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HZB Helmholtz Zentrum Berlin

CHARITÉ

BHT Berliner Hochschule für Technik

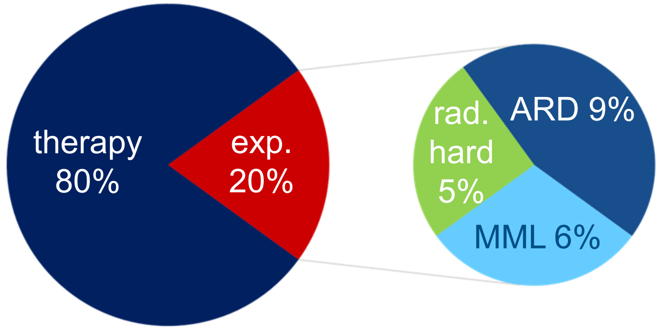
Universität der Bundeswehr München

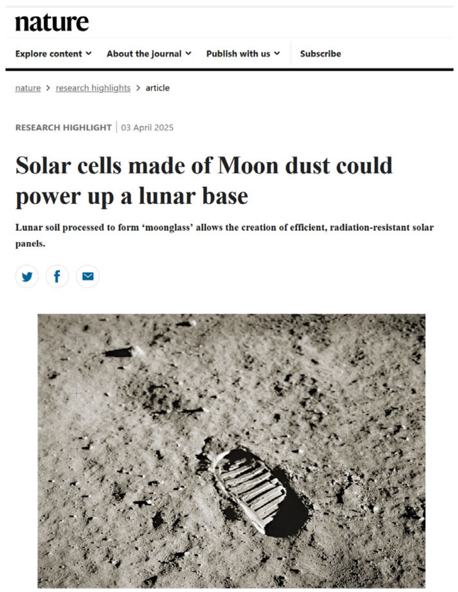
development in proton therapy: FLASH and minibeams at the HZB cyclotron

Proton Accelerator: Beam Time Distribution

- main use of accelerator: therapy of ocular tumours in collaboration with CHARITÉ - university hospital Berlin
- accelerator research and development (***ARD***)
- life sciences (***MML***)
- radiation hardness tests on electronics and solar cells for space (link to research field ***energy***)
- example: Perovskite/Perovskite Tandem cells extra-ordinarily stable
- research highlight by nature

(2025) 10.1038/d41586-025-00971-x

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RESEARCH HIGHLIGHT | 03 April 2025

Solar cells made of Moon dust could power up a lunar base

Lunar soil processed to form 'moonglass' allows the creation of efficient, radiation-resistant solar panels.

Adv. Energy Materials (2021) 10.1002/aenm.202102246

Springer, Energy harvesting and Storage (2022) 10.1007/978-981-19-4526-7

RSC Adv. (2023) 10.1039/D3RA03846G

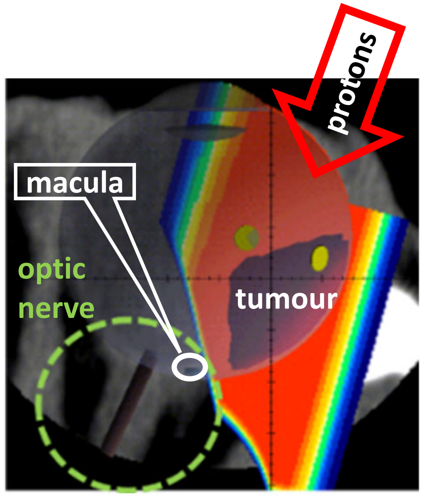
Device (2025) 10.1016/j.device.2025.100747 (2025)

Proton Therapy of Ocular Tumours: Status

- HZB cyclotron: proton energy of 68 MeV, ideal for ocular treatments (~ 25 mm diameter)
- extremely sharp distal dose fall-off (90% to 10%) < 1 mm
  → better reduction of side effects (loss of vision) in contrast to high-energy cyclotrons
- sufficient beam current, treatment time < 1 minute/fraction

- > 25 years successful treatment in collaboration with CHARITÉ
- local tumour control: 96% eye retention rate: 95%
  → one of the world leading centres in ocular proton therapy

- successful interdisciplinarity: ophthalmologists, radiation oncologists, medical physicists, accelerator physicists, and engineers



