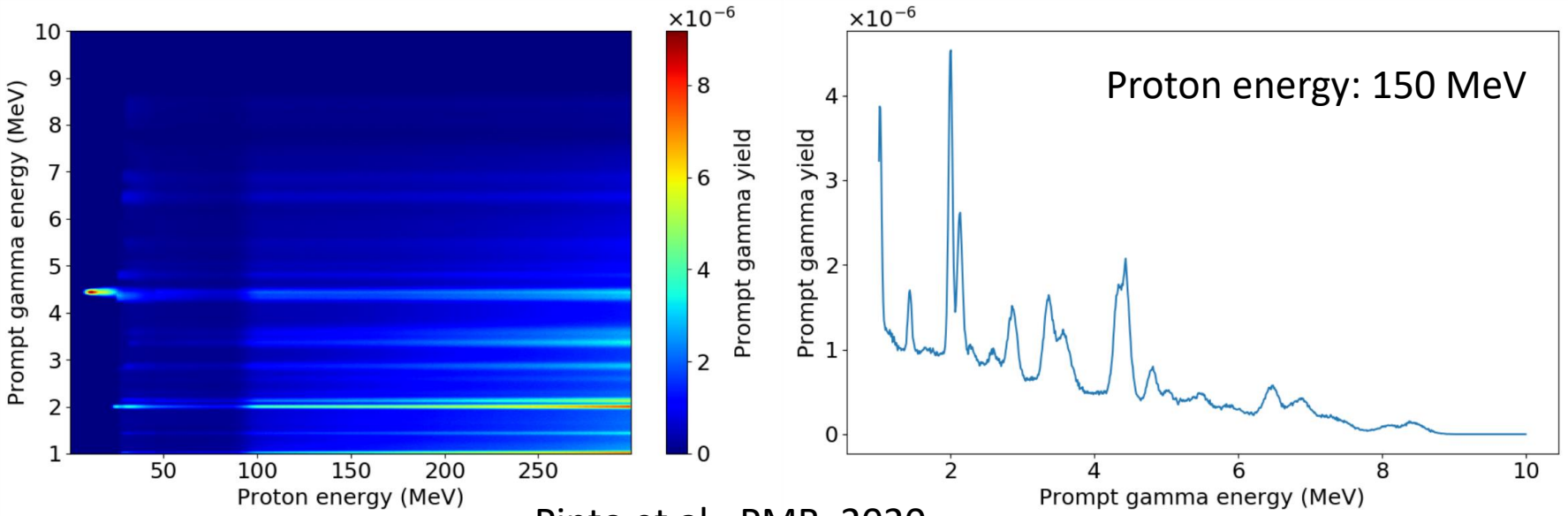


- Contrary to PET monitoring, PG monitoring requires taking into consideration energy thresholds
  - e.g. knife-edge camera: 3-6 MeV
- Other devices/groups consider different energy thresholds
  - Min et al. (2008) propose 4-10 MeV
- What about PG spectroscopy? What about the need to know the energy spectrum per voxel to propagate the prompt γ-rays?
- Should the filtering implementation be site/camera dependent? No!
  - It requires considerable time for deployment
  - It limits the possibilities for the users

Beyond just MC: Filtering approach

- Solution: development of filters for a broad energy range and use a look-up table for yield correction

- The LUT is also used to estimate the energy spectrum per voxel by knowing the average proton energy

