Metrology for Advanced Radiotherapy using Particle Beams with Ultra-High Pulse Dose Rates (UHDpulse)

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Table of Content

FLASH Radiotherapy – A Very Short Introduction

- FLASH radiotherapy (FLASH-RT) is a promising cancer treatment that involves an almost instantaneous delivery of a high radiation dose in only a few radiation pulses of ultra-high dose rate.
- Not a new concept! It’s know since the ‘60 that delivering the total required dose in a single ns-pulse of X-rays shows a significant increase of cell survival compared to conventional radiation treatments.
- In the last few years FLASH-RT has gained renewed interest after it was demonstrated, with the use of linear accelerators and *in vivo,* it significantly reduces the undesired side effects to healthy tissue compared to conventional radiotherapy: FLASH effect

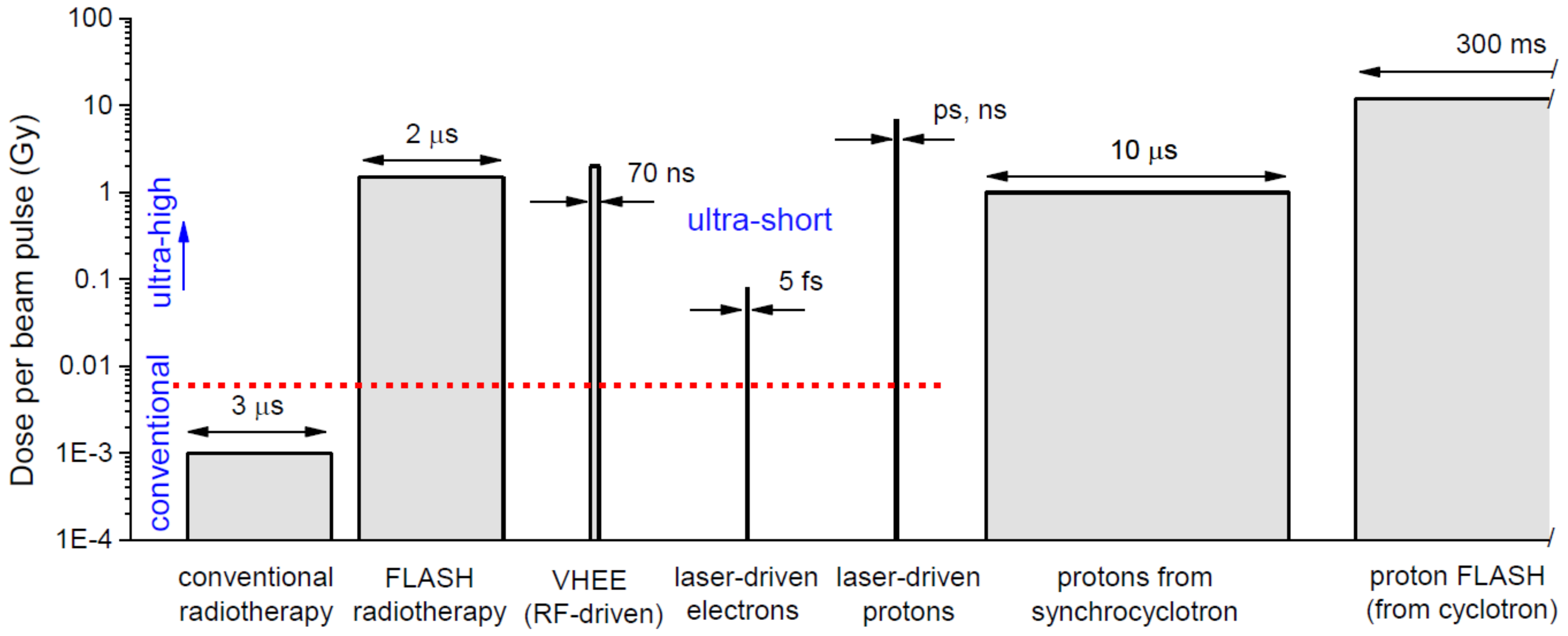
FLASH Radiotherapy – A Very Short Introduction

- The FLASH effect is observed with photons, proton, and electrons.
- Most of the pre-clinical trials involved electron beams with energies not exceeding 20 MeV.
- The limited energies achievable in the average medical electron beams are suitable only for superficial and shallow treatments.
- Very High Energy Electrons (VHEE) beams with energies above 100 MeV would allow for effective deep-seated tumour treatments → this would require huge conventional accelerator systems.

