# **Computational and experimental methods** applied for treatment planning, quality assurance, and research **at the clinically operating proton therapy facility**

**Antoni Rucinski, IGFAE Workshop, 10.05.2023**
antoni.rucinski@ifj.edu.pl

# Witnessing PT development in Europe

## My story


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

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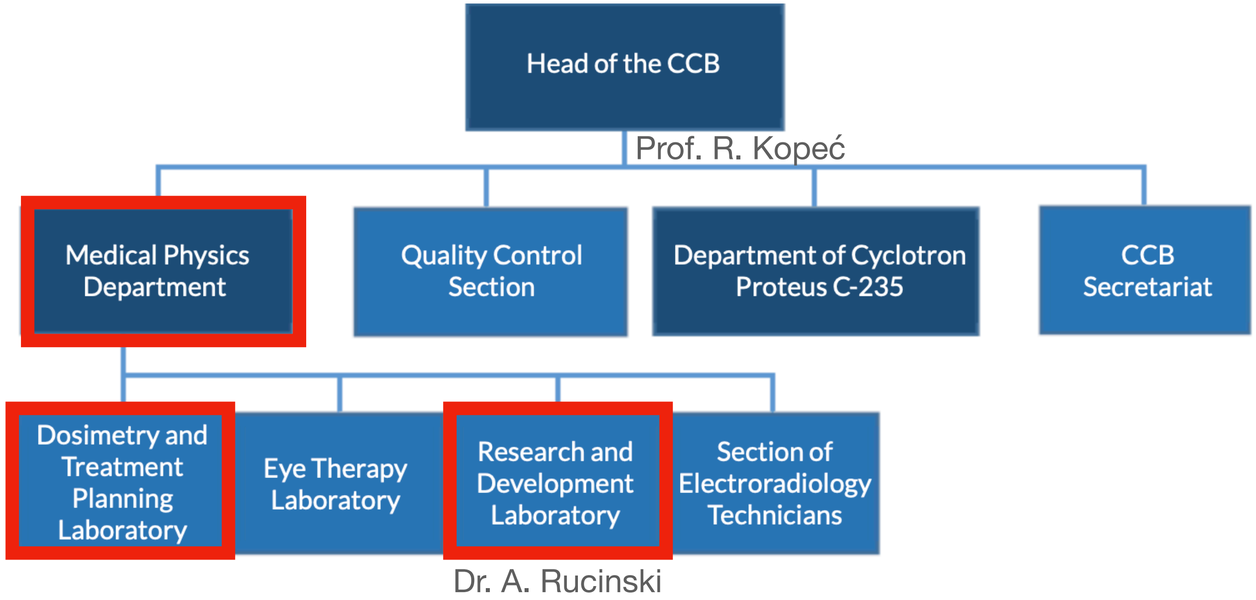
# CCB Kraków proton center

## Structure and relevant data/equipment


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

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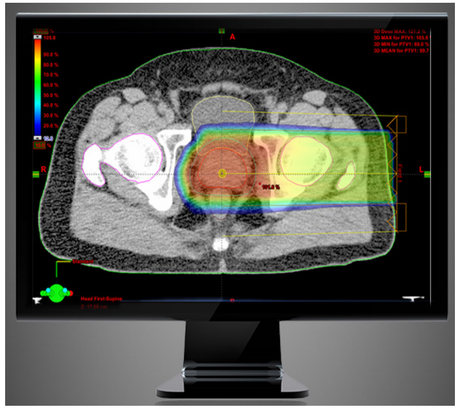
# Translational research at CCB proton center

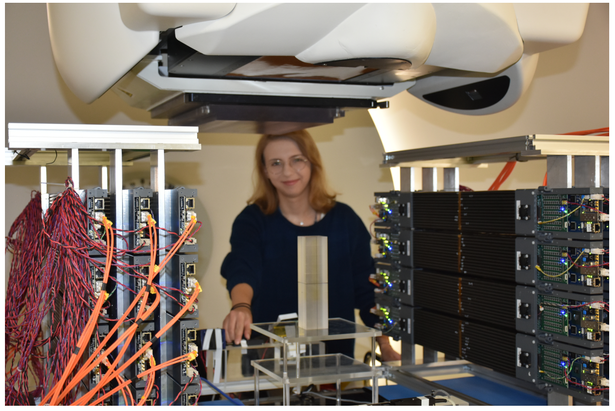
## Physics, radiation biology, and oncology to improve clinical protocols

Computations and modelling ⟷ Experiments



Biologically and LET weighted treatment planning

Quality assurance



Detectors for range monitoring for therapy adaptation

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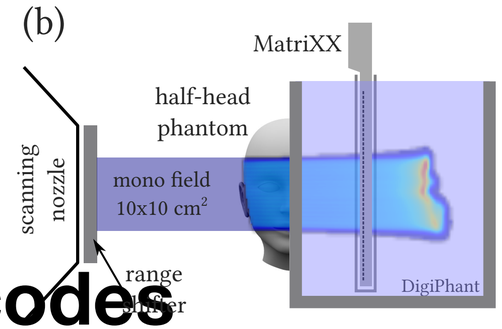
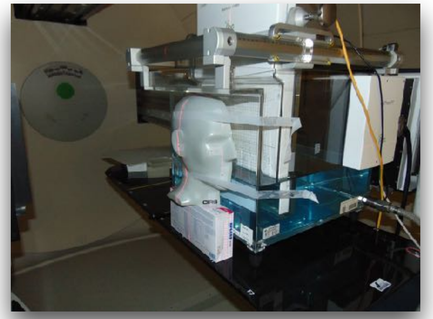
# Beam modeling

