Computational and experimental methods applied for treatment planning, quality assurance, and research **at the CCB Krakow proton therapy center**

Antoni Rucinski, Symposium on new trends in nuclear and medical physics, 20.10.2023
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Witnessing PT development in Europe

My story

1	2004 -2009	Warsaw Technical University Universität Stuttgart (Erasmus Fellow)	MSc
2	2010 -2013	University of Heidelberg	PhD
3	2013 -2014	University Clinic Heidelberg SLK-Kliniken Heilbronn	MPE
4	2015 -2016	INFN & Sapienza University of Rome	Postdoc
5	2017 - now	Institute of Nuclear Physics Polish Academy of Sciences CCB Kraków Proton Beam Therapy Centre	Assistant Professor

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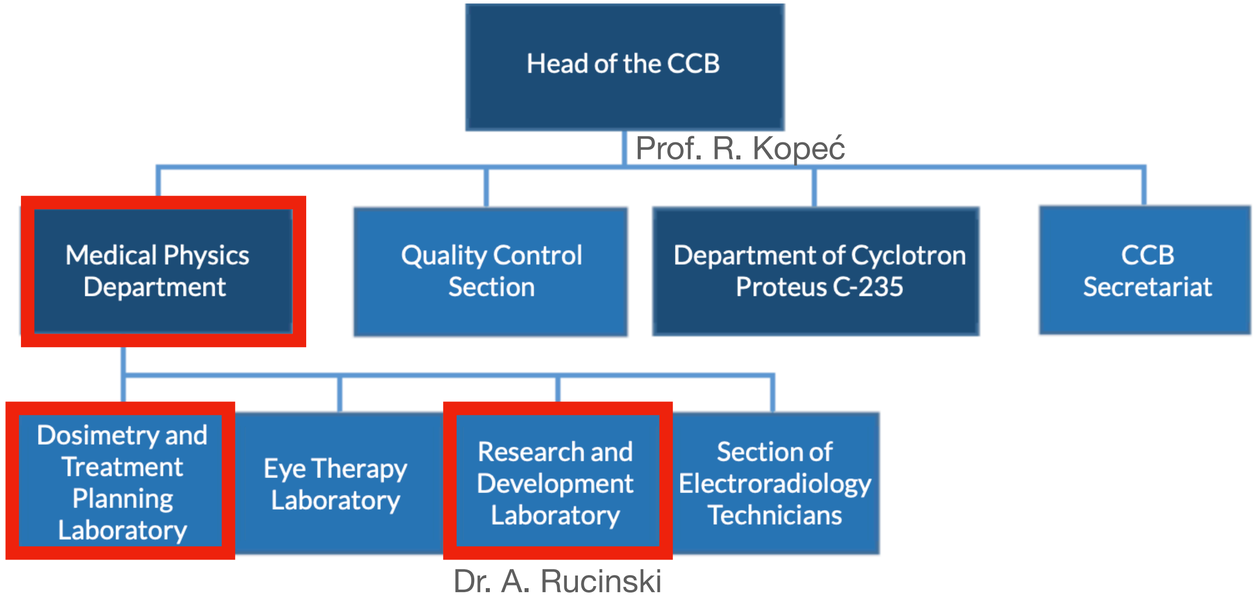
CCB Kraków proton center

Structure and relevant data/equipment



- Access to proton beams in Gantry rooms for experiments
- Anonymized patient data for TP studies and protocol development
- Radiobiology labs equipped to perform in vitro experiments (from 2023)

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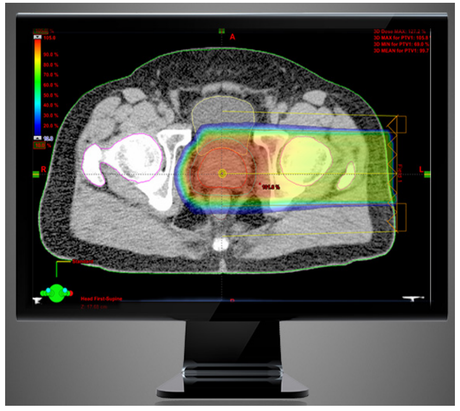
Translational research at CCB proton center

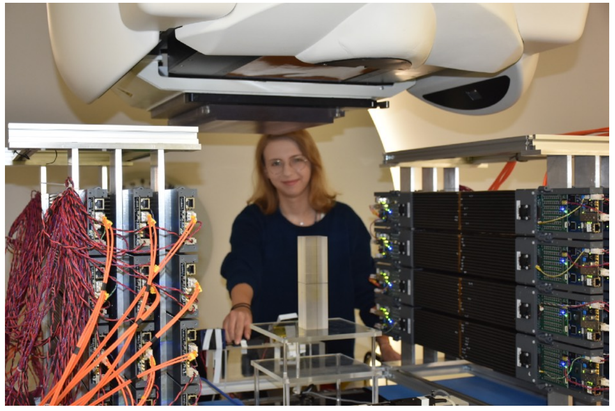
Physics, radiation biology, and oncology to improve clinical protocols

Computations and modelling ⟷ Experiments



Biologically and LET weighted treatment planning

Quality assurance

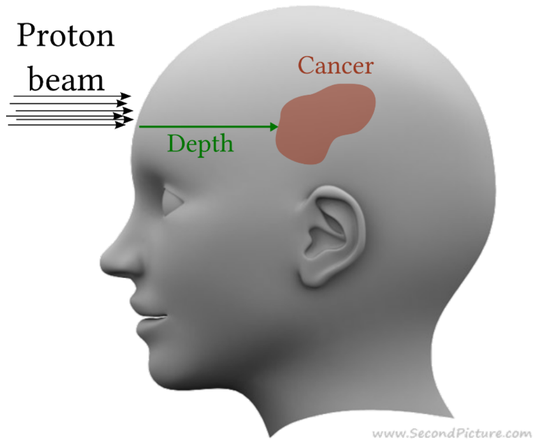


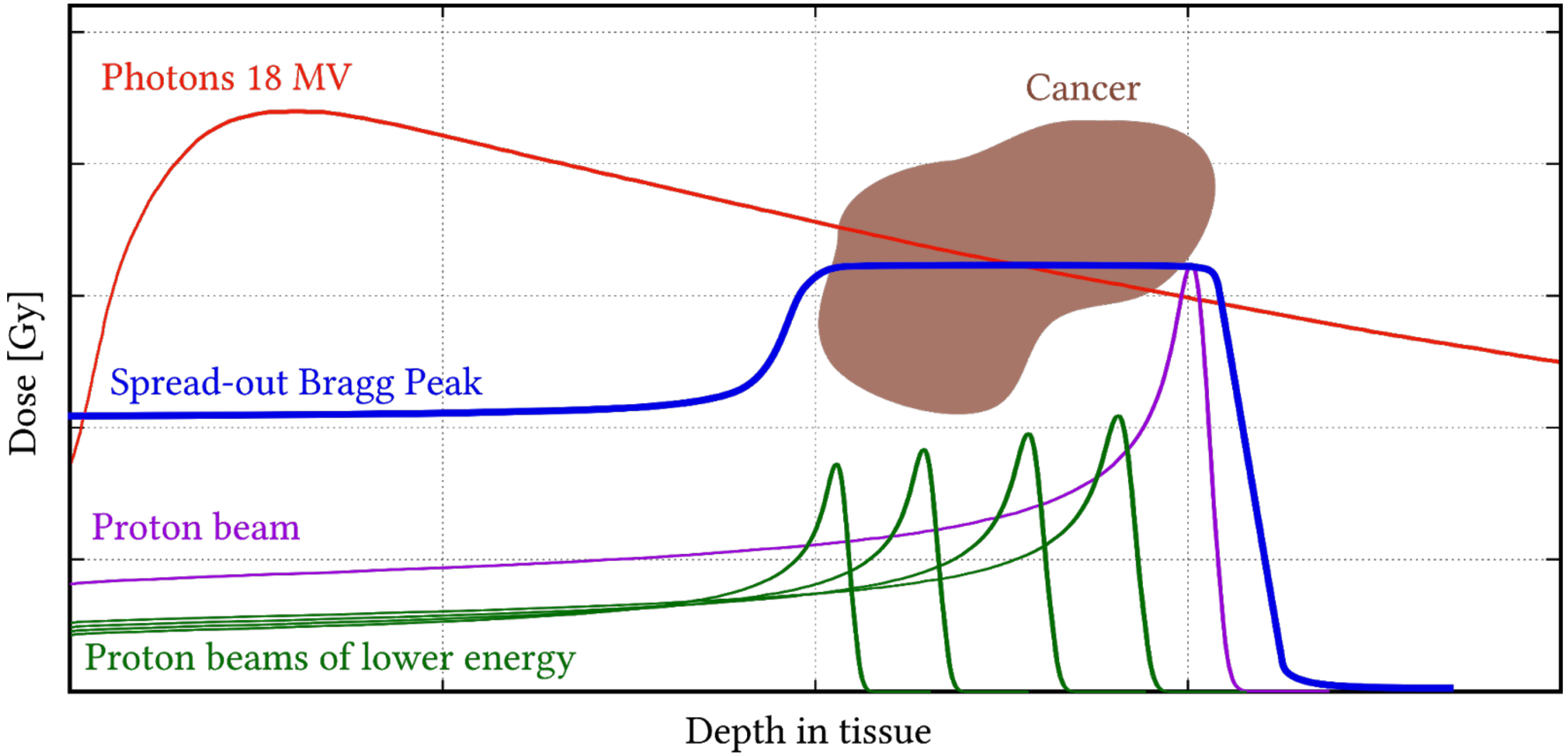
Detectors for range monitoring for therapy adaptation

CCB antoni.rucinski@ifj.edu.pl

Proton therapy

Advancement in beam delivery: Pencil beam scanning, energy & intensity modulation





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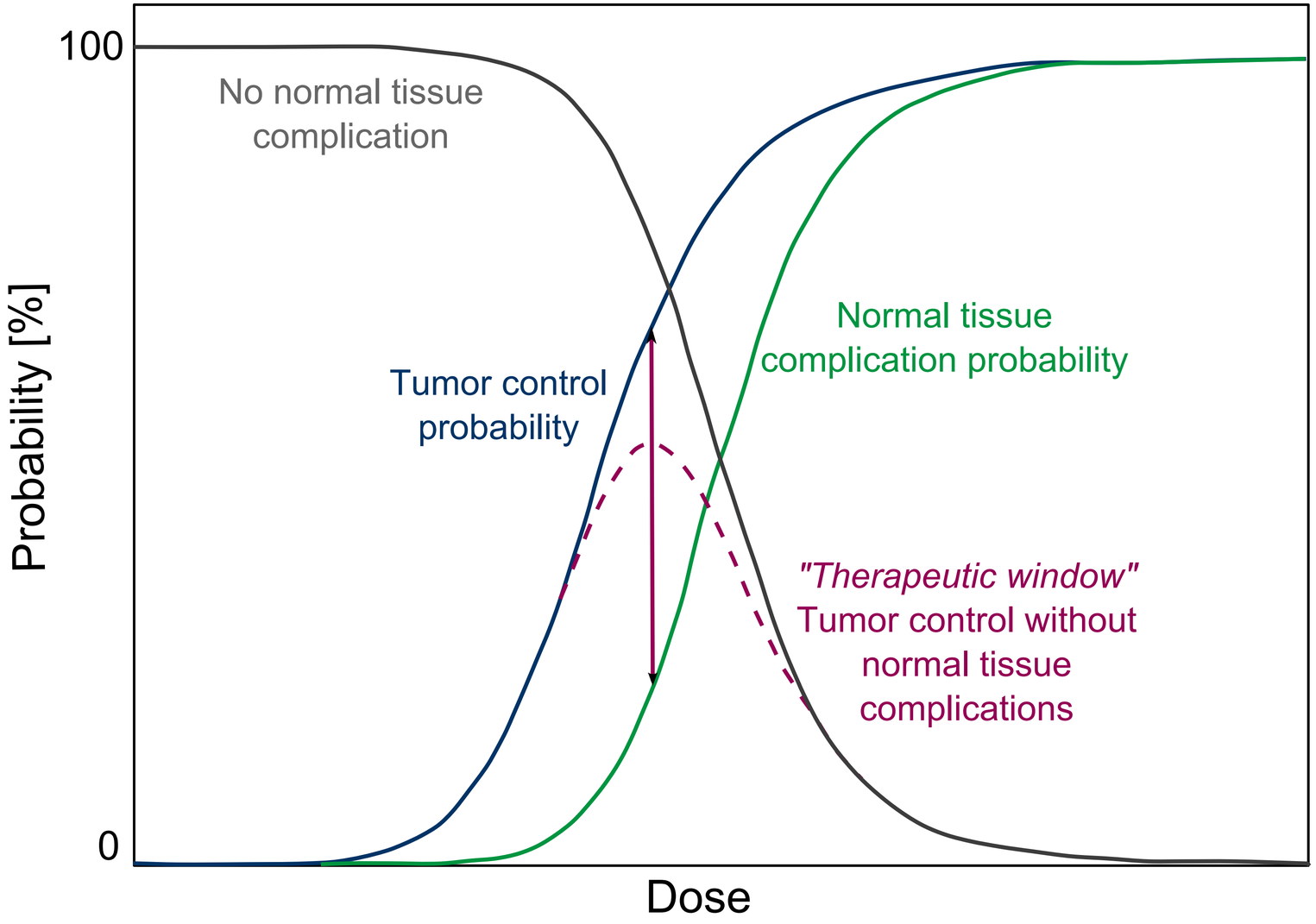
Photons vs. particles



