FLASH experiments at the “Dresden platform for high dose rate radiobiology”

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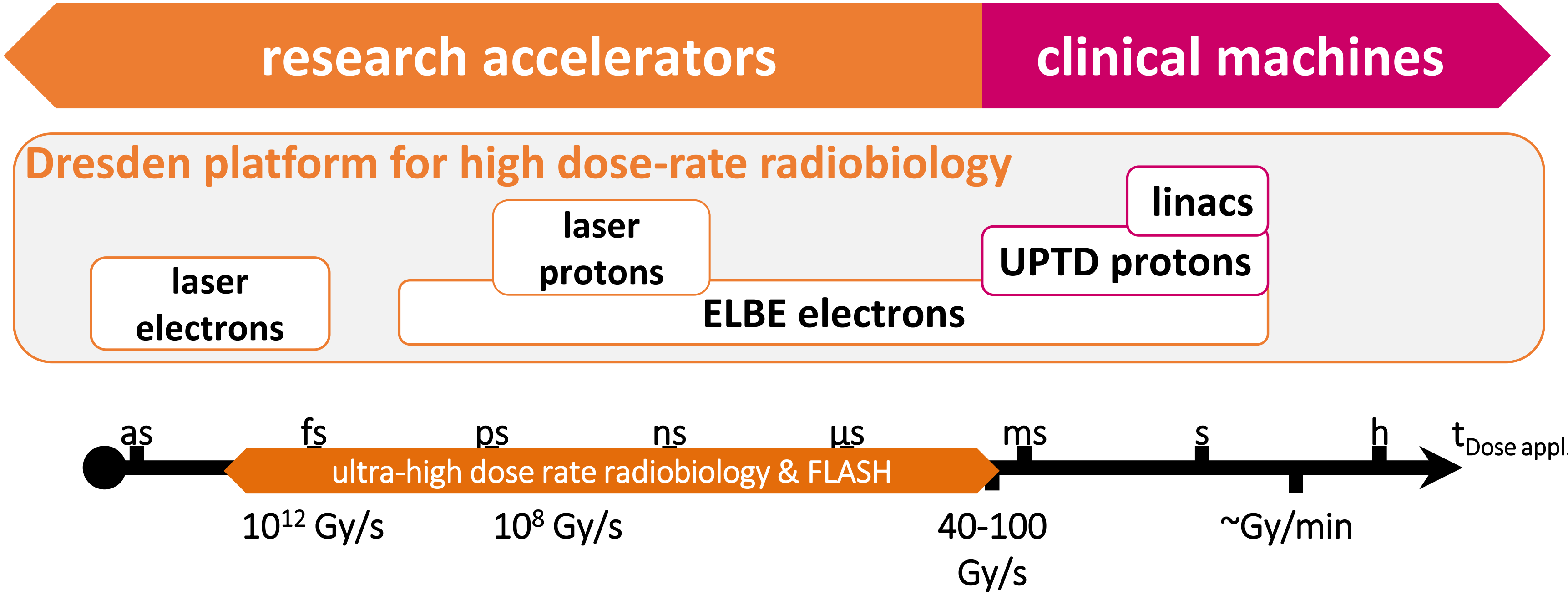
HZDR
HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

Dresden platform for high dose rate radiobiology



Dresden platform provides possibility to perform radiobiological experiments

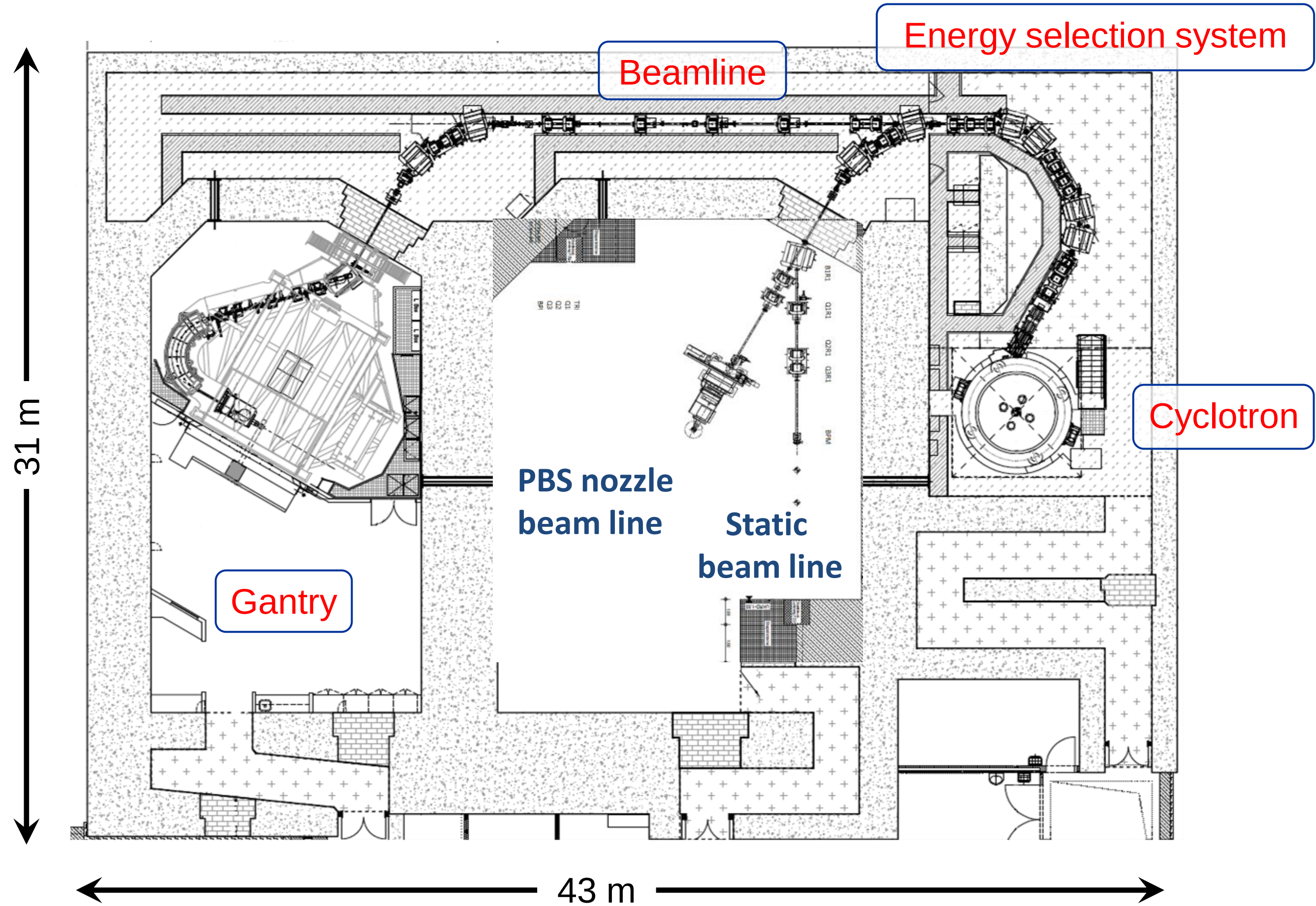
- Clinical and experimental electron and proton beams
- Huge range of dose rates covering physical, chemical and biological reaction times
- Experience with cell and animal studies at accelerators