This is were lasers come into play!

The Use of Laser-Driven Accelerators in FLASH-RT

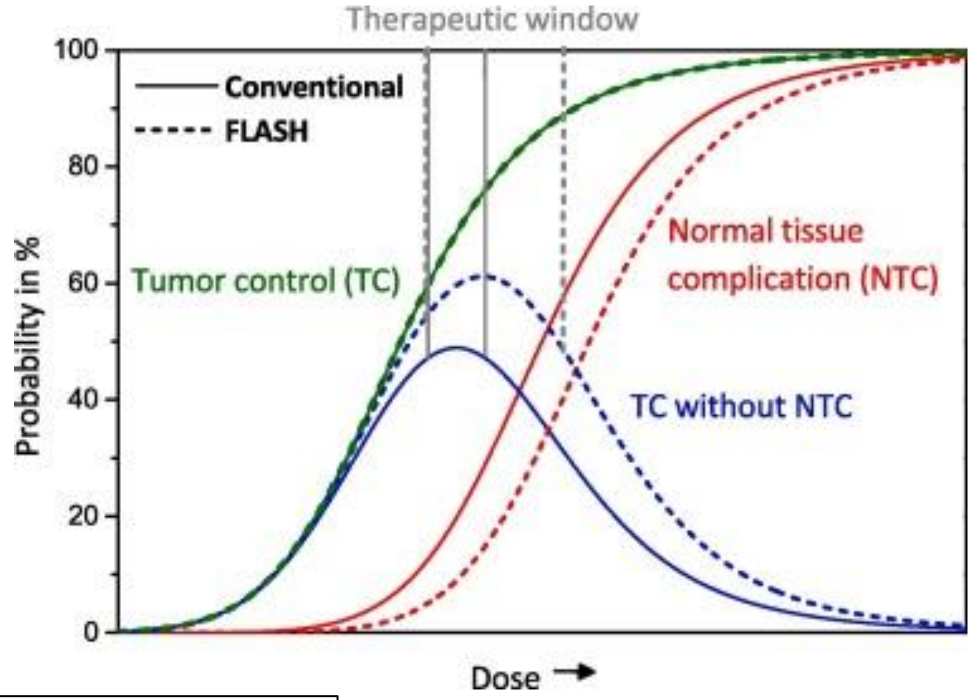
- Laser-driven accelerators are a compact and cost-effective solution for FLASH-RT with VHEE as well as with protons.
- They can deliver ultra-short radiation pulses of ultra-high dose rates: up to 10^9 -10^{12} Gy/s



A. Schuller et al. Phy. Med. 80 (2020) 134-150

Metrological Issues in FLASH-RT

- Before implementation in clinical practice, a method to precisely measure radiation doses at these ultra-high pulse dose rates is required to ensure reliable delivery of prescribed doses to patients.
- <u>FLASH-RT as well as VHEE and laser-driven beams present significant metrological challenges</u> as there are significantly higher dose rates during each radiation pulse than for radiation pulses from conventional medical accelerators.