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Photons vs. particles

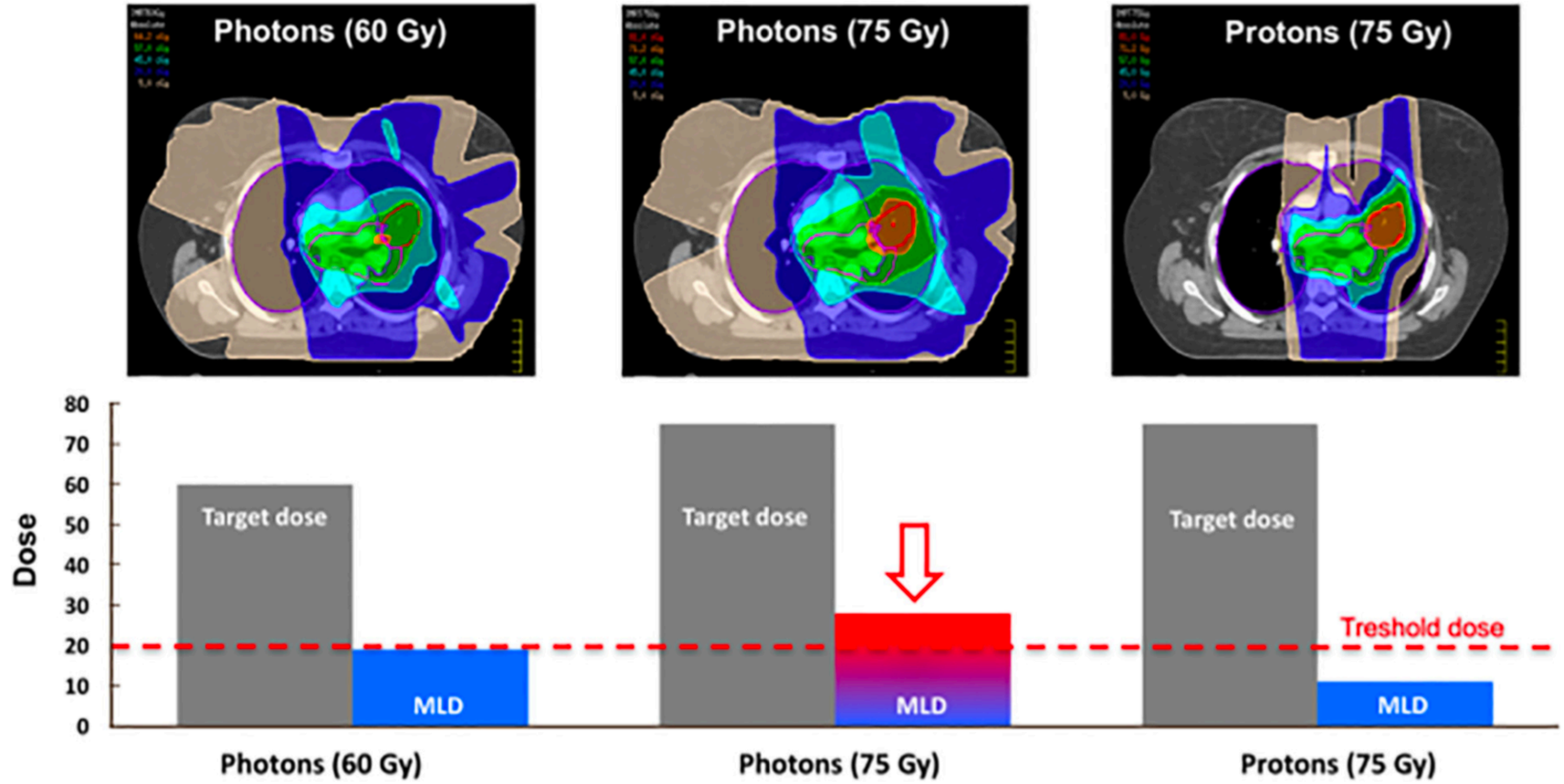


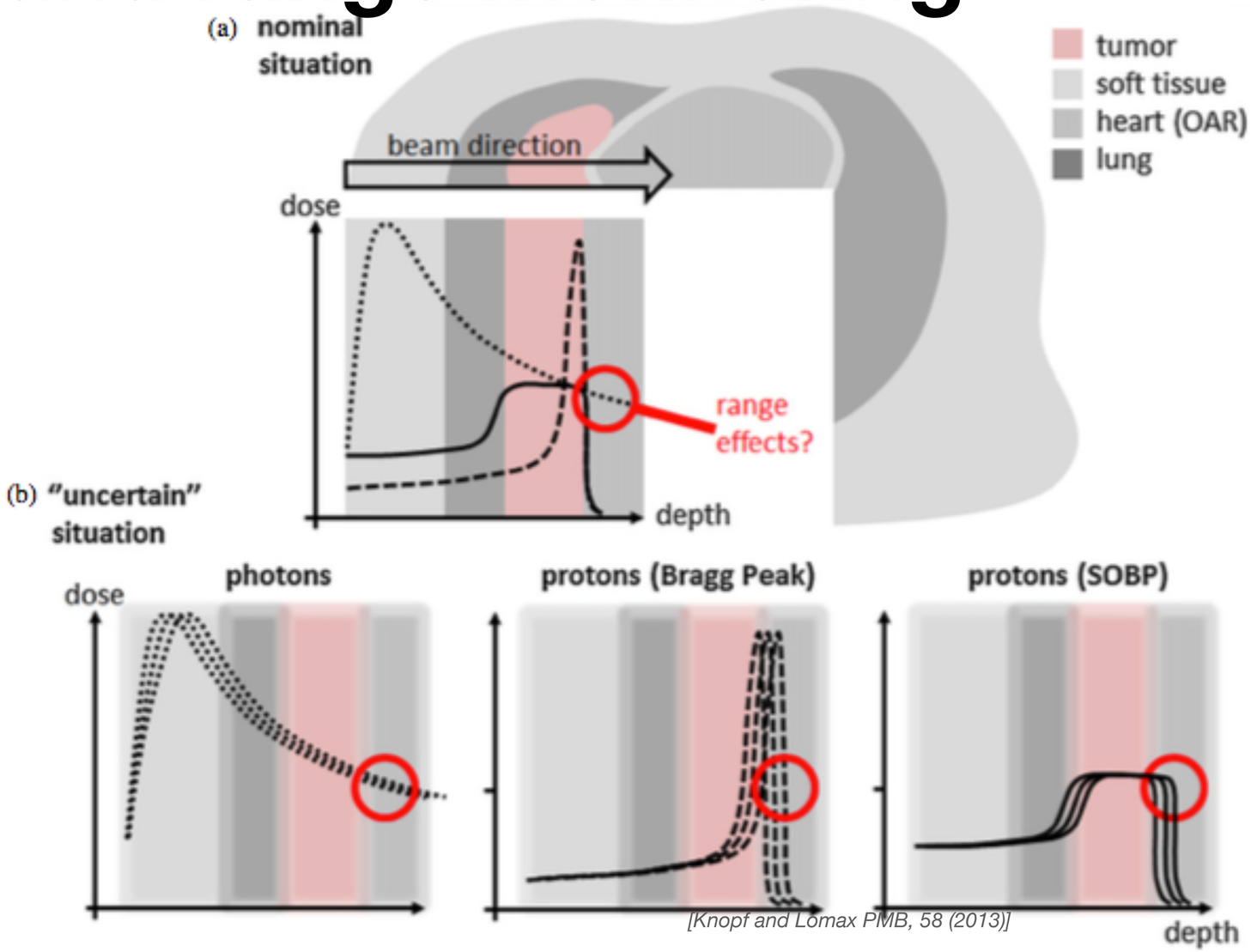
Fig. 3. Example for a proton therapy-directed randomized control trial for non-small cell lung cancer patients (NSCLC) to test the therapeutic ratio relative to photon treatment consisting of three arms: (A) current standard, 60 Gy photons; (B) dose escalation, 75 Gy photons; (C) dose escalation, 75 Gy protons. For the three arms, treatment plans as well as target dose and mean lung dose (MLD) are compared for the same patient. The proton arm aims at escalating the target dose without increasing dose to normal tissues, i.e., improving local control without increasing toxicity.

Lühr et al. Radiotherapy and Oncology 128 (2018) 56–67

Uncertainties and range monitoring

Scanned particle beams

- Favourable dose deposition profile (BP)/Increased Radiobiological effectiveness/high precision of beam application
- High sensitivity for range variations (patient positioning/organ motion)



[Knopf and Lomax PMB, 58 (2013)]

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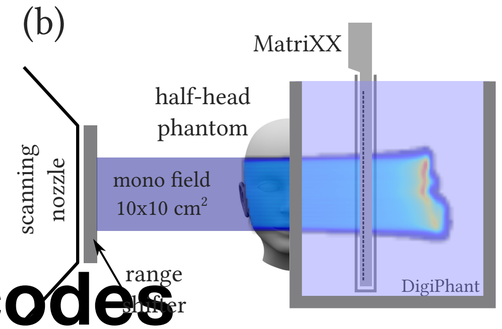
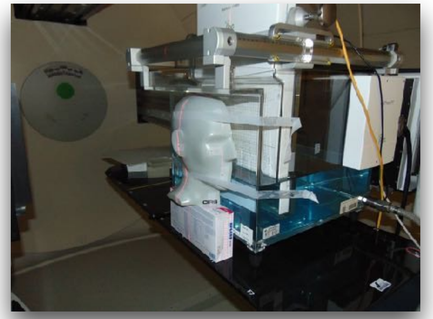
Beam modeling