Dosimetry for such experiments depends on the individual requirements and beam properties of the different facilities.

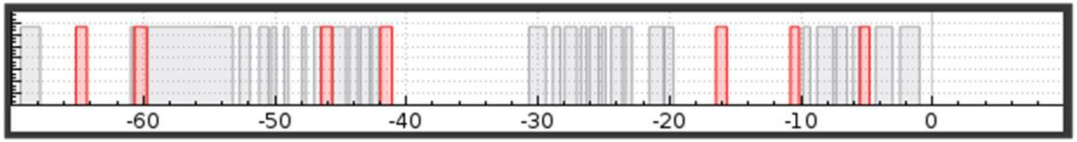
University Proton Therapy Dresden

IBA Proteus Plus system:

- isochronous cyclotron
- 230 MeV primary proton energy
- down to 70 MeV from degrader-based energy selection system
- Max. cyclotron current: 500 nA (radiation protection limit)



Experiments in parallel with patient treatment



University Proton Therapy Dresden

Experimental Area at University Proton Therapy Dresden (EA-UPTD)

EMPIR

Experiments performed by UHDpulse partners:

- NPL: graphite calorimetry, ionization chamber dosimetry, CMOS detector tests
- Advacam: dosimetry using pixel sensors

Experiments performed by externals within MRgRT-DOS:

- NPL, PTB: alanine and ionization chamber dosimetry in magnetic fields

University Proton Therapy Dresden: fixed beam line

IBA Proteus Plus system:

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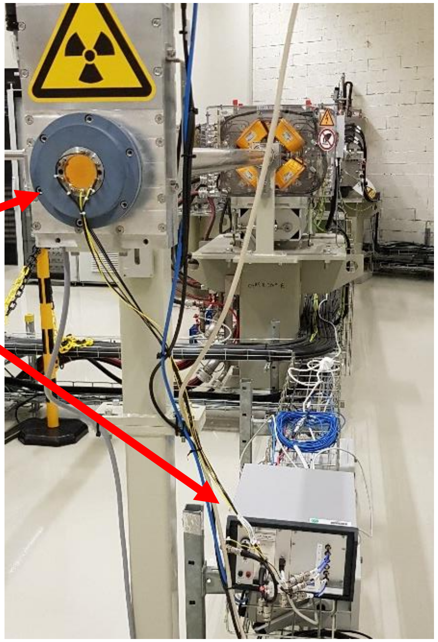
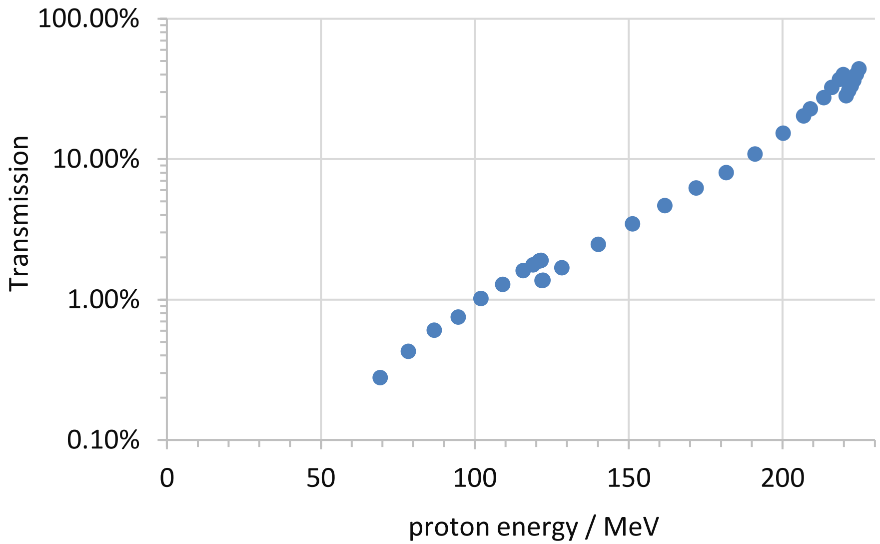
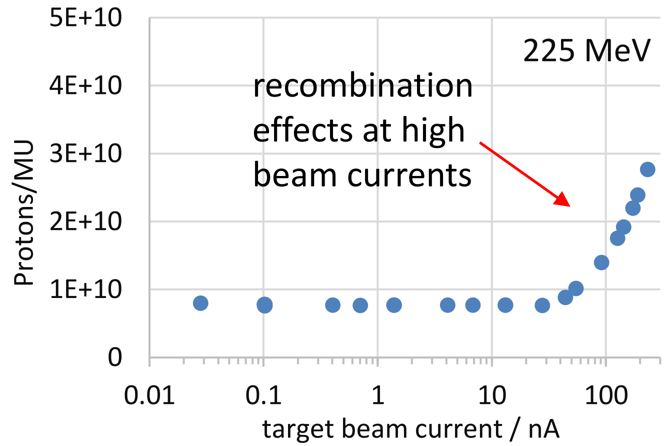
In-house developed beam control for static pencil beam delivery



