Assessment of biological effects of clinical and secondary irradiation in proton therapy by dosimetric measurements and simulations

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1- Background and Objective

- Proton therapy offers superior dose distribution → Higher dose to the tumor, lower dose to the normal tissues.
- Protons can create different particles as they travel through the body which could lead to local and distant dose deposition.
- The radiation induced biological effects depend on many parameters (e.g. particle type, energy, linear energy transfer [LET], cell and tissue type…) and are loaded with uncertainties due to a high variability of the parameters influencing the response.

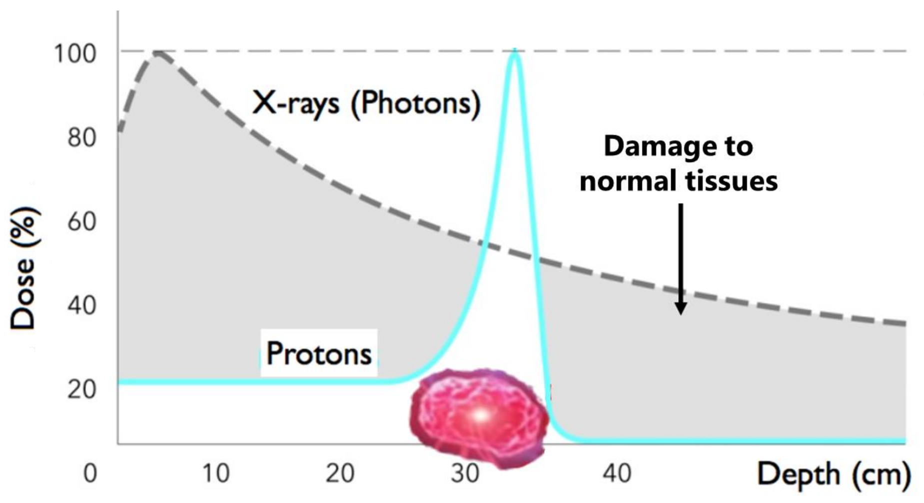

Fig 1. Percentage depth dose curves for photons vs protons.

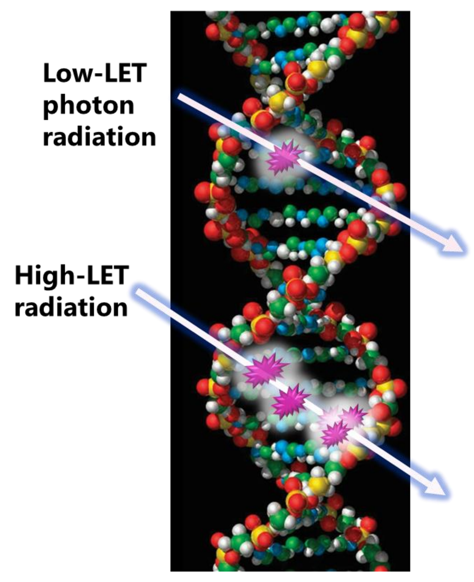

Fig 2. DNA damage caused by low vs high-LET radiation

Goal: Biophysical characterization of the primary and secondary radiation fields in proton therapy using a Timepix detector, Monte Carlo simulations and biological assays to score DNA damage

2- Materials and Methods

A. Characterization of the MiniPIX-Timepix detector for proton therapy applications

- Rotation scan of proton beams with MiniPIX-Timepix detectors (**fig 3**) at the cyclotron NPI-CAS Rez-Prague (12, 22, 31 MeV) and the proton cyclotron UJF-PAN Krakow (70, 100, 200 MeV).
- Measurements in mixed fields (CERF facility, CERN) and neutron sources (VDG accelerator-CTU, AmBe and ^{252}Cf at LNK) of different energies and with different neutron converters.
- Monte Carlo simulations using TOPAS including the full detector geometry.