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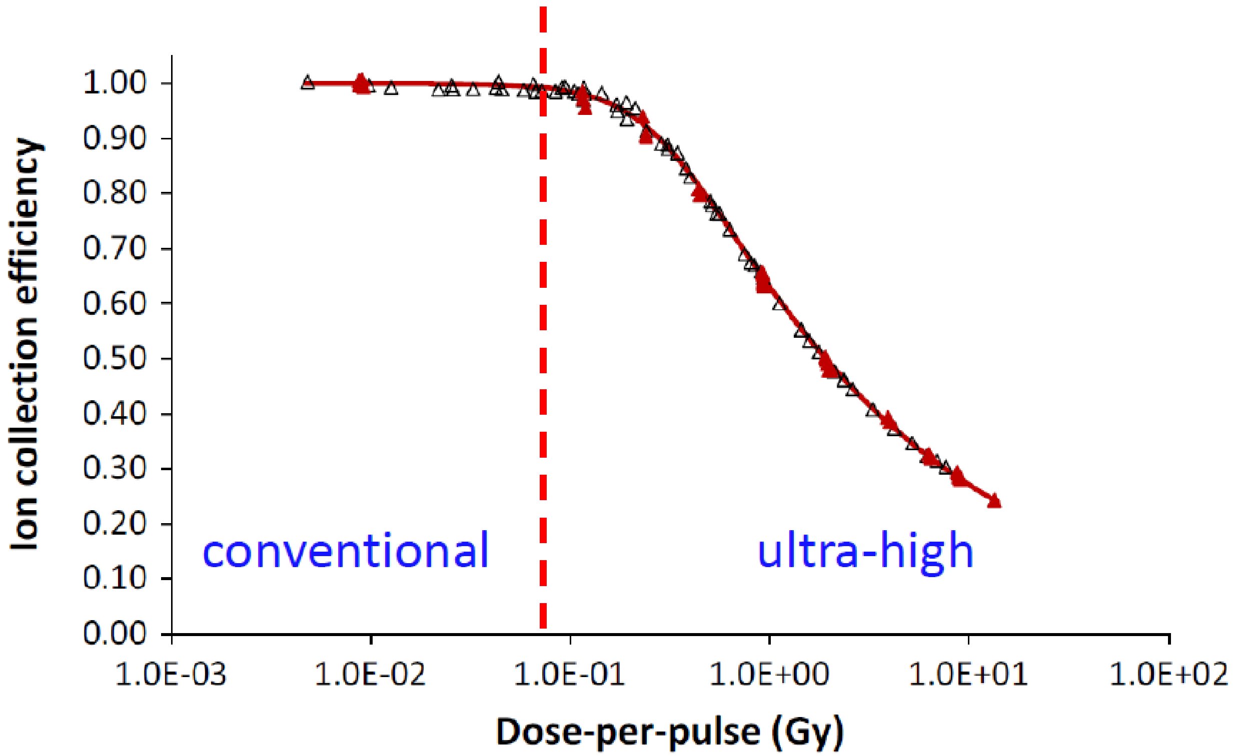
Metrological Issues in FLASH-RT

- The established active detectors for real-time dosimetry as ionization chambers or diodes start to fail when the dose rate/dose-per-pulse is increased beyond what is used in conventional radiotherapy.
- The red dashed line in the figure indicates an upper limit, where the ion collection efficiency of a common ionization chamber starts to deviate considerably from unity.



typical behavior of ordinary ionization chambers

Petersson et al., Med Phys 44 (2017) 1157
DOI: 10.1002/mp.12111

The UHDpulse Project

- UHDpulse – Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates is a recently started European project aimed at developing and improving dosimetry standards for FLASH-RT, VHEE radiotherapy, and laser-driven medical accelerators.
- Joint Research Project in the framework of the European Metrology Programme for Innovation and Research (EMPIR).
- Started in 2019, its initial duration was of 3 years. A one-year extension was granted to compensate for delays due to the covid-19 pandemic.

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

The UHDpulse Project: Objectives

- To develop a metrological framework, including SI-traceable primary and secondary reference standards and validated reference methods for dosimetry measurements for particle beams with ultra-high pulse dose rates.
- To characterise the response of available detector systems in particle beams with ultra-high dose per pulse or with ultra-short pulse duration.
- To develop traceable and validated methods for relative dosimetry and for the characterisation of stray radiation outside of the primary pulsed particle beams.
- To provide input data for future Codes of Practice for absolute dose measurements in particle beams with ultra-high pulse dose rates.