Segmented ionisation chamber (in-house/PTW)

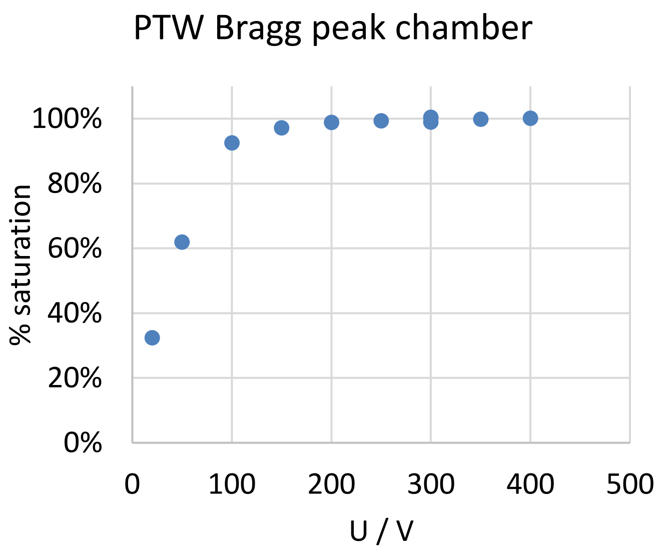
45% transmission at 225 MeV

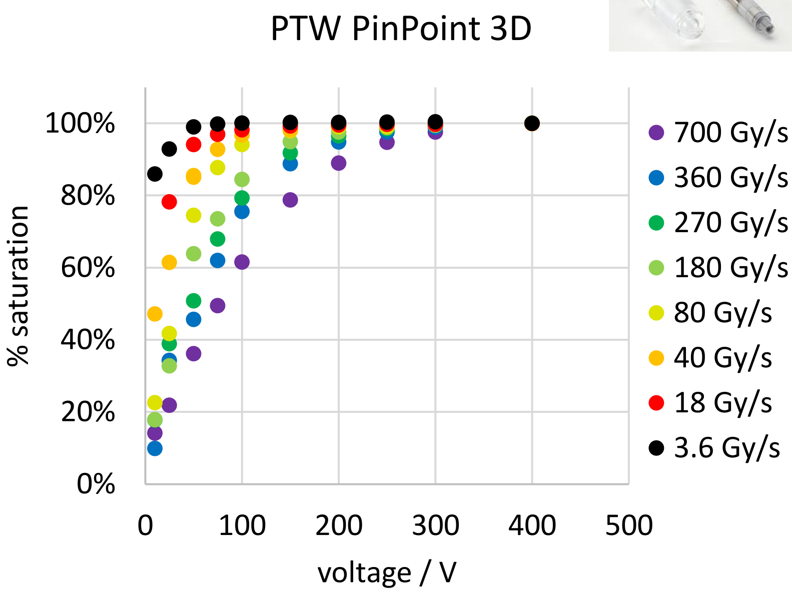




University Proton Therapy Dresden: fixed beam line

Recombination effects in ionization chambers at UHDR





2 mm air gap: 2000 V/cm @ 400 V

1.45 mm radius: 2750 V/cm @ 400 V

max. voltage according to manual: 500 V

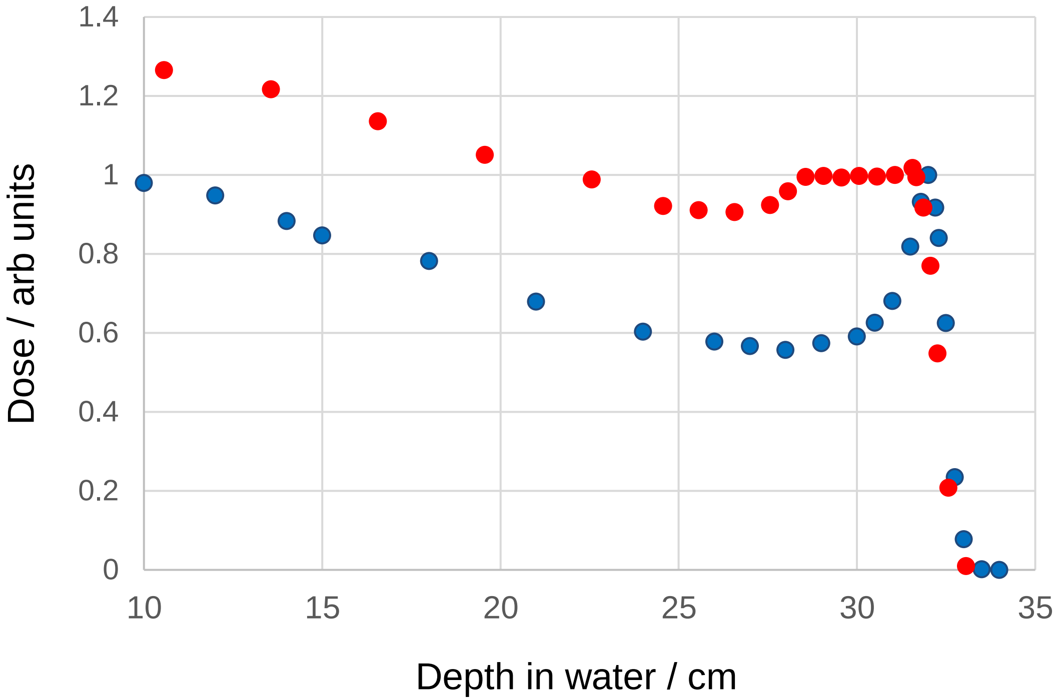
University Proton Therapy Dresden: further developments