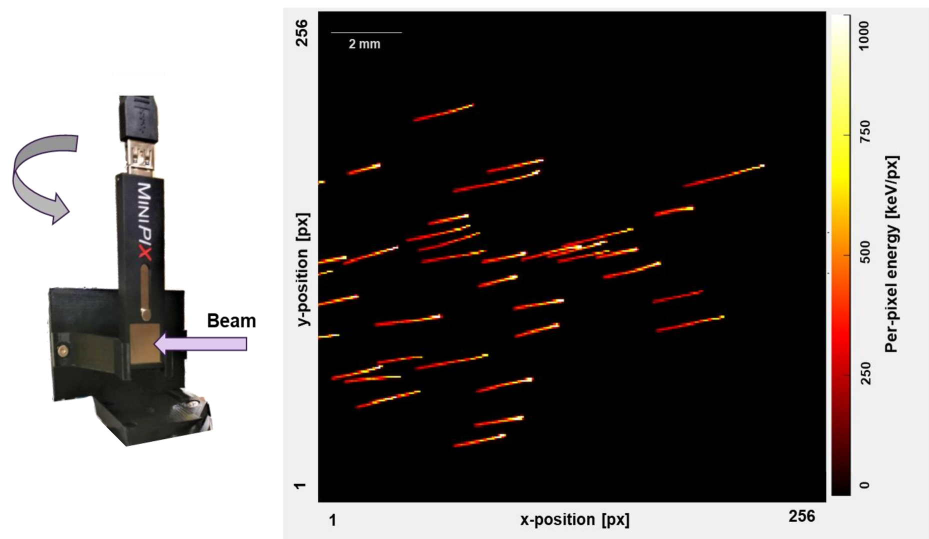

Fig 3. MiniPIX-Timepix detector placed in the primary beam on a rotation stage driven by a stepper motor (left). Timepix frame showing single proton tracks and per pixel energy (right).

B. Characterization of the secondary radiation field in proton therapy for different irradiation conditions

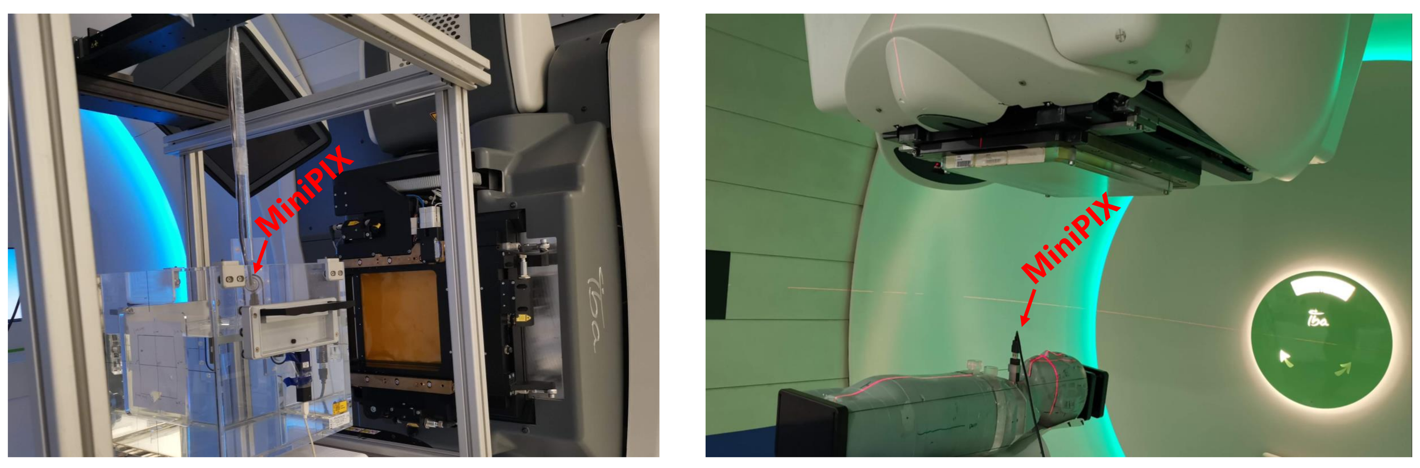

Fig 4. Measurements at various positions out-of-field. In a water phantom to investigate the impact of apertures and field size on the secondary radiation field at Particle (Proton therapy) center of UZ Leuven (left). In an anthropomorphic phantom receiving a realistic clinical plan for a pediatric localized brain tumor at WPE center in Essen, Germany (right).