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UHDPulse Project: Consortium

- 5 National Metrology Institutes: leaders in the field of dosimetry
- 2 academic hospitals: pioneers in FLASH-RT
- 3 universities: experts in detector development and pioneer in laser-driven beams
- 3 national research institutes: pioneers in detector development and laser-driven beams and dosimetry experts
- 1 European research institute: expert in laser-driven beam research
- 2 companies: experts in detector development

UHDpulse Workpackages

The partners will fulfill the aim of the project in 4 technical Work Packages

WP1: Primary standards

- Definition of reference conditions
- Reference radiation fields
- Adapting primary standards (water calorimeter, Fricke dosimeter)
- Prototype graphite calorimeters for laser-driven beams

WP2: Secondary standards, relative dosimetry

- Transfer from primary standards
- Characterizing established detector systems
- Formalism for reference dosimetry for future Code of Practice

WP4: Detectors and methods outside primary beam

- Active detection techniques for pulsed mixed radiation fields of stray radiation and pulsed neutrons
- Methods with passive detectors

WP3: Detectors for primary beam

- Novel and custom-built active dosimetric systems
- Beam monitoring systems

- ELI Beamlines is a partner in the UHDpulse project.
  - It serves as an irradiation facility
  - It leads the effort for several activities in 2 separate Work Packages

WP4: Detectors and methods outside primary beam

- Active detection techniques for pulsed mixed radiation fields of stray radiation incl. pulsed neutrons
- Methods with passive detectors

WP3: Detectors for primary beam

- Novel and custom-built active dosimetric systems
- Beam monitoring systems

Why use passive detectors?

- Secondary radiation fields are present with all therapeutic beams
  - They have the same pulse structure as the primary beam
  - They are composed of radiation of different types/energies
  - They cause parasitic doses to healthy tissues/organs → These secondary fields must be well described and understood

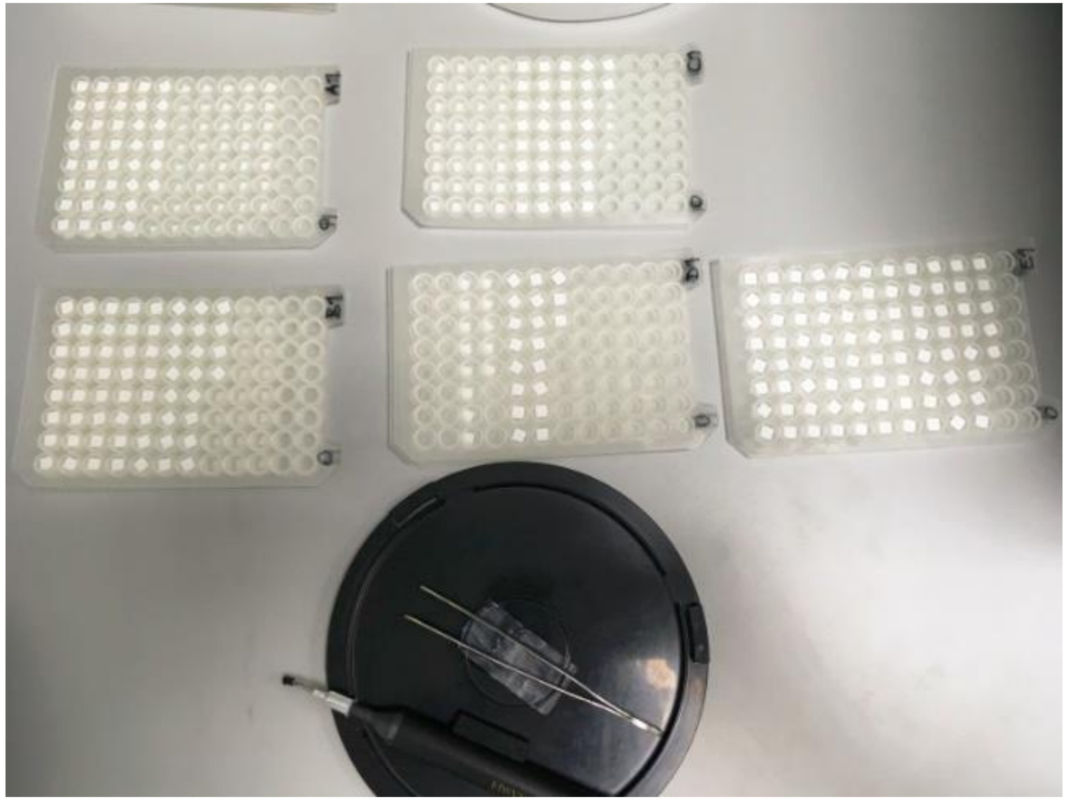
Passive detector can be safely used in the context of short pulse durations and are not effected by electromagnetic pulse

Thermoluminescence and Optically Stimulated Luminescence

- Thermoluminescence (TL) and Optically Stimulated Luminescence (OSL) are two of the most important techniques used for passive radiation dosimetry.
- The luminescence radiation emitted by the irradiated material is directly correlated to the dose deposited by the impinging ionizing radiation
  - TLD: readout is performed using a heat source
  - OSL: the release of trapped charges is accomplished by shining a laser on the material.