## Eclipse TPS, Fred and GATE MC codes

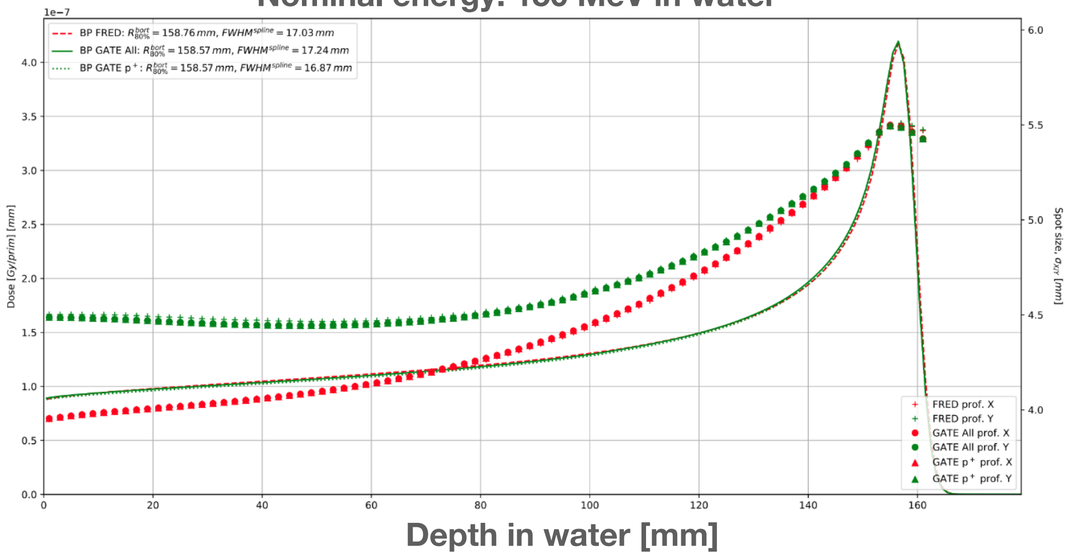


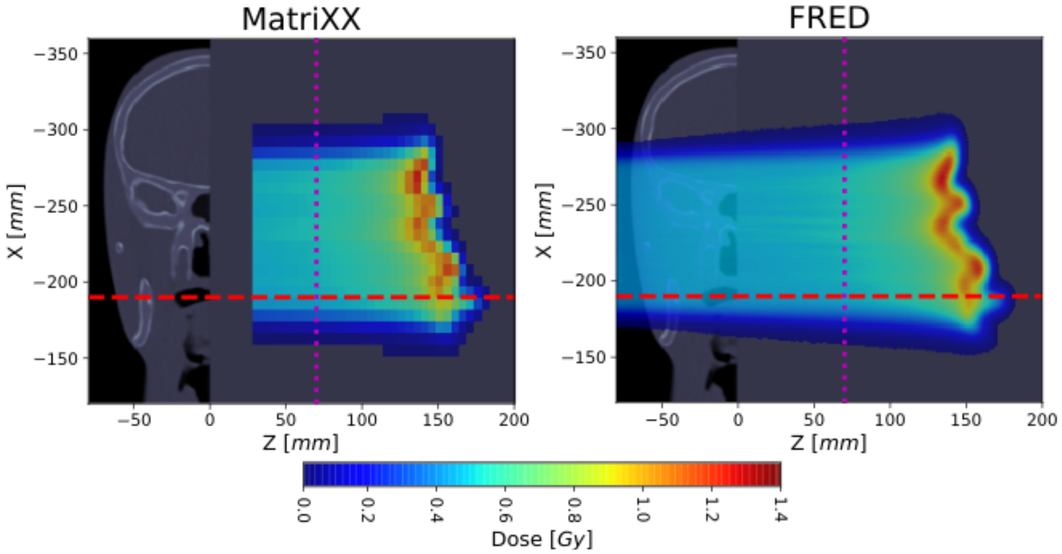



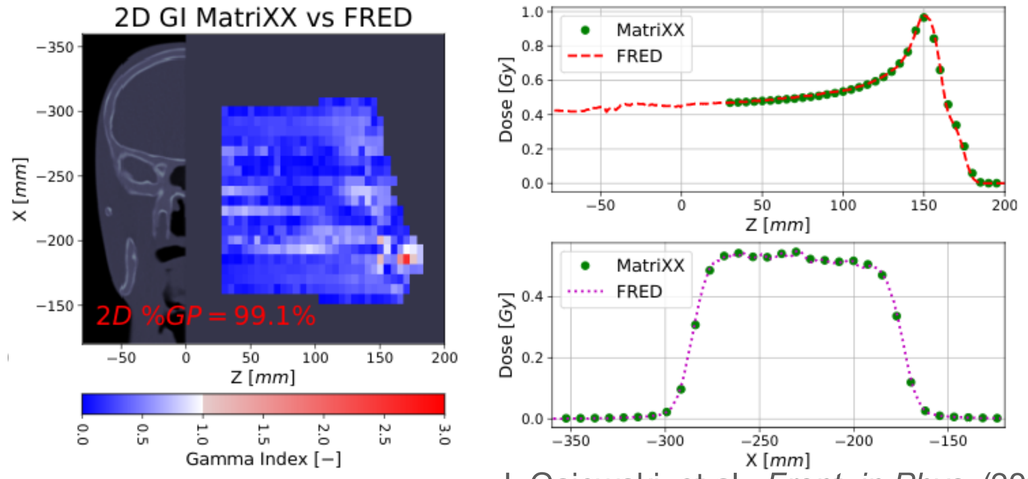
Experimental validation

- 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




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

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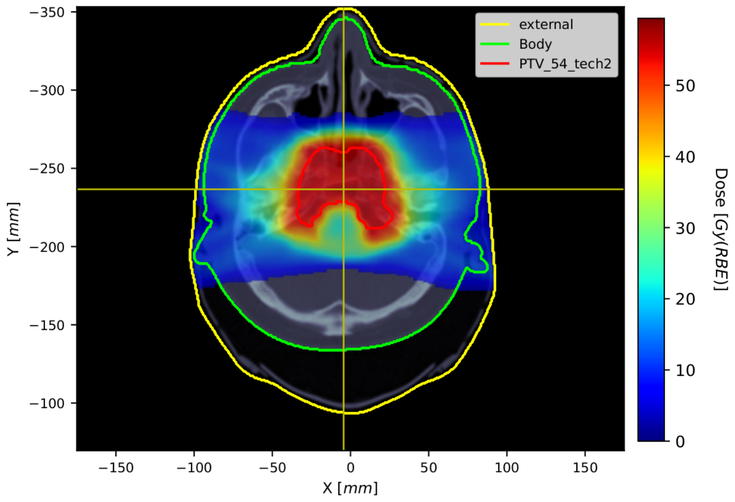
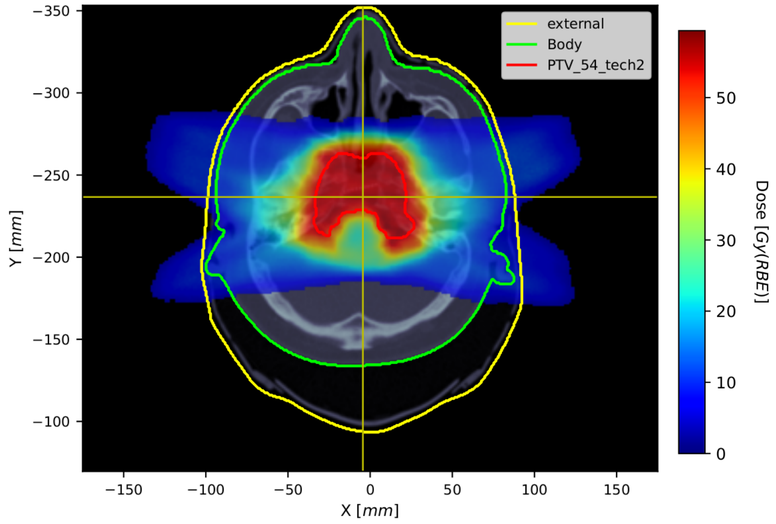
# Dosimetric cross-validation TPS-GATE-FRED

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

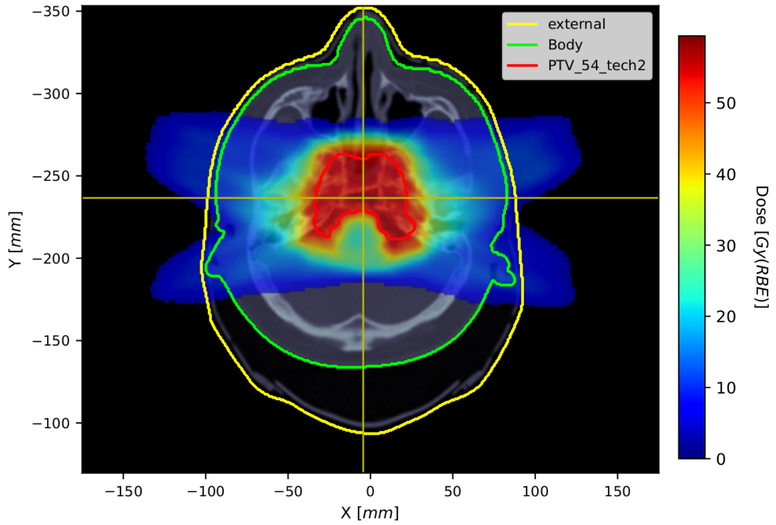
TPS



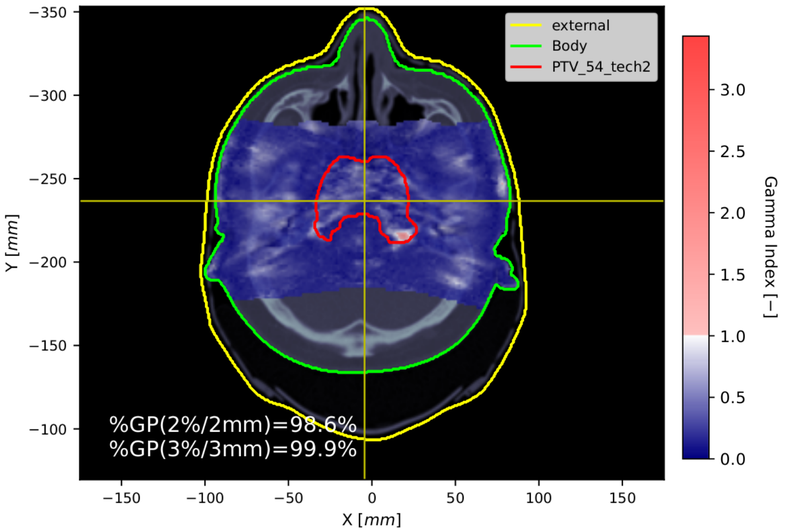

FRED




GATE




Gamma Index (*3mm/3%*)




Silesian University of Technology

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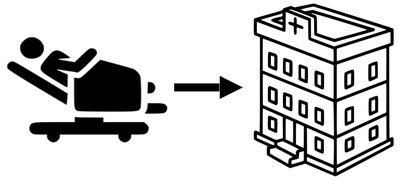
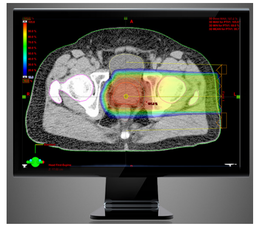
# Computational Patient QA with FRED and GATE



Diagnosis and treatment protocol

Computed tomography

CT calib. (HU to RPSP)



Treatment planning

Beam model (commissioning)

Experimental dose measurement

Time consuming process

Plan verification

Computational patient QA

Plan irradiation

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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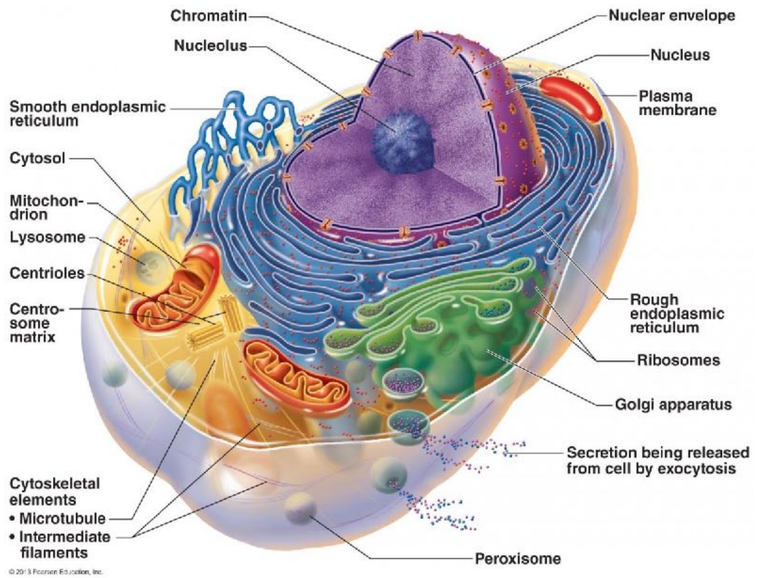
# Advances in radiobiological modeling

## Dose: Macroscopic concept

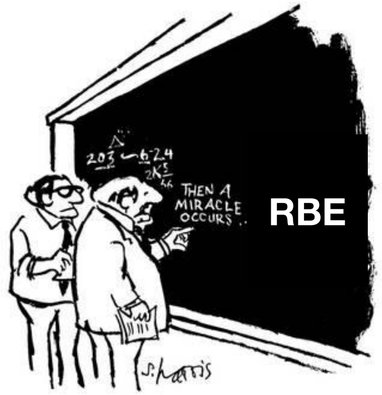
*From: http://www.ptw.de*

?