Eclipse TPS, Fred and GATE MC codes

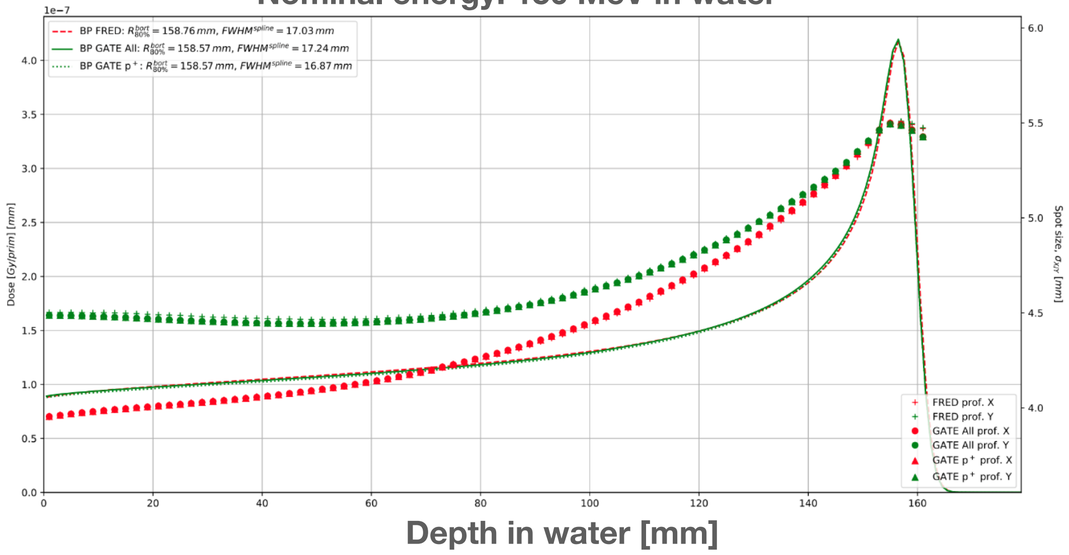


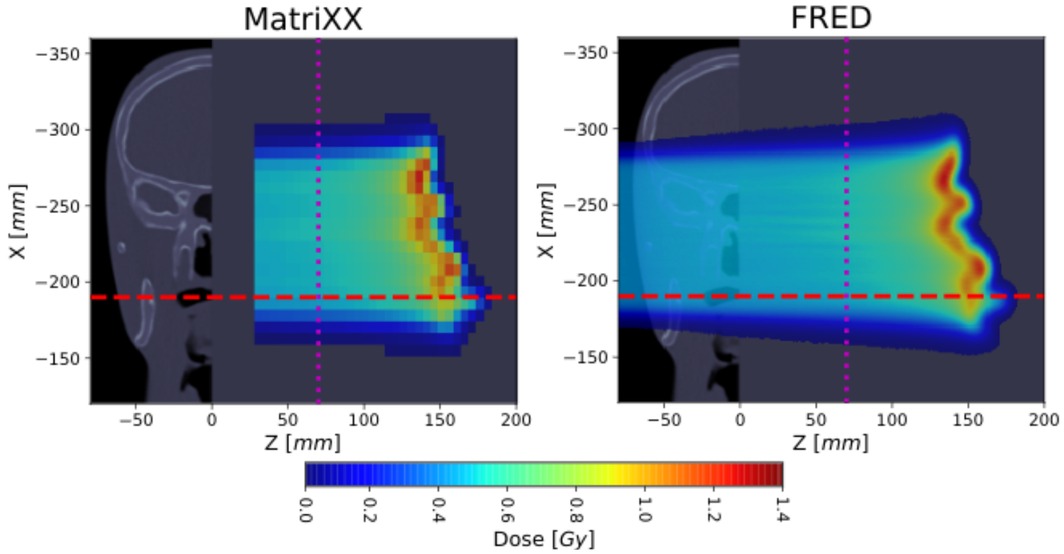


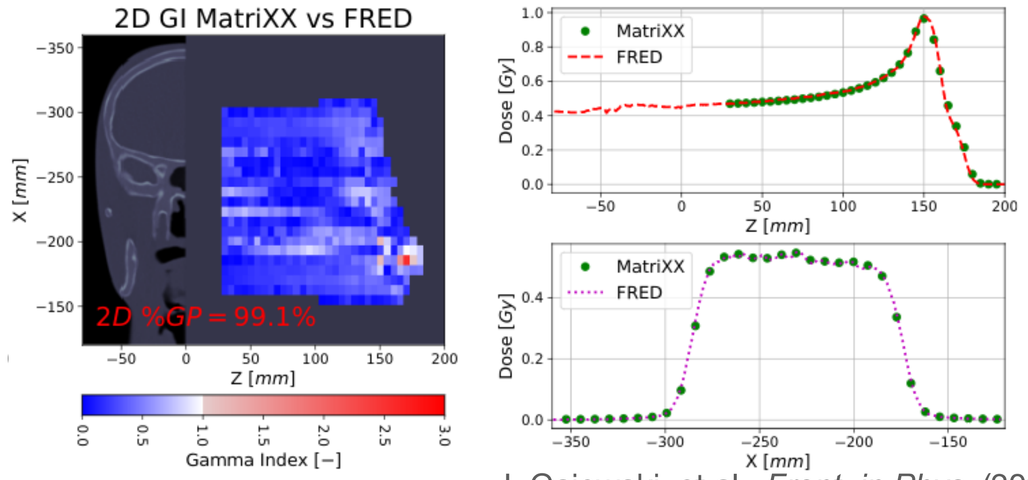
Experimental validation

- Beam model based on 9 parameters for 17 beam energies:
- Initial energy, energy spread
- Lateral propagation (6 emittance parameters)
- Dosimetric calibration
- Range shifters
- Gantry/patient rotations + isocenter shifts

Nominal energy: 150 MeV in water







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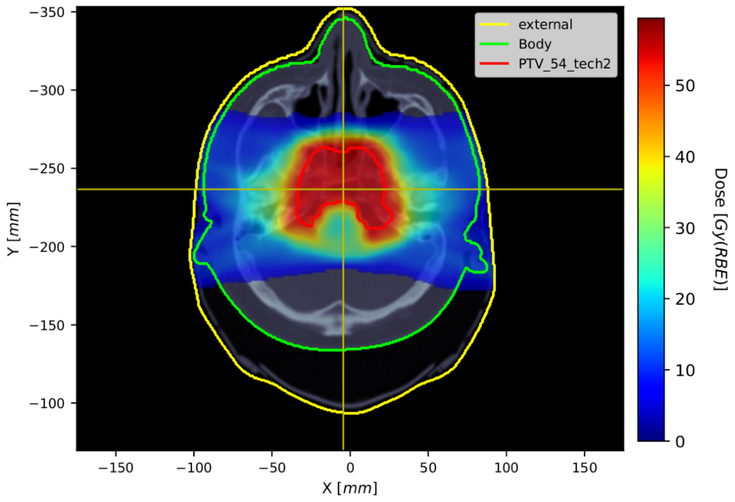
J. Gajewski, et al., *Front. in Phys.* (2021)

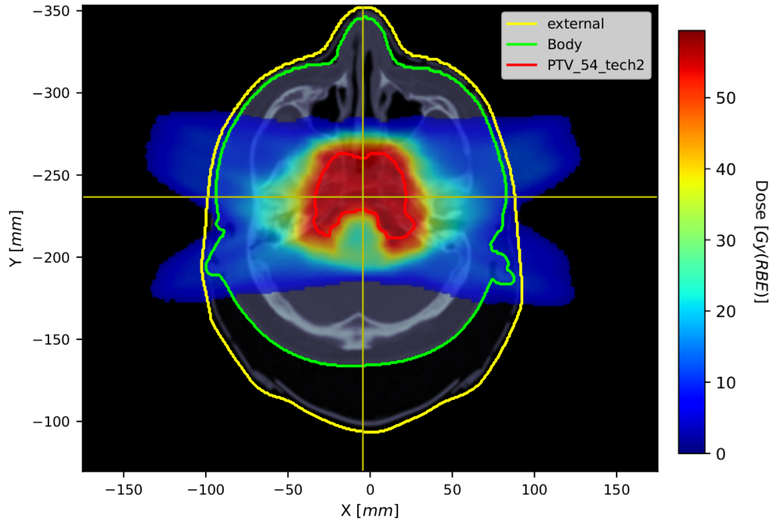
Dosimetric cross-validation TPS-GATE-FRED

- 35 patient treatment plans
- precise physics
  - *QGSP_BIC_HP_EMZ*
  - *0.1 mm prod. cuts*
- GATE on ZIEMOWIT cluster

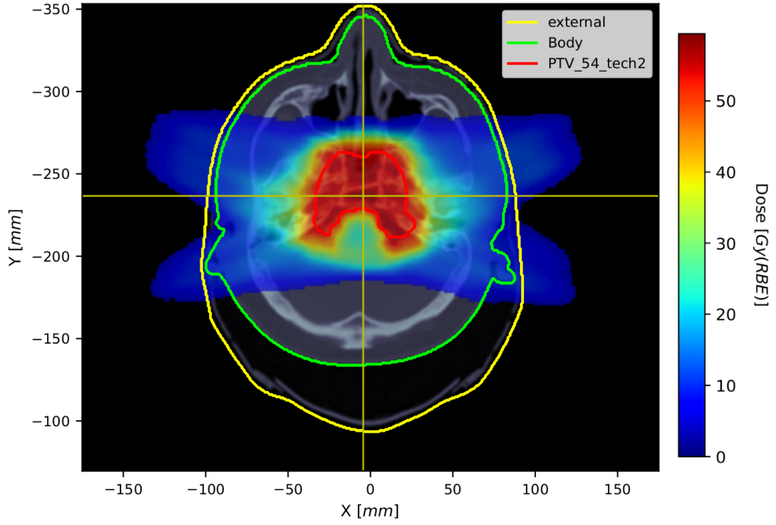
TPS



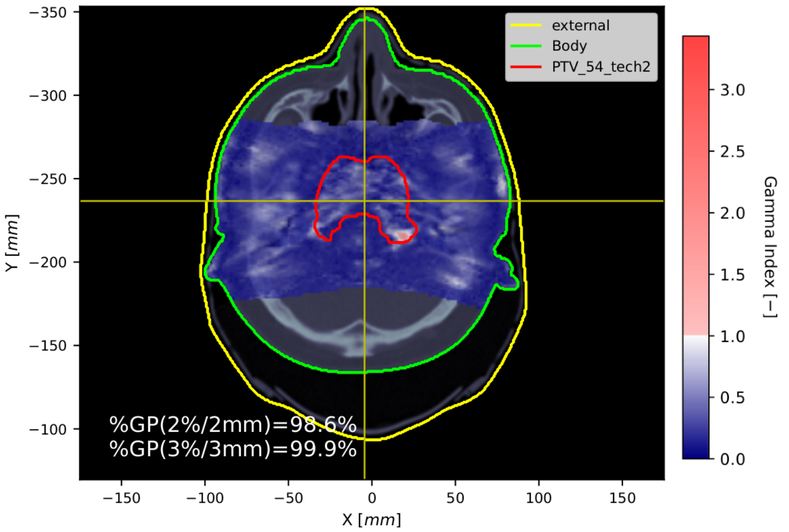
FRED



GATE



Gamma Index (*3mm/3%*)



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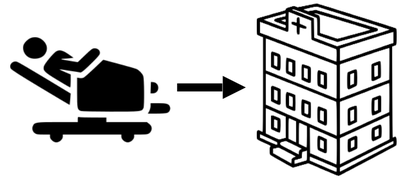
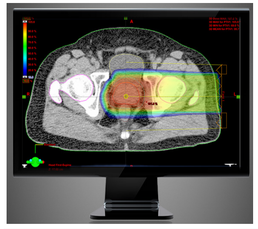
Computational Patient QA with FRED and GATE



Diagnosis and treatment protocol

Computed tomography



Treatment planning

Experimental dose measurement

Time consuming process

Plan verification

Plan irradiation

CT calib. (HU to RPSP)

Beam model (commissioning)

Computational patient QA

Log-based patient QA

Monte Carlo calculations

GATE

Fred

SCIENCE FOR THE SOCIETY

Grant for computational patient QA workflow implementation

+

simultaneous LET and dose optimisation

myQA® iON

iba

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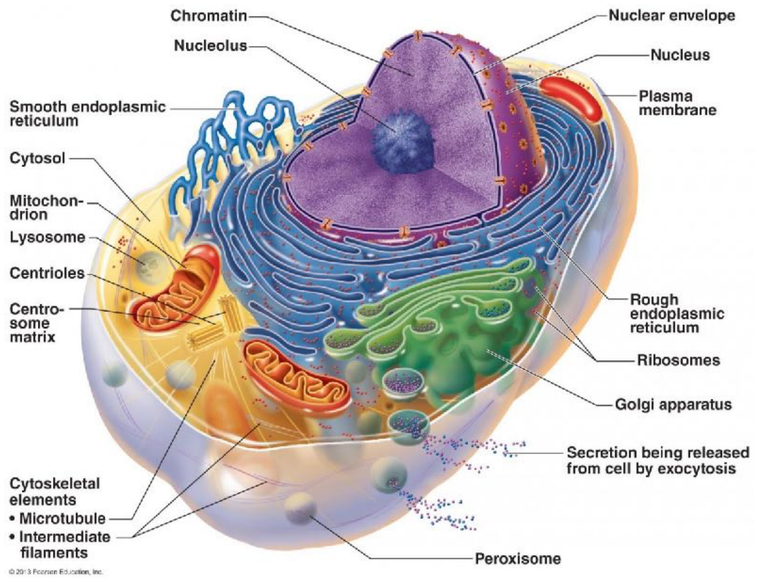
Advances in radiobiological modeling

Dose: Macroscopic concept

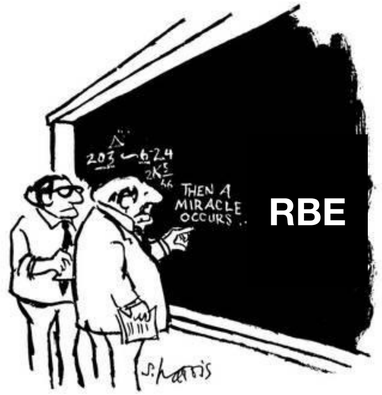
From: http://www.ptw.de

?