- Generation of SOBP from single pencil beam
- Proton energy: 225 MeV
- Dose rates in the SOBP up to 700 Gy/s

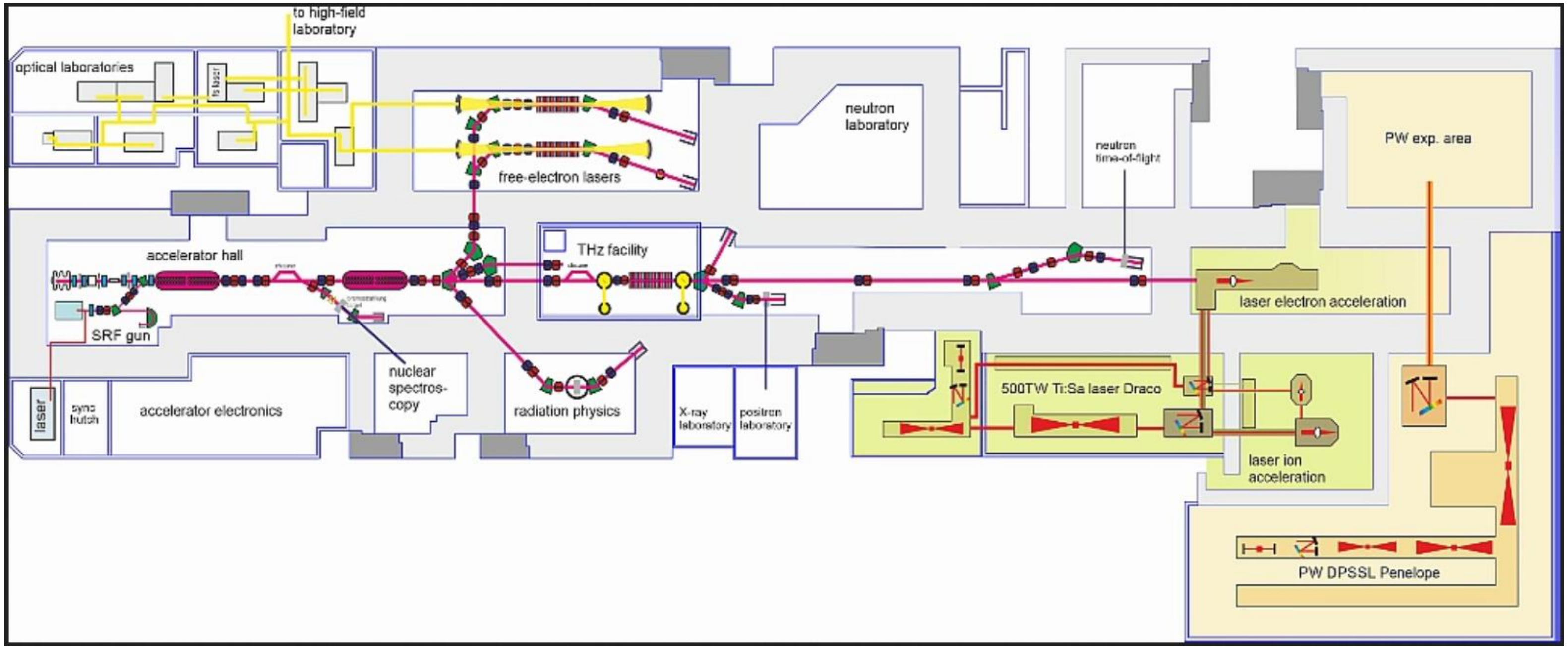
3D-printed range modulator

Modulator provided by
Uli Weber, GSI

Simeonov et al., Zeitschrift für Med. Phys. 2020