OSL Dosimeters @ ELI Beamlines

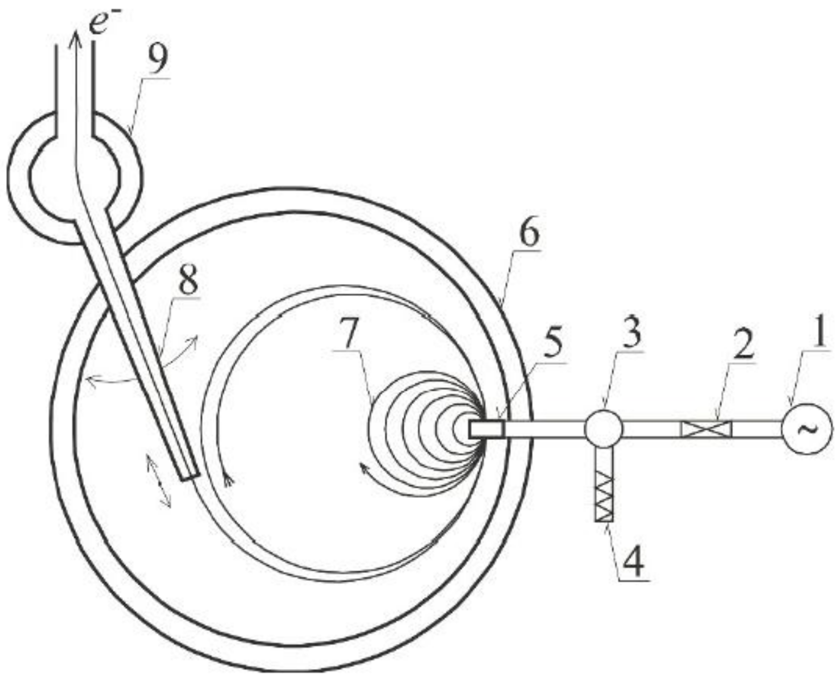
- Dry pressed chips of BeO,
  - 4.7 x 4.7 x 0.5 mm^3
- Low cost and easy availability
- Good dosimetric properties:
  - high sensitivity to ionizing radiation
  - wide linear dose response (~1 μGy - few Gy)
  - effective atomic number similar to human soft tissue (Z_{eff}=7.2)
- Emission bands: ~310 nm and ~370 nm (dominant)
- As BeO is sensitive to visible light: light-tight packaging



- Monte Carlo Simulations are exploited to optimize detector parameters and design.
- ELI Beamlines houses a strong FLUKA Monte Caro team
  - The FLUKA code is a general purpose Monte Carlo code for the interaction and transport of hadrons, leptons, and photons from keV (with the exception of neutrons, tracked down to thermal energies) to cosmic ray energies in any material.
  - https://fluka.cern/
- Validation of the methodology is being performed in conventional radiation fields that act as references.

Data Taking at Mikrotron

- The MT 25 Mikrotron is a cyclic electron accelerator of the Nuclear Physics Institute of the Czech Academy of Sciences located in Prague.