## 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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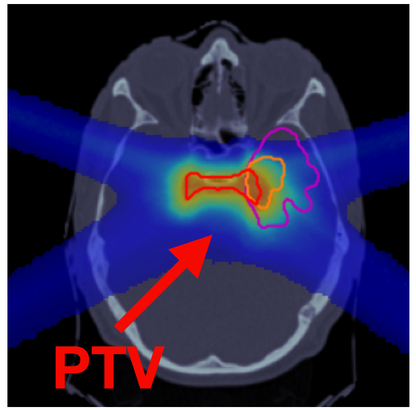
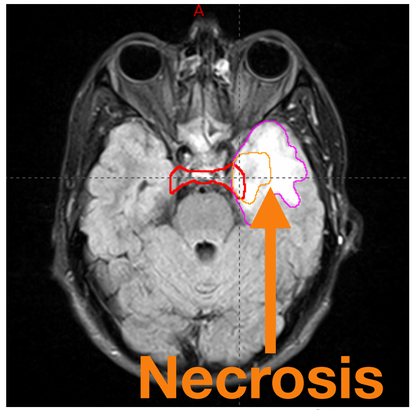
# MC to support LET and biologically weighted TP

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

**Dose** RBE=1.1

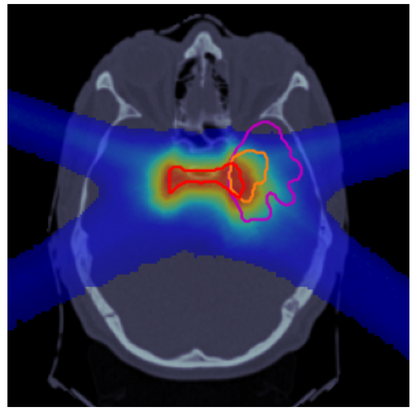



Post treatment **MRI**

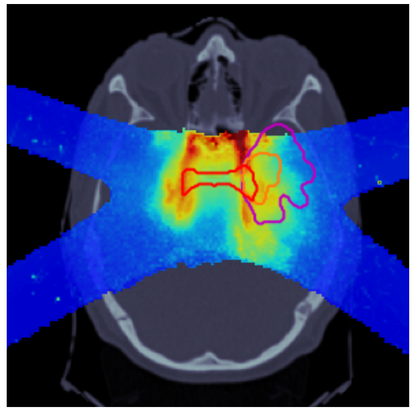



Stage II

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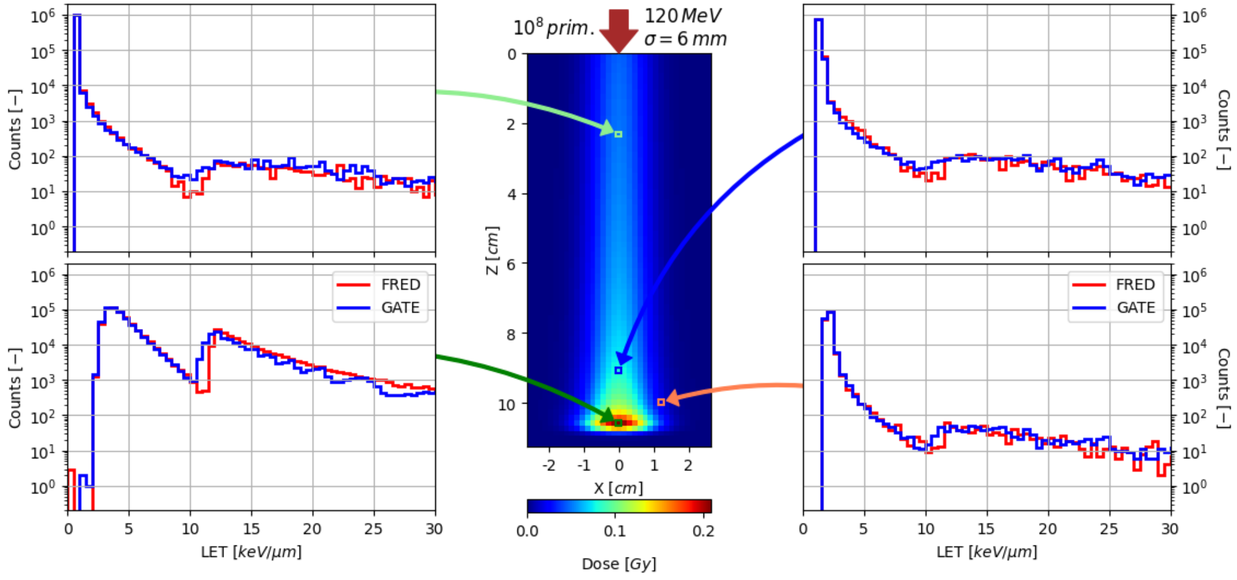
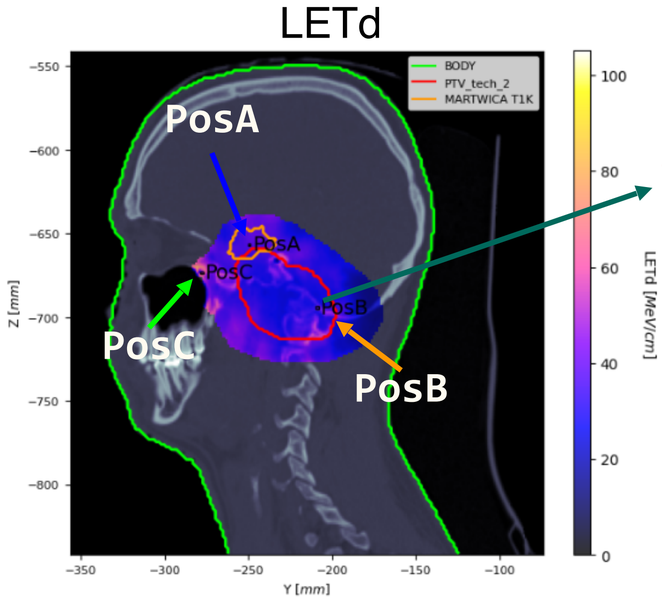
Garbacz et al. 2021 M. Garbacz, https://doi.org/10.1016/j.radonc.2021.08.015
Garbacz et al. 2022 https://doi.org/10.1186/s13014-022-02022-5

# Computational LET QA

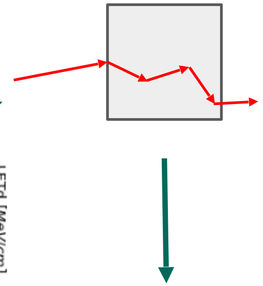
Not only the **averaged LET** (e.g. LETd) but
the whole **LET spectra** in a voxelized geometry