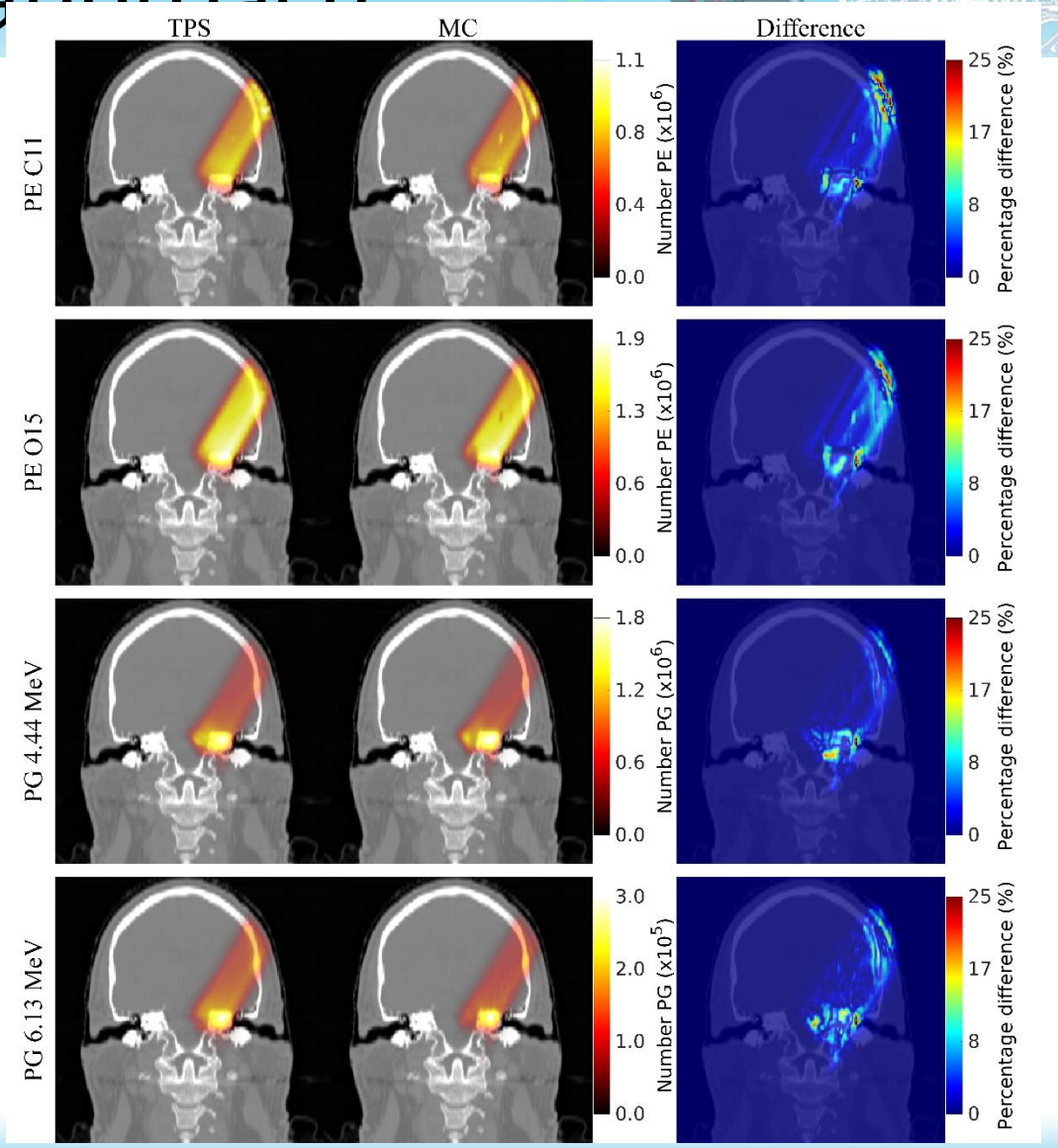


Pinto et al., PMB, 2020

Carbon target

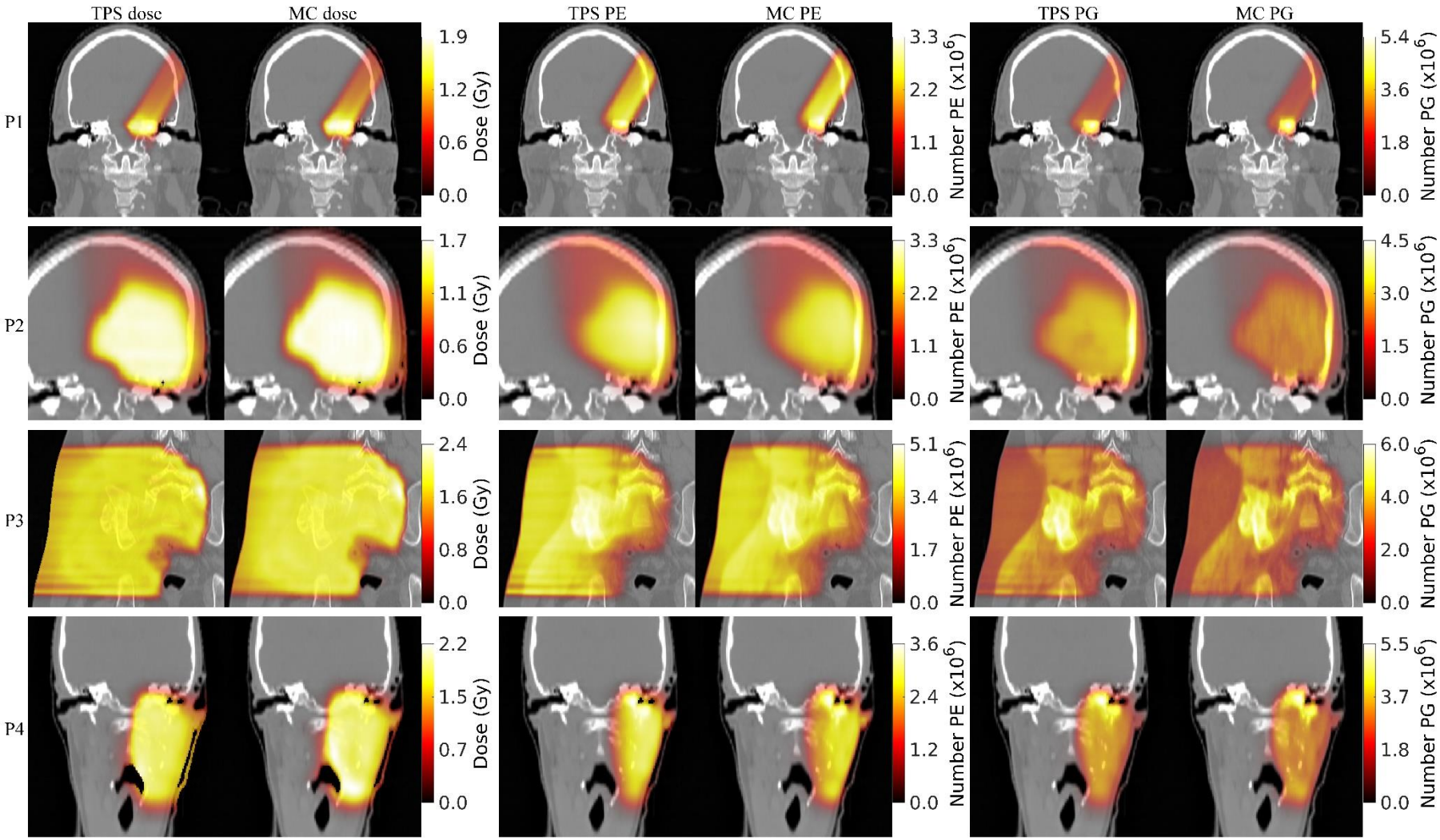
Beyond just MC: Filtering approach

- Possibility to select energy windows but also the peaks of characteristic emission
- PET: possibility to select specific positron emitters or nuclear reactions
- PG: possibility to select specific target nucleus