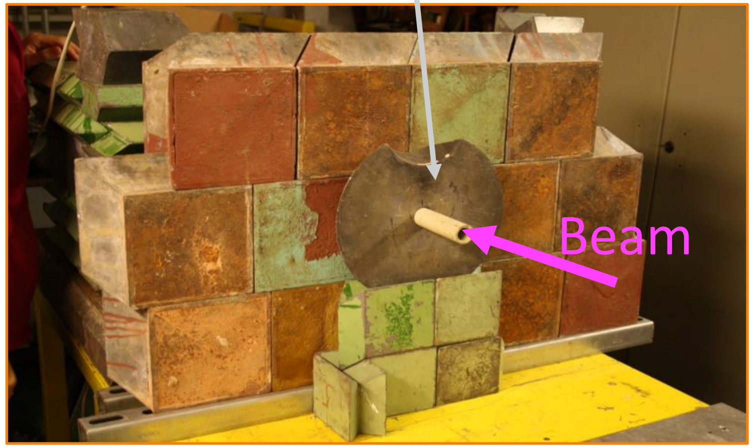
Schematic layout of the MT 25 [58]. 1) Magnetron, 2) Phase shifter, 3) Circulator, 4) Water load, 5) Accelerating cavity, 6) Main magnet, 7) Electron trajectories, 8) Adjustable beam extractor, 9) First deflector

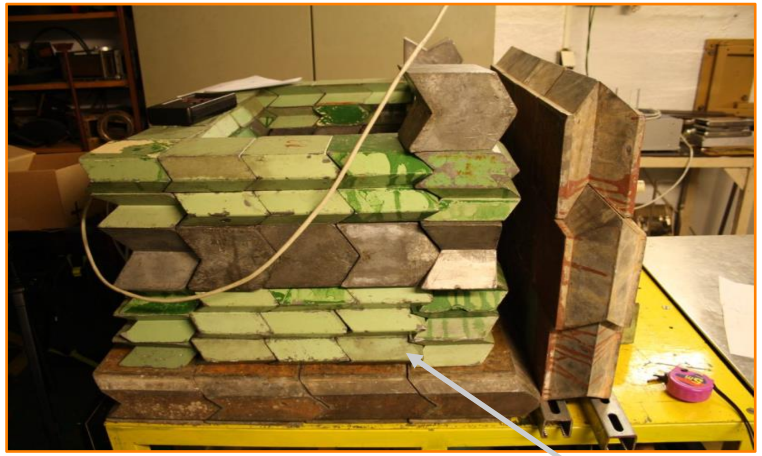
- Energy: 1-25 MeV
- Pulse length: 3.5 μs
- Repetition rate: 423 Hz
- Mean maximum current: 30 μA
- Angular divergence: 12°

Data taking at Mikrotron

- Lead bunker to shield background radiation
  - ~75 x 40 x 50 cm
  - 3 mm diameter brass collimator in the wall
- Plexiglass phantom (~25 x 25 x 1.3 cm)
- Dosimeters:
  - ELI-BL **OSL**
  - NPI TLD
  - ELI-BL **GAF**
  - CERN DIS
- 8 cm polyethylene moderator
- 4.2 Gy on the center of the phantom (measured with IC)

Plastic pipe
(Ø=2 cm)