Cell inactivation: Microscopic concept



RBE modeling



"I think you should be more explicit here in step two."

RBE modeling:
- Phenomenoligical
- Microdosiemtric

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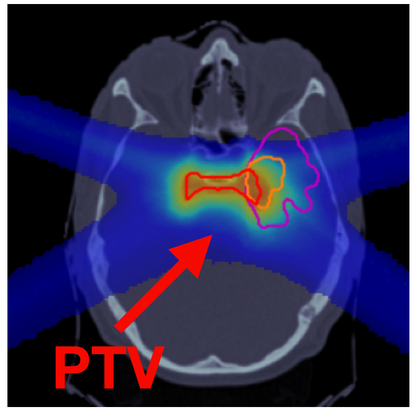
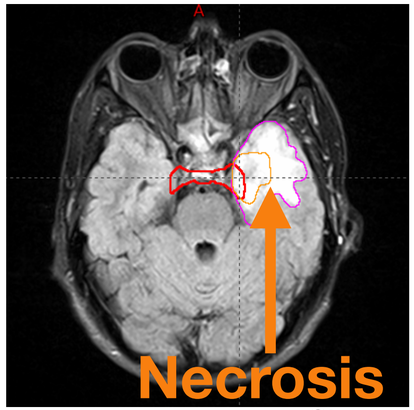
MC to support LET and biologically weighted TP

Chordoma, 74 Gy(RBE), 2Gy(RBE)/Fx, 4 radiation fields

Dose RBE=1.1

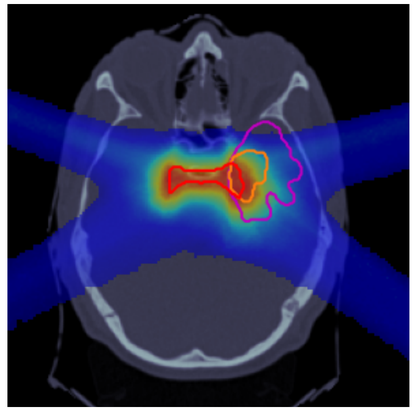


Post treatment **MRI**

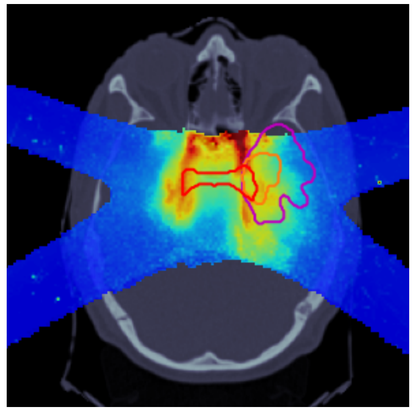


Stage II

RBE-weighted dose*



LET$_d$



*Dose computed with GPU-accelerated MC code (FRED) according to variable RBE model proposed by (A McNamara et al. 2015, PMB)

- **<u>Hypothesis</u>**
  - LET spectrum (not LET$_d$) in a voxel is essential for biological effect
  - High-LET particles cause complex DNA damage
- **<u>Impact/Application</u>**
  - Commissioning and validation of MC-TPS
  - Biologically and LET-weighted treatment planning

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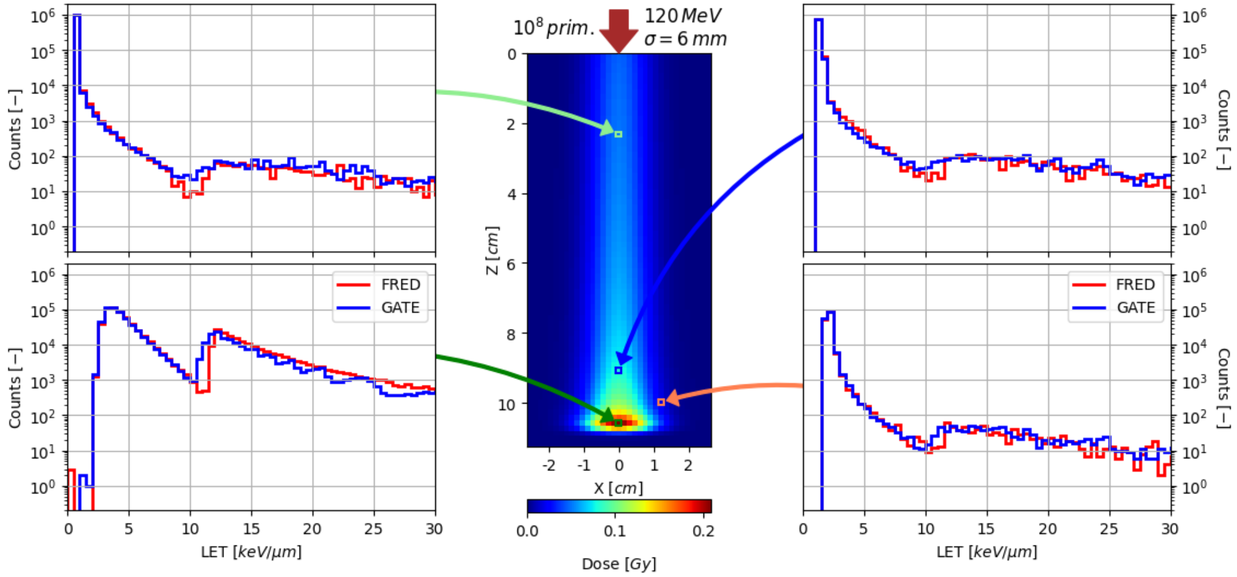
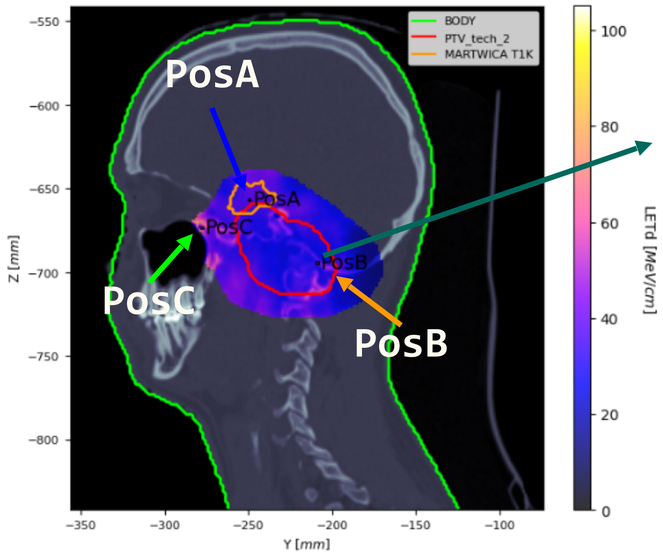
Garbacz et al. 2021 https://doi.org/10.1016/j.radonc.2021.08.015
Garbacz et al. 2022 https://doi.org/10.1186/s13014-022-02022-5

Computational LET QA

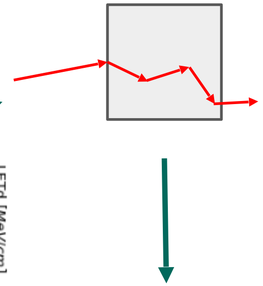
Not only the **averaged LET** (e.g. LETd) but
the whole **LET spectra** in a voxelized geometry



LETd



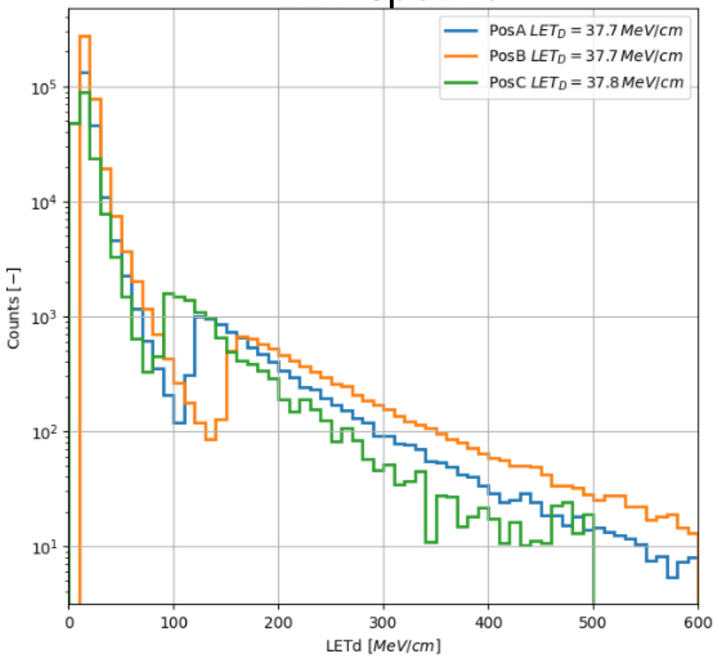
CT voxel



LET scored for each particle depositing energy

Spectra stored in Multi-component image (each voxel is a histogram)

LET spectra



Fred

GATE

Collaboration

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The National Centre for Research and Development