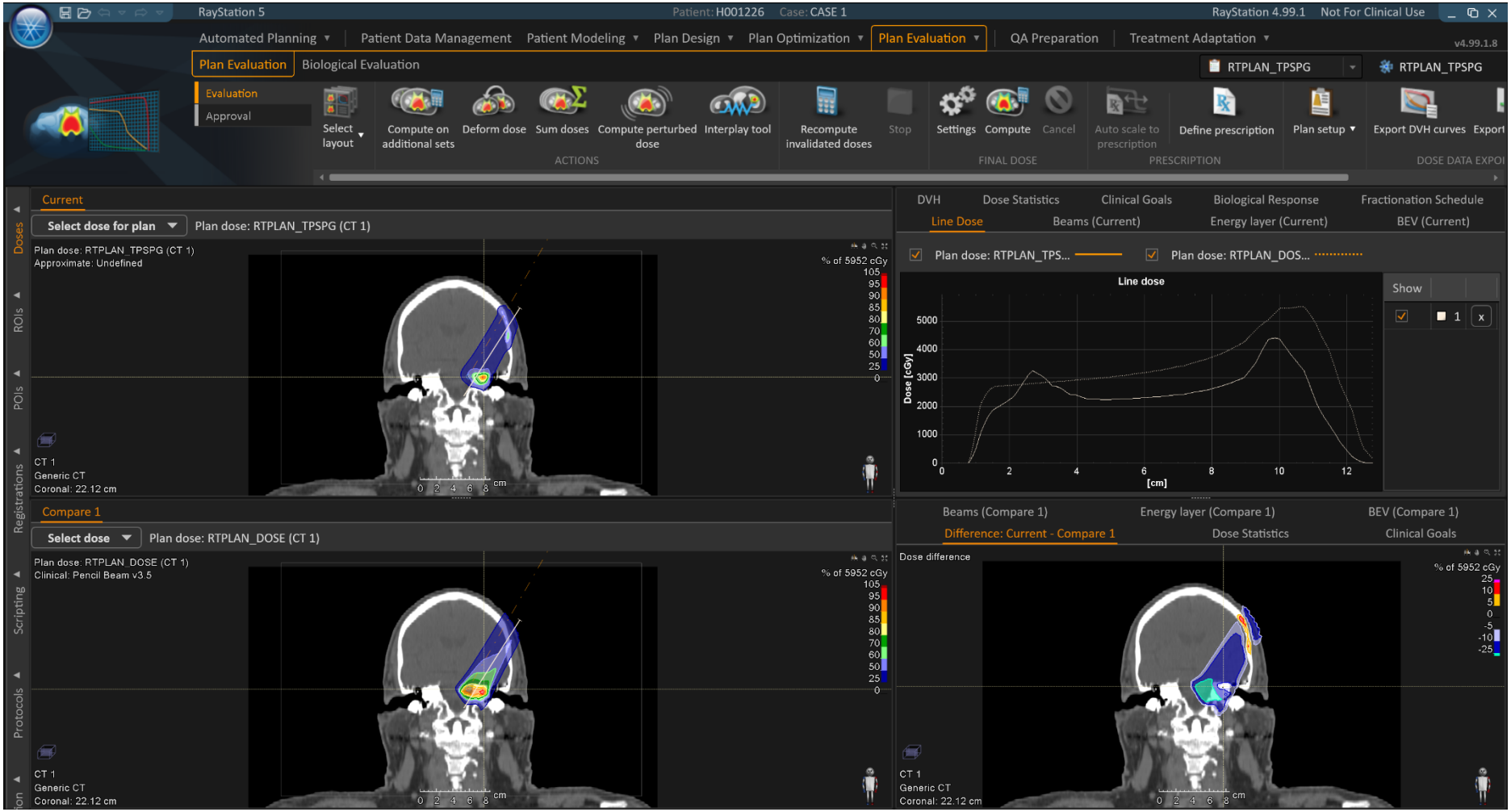
Pinto et al., submitted

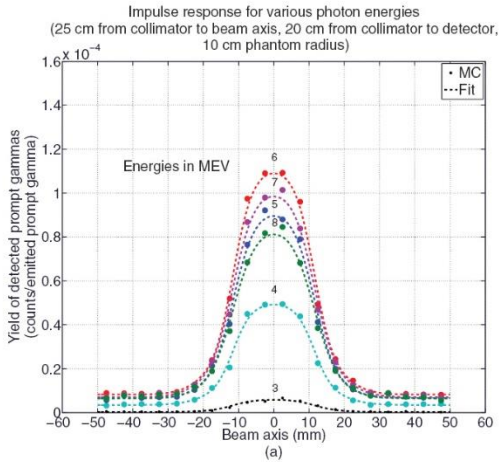
Beyond just MC: Filtering approach

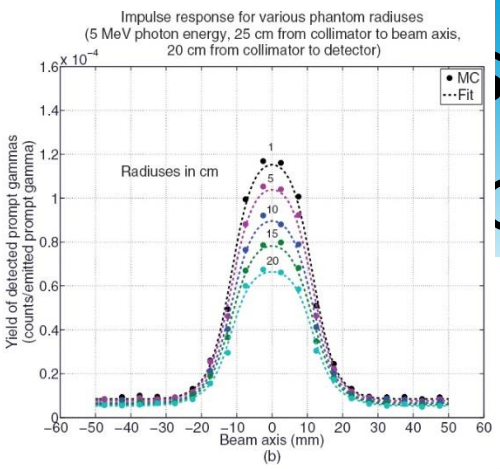


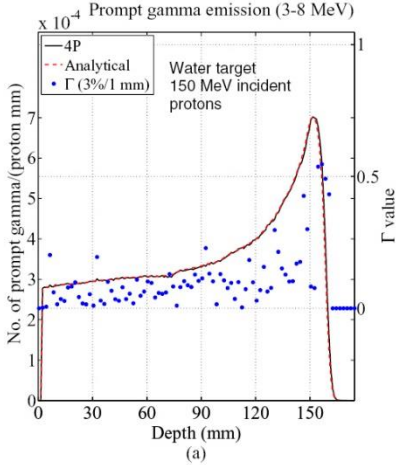
Pinto et al., submitted

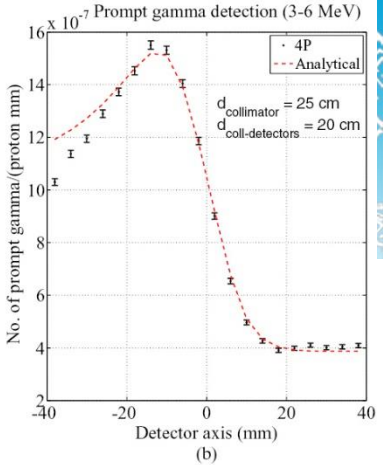
Beyond just MC: Filtering approach

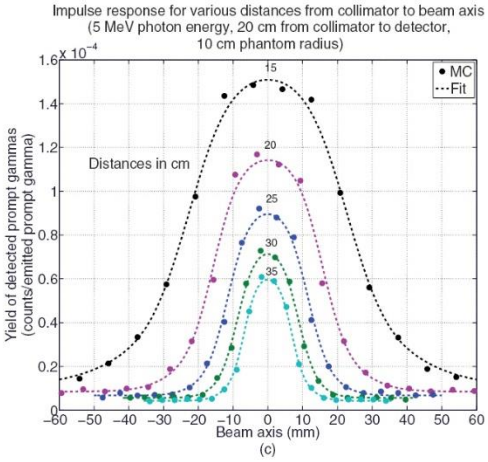


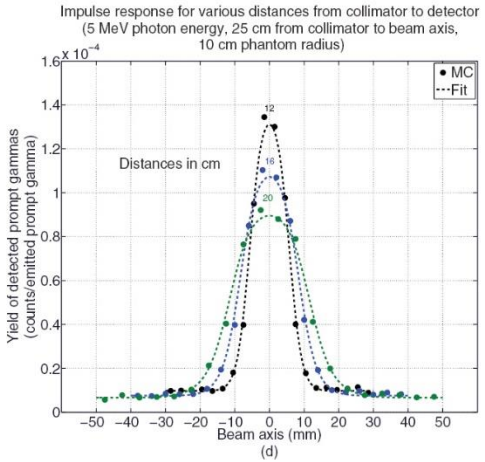