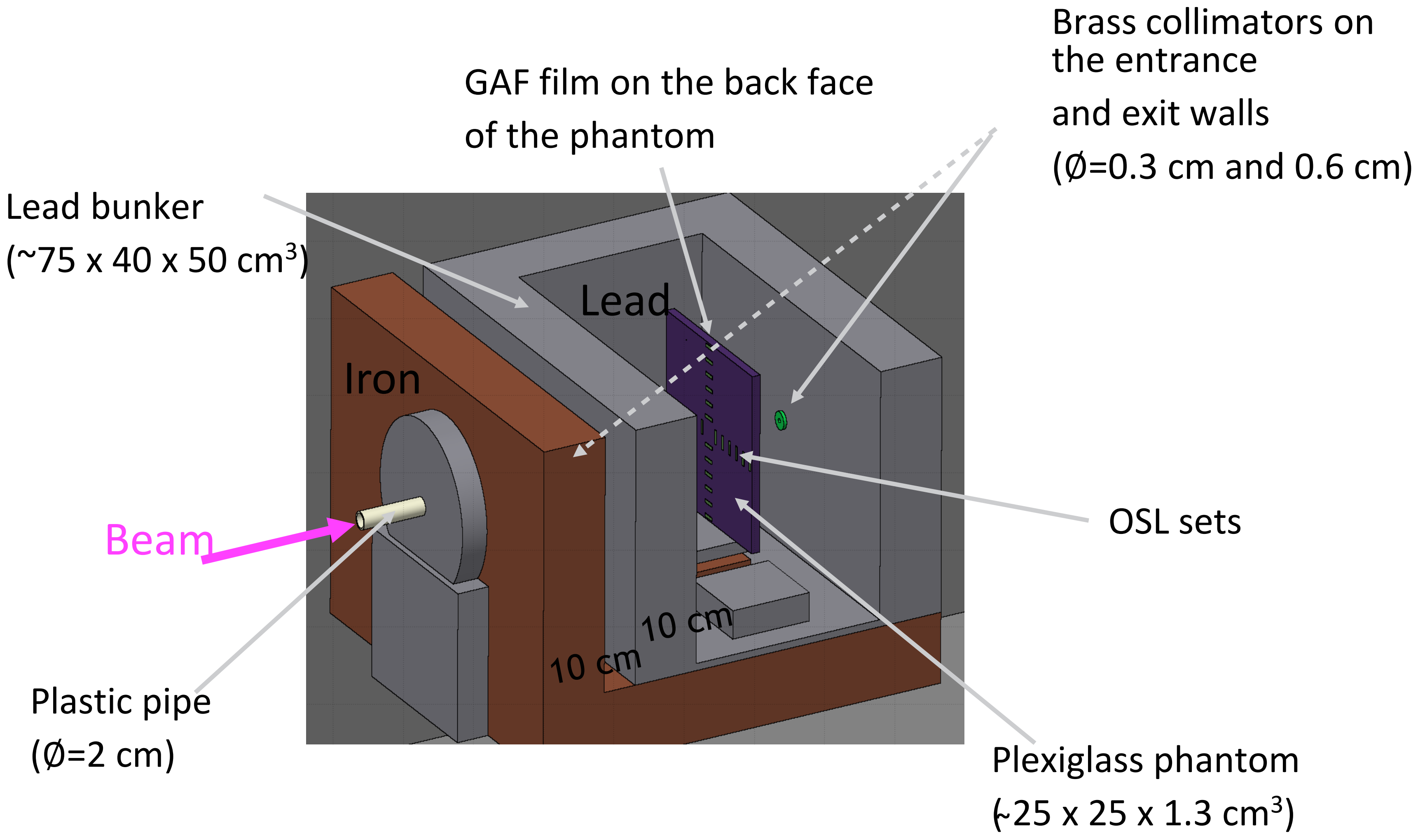


Lead bunker
(~75 x 40 x 50 cm^3)

Plexiglass phantom
(~25 x 25 x 1.3 cm^3)