> 5000 patients @ HZB = 10% of worldwide proton treated eye tumours

Int. Jour. Radiation Oncology Biology Physics 120 (2024) 10.1016/j.ijrobp.2024.06.017

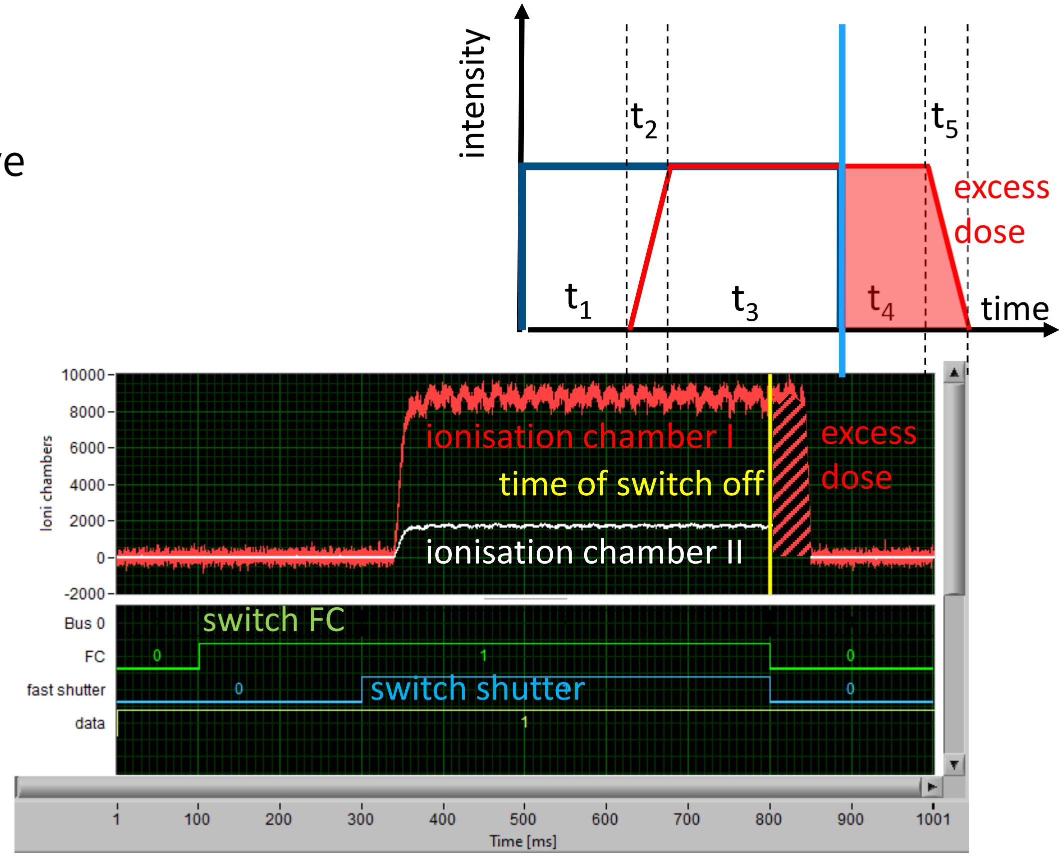
Aspiration: Maintain Tumour Control – Reduce Side Effects

Theme	Requirement	Challenge
FLASH:	extremely high dose rates of > 40 Gy/s applied in short times (< 0.5 s)	
	high dose rates = high beam intensities short delivery times	saturation effects in beam monitors short reaction times on electronics and interlocks
Minibeams:	spatial fractionated beams	
	beam spots < 0.5 mm	positioning and dose precision
beams:	sharper lateral dose fall-off, higher Linear Energy Transfer (LET)	
	broad He-beam with adequate dosimetry	radiobiological effectivity has to be investigated
ARD:	beam delivery, dosimetry, beam diagnostics	
	high beam intensities excellent energy spread	this combination: rare

research driven by users, ARD contributes to MML MLI

FLASH: Beam Delivery – Control System

- ideal: instant opening and closing of the beam shutter without any delays
  ⇨ instantaneous, rectangular intensity (dose rate) curve
- reality: delays and opening/closing times
- required precision for dose application: ± 1.5%
- 10 kHz feedforward control of dose delivery using FPGA + LabVIEW compensates excess dose