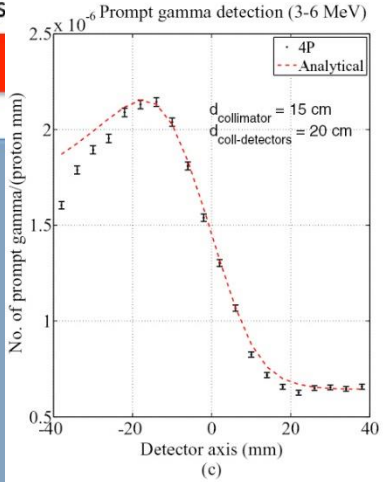


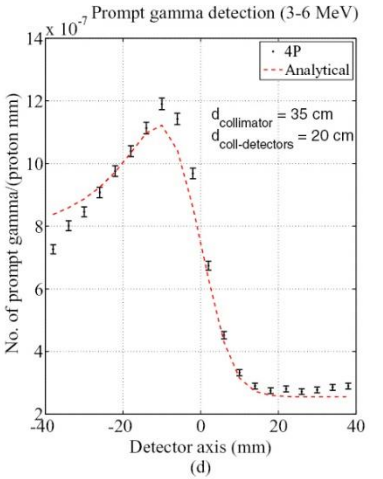


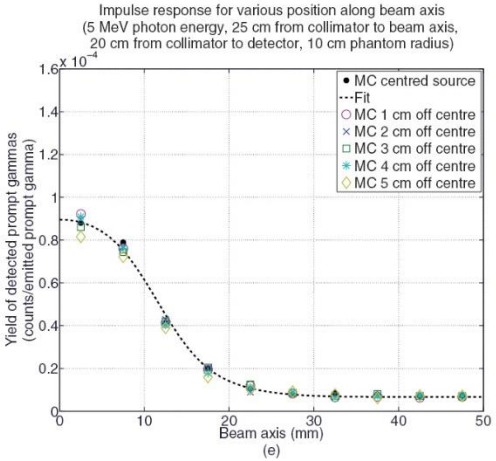




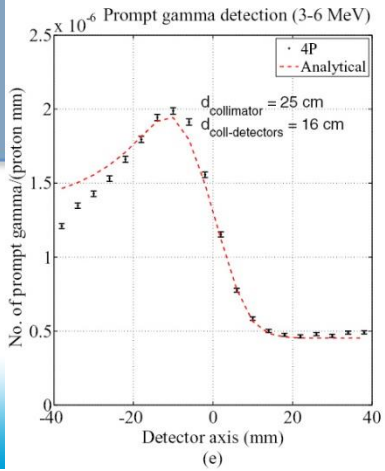


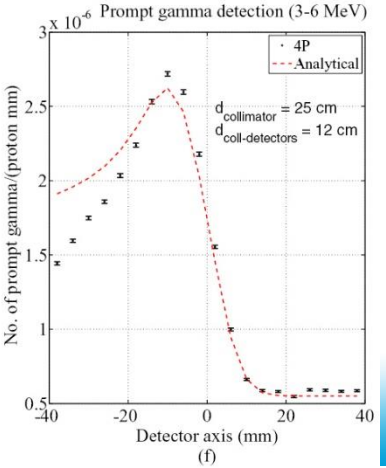






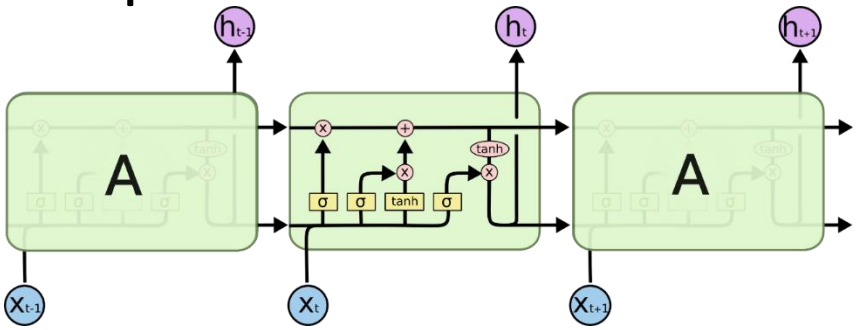
Sterpin et al., PMB, 2015





Beyond just MC: LSTM-RNN

- Long Short Term Memory (LSTM) Recurrent Neural Networks (RNN)
- Repeated modules, information passed to next module