LETd




CT voxel

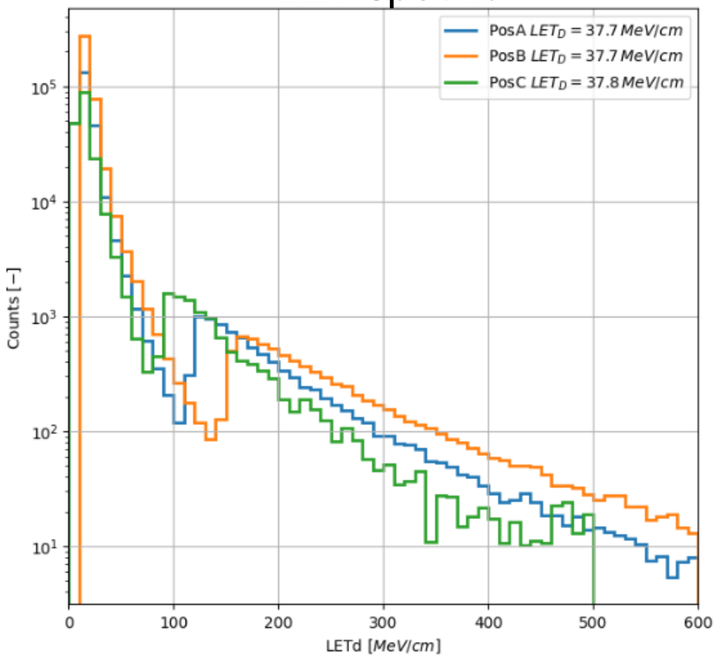


LET scored for each particle depositing energy

TK

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

LET spectra




Fred

GATE

Collaboration

SAPIENZA
UNIVERSITÀ DI ROMA

The National Centre for Research and Development

Grant for characterisation of mixed radiation fields in proton therapy

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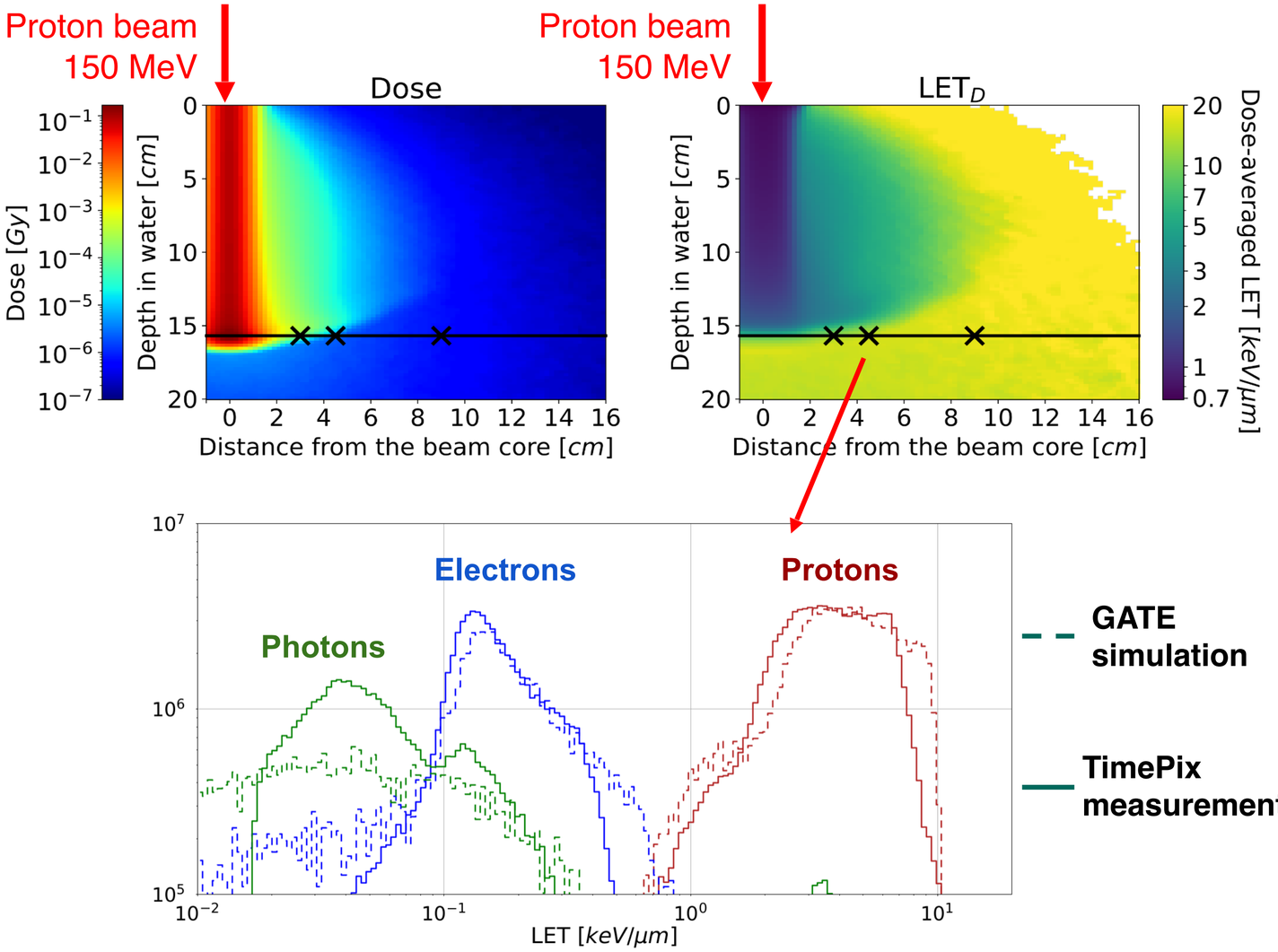
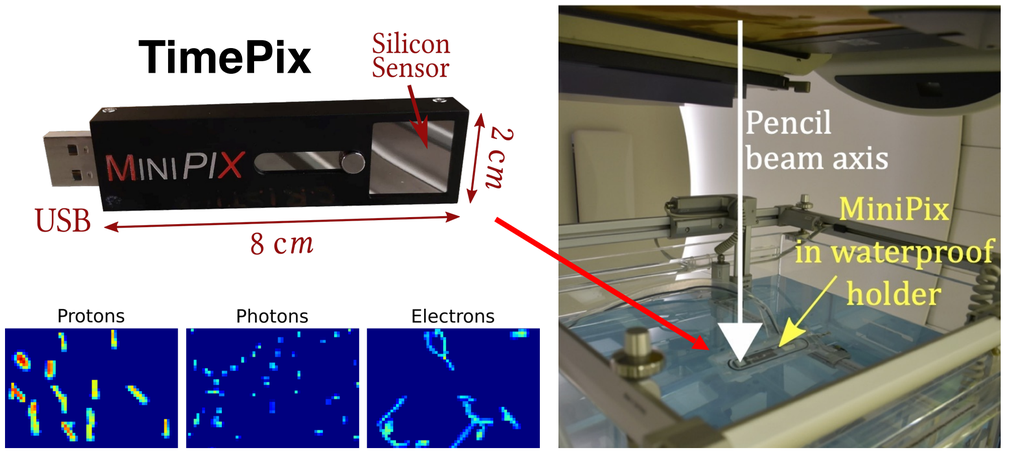
# Experimental LET QA




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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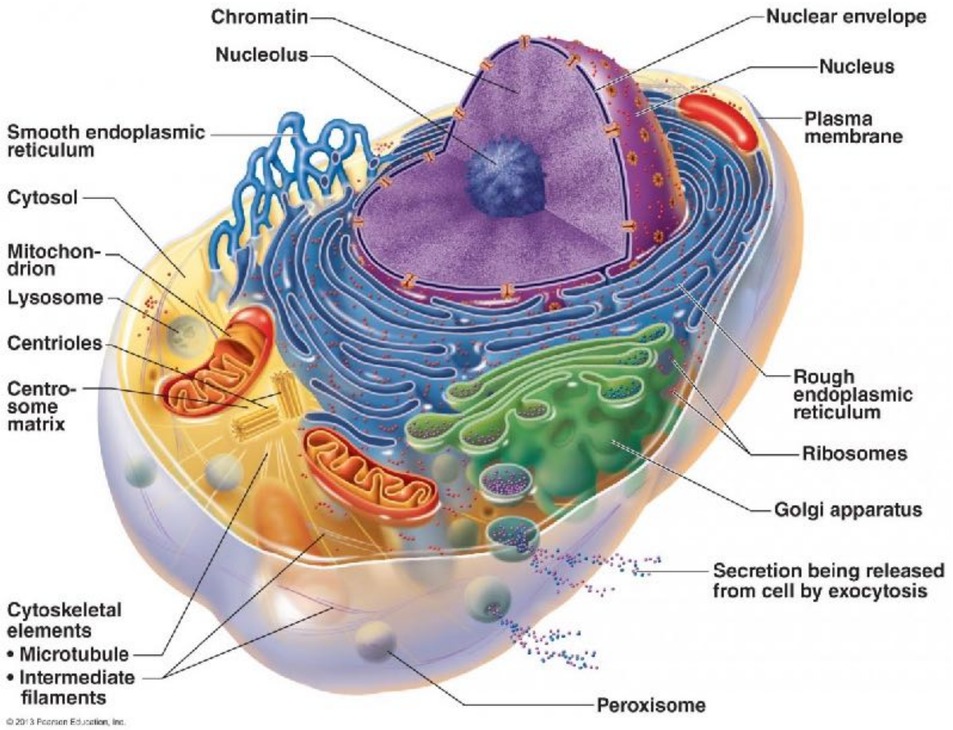
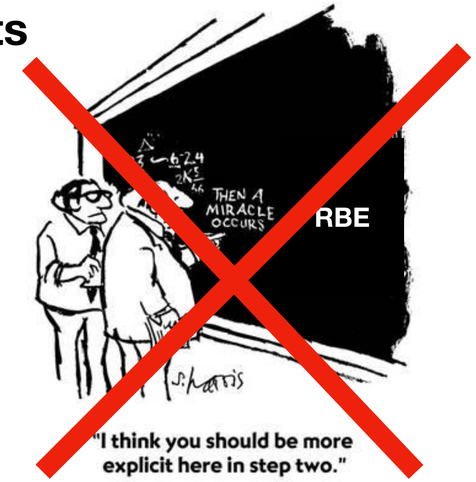
# Dose becomes inadequate at microscopic levels

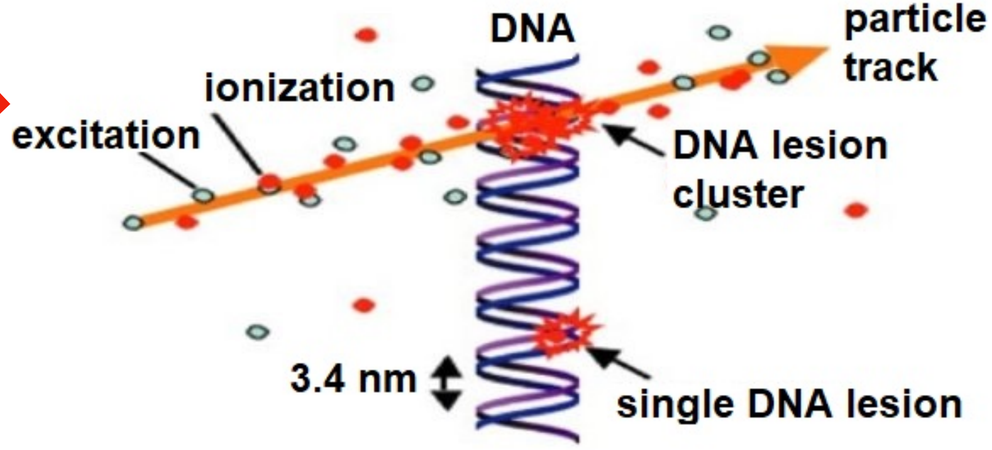
## The hypothesis: Similar clustering leads to similar biological effect