Grant for characterisation of mixed radiation fields in proton therapy

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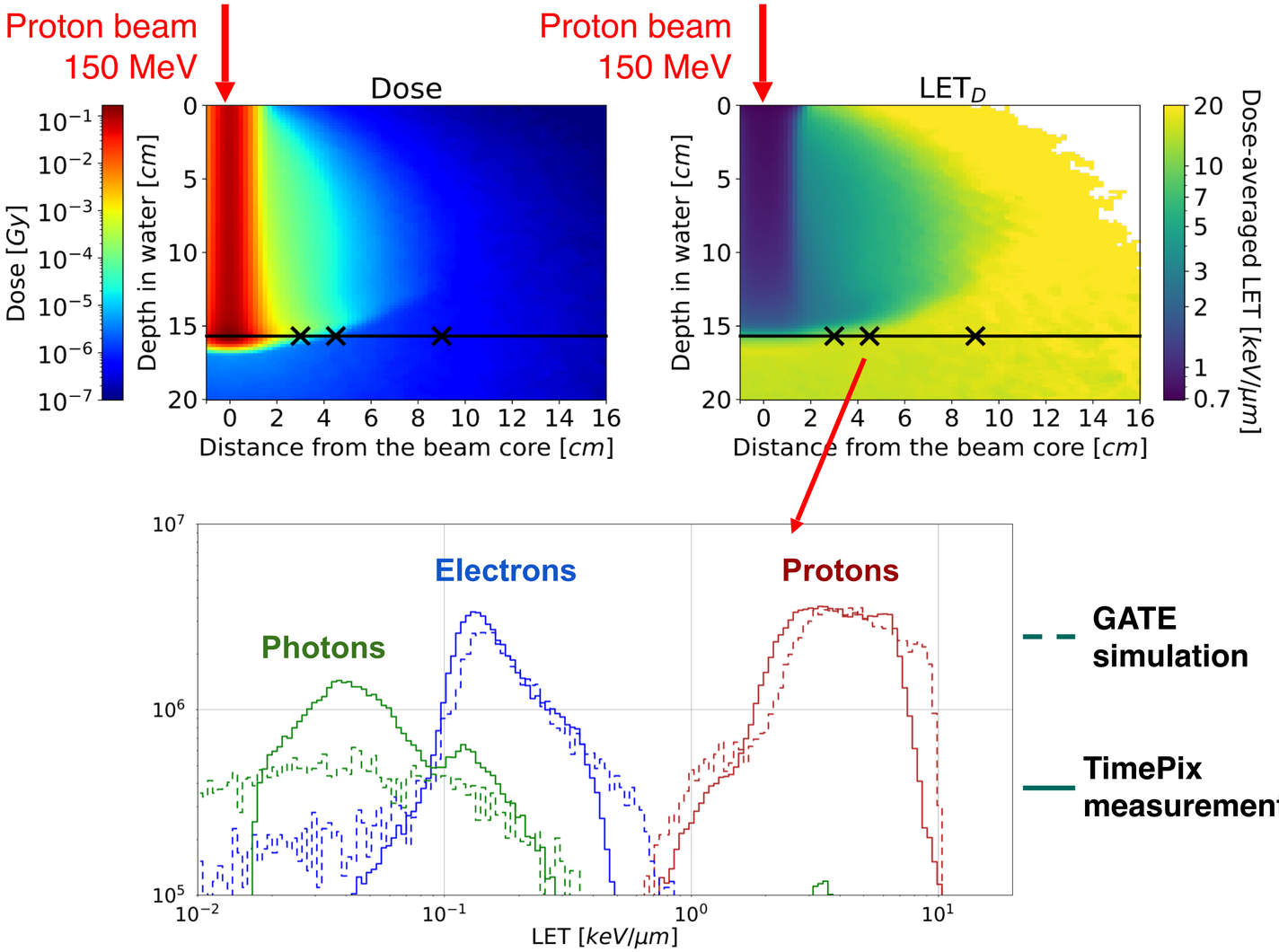
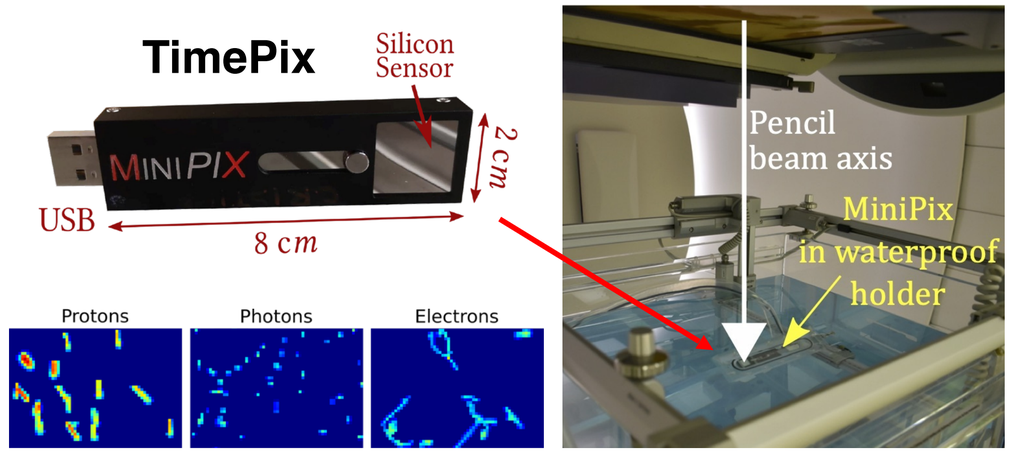
Experimental LET QA





Monte Carlo for detector development

- Depositions in TimePix simulated in GATE and FRED
- TimePix response with Geant4-based AllPix²

Collaboration

ADVACAM Imaging the Unseen

The National Centre for Research and Development

Grant for characterisation of mixed radiation fields in proton therapy

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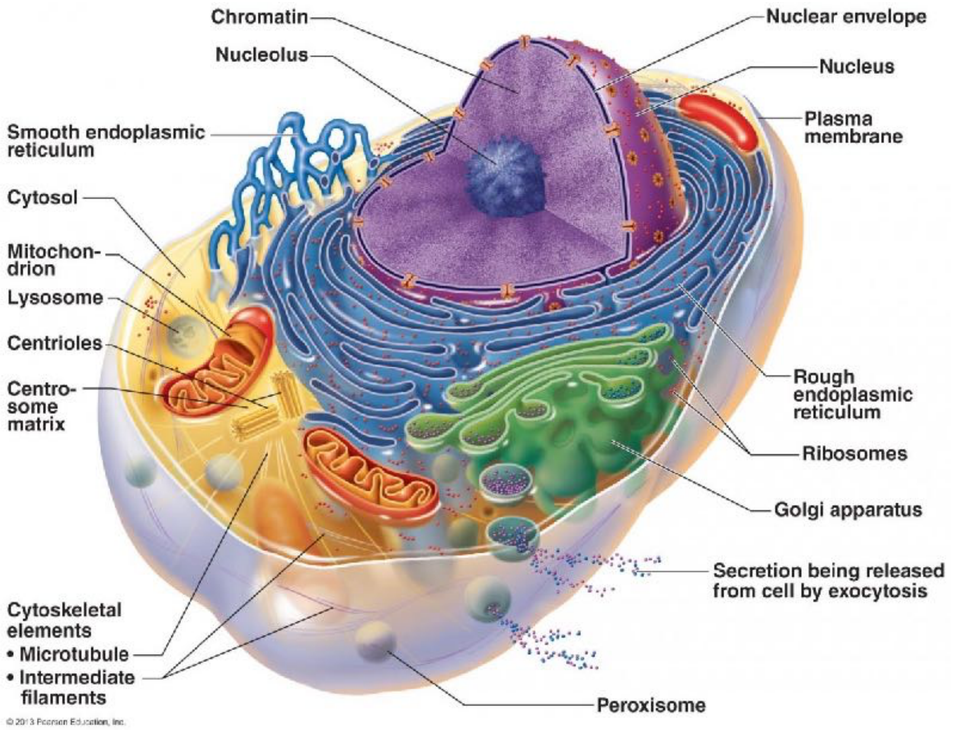
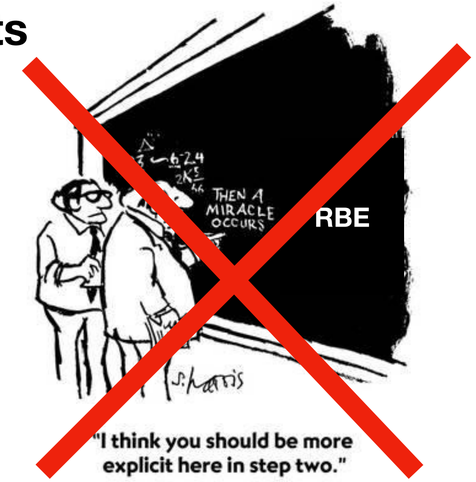
Stasica et al. 2020, https://doi.org/10.3389/fphy.2020.00346
Stasica et al. 2023, https://doi.org/10.1088/1361-6560/acc9f8

Dose becomes inadequate at microscopic levels

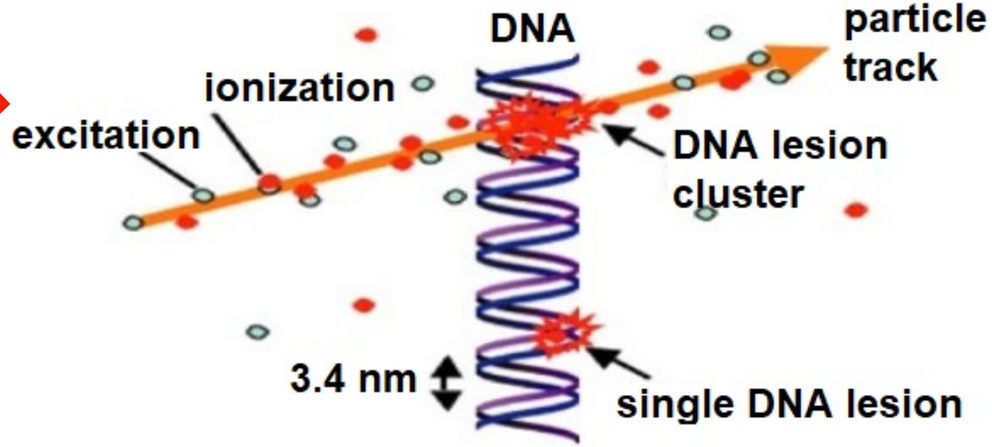
The hypothesis: Similar clustering leads to similar biological effect

Cell/DNA damage: Micro/nano-scopic concepts





Local ionization cluster size on the nanometer scale is the starting condition for all subsequent processes that lead to the observed DNA damage



- **Radiation damage is a stochastic quantity on the micro- and nanoscopic level, there fore the modeling solution must use micro- and/or nanodosimetric distributions rather than average quantities (LET, absorbed dose).**

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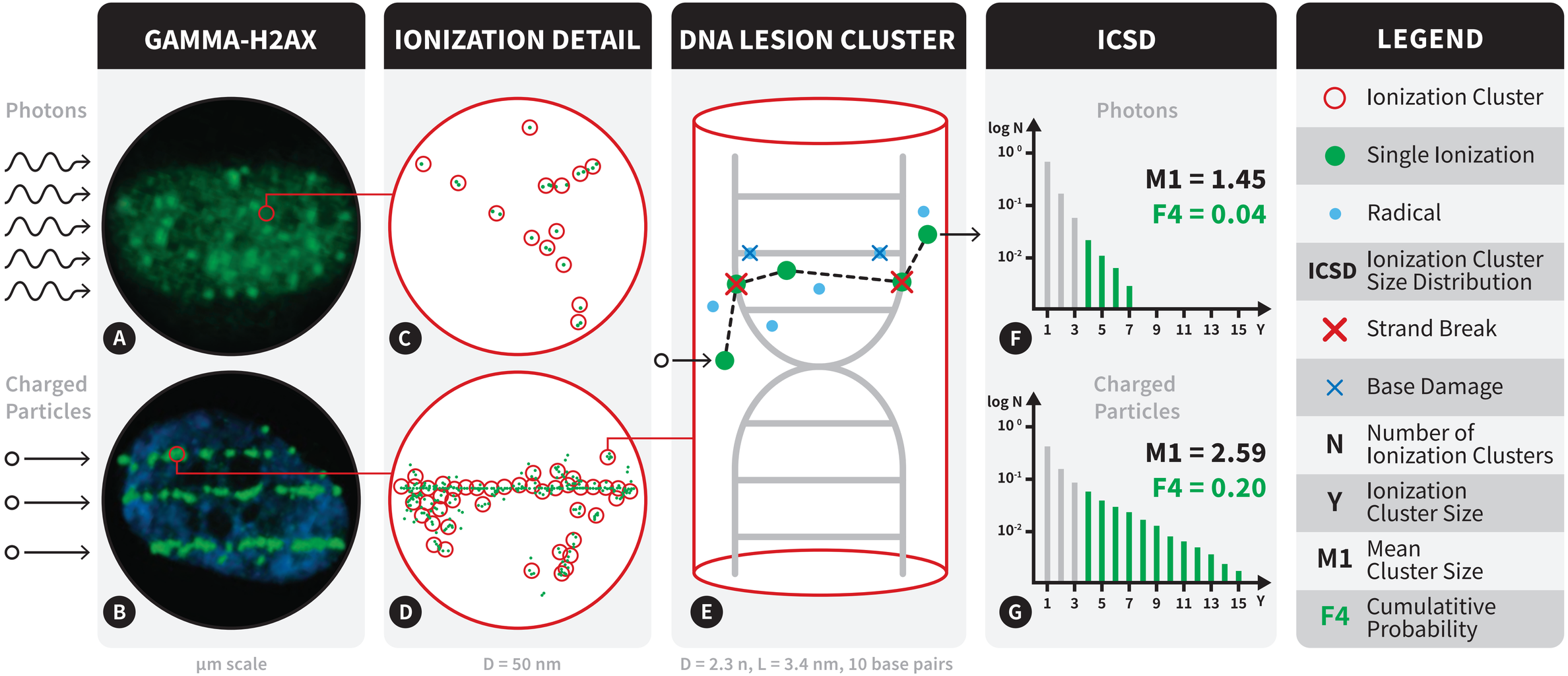
Ionization detail parameters and cluster dose Principles and concepts

ProtoTerra PhD students work with LLU, CA, USA & Krakow on ID detector & TP approach