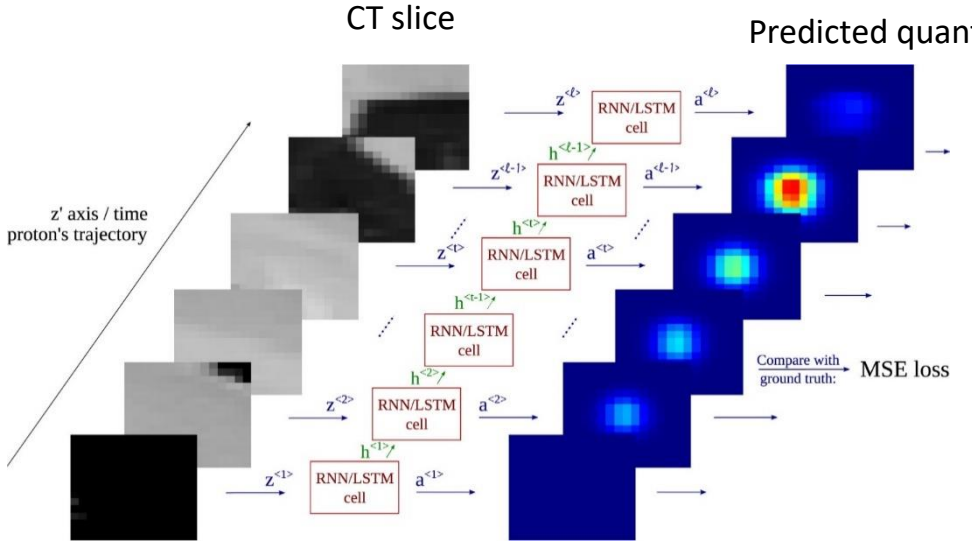
https://colah.github.io/posts/2015-08-Understanding-LSTMs/

- Emulates “memory”: a module learns from input but also from info from previous module
- Used for time series learning

Contact: G.Dedes@physik.uni-muenchen.de

Beyond just MC: LSTM-RNN

- PG distribution as “time” series: next depth in patient -> next step in “time”



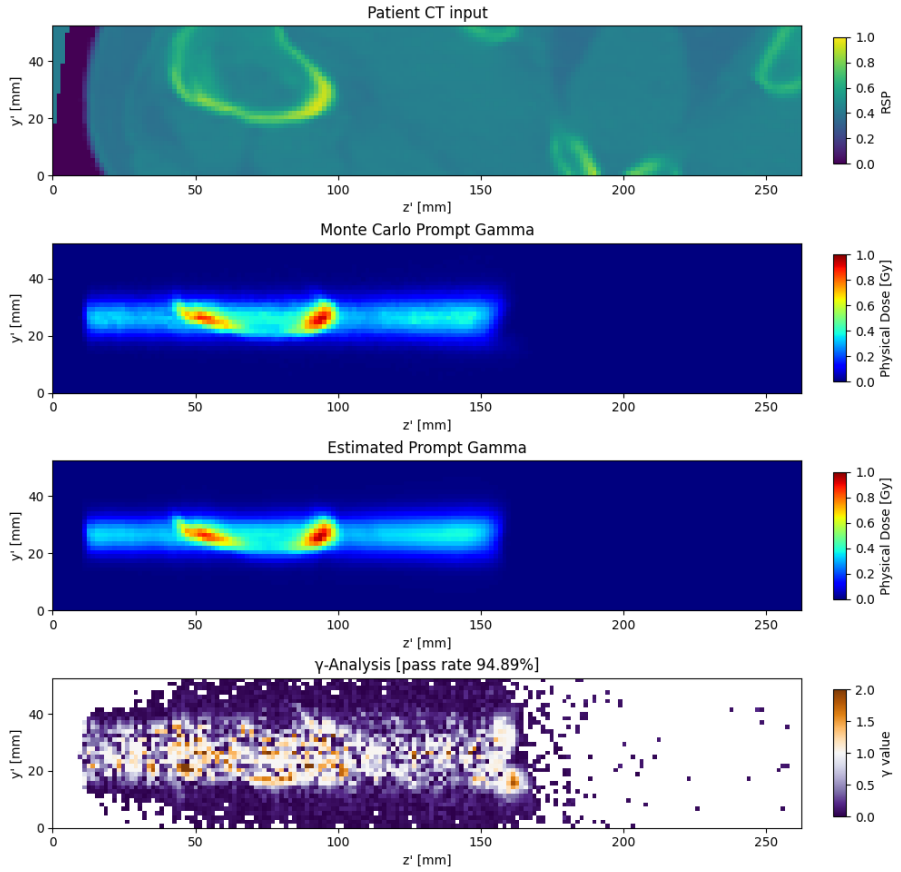
Med Phys. 2021 Apr;48(4):1893-1908. doi: 10.1002/mp.14658

- Applied to dose by Heidelberg group (Neishabouri et al., doi: 10.1002/mp.14658)

Contact: G.Dedes@physik.uni-muenchen.de

Beyond just MC: LSTM-RNN

- LMU PG project (Dedes, Kriechbaum)
- 3D - PG prediction on prostate anatomy
- ~1 day training on low-end GPU
- ~10 ms prediction time per PB



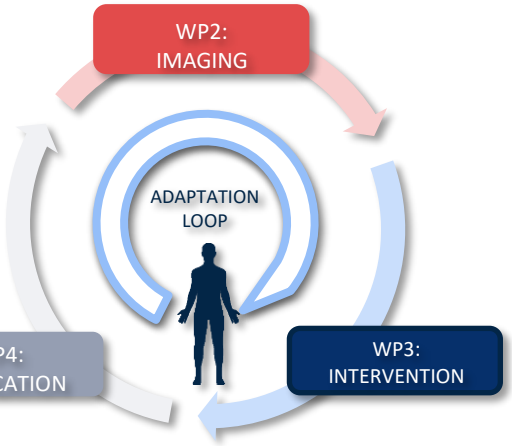
Contact: G.Dedes@physik.uni-muenchen.de

Beyond just MC: Dose reconstruction

ESR14: Dose reconstruction strategies using secondary prompt gamma radiation in proton therapy

Beyond just MC: Dose reconstruction

Fast prompt gamma-based dose verification



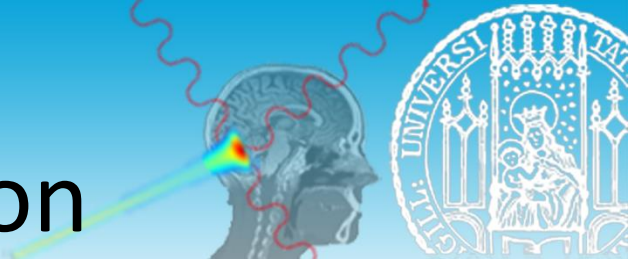
Reconstruction of a few exploratory pencil beams

deviations?