**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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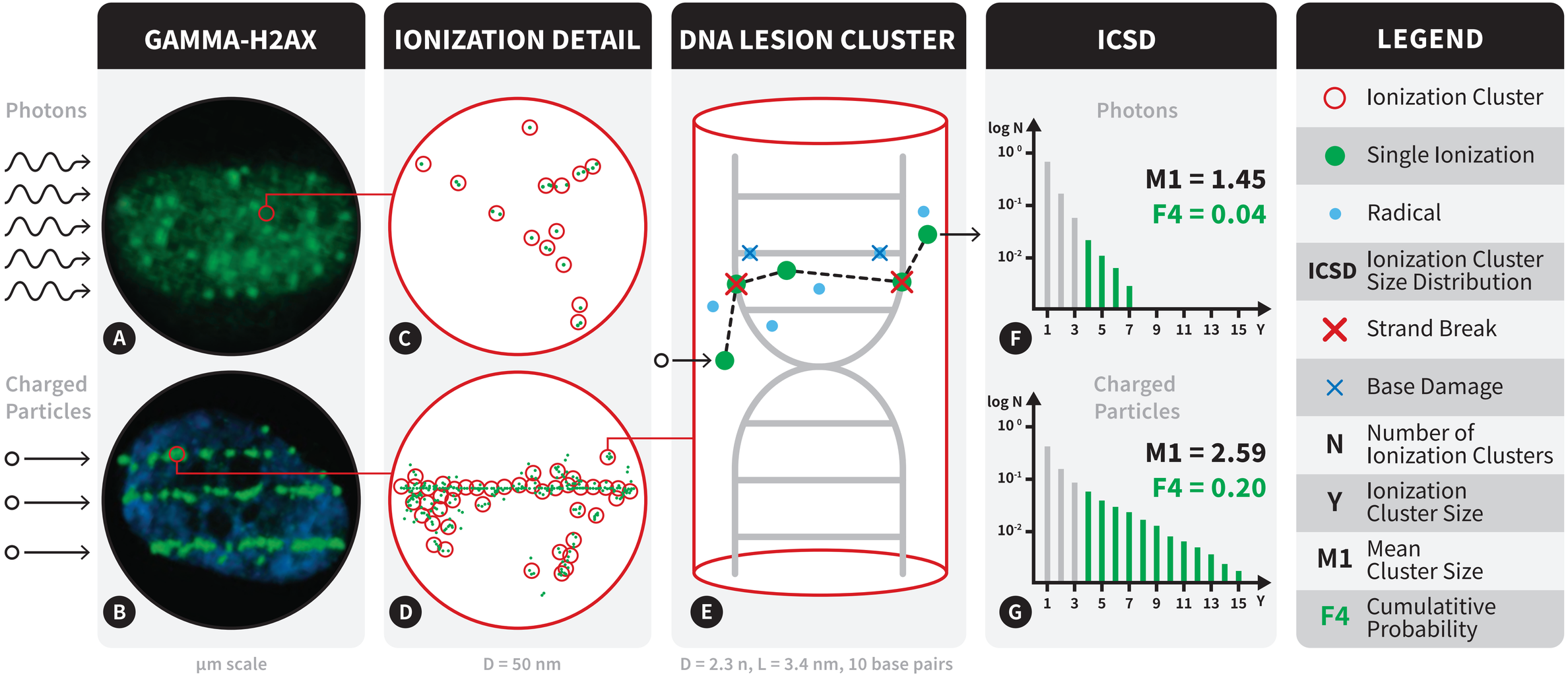
# Ionization detail: principles and concepts

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

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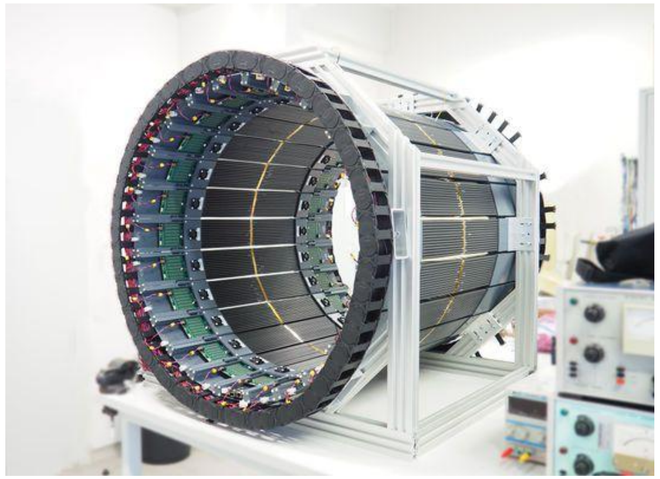
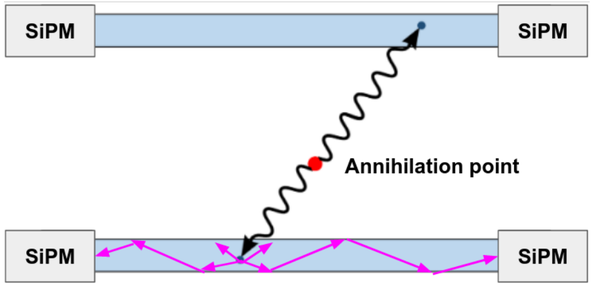
Rucinski A, Biernacka A & Schulte R 2021 *Applications of nanodosimetry in particle therapy planning and beyond* PMB 66(24), 24TR01. URL: https://doi.org/10.1088/1361-6560/ac35f1