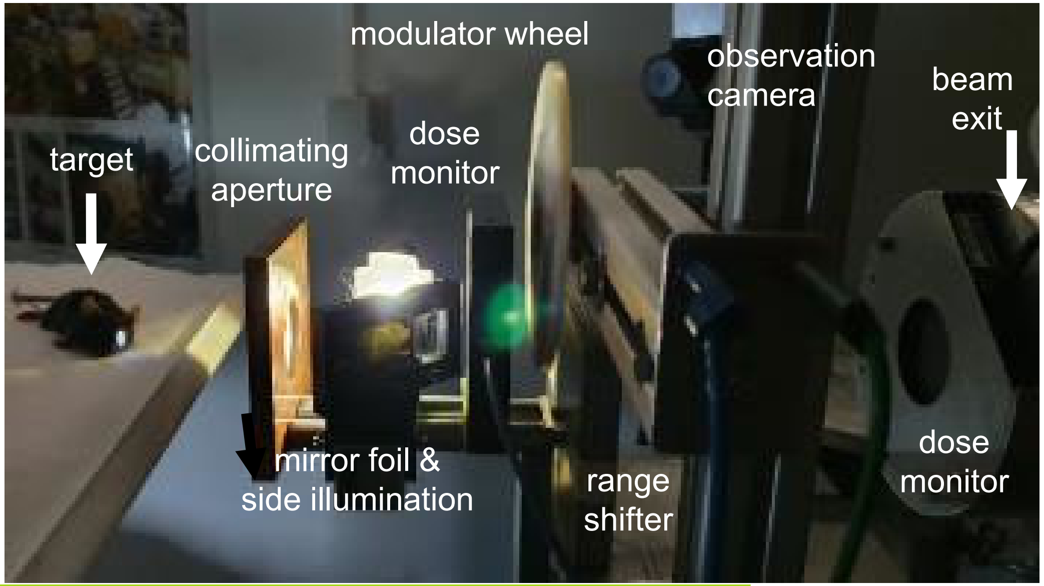
reproducibility meets clinical specifications

Proc. ICALEPS (2023) 10.18429/JACoW-ICALEPCS2023-MO3BCO07

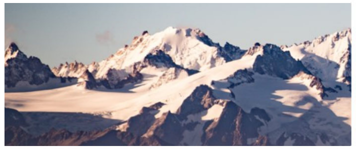
HZB Helmholtz Zentrum Berlin CHARITÉ

FLASH: First Results

- compact nozzle for a flat 6 mm irradiation field and 5 mm <u>spread-out Bragg peak</u> within clinical specs (**no shoot through**)
- irradiation of **single** mice eyes
- mode switching in 30 min – radiation properties unaffected
- conventional: 0.25 Gy/s: 15 Gy in 60 s
- FLASH: 75 Gy/s: 15 Gy in 0.2 s



Medical Physics (2021) doi:10.1002/mp.14730
Cells (2025) doi:10.3390/cells14040298



WILEY

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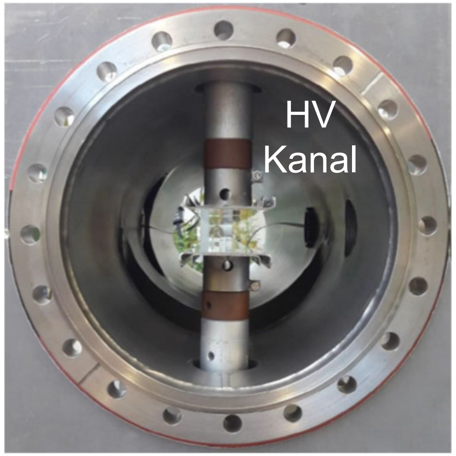
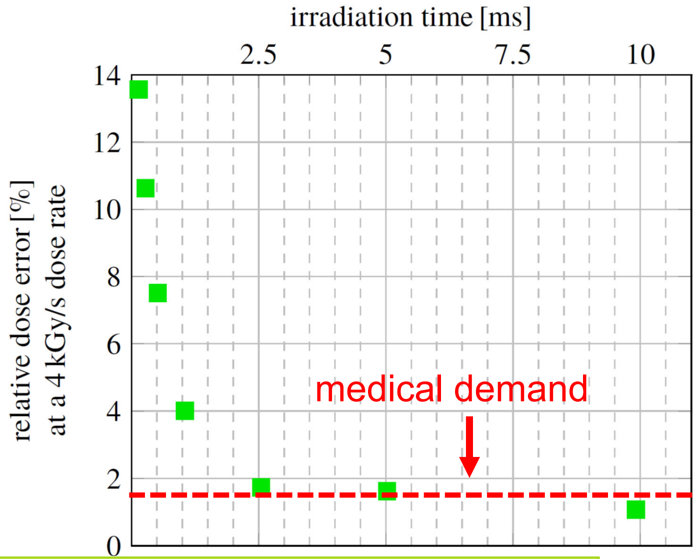
world-wide first FLASH irradiation of eyes