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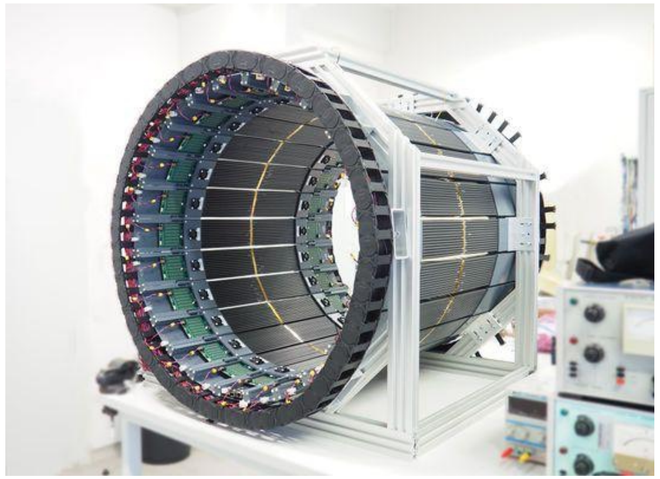
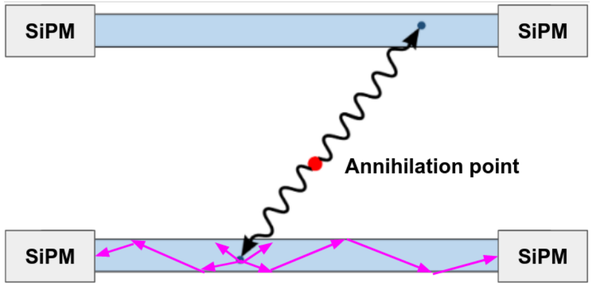
Rucinski, Biernacka & Schulte 2021 *DOI*: https://doi.org/10.1088/1361-6560/ac35f1
Faddegon, …, Rucinski, 2023 DOI: https://doi.org/0.1088/1361-6560/acea16

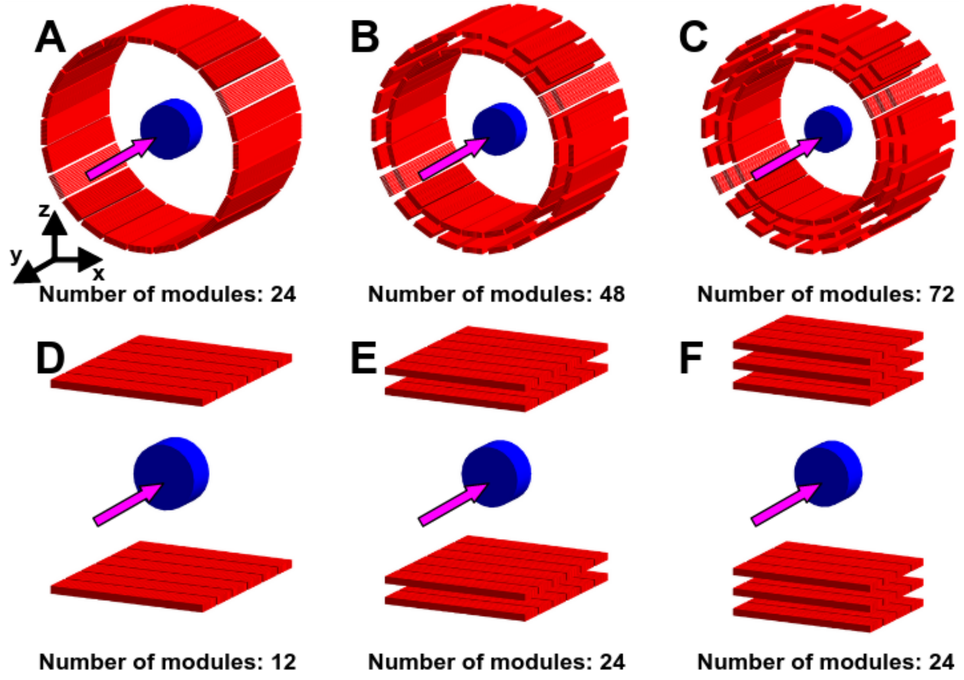
J-PET for range monitoring in PT

J-PET operation principle





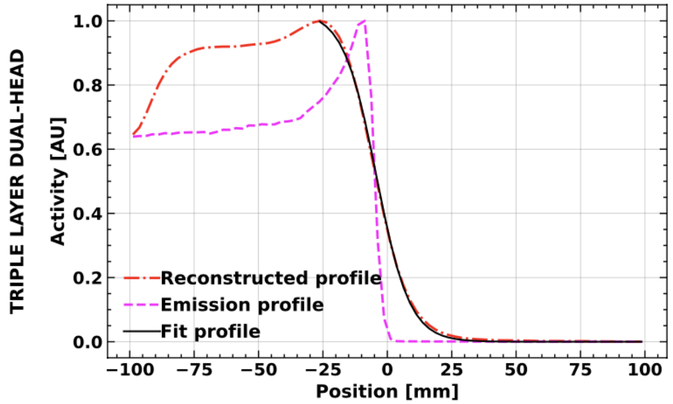
Sensitivity



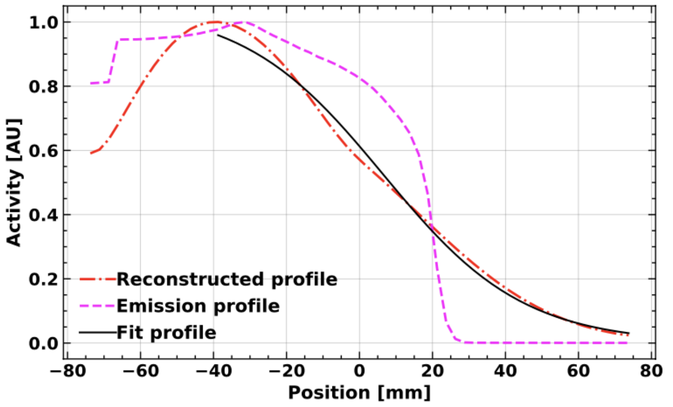
Setup	SPB			SOBP		
	$\eta[10^{-6}]$	$\sigma(\eta)[10^{-6}]$	$\overline{H}$	$\eta[10^{-6}]$	$\sigma(\eta)[10^{-6}]$	$\overline{H}$
Single layer cylindrical	9.45	0.29	1.0	3.64	0.22	1.0
Double layer cylindrical	27.41	0.80	2.9	10.76	0.65	2.9
Triple layer cylindrical	45.72	1.26	4.8	18.00	1.11	5.0
Single layer dual-head	3.79	0.13	0.4	2.45	0.19	0.7
Double layer dual-head	10.55	0.35	1.1	7.21	0.56	2.0
Triple layer dual-head	10.22	0.26	1.1	8.92	0.78	2.4

Range estimation

SPB



SOBP



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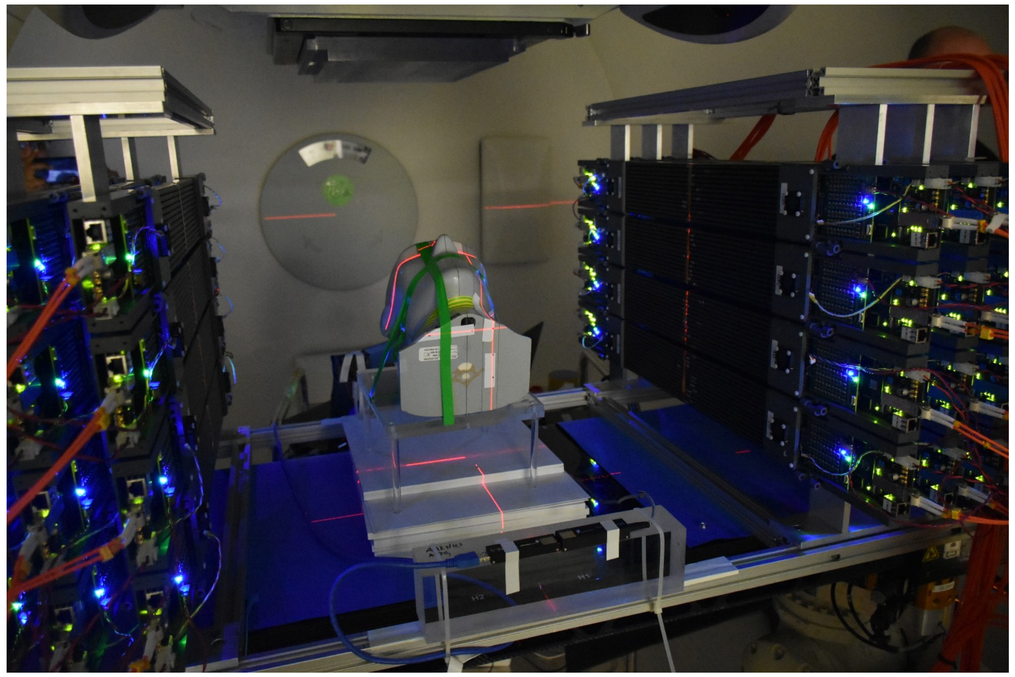
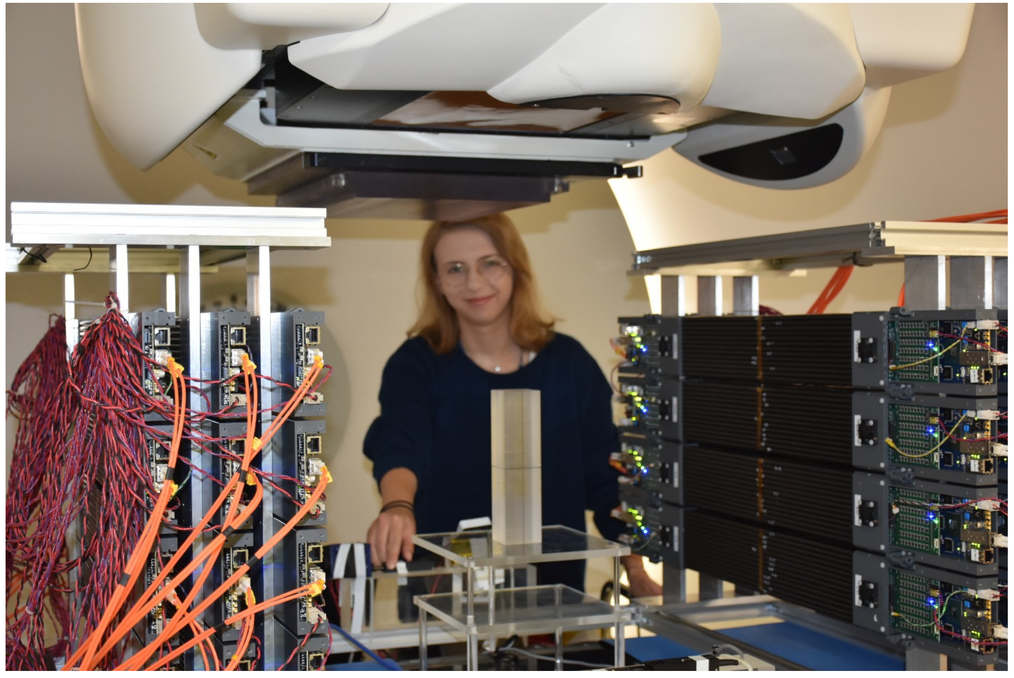
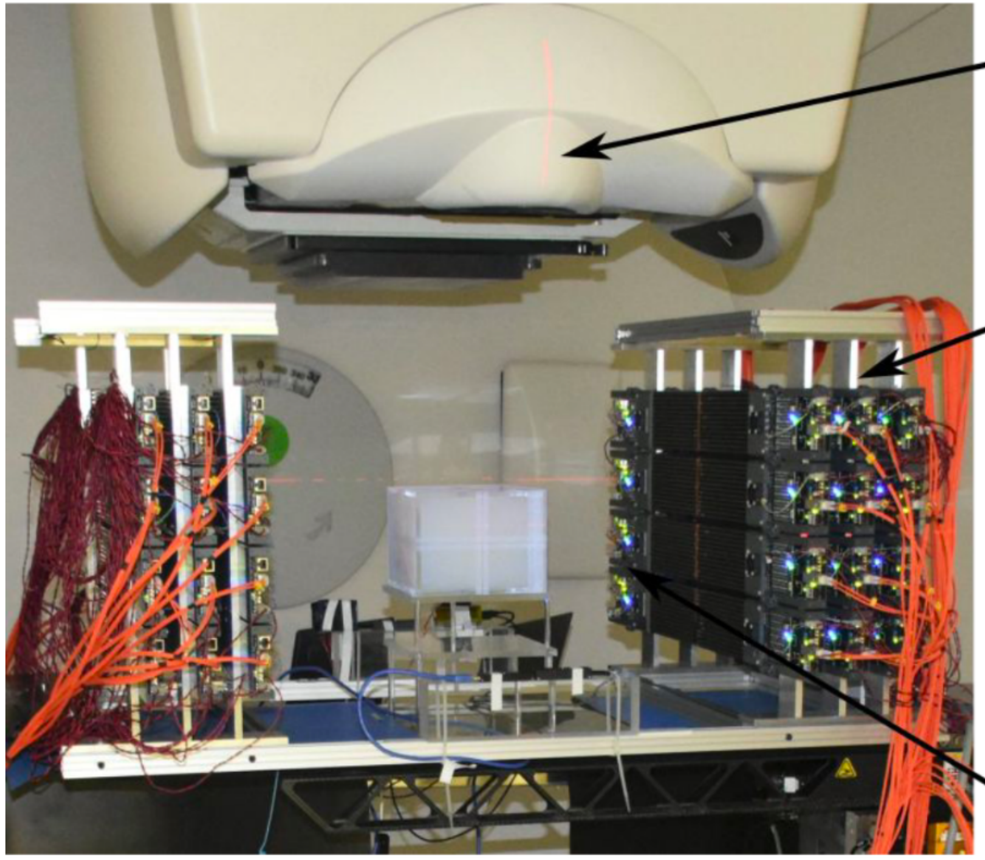
J-PET & proton beams 2021