3- Results

A. High-resolution angular sensitive LET measurements of protons in full field-of-view using a compact single-layer Timepix detector

- Pixel clusters were analyzed in detail in terms of morphological, spectral and tracking parameters.
- Parameters relevant for this work:
  - Deposited energy
  - 2D projected track length
  - Cluster roundness and linearity

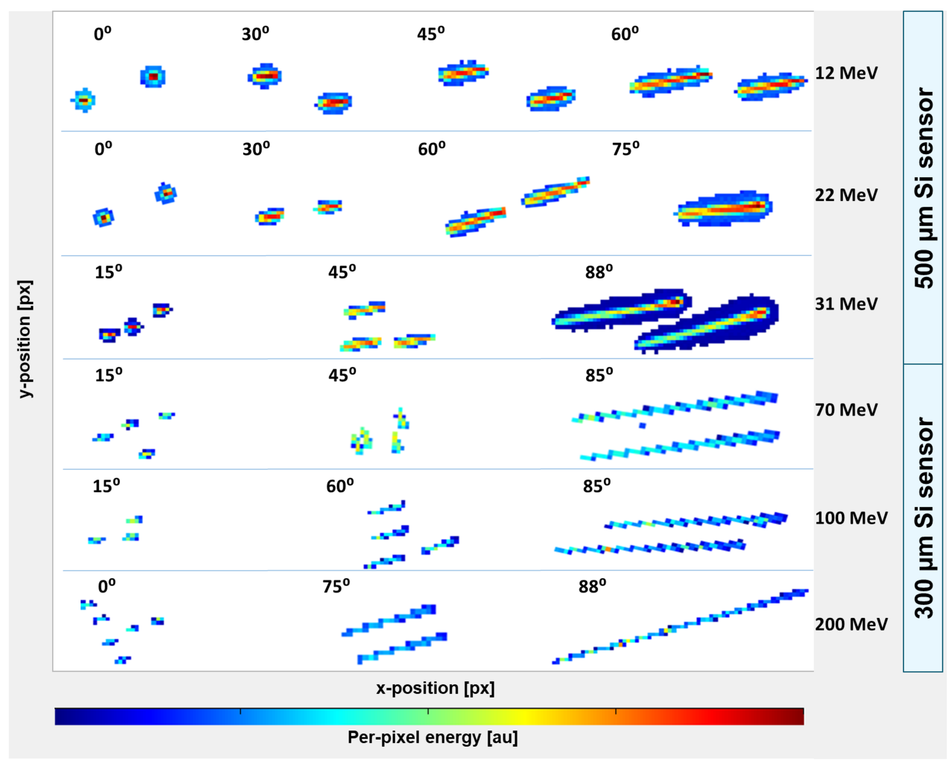

Fig 5. Pixel clusters created by protons of different energies and angles

Reconstructed angular distributions of protons

- We developed a model that calculates the proton's incident angle based on the track's morphology.
- An agreement within 2^{0} was found between the reconstructed and true angles.
- The directional detection has been extended down to normal incidence.