FLASH: Upgrade – Faster Beam Switching

- first FLASH experiments: t_{irr} = 200 ms (scissor-like mechanical shutter: 10 ms for beam-on, 5 ms for beam-off)
- design and installation of electrical shutter for both injectors: 0.3 ms for beam-on, 0.4 ms for beam-off
- now: 10 ms pulses with dose-delivery precision of better than 1.5% possible



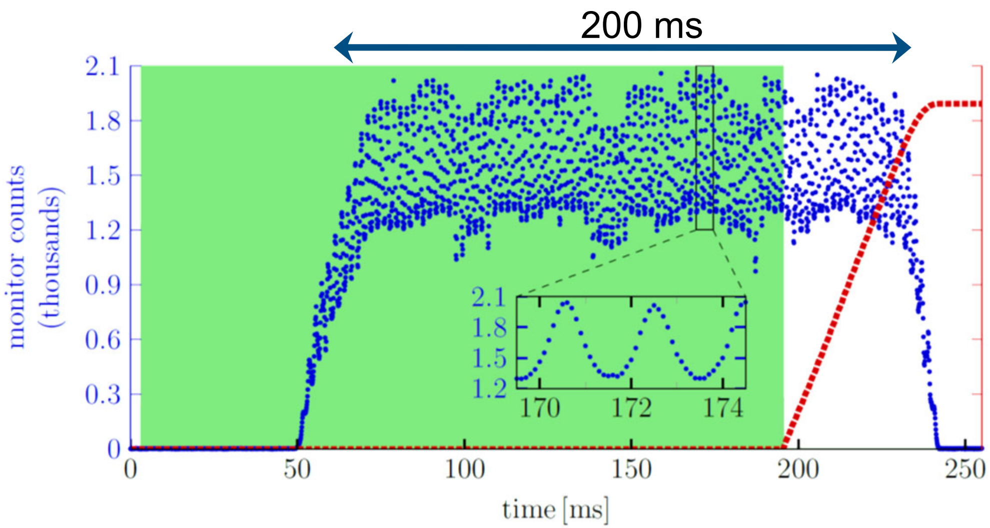


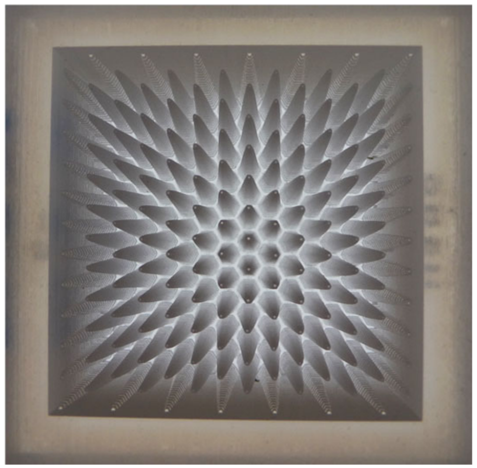
decrease FLASH time by factor 20 while maintaining clinical specifications

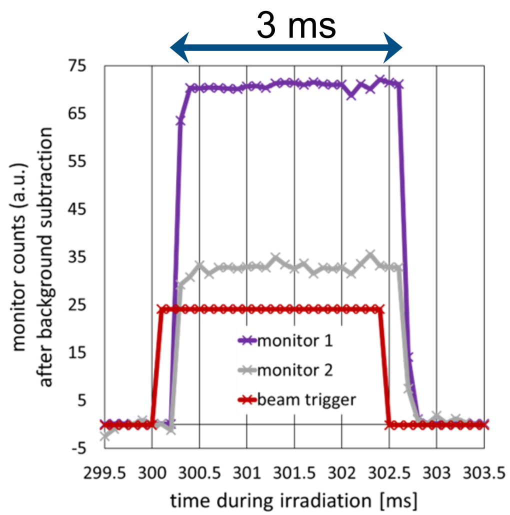
Proc. Cyclotrons (2023)
10.18429/JACoW-CYCLOTRONS2022-MOPO011