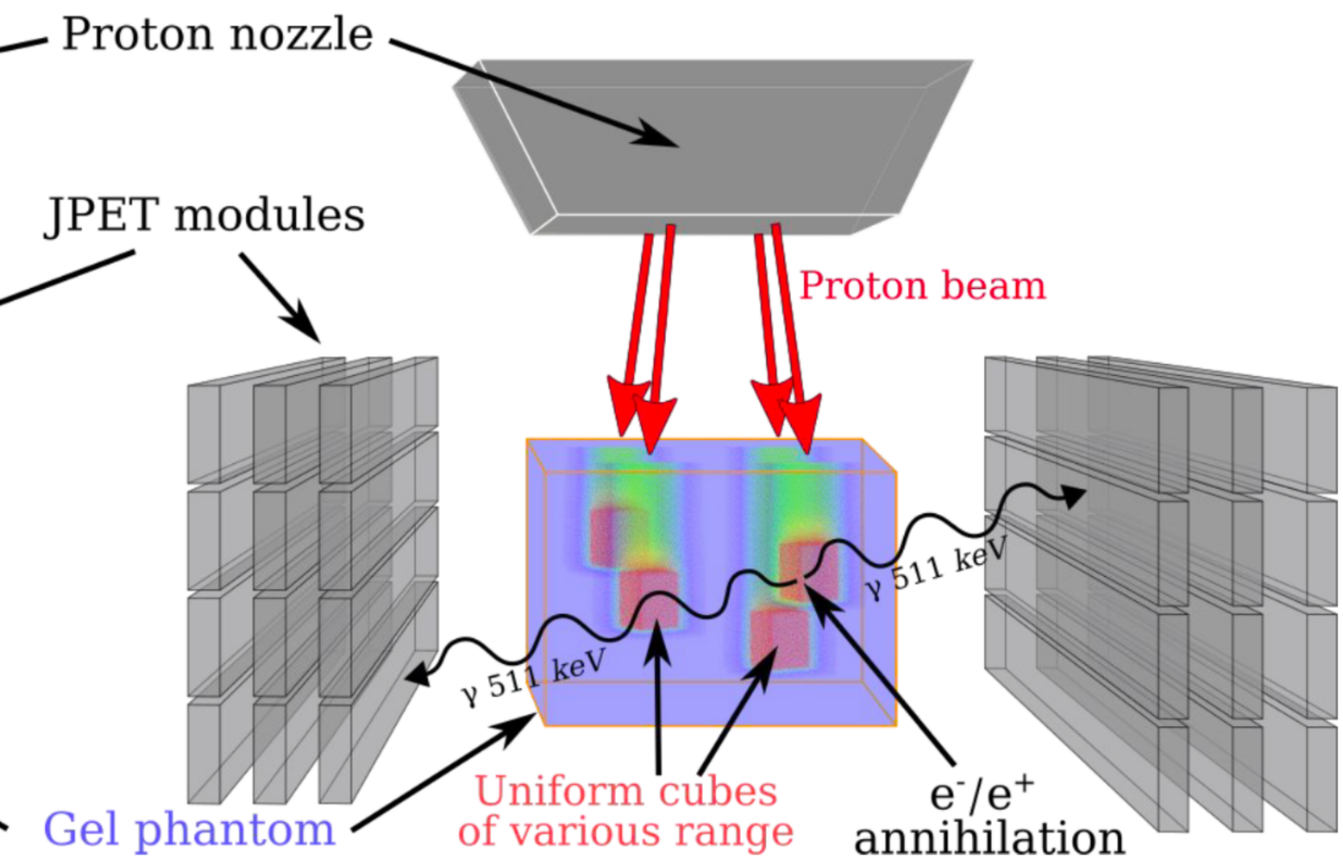




J-PET for range monitoring in PT

Experimental validation with proton beams at CCB





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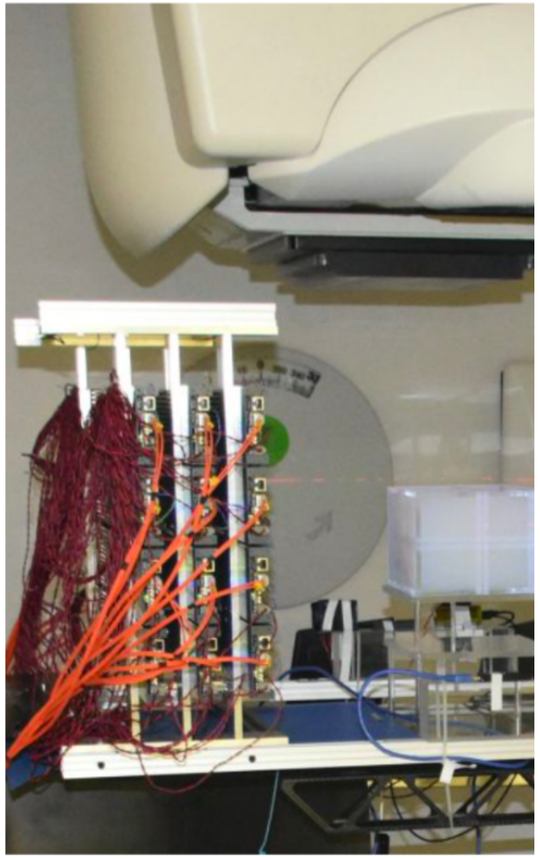
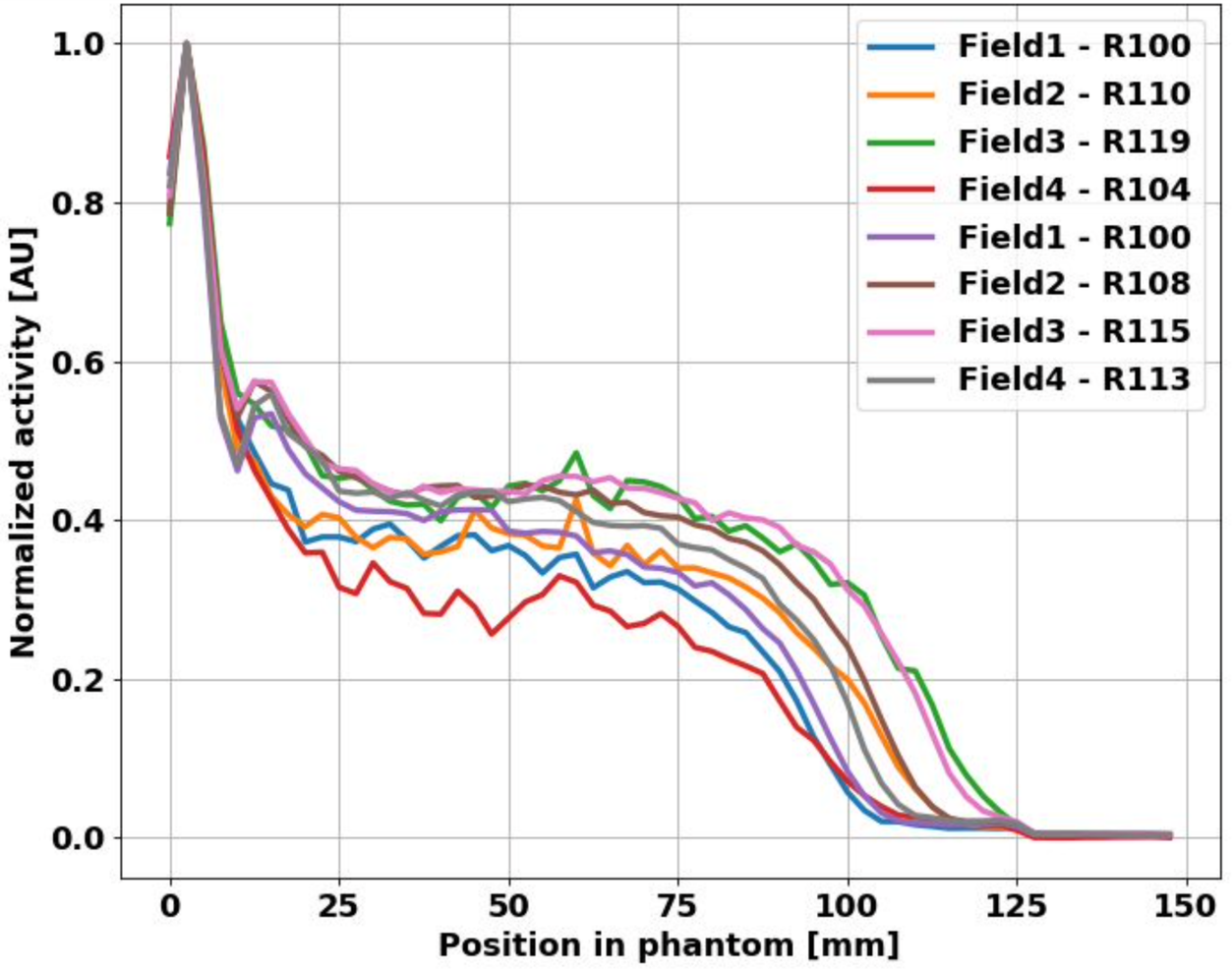
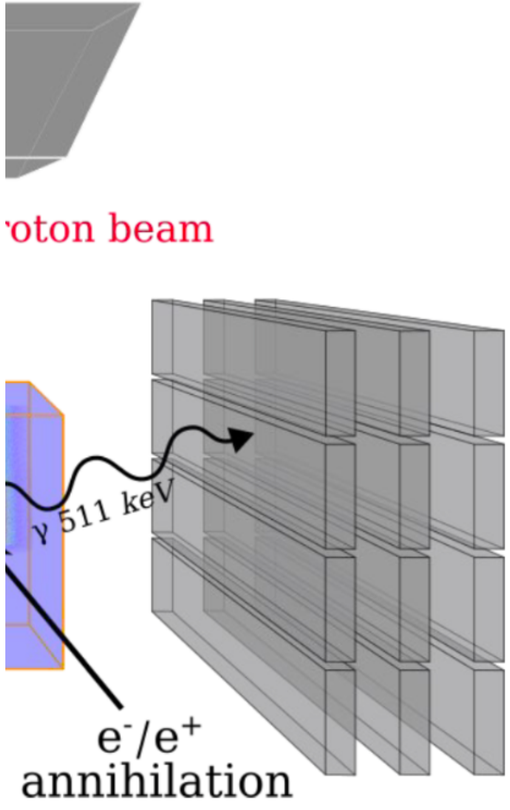
J-PET for range monitoring in PT