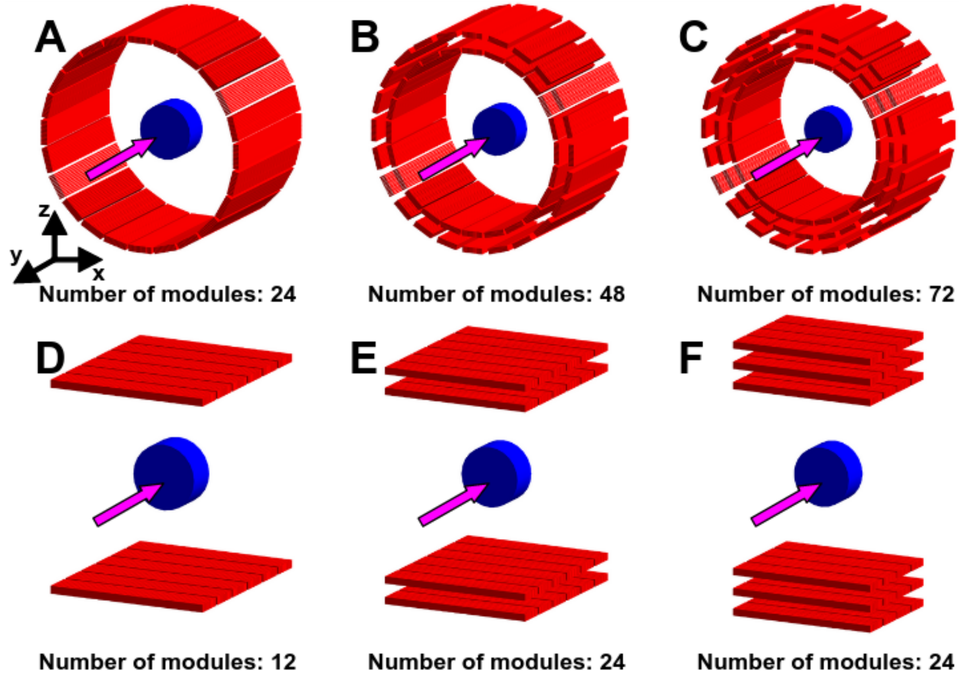
# J-PET for range monitoring in PT

## J-PET operation principle





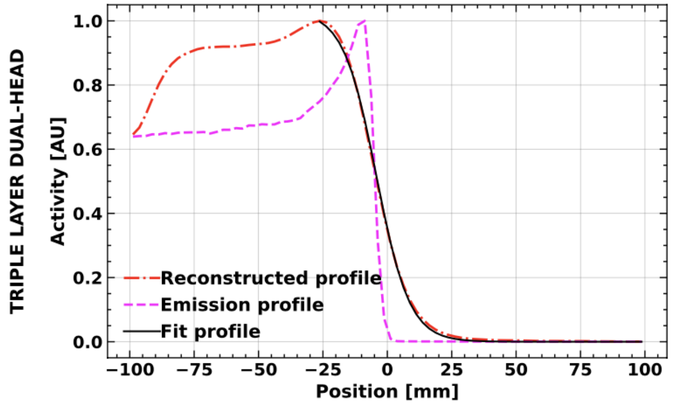

## Sensitivity



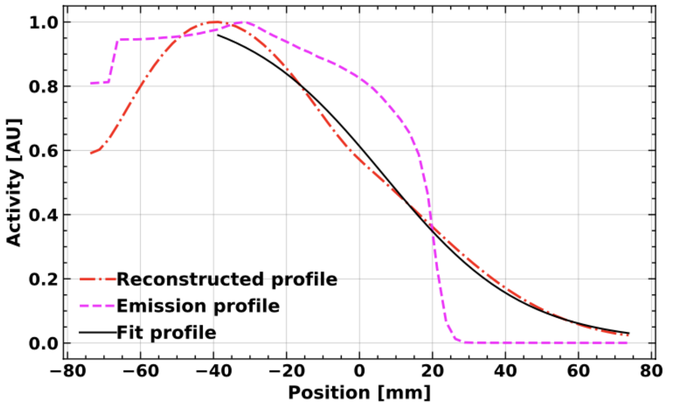

| Setup | SPB | | | SOBP | | |
|---|---|---|---|---|---|---|
| | $\eta[10^{-6}]$ | $\sigma(\eta)[10^{-6}]$ | $\overline{H}$ | $\eta[10^{-6}]$ | $\sigma(\eta)[10^{-6}]$ | $\overline{H}$ |
| Single layer cylindrical | 9.45 | 0.29 | 1.0 | 3.64 | 0.22 | 1.0 |
| Double layer cylindrical | 27.41 | 0.80 | 2.9 | 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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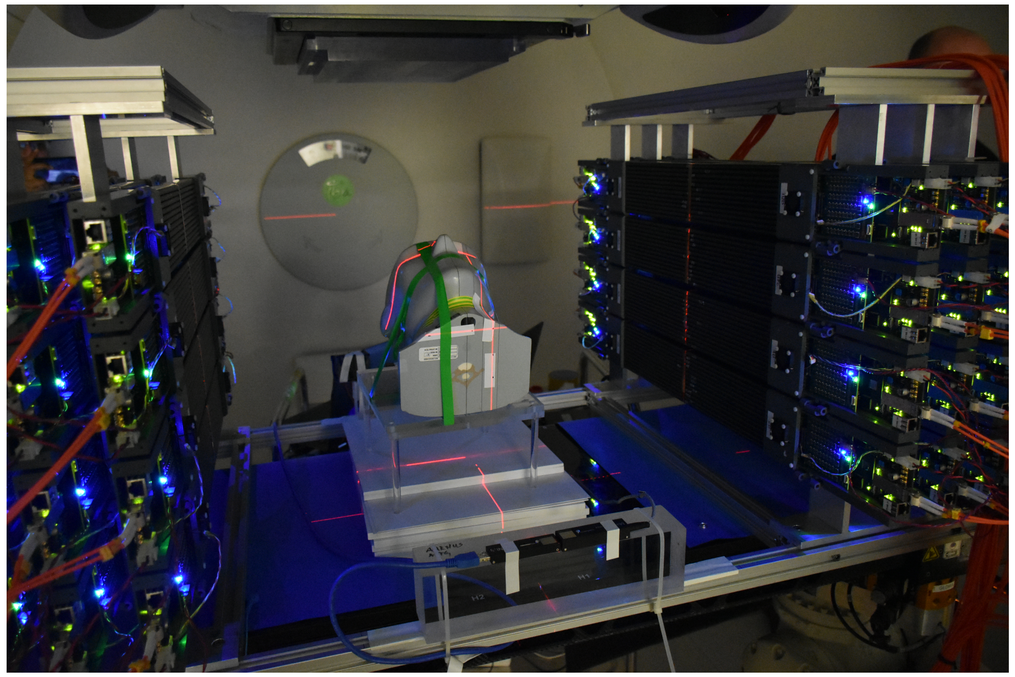
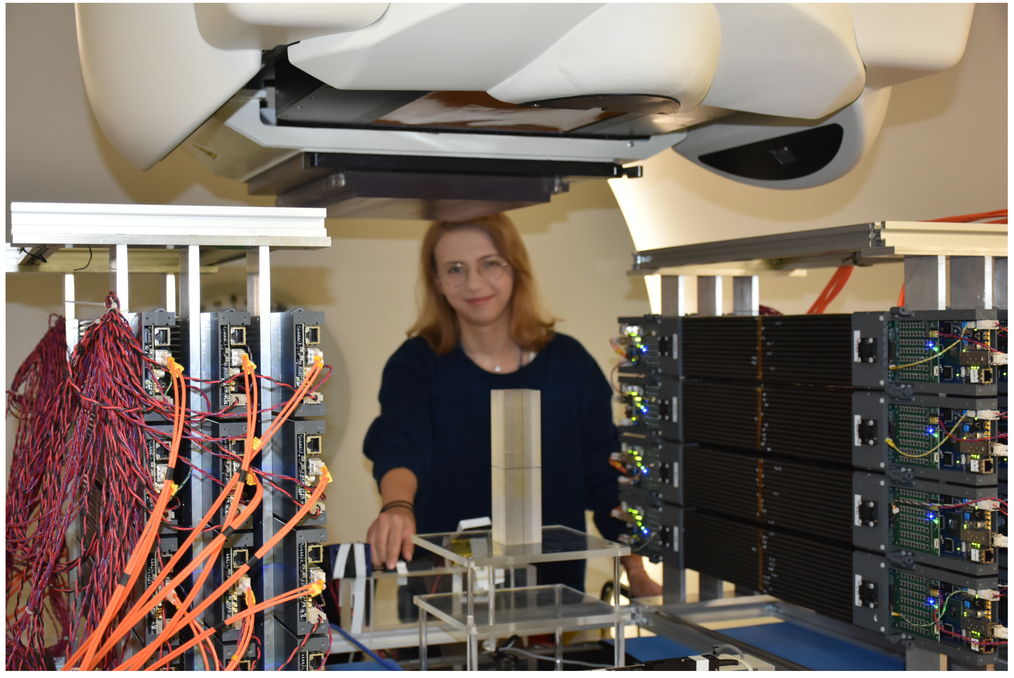
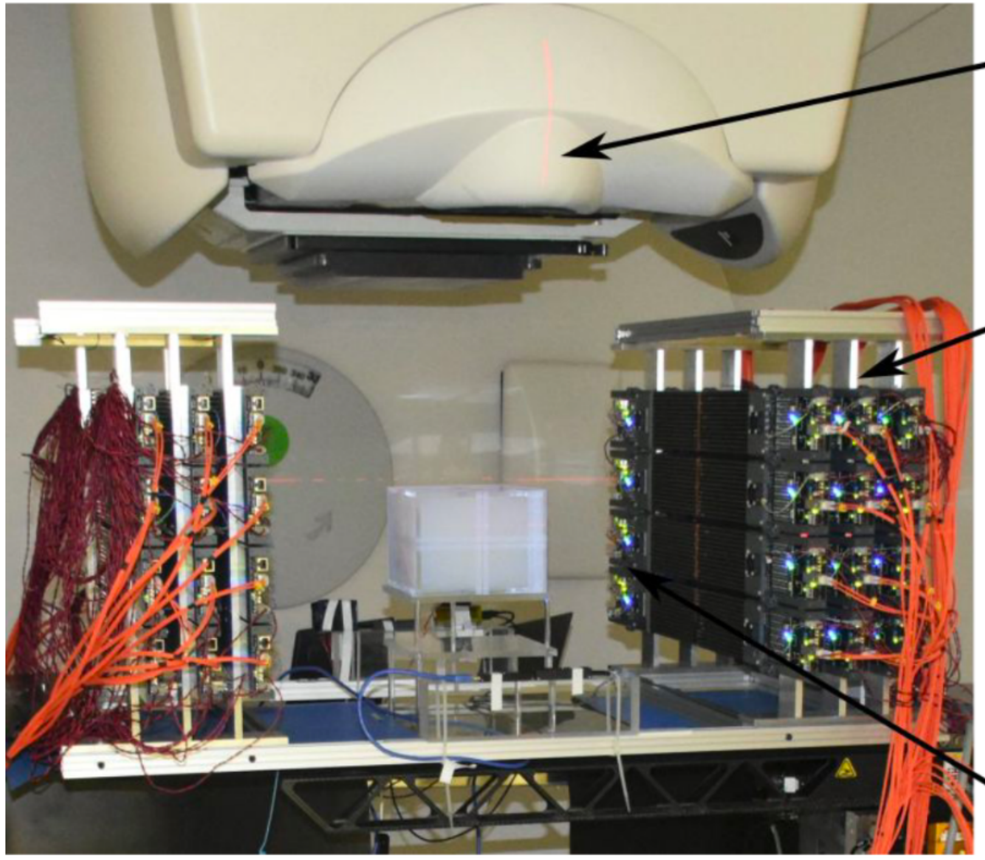
# J-PET & proton beams 2021