Send information to adapt the plan

- good PG-dose correlation
- sufficient statistics

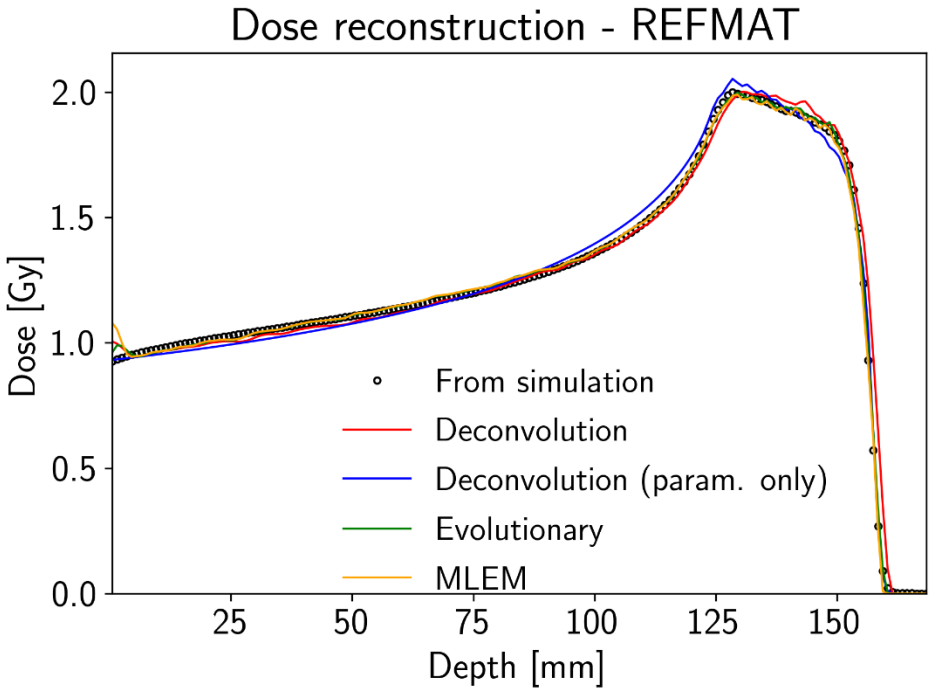
Beyond just MC: Dose reconstruction



- **Research and development of methods for dose reconstruction that can be applied in real-time**
  - **Deconvolution approach** (Remmele et al., PMB, 2011)
  - **Deconvolution approach in terms of $\widetilde{Q}_v$ functions parameters**
  - **Evolutionary algorithm** (Schumann et al., PMB, 2016; Hofmann et al., PMB, 2019; Yao et al. Nucl. Sci. Tech., 2023)
  - **Maximum likelihood expectation-maximization** (MLEM) (Masuda et al., PMB, 2019; Masuda et al., PMB, 2020)

Beyond just MC: Dose reconstruction

PROTONS, SOBP



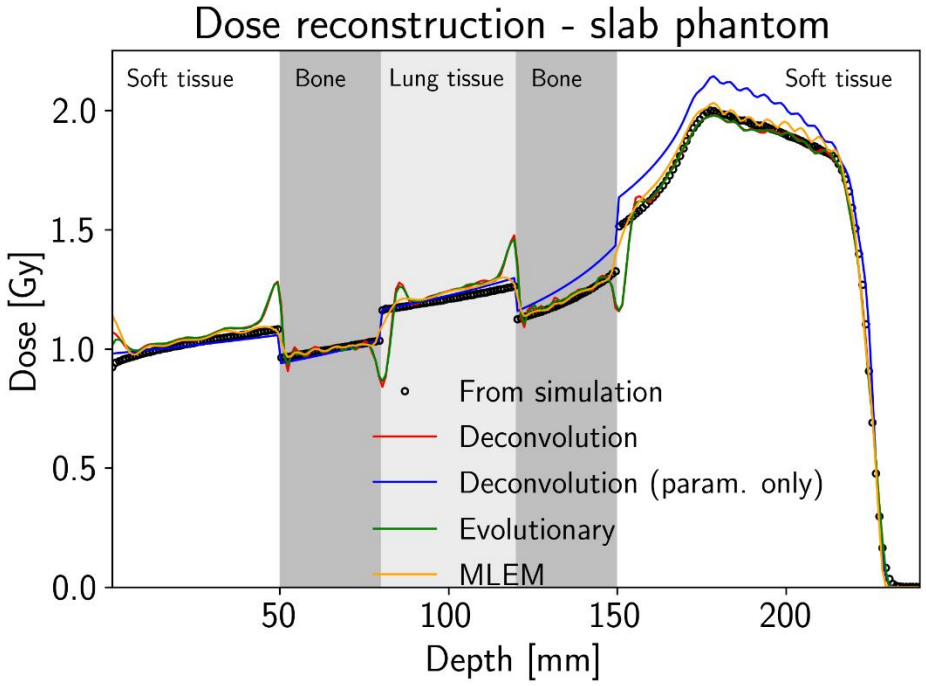
Metric	Deconvolution	Deconvolution (param. only)	Evolutionary	MLEM
NRMSE ($\times 10^{-2}$)	1.78	2.76	1.33	1.94
ΔR_{80} (mm)	0.69	0.98	0.46	0.71
ΔR_{50} (mm)	-0.07	-0.29	0.07	0.13
ΔR_{10} (mm)	-0.21	0.06	-0.20	0.14

Average % differences between the weights of contributions:

- -3.23 % ± 0.80 % for deconvolution approach;
- 4.49 % ± 0.94 % for deconvolution approach in terms of $\tilde{Q}_\nu$ functions parameters;
- -2.54 % ± 0.62 % for evolutionary algorithm;
- -4.65 % ± 0.65 % for the MLEM

Beyond just MC: Dose reconstruction

PROTONS, SOBP SLAB PHANTOM



Metric	Deconvolution	Deconvolution (param. only)	Evolutionary	MLEM
NRMSE ($\times 10^{-2}$)	5.47	5.66	5.28	2.82
ΔR_{80} (mm)	0.71	0.81	0.68	0.82
ΔR_{50} (mm)	0.17	-0.55	0.31	0.51
ΔR_{10} (mm)	-0.22	0.25	-0.29	0.38