FLASH: Upgrade – Accuracy

- use of modulator wheel = dose changes over time, no problem for “long” irradiations
- replace by 3D-printed ridge filter ⇨ flat curve over short times







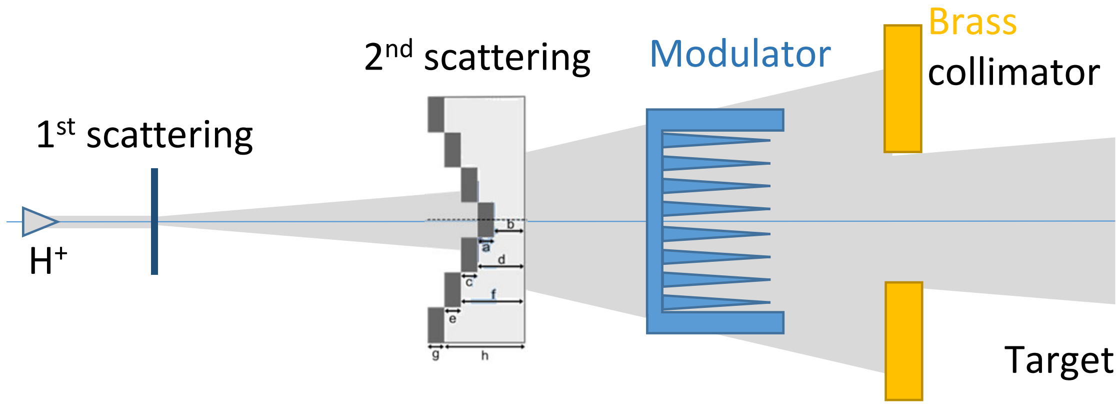
enhanced stability over time

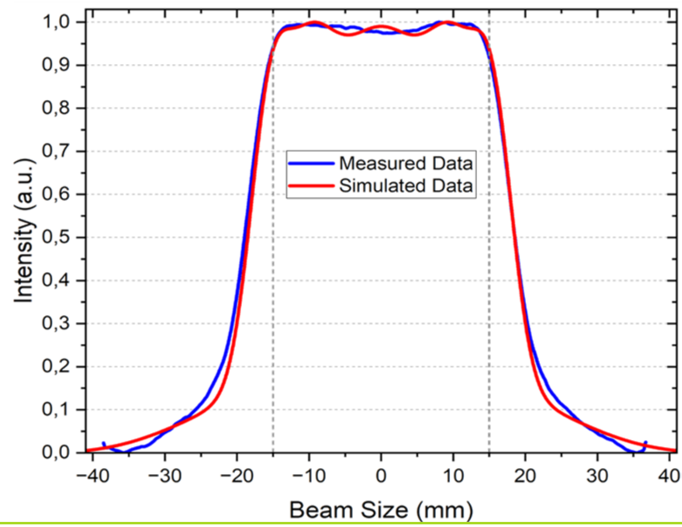
Flash Radiotherapy & Particle Therapy (2022) 10.14293/S2199-1006.1.SOR-.PPRDNQW.v1

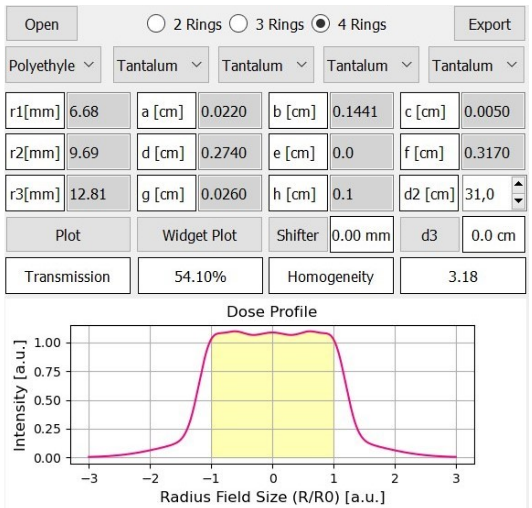
FLASH: Upgrade – Nozzle ⇨ Intensity

- Python GUI **optimizer** for calculating dual-scattering nozzles with up to 4 rings:

- irradiation field: **30 mm**
  beam transmission: increased from 10% ⇨ 54% in the homogenous field-part



