High dose rate in vivo proton irradiation based on a laser plasma proton accelerator

U. Schramm

Institute for Radiation Physics and Oncoray
Helmholtz-Zentrum Dresden-Rossendorf

MT ARD

ATHENA
The Helmholtz-Project for Laser-Plasma-Acceleration

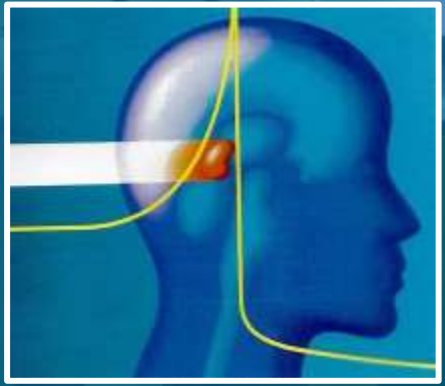
OncoRay

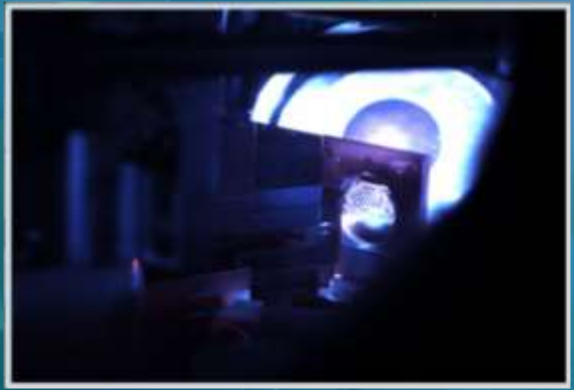
HZDR
HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

Laserlab-Europe Symposium “Lasers Fighting Cancer” May 2021

Motivation (in the early times of laser acceleration)

- compact (cheap) accelerator to replace clinical proton therapy source
  [T. Bortfeld, J. Loeffler, Nature 2017: shrink accelerators, sharpen beams, broaden coverage]