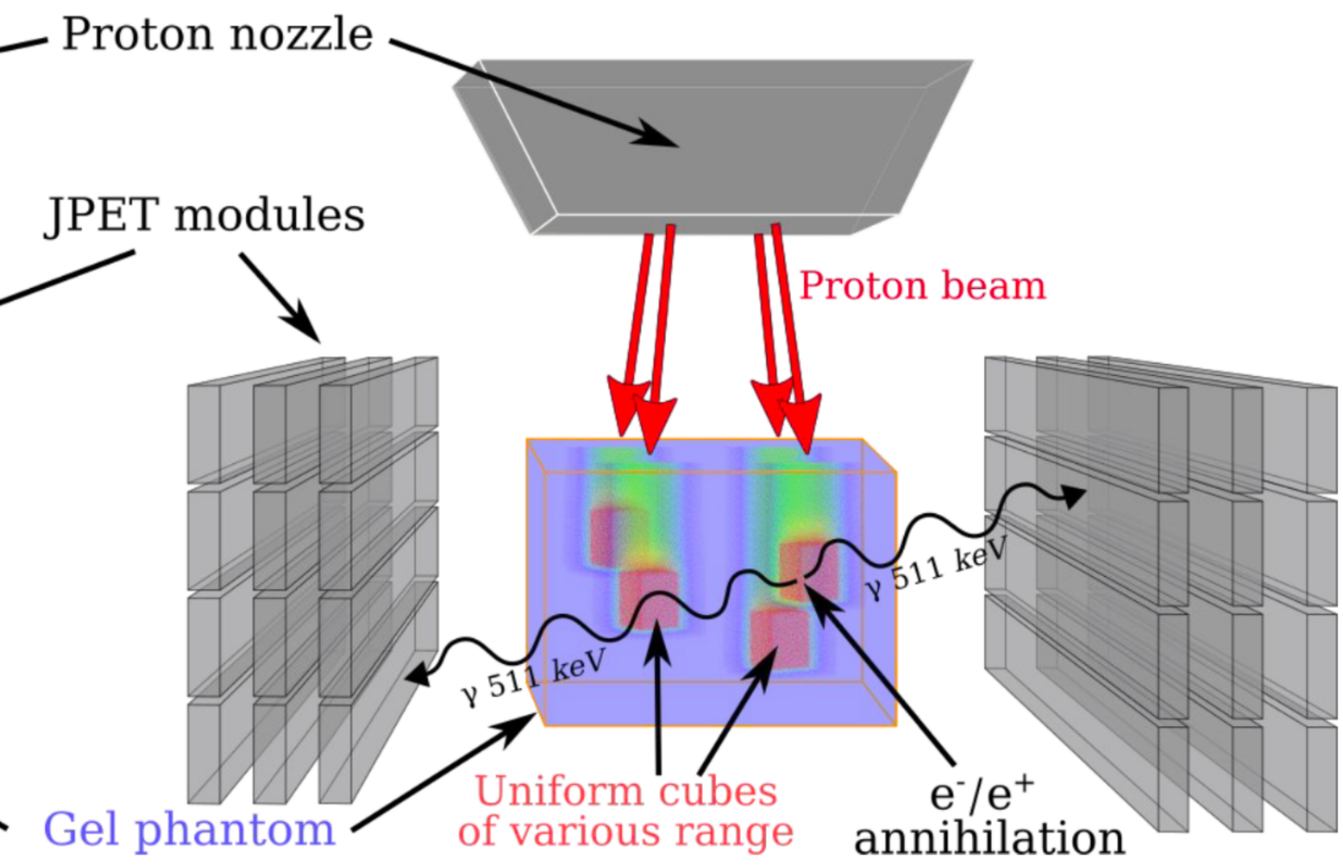




# J-PET for range monitoring in PT

## Experimental validation with proton beams at CCB



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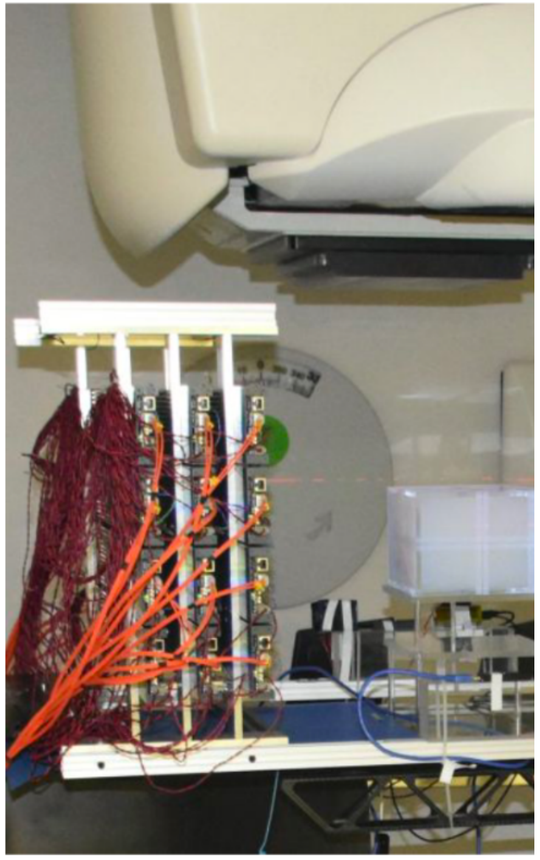
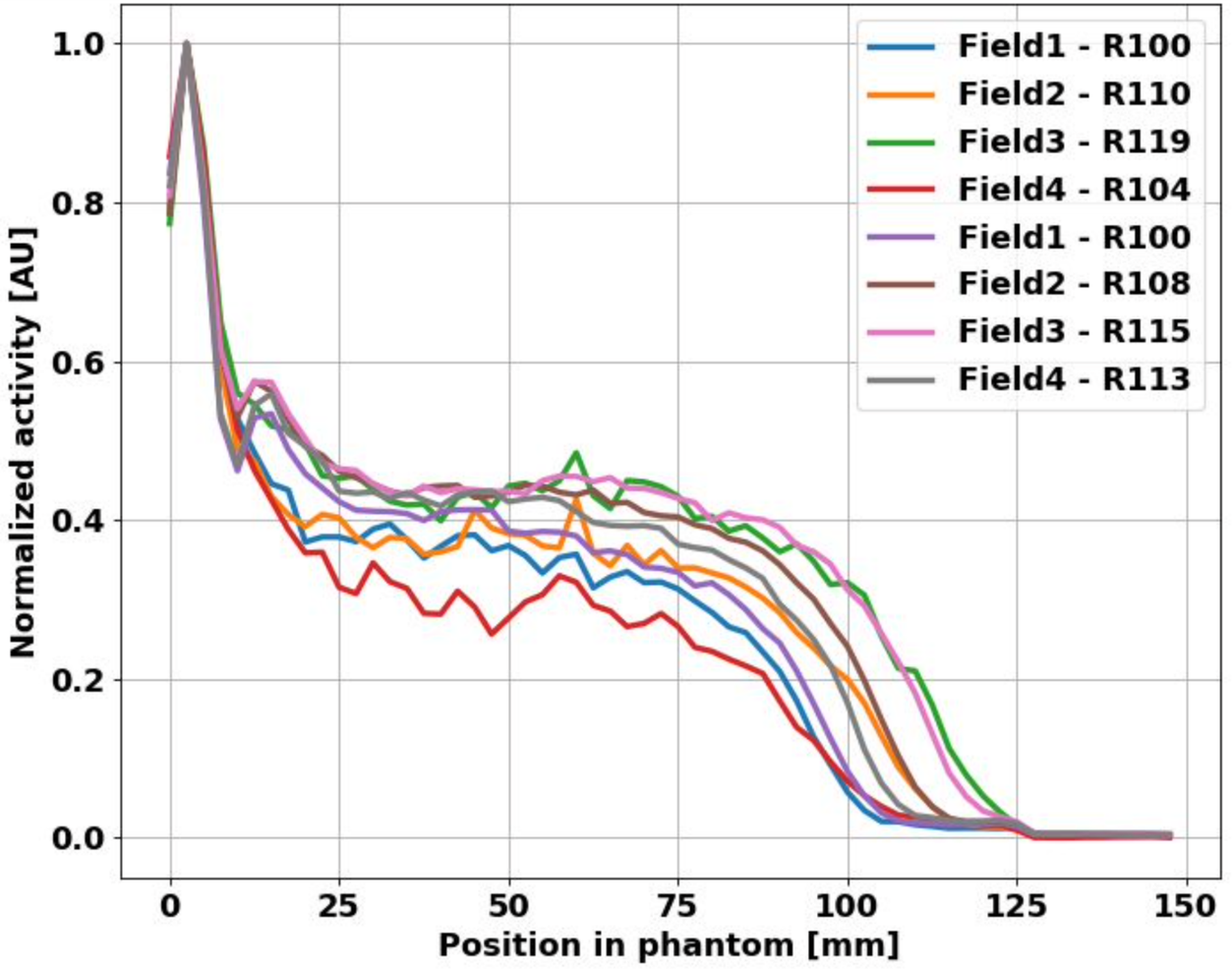
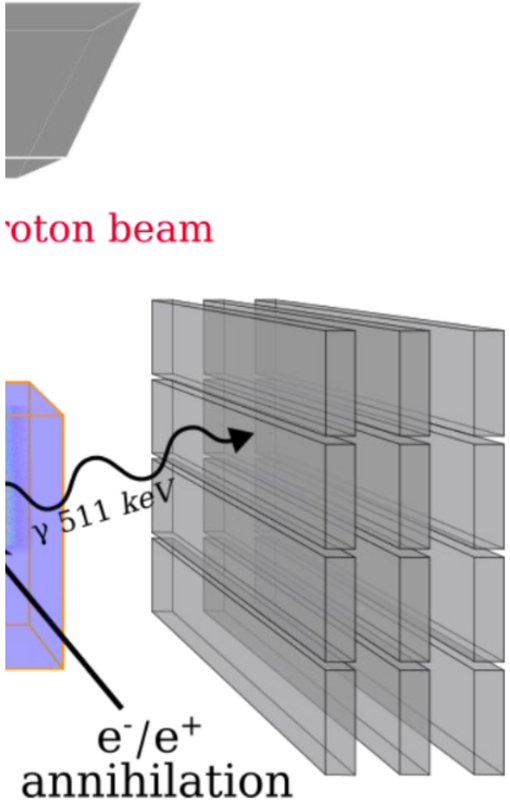
# J-PET for range monitoring in PT

## Experimental validation with proton beams at CCB



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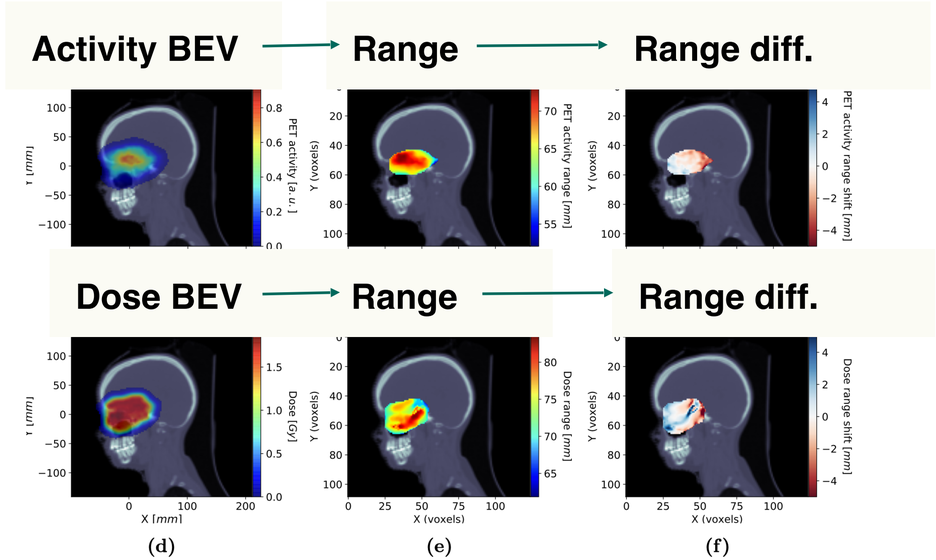
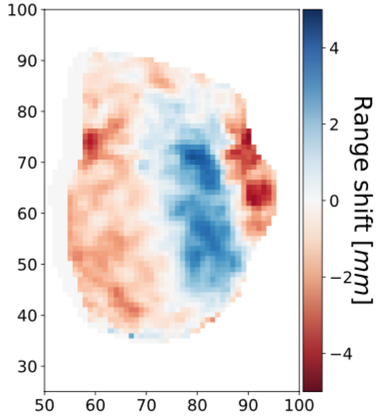
# Range shift detection in patients