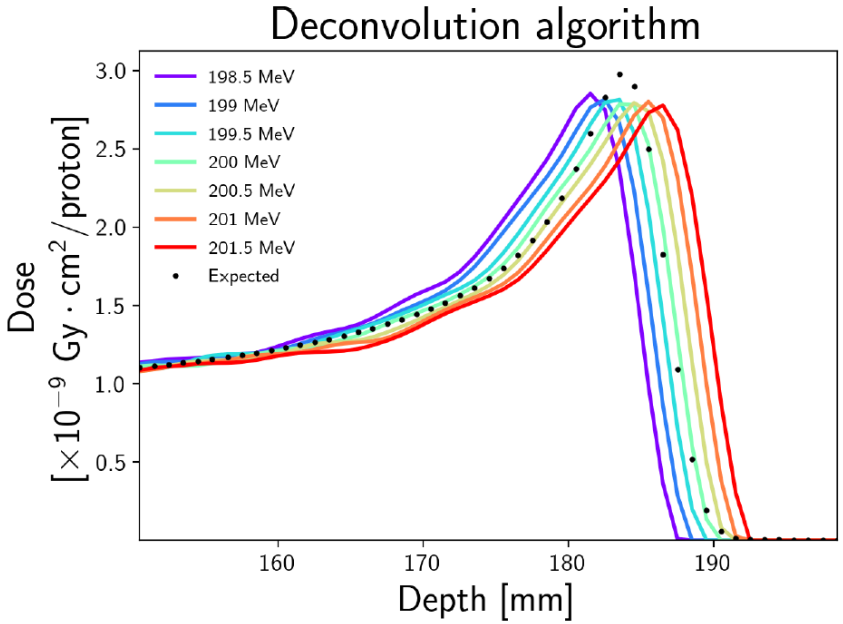
Average % differences between the weights of contributions:

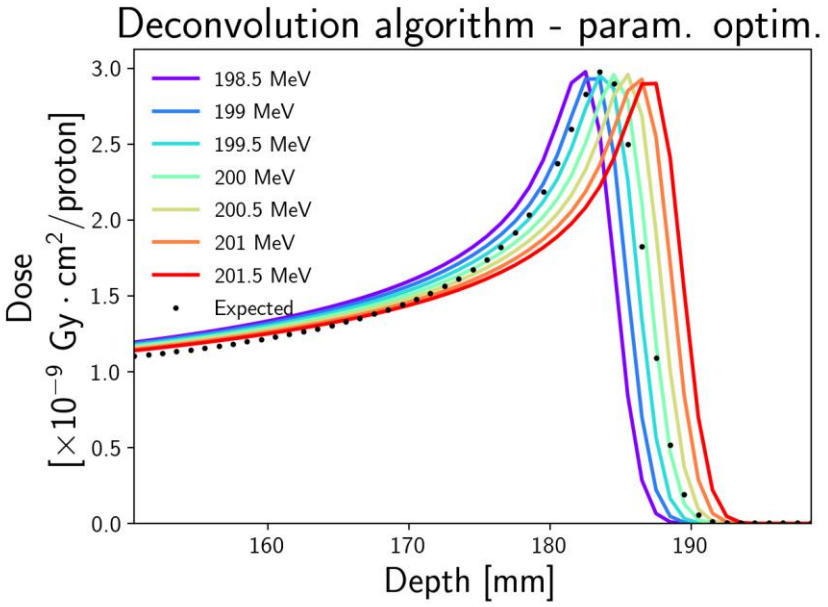
- -0.99 % ± 0.97 % for deconvolution approach;
- 15.34 % ± 3.11 % for deconvolution approach in terms of $\tilde{Q}_\nu$ functions parameters;
- -0.06 % ± 1.1 % for evolutionary algorithm;
- 3.65 % ± 0.71 % for the MLEM

Beyond just MC: Dose reconstruction

RANGE SHIFTS ANALYSIS

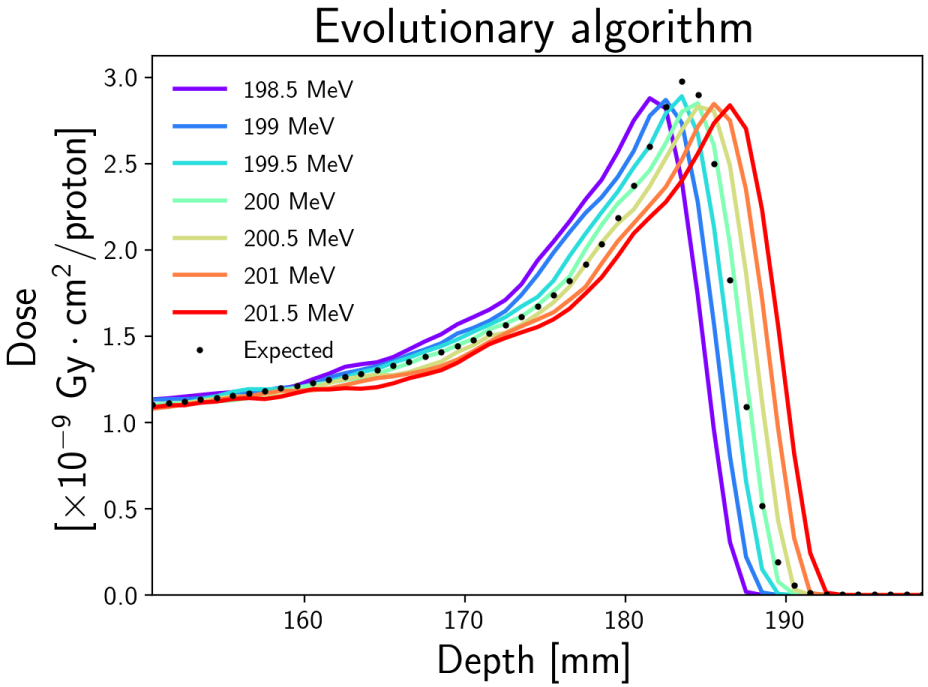
- Proton range shift approximated by a change in the initial energy of the proton beams.
- PG profiles considered as coming from protons of initial energy equals to:
  198.5 MeV, 199 MeV, 199.5 MeV, 200.5 MeV, 201 MeV and 201.5 MeV
- Analysed as if the initial energy would be 200 MeV.