UHDR experiments at HZDR: ELBE and DRACO



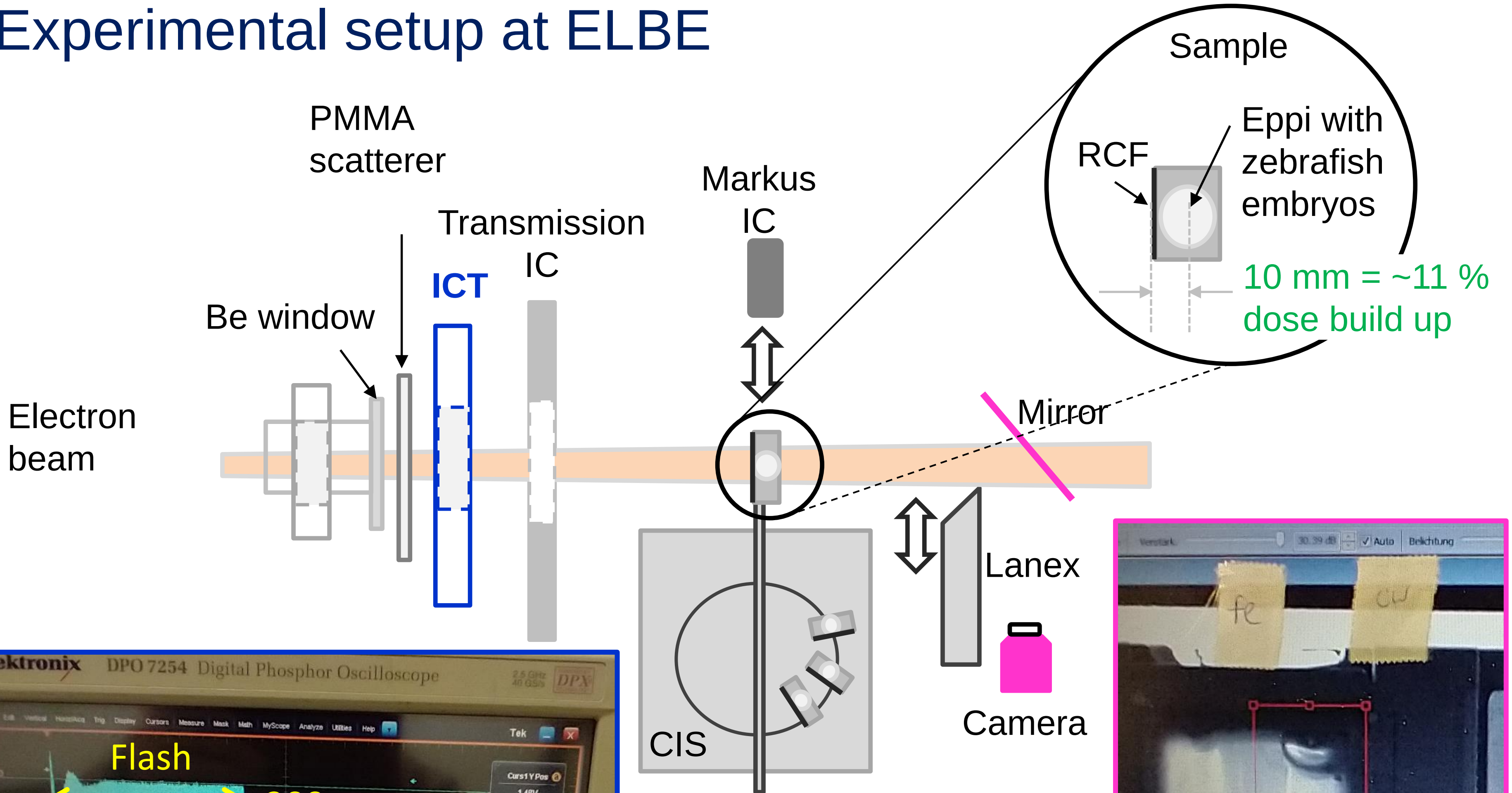
Electron accelerator ELBE

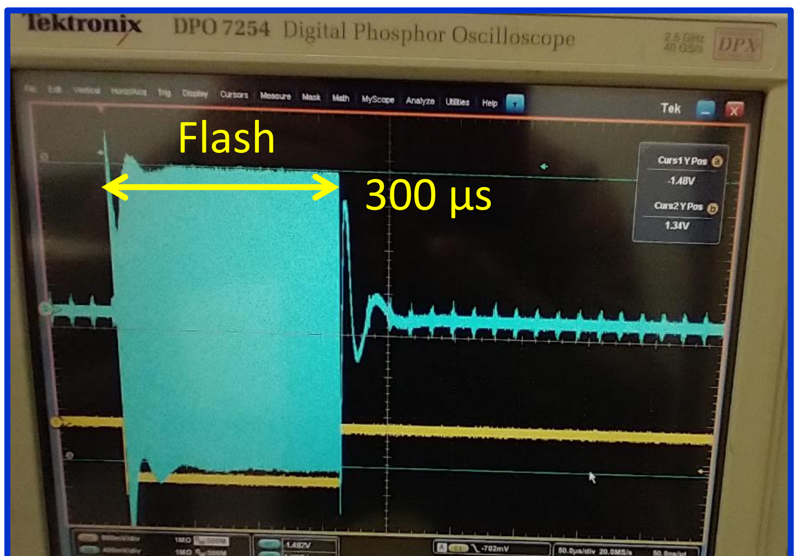
- 30 MeV electron beams with flexible adjustable pulse structure
- Mean dose rates up to 10.000 Gy/s