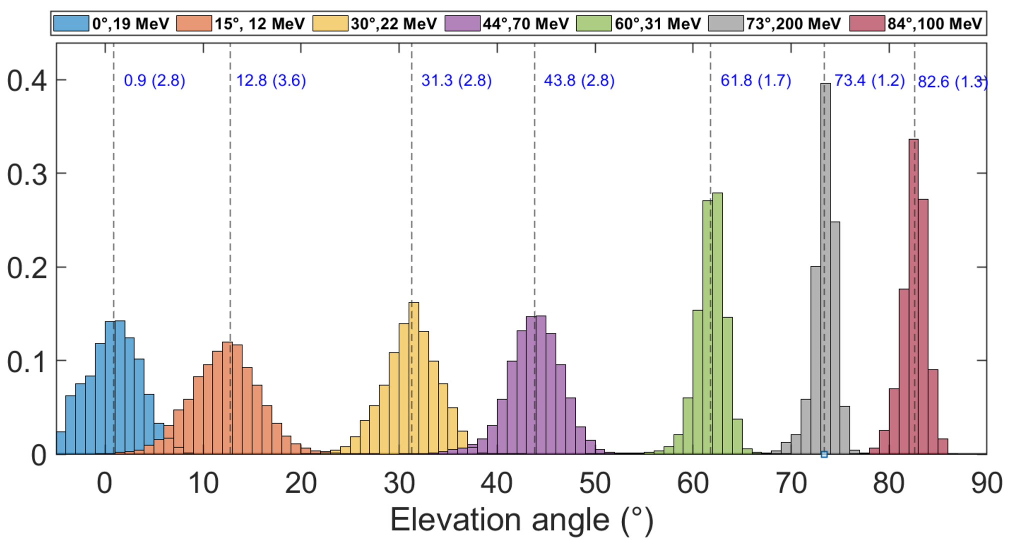

Fig 6. Angular distributions derived from morphological cluster parameters. True angles shown in legend.

LET of protons for wide-range energy and direction

- The track length in the sensor was calculated using the new model.
- Frequency-averaged LET (LET_F) from measurements and simulations were calculated and compared with estimates based on a lookup table (PSTAR).
- Experimental LET_F agreed within 12% and 10% with simulations and LET estimates based on PSTAR, respectively.

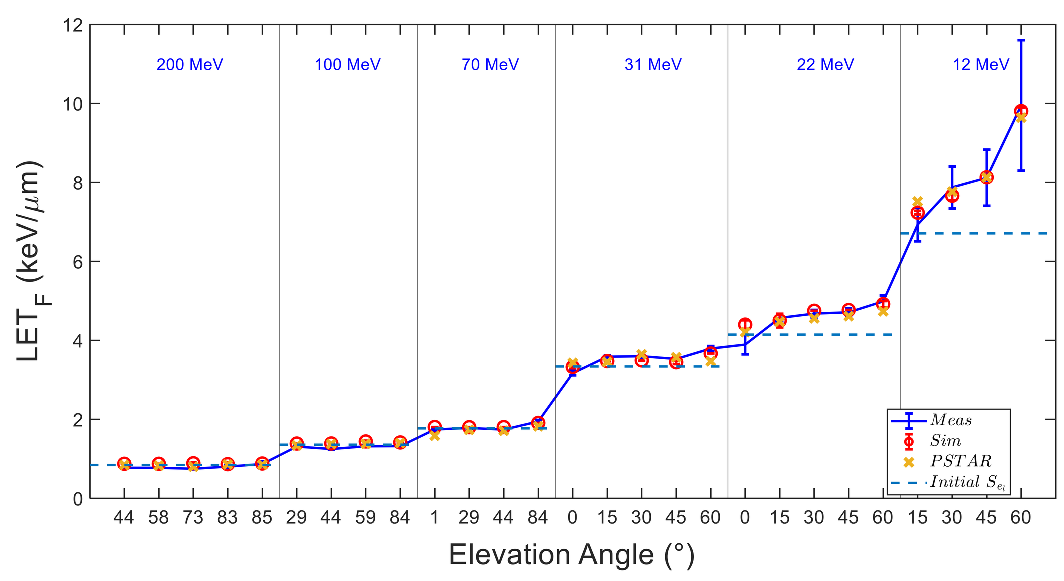

Fig 7. Measured and simulated LET_F compared with LET based on PSTAR and initial stopping power.

B. DNA damage database from published *in vitro* and *in silico* studies

- Includes over 100 ions experiments and 40 simulations.
- Damage yield for different cell lines, radiation qualities, biological assay, simulation codes and parameters.
- Will be coupled with energy/LET spectra from Timepix to predict DNA damage and validate with experiments.

4- Summary

- The MiniPIX was characterized with protons (12 – 200 MeV) and neutrons (1 – 10^3 MeV).
- We developed an improved method to assess the incident angle and LET of protons using single-layer Timepix detectors in full field-of-view and for a wide range of proton energies (12 - 200 MeV).
- The agreement between measurements, simulations and estimates based on PSTAR in terms of deposited energy was 5% (results not shown here) and 12 % for LET_F.

5- Future work

- Detailed analysis of the out-of-field water and anthropomorphic phantom measurements will be performed in terms of energy, LET and angular distributions per particle type.
- Comparison of the impact of different irradiation conditions on the generated secondary radiation field.
- In-field and out-of-field biophysical characterization of a clinical proton beam (approved and funded beam time at PARTREC, Groningen).