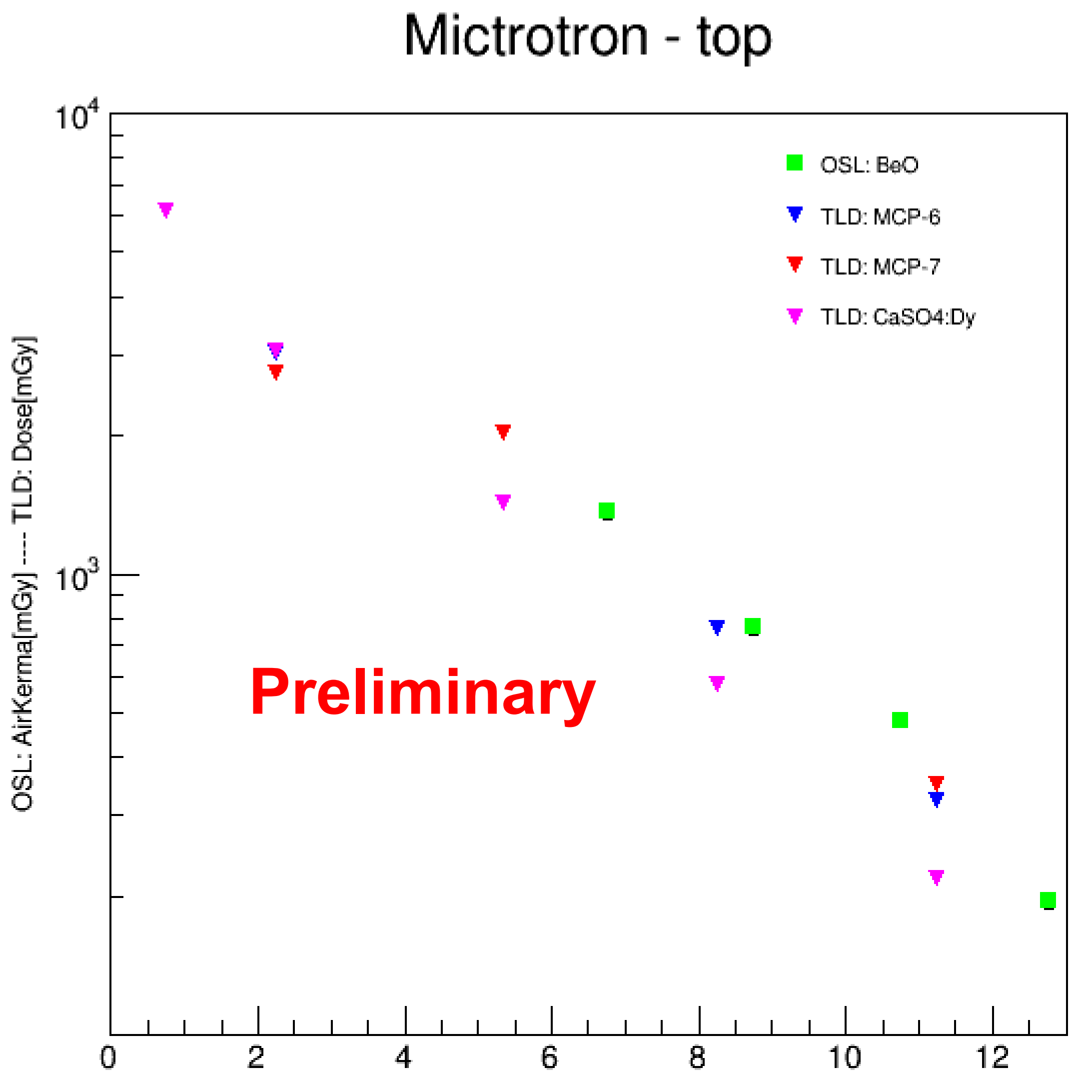
FLUKA Geometry

FLUKA Geometry of the experimental setup at Mikrotron in 01/2020



Datataking Mikrotron 01/2020:Preliminary results

- General good agreement of data especially considering
  - Geometry: positioning of detectors
  - OSL measure AirKerma, TLDs measure Absorbed Dose
  - The different TLDs used have significantly different sensitivities to neutrons.



Conclusions

- FLASH-RT is a “trending” and promising cancer treatment under development
- Laser-driven particle accelerators are considered a compact and cost-effective solution for this kind of radiotherapy → deep-seated tumour treatment possible
- FLASH-RT and laser-driven beams present significant metrological challenges
  - They have significantly higher dose rates during each radiation pulse than for radiation pulses from conventional medical accelerators.
  - The established active detectors for real-time dosimetry as ionization chambers or diodes start to fail when the dose rate/dose-per-pulse is increased beyond what is used in conventional radiotherapy.

Acknowledgements *This project 18HLT04 UHDpulse has received funding from the EMPIR programme cofinanced by the Participating States and from the European Union’s Horizon 2020 research and innovation programme.*

Conclusions

- The European project “Metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates” – UHDpulse aims at developing metrological tools needed to establish traceability in absorbed dose measurements of ultra-high pulse dose rate particle beams.
- These tools are necessary
  - for accurate comparison of radiobiological effectiveness of different irradiation modalities and sites (pre-clinical studies)
  - to enable future clinical application of these beams.

Acknowledgements *This project 18HLT04 UHDpulse has received funding from the EMPIR programme cofinanced by the Participating States and from the European Union’s Horizon 2020 research and innovation programme.*

Further References

- UHDpulse Official webpage: http://uhdpulse-empir.eu/
- UHDpulse review paper: https://doi.org/10.1016/j.ejmp.2020.09.020

EMPIR EURAMET

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

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