Laser accelerator DRACO

- High power laser: 20 J in 30 fs
- Mean proton dose rates up to 10^9 Gy/s

Experimental setup at ELBE



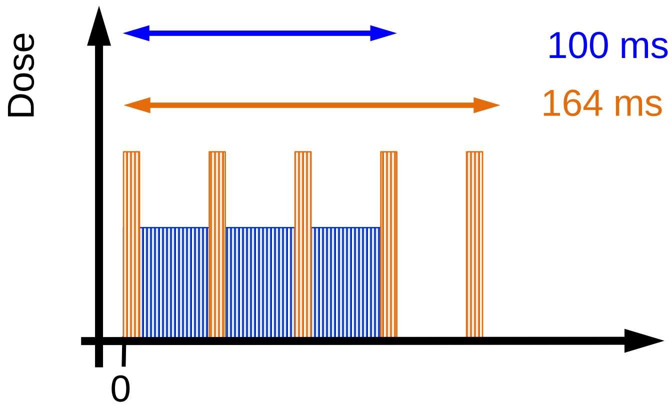


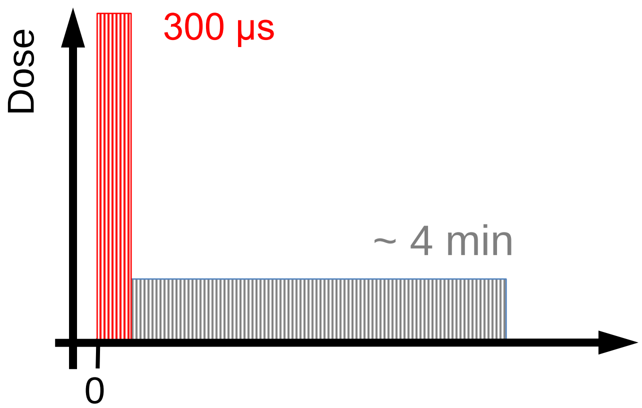
Beam position changes for different regimes

UHDR experiments at ELBE – Pulse structures

LET independent investigation of beam pulse structure influence at **research electron linear accelerator ELBE**

Variable pulse time structure and tunable bunch charge over broad range allow to mimic pulse structure of clinical proton accelerators (**isochronous** and **synchrocyclotron**)





Flash$_{cyclo}$ (290 Gy/s | 10^6 Gy/s)

Flash$_{synchro}$ (177 Gy/s | 10^9 Gy/s)

Reference (0.12 Gy/s | 10^3 Gy/s)

Flash$_{max}$ (10^5 Gy/s | 10^9 Gy/s)

Karsch et al.: Radiother Oncol 2022

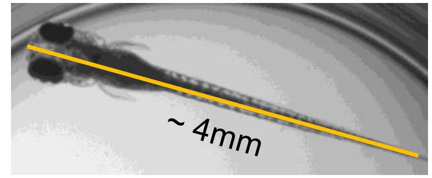
Zebrafish experiments at ELBE

Model: **Wildtype zebrafish embryo**, 24 hours old

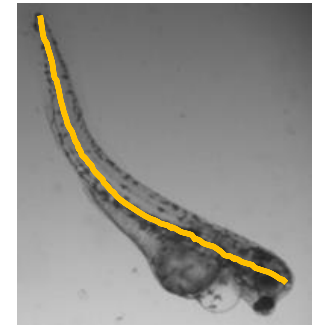
- Small vertebrate *in vivo* model for normal tissue response

~ 1mm

4 days



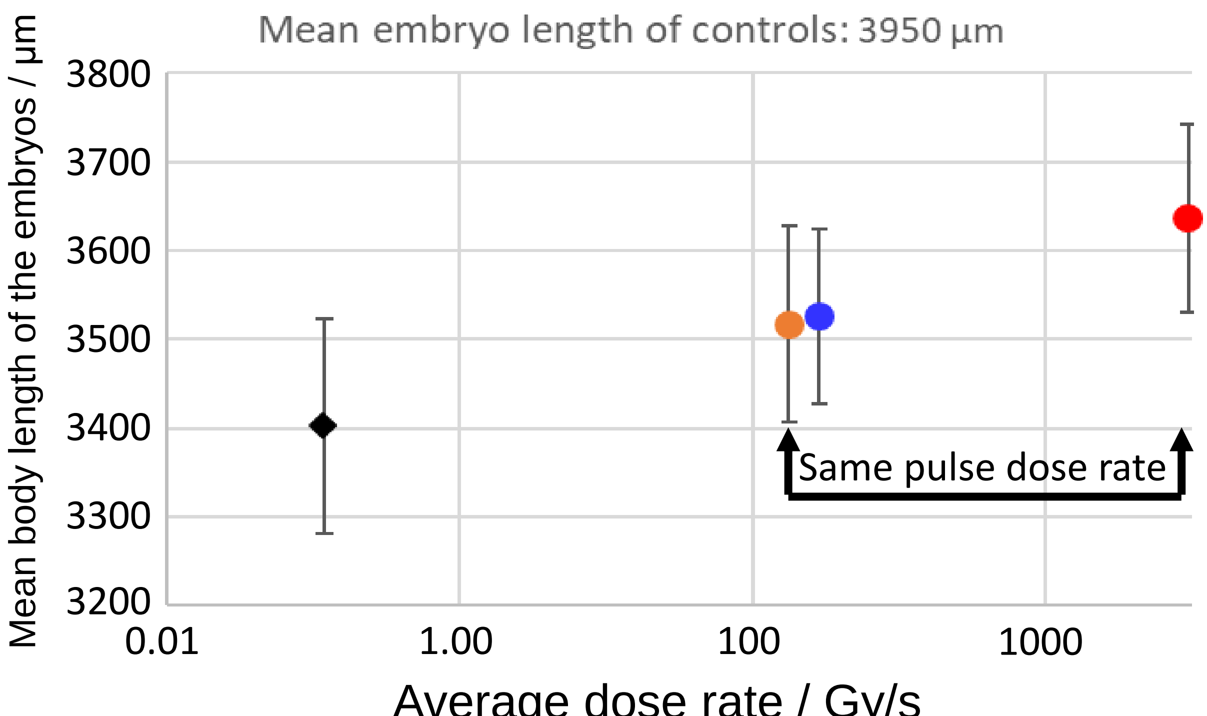
Unirradiated control



Irradiated embryo

Szabo et al. PLoS One 2018;
Beyreuther et al. Radiother Oncol 2019

Endpoint: radiation induced length reduction



L. Karsch et al. Radiother Oncol 173:49-54 (2022)

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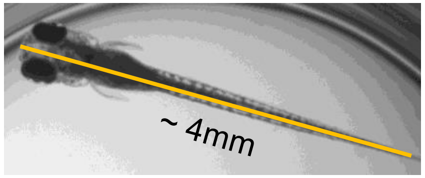