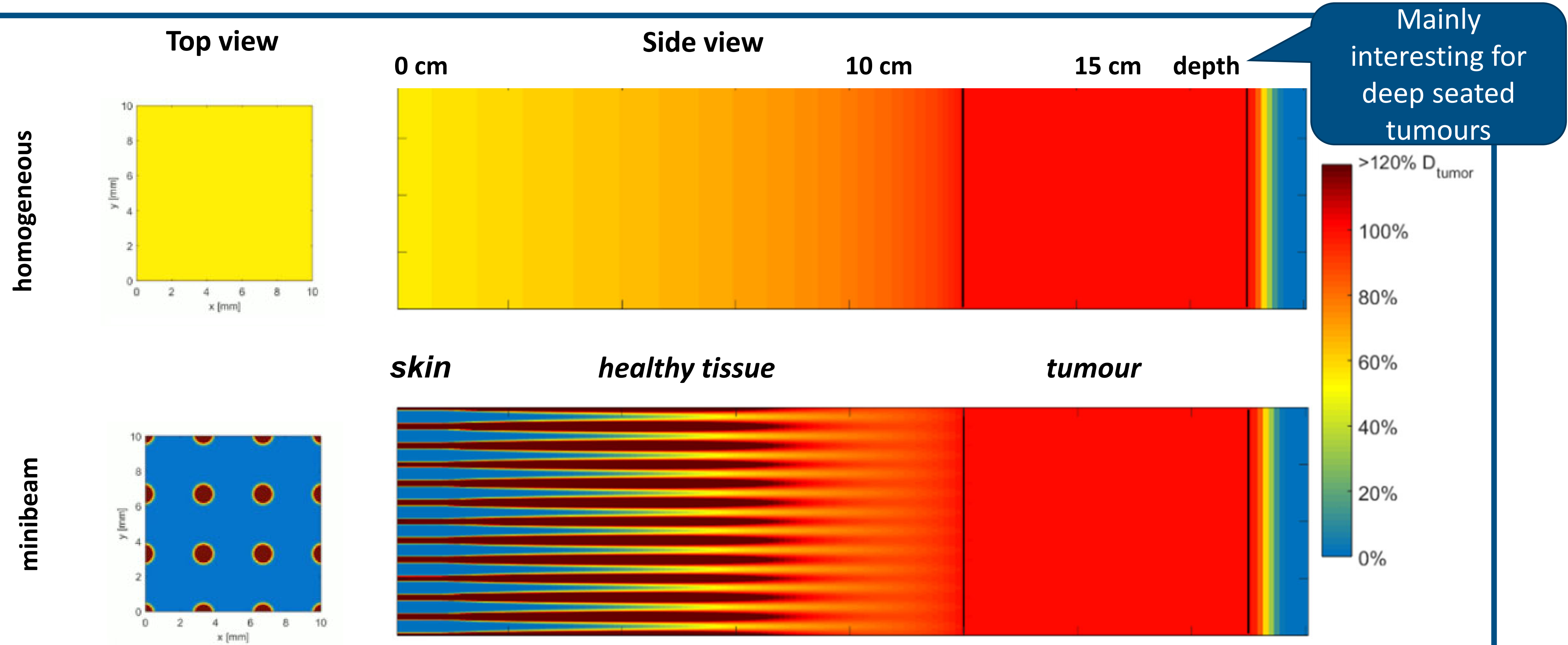




FLASH for human eyes feasible

Proc. IPAC (2024) 10.18429/JACoW-IPAC2024-THPR50

Proton Minibeam Radiotherapy (pMBRT) - the concept of spatial fractionation



Beam sizes σ: 100 µm to 1mm
Centre-to-centre distance mm range

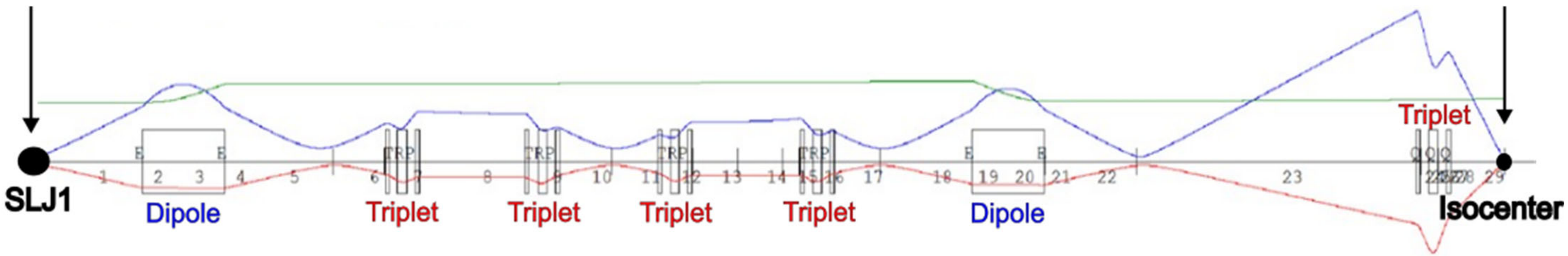
- **Tissue sparing, reduced side effects**
- **Normal tumour control**

Slide by Prof. Dr. Judith Reindl **judith.reindl@unibw.de**

Spatial Fractionation MINIBEE

- installation of a Small Animal Radiation Research Platform (SARRP) at dedicated beamline, project funded by federal ministry of defence: 3.5 M€
- beam line simulations performed with Codes: Trace3D + Georges Python library // BDSIM (Geant4)
- no special quadrupole required for minibeams at isocentre:

σ_x [µm]	σ_y [µm]	σ'_x [mrad]	σ'_y [mrad]	Transmission
49.1	50.3	4.6	2.57	2.5%



unique: Small Animal Radiation Research Platform with minibeam

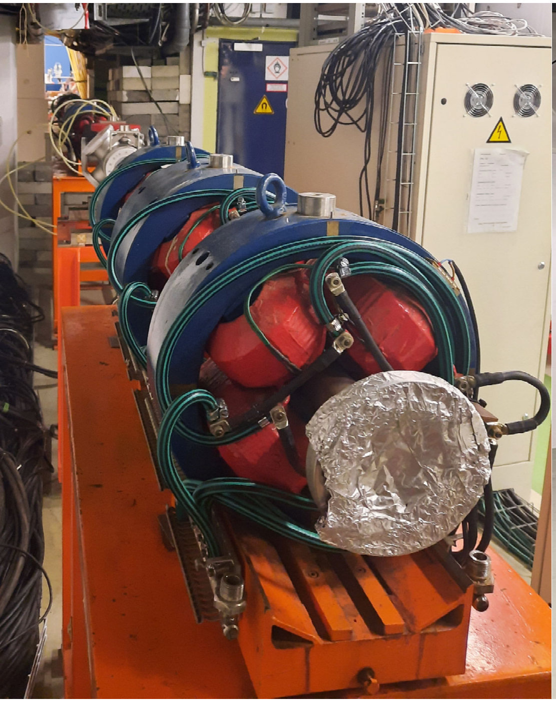
Proc. IPAC (2024) 10.18429/JACoW-IPAC2024-THPR62

HZB Helmholtz Zentrum Berlin

Universität der Bundeswehr München

MINIBEE – Set Up

- open wall to cyclotron vault and install radiation monitors ☑
- install new beam-line and install SARRP ☑
- in progress: commissioning and control system
- to do: licensing



Future: Need for New Ideas

- challenges:
  - aging accelerator infrastructure
  - maintaining excellent clinical standard and accompanying research
- hot research topics – further reduction of side effects:
  - potential future: FLASH Radiotherapy → extremely high beam intensities
  - Helium-ions: sharper lateral dose fall-off, higher radiobiological efficiency
- = <u>impossible</u> at standard commercial proton therapy accelerators

solution: customized, innovative design of compact, superconducting cyclotron incorporating FLASH & He therapy: He^{2+} 280 MeV and H_2^+ 140 MeV

~ same range in water, ideal for eyes

~ same magnetic rigidity

commercial solution not available ⇨ develop new design

AIMA DEVELOPPEMENT
Accelerators for Industrial and Medical Applications

Summary

- more than 5000 eye patients conventionally treated in collaboration with Charité – Universitätsmedizin Berlin
- user operation & research:
    - MiniBEE project with Uni. Bundeswehr München in full thrust, experiments in 2026
    - FLASH delivery of kGy/s down to few ms irradiation-time within clinical specs
    - plans for clinical FLASH application to human eyes (organoids, iris melanoma, patients)
    - phase I CDR for compact cyclotron with scientific case finished

Thank you for your attention

patient apertures