## Patient simulation studies with J-PET

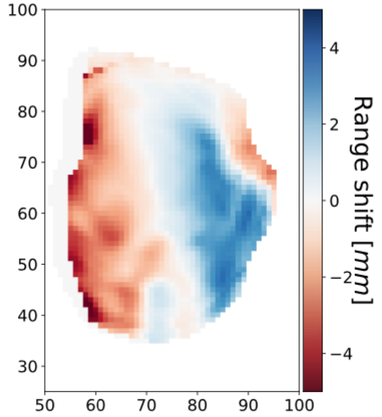
**94 patients x 27 scenarios**
**(24 shifts + 2 CT cal. + reference)**



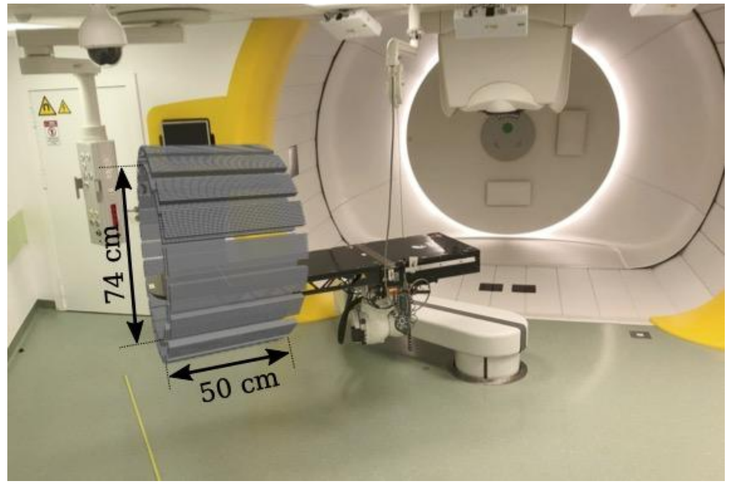

PET image



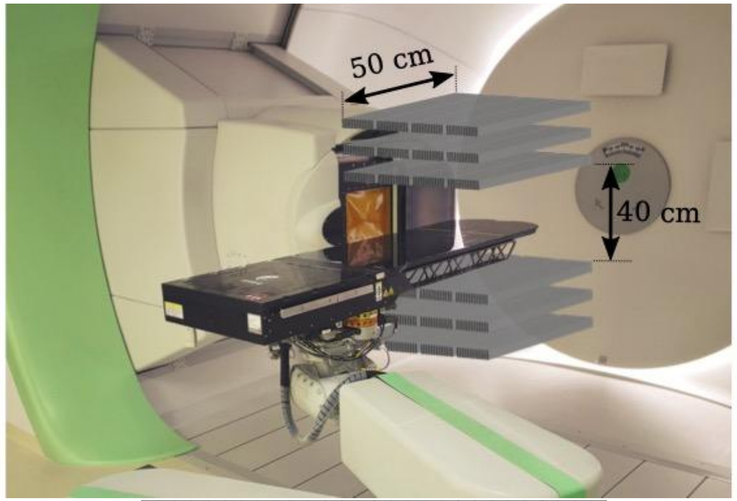

Dose image

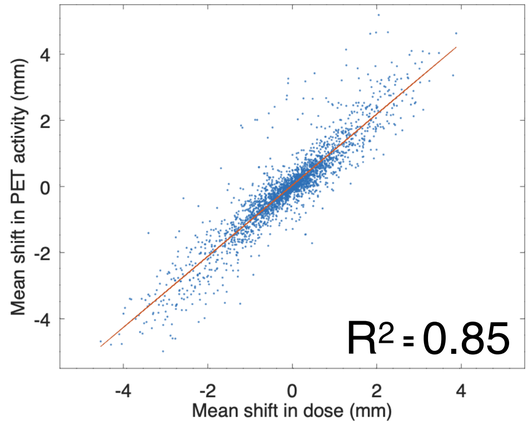


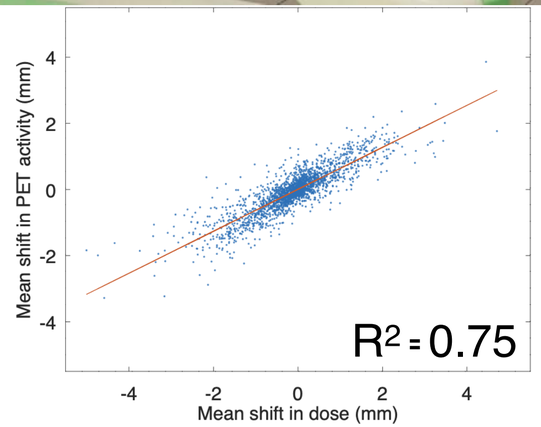

In-room PET imaging protocol




In-beam PET imaging protocol





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) provisionally accepted



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# 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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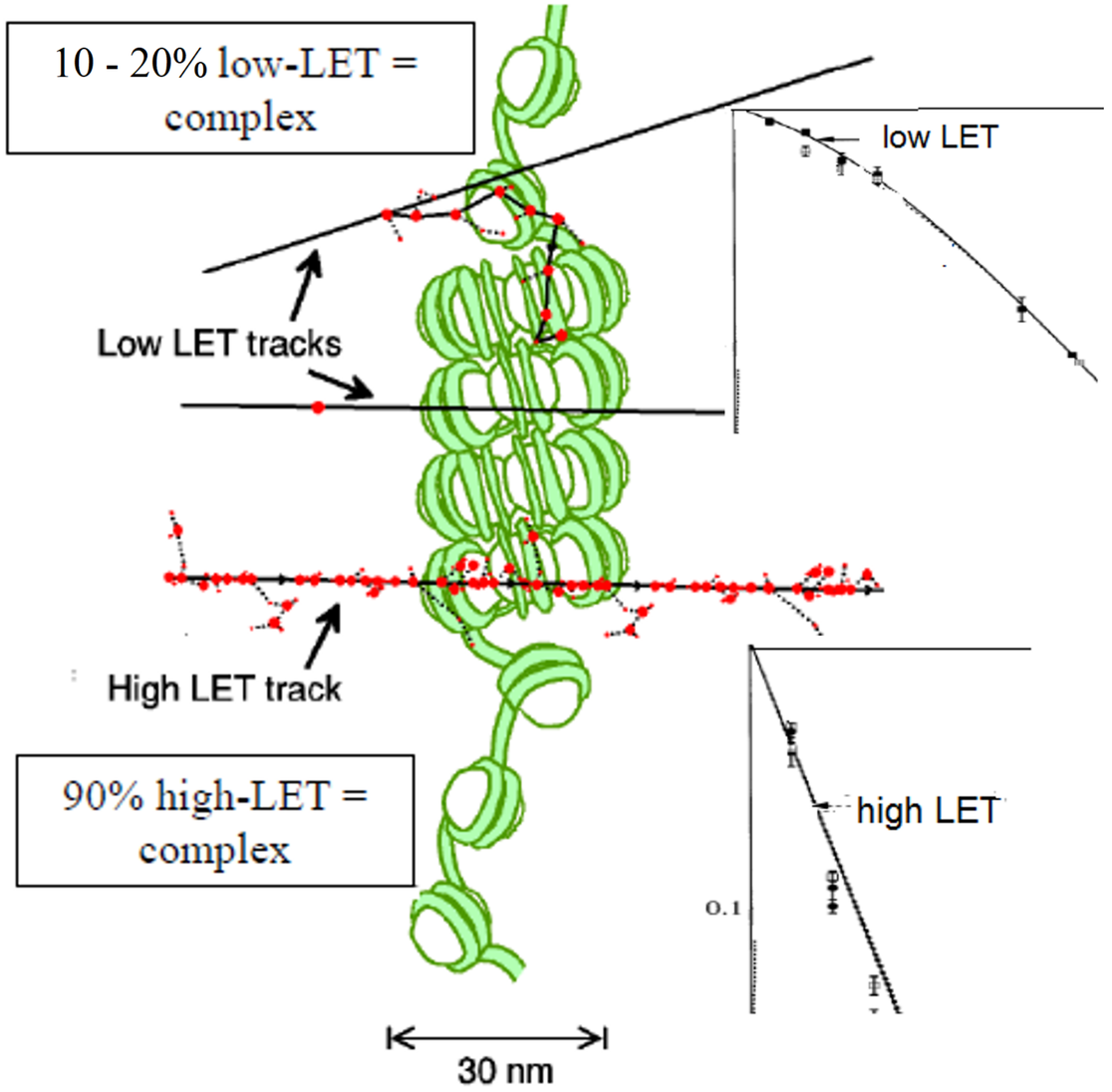
# The hypothesis: Similar clustering leads to similar biological effect

- 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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