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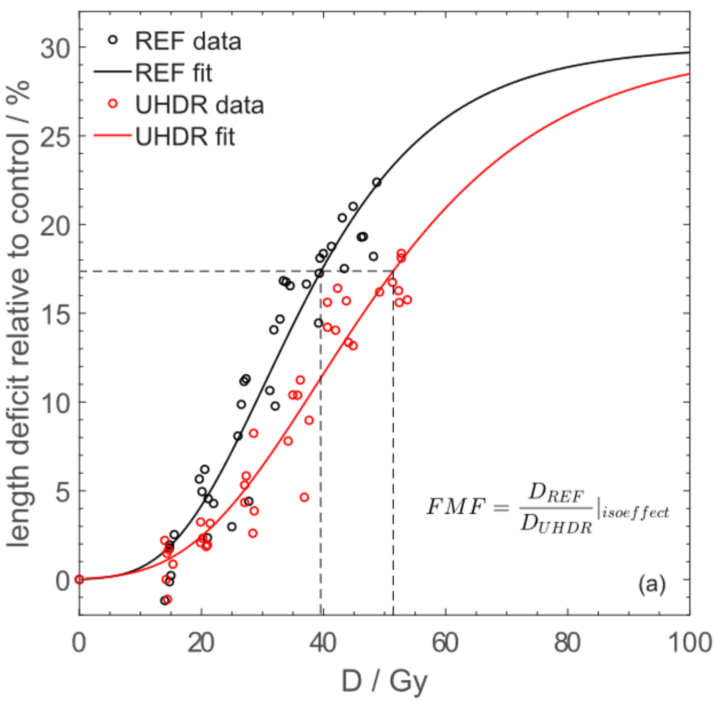
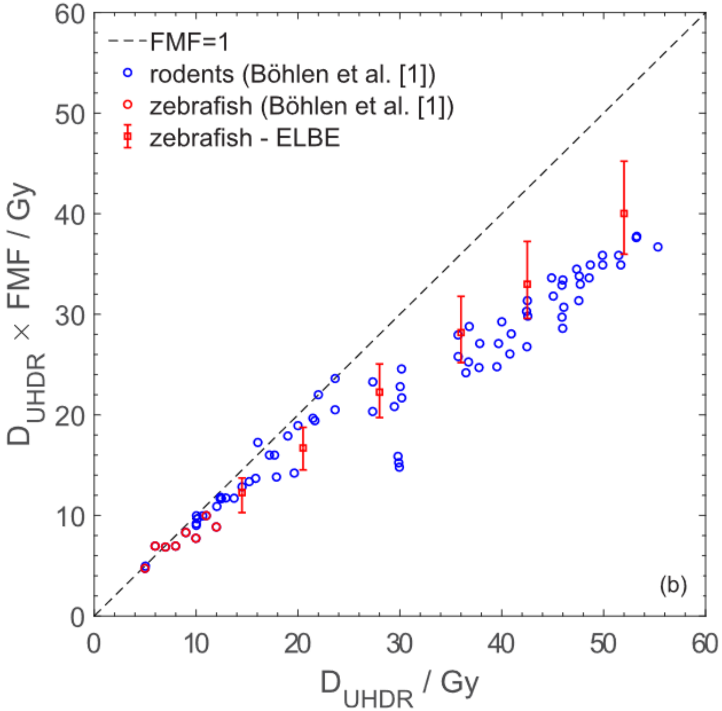
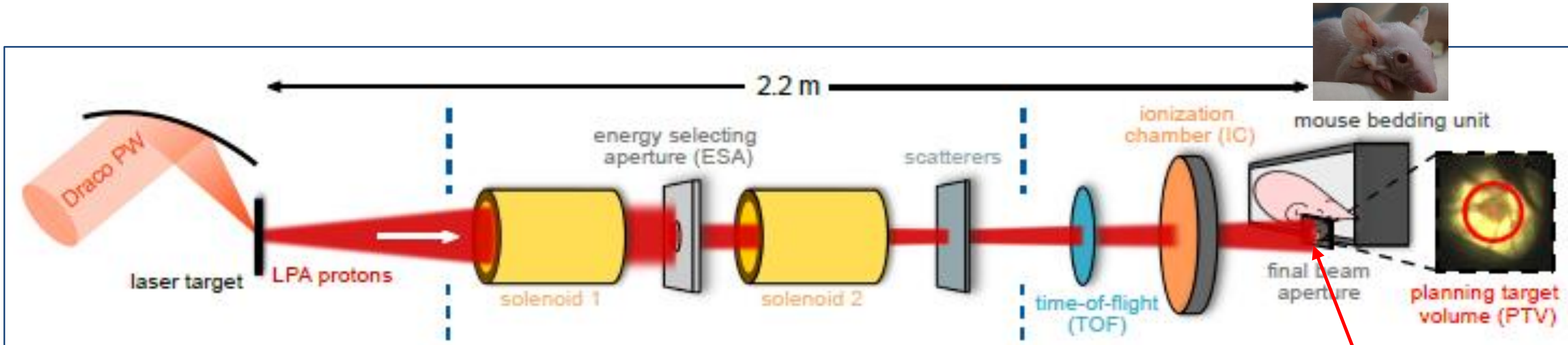