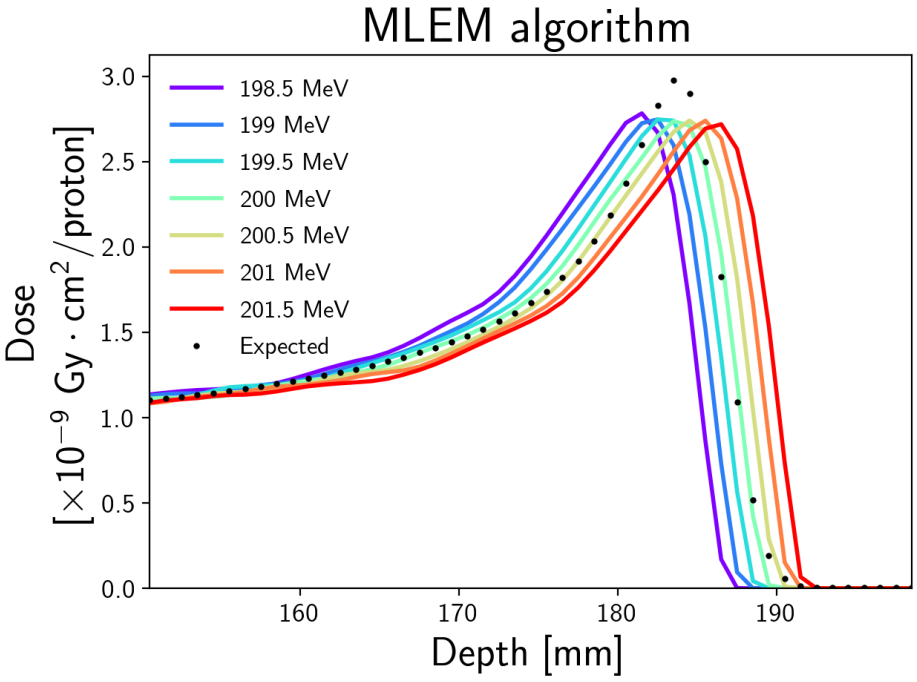


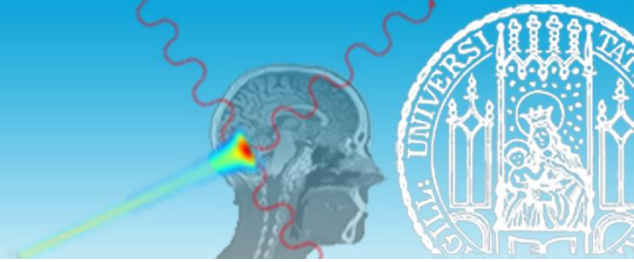


Beyond just MC: Dose reconstruction

RANGE SHIFTS ANALYSIS





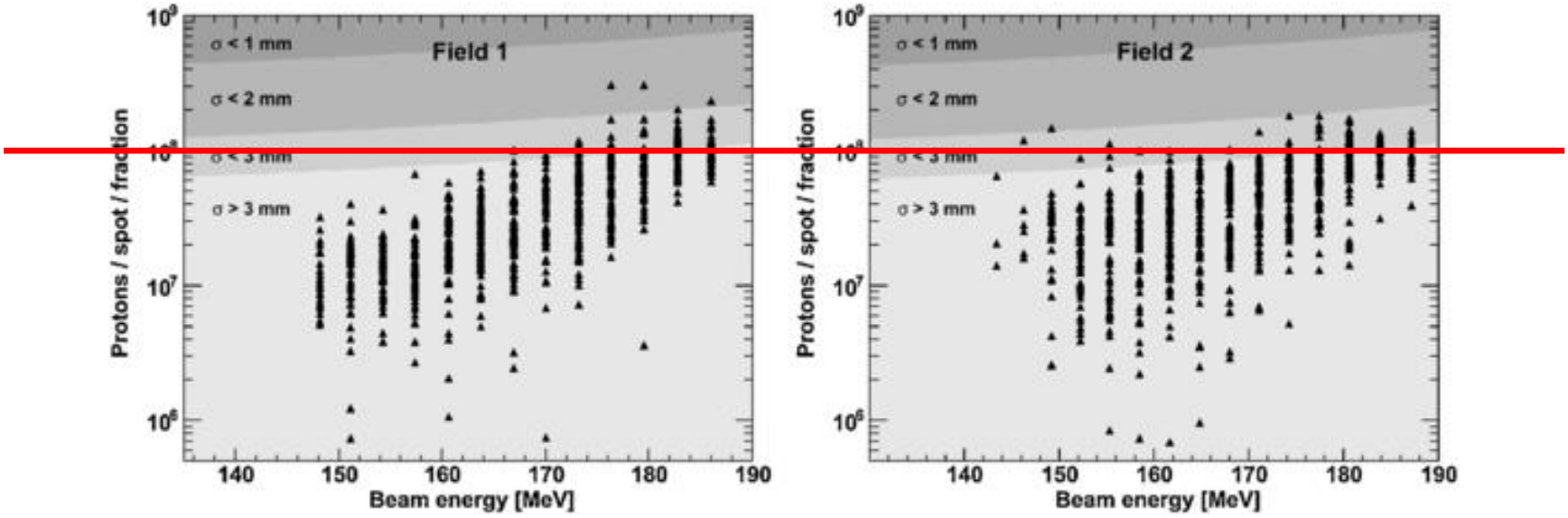


FINAL REMARKS

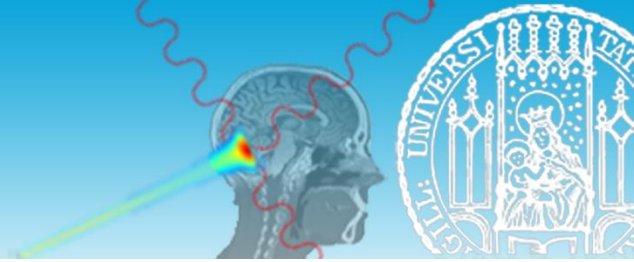
Final remarks

- MC tools are just that: ***tools***!

- In proton monitoring research **avoid a common pitfall**: more than ~10^8 protons per spot is **not** a typical treatment scenario in conventional fractionation



Smeets et al., PMB, 2012



Thanks!