Experimental validation with proton beams at CCB







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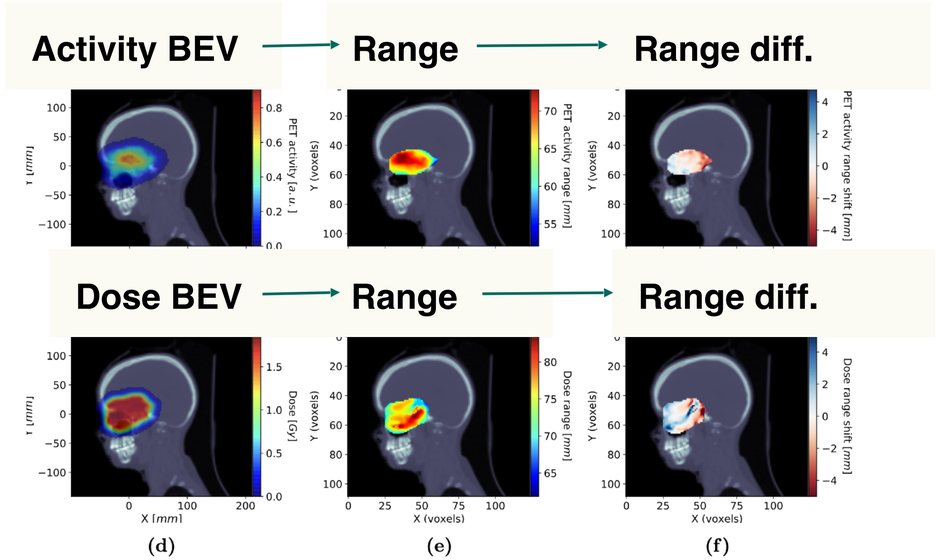
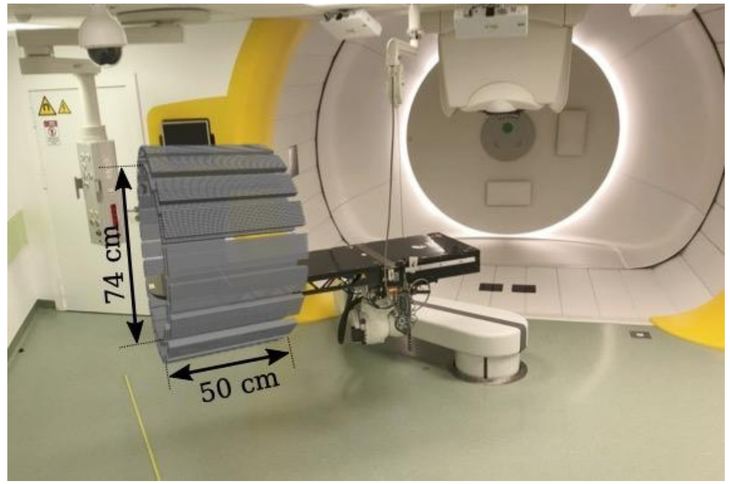
Range shift detection in patients

Patient simulation studies with J-PET

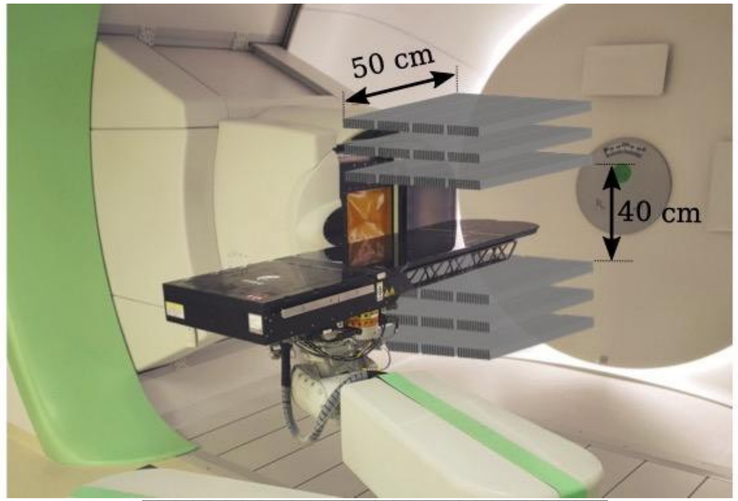
94 patients x 27 scenarios
(24 shifts + 2 CT cal. + reference)



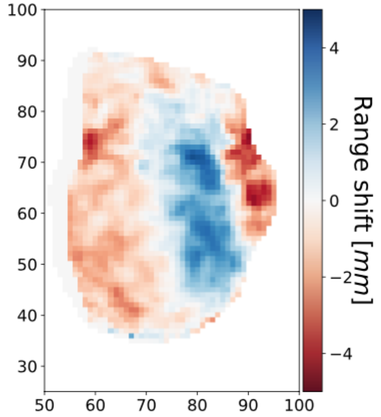
In-room PET imaging protocol



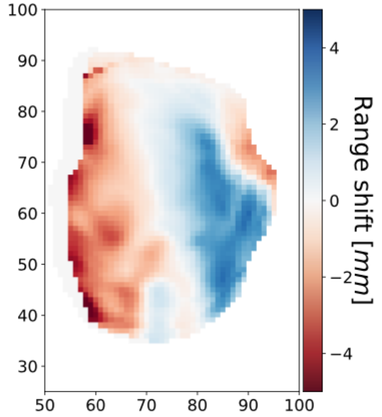
In-beam PET imaging protocol

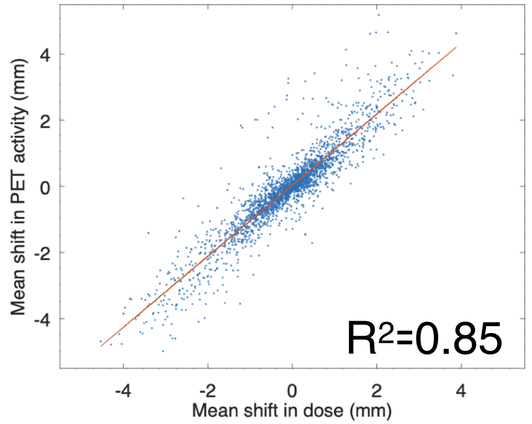


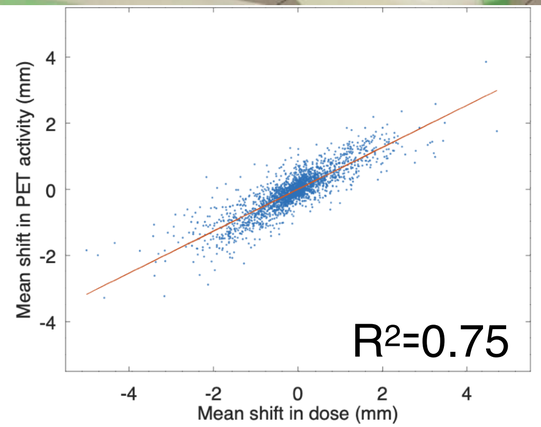
PET image



Dose image







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K. McNamara et al. 2022 https://doi.org/10.1088/1361-6560/aca515
D. Borys et al. 2022 https://doi.org/10.1088/1361-6560/ac944c
K. Brzezinski, et al., PMB (2023) https://doi.org/10.1088/1361-6560/

Summary

- **Proton therapy facility offers to medical physics research:**
  - Access to proton beams in Gantry rooms for experiments
  - Anonymised patient data for TP studies and protocols development
  - Radiobiology labs equipped to perform in vitro experiments
- **In CCB Krakow proton center**
  - MC based patient QA - Dose evaluation
  - MC to Support treatment planning - LET evaluation
  - Detector development - J-PET and TimePix
  - Ionisation detail based treatment planning

Thank you

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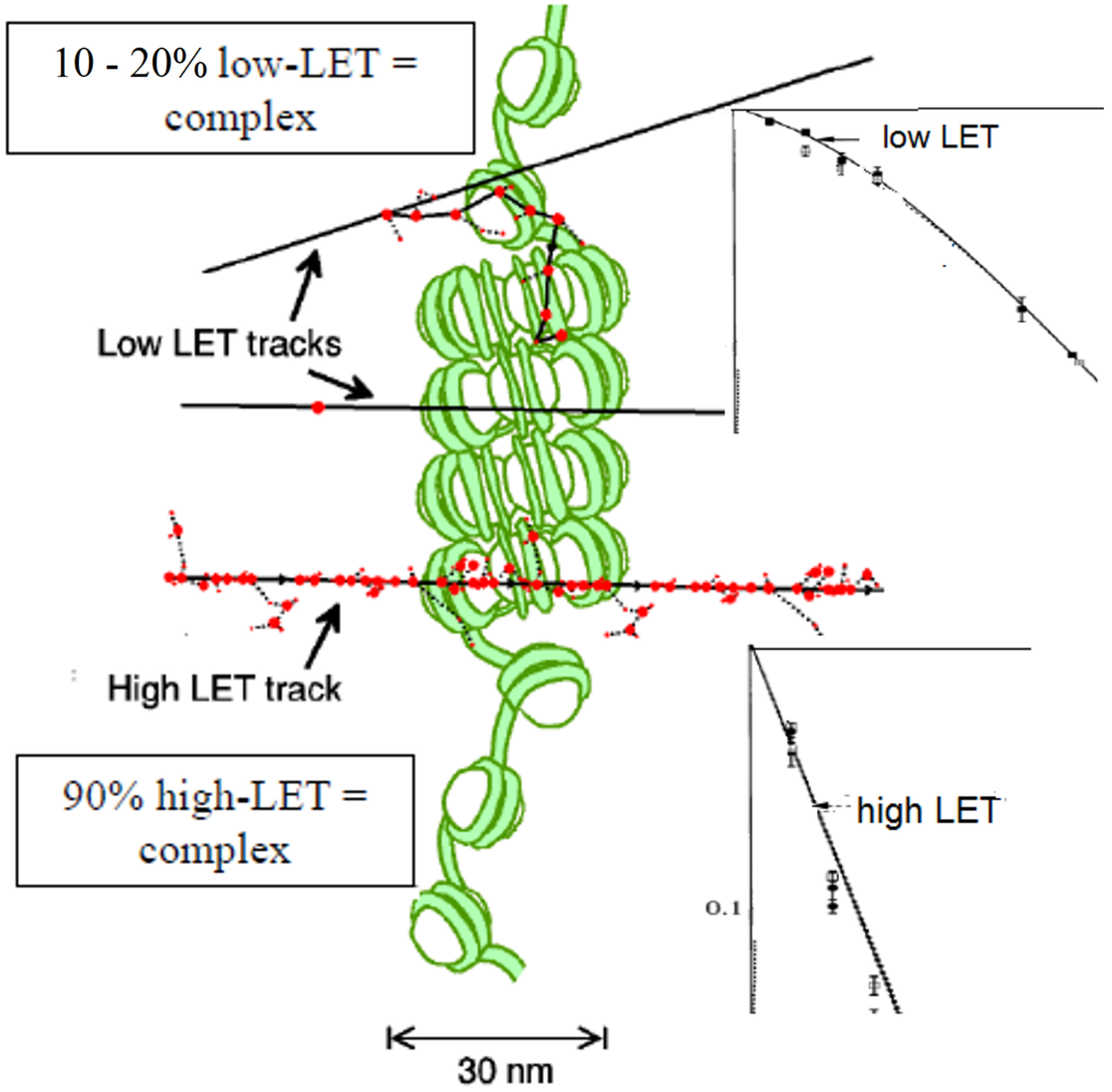
The hypothesis: Similar clustering leads to similar biological effect

- Local **ionization cluster size** on the nanometer scale is the starting condition for all subsequent processes that lead to the observed DNA damage
- The **complexity of the damage** determines the **repair pathways** chosen by cells and, in turn, will dictate the **final biological outcomes** that are important for RT
- **Complex DNA damage** caused by ionization clusters in short DNA segments is responsible for **cell death/dysfunction/DNA mutation**



Courtesy of Dudley Goodhead

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