F. Horst et al, In Regard to Boehlen et al., accepted in IJROBP (2023)

DRACO laser: proof-of-concept animal study

- Pilot campaign with 92 mice prove applicability for preclinical *in vivo* studies, incl. all necessary controls and reference irradiation at clinical proton accelerator



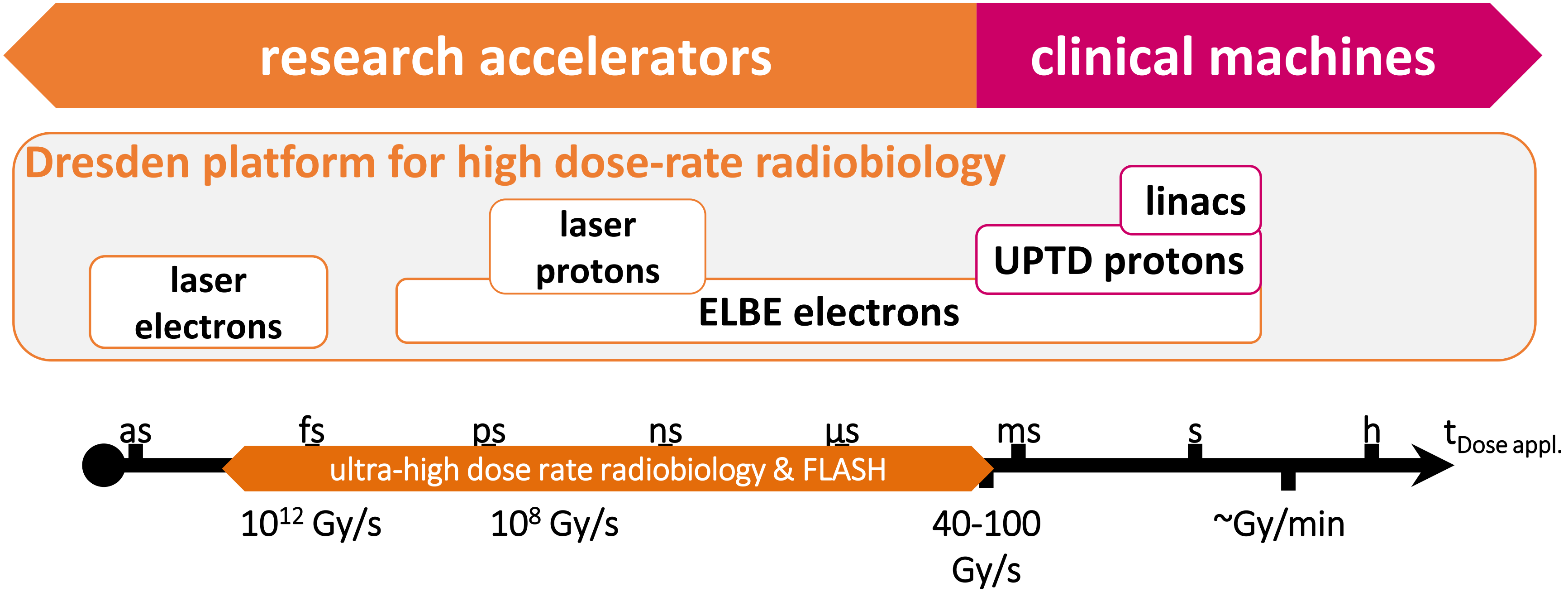
online monitoring of proton spectra

EBT3 film for reference dose

	UPTD	Draco
Energy spectrum	Monoenergetic, 70 – 230 MeV	Exp. spectrum, <60 MeV
Pulse frequency	100 MHz	≤ 10 Hz
Dose per pulse	10^{-8} Gy	≥ 0.6 Gy
Pulse dose rate	~ Gy/s	$>10^9$ Gy/s

Kroll et al., Nature Physics 2022; 18:316–22 Beyreuther et al. PLoS One 2018

Summary



Dresden platform provides possibility to perform high dose rate experiments

- Clinical and experimental electron and proton beams that provide a huge range of dose rates for physical, chemical and biological experiments
- Challenges for dosimetry (small fields, high dose rates): specific solutions realized for several experimental setups

Thanks for your attention!

Related publications

… on **dose rate dependence of different dosimeters**

Karsch et al.: Z Med Phys 21 (2011) 4
Richter et al.: Rad Meas 46 (2011) 2006
Karsch et al.: Med Phys 39 (2012) 2447
Karsch et al.: Z Med Phys 24 (2014) 210
Karsch: Phys Med Biol 61 (2016) 3222
Karsch Med Phys 43 (2016) 6154
Gotz et al.: Phys Med Biol 62 (2017) 8634
Gotz et al.: Med Phys 46 (2019) 3692

… and on **dose rate dependence of biological response *in vitro***

Kraft et al. New Journal of Physics, 12(8) (2010) 085003.
Beyreuther et al.: Int J Radiat Biol 91 (2015) 643
Laschinsky et al.: Radiat Environ Biophys 55 (2016) 381

… and on **FLASH effect *in-vivo* (zebrafish)**

Beyreuther et al.: Radiother Oncol 139:46-50 (2019)
Pawelke et al.: Radiother Oncol 158:7-12 (2021)
Kroll et al., Nature Physics 18:316–22 (2022)
Karsch et al.: Radiother Oncol 173:49-54 (2022)
Jansen et al.: Radiother Oncol 175:193-196 (2022)
Horst et al.: accepted in IJROBP (2023)