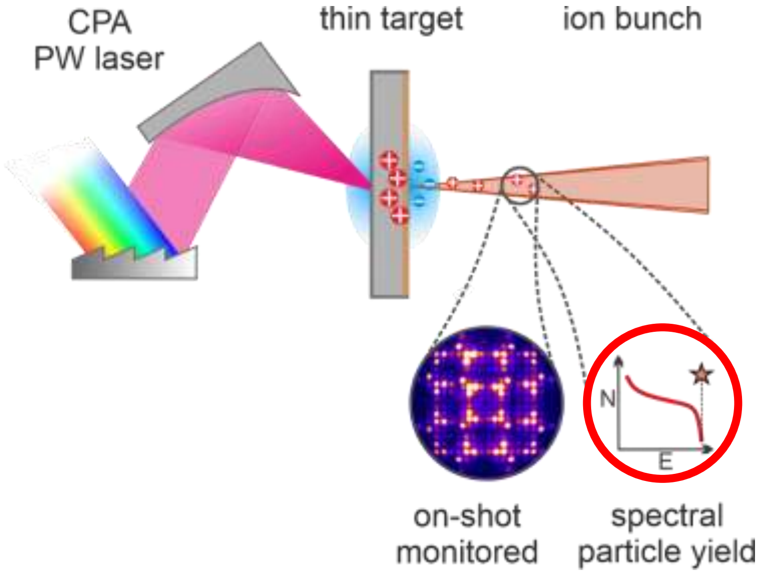


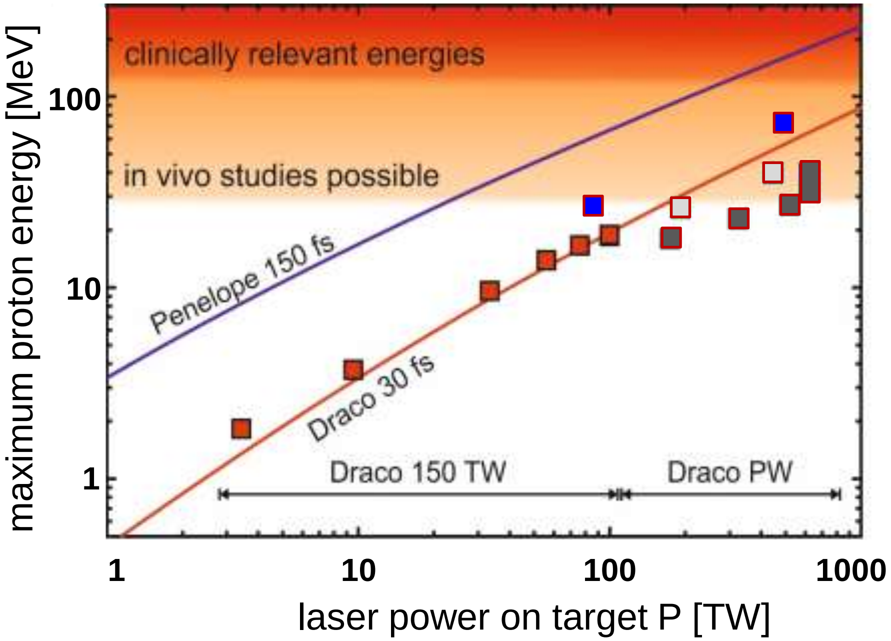


meter-scale -> micron scale

S. Kraft et al. NJP 12 (2010) 085003,
K. Zeil et al. APB 110, 437 (2013)

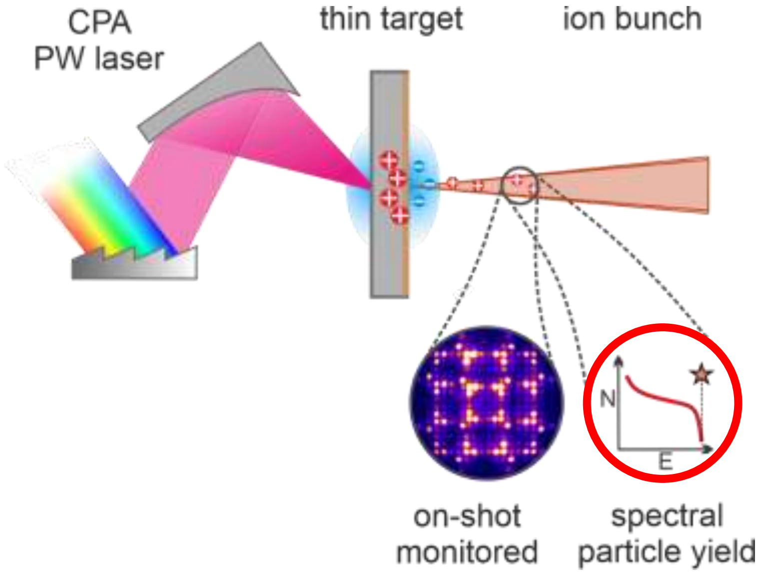
Upscaling of laser accelerated proton beam energies …

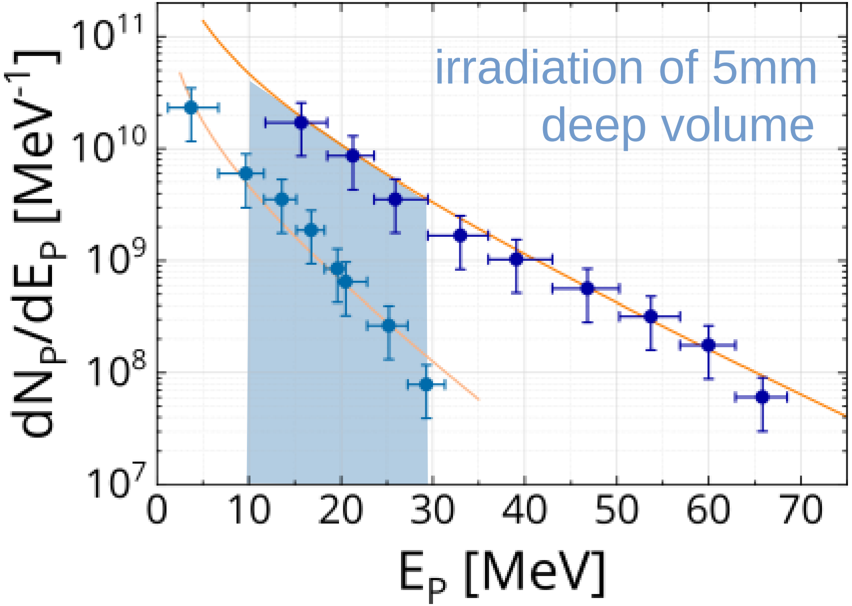




- increased laser energy
- dedicated targetry
- improved and monitored laser and plasma control

Upscaling of laser accelerated proton beam yields …





- reduced sensitivity to cut-off fluctuation
- reproducible depth dose profile and control

Motivation (today)

- *exploit unprecedented source characteristics*

  -> extreme dose rates (10s of Gy in nanosconds)
  -> broad energy range -> single pulse depth dose shaping

Prerequisites

- *Sufficient energy to penetrate volume (>30 MeV protons)*
- *Sufficient particle yield (pulse dose rate and average)*
- *Absolute dose control and metrology in 3D*
- *Stability (laser accelerator availability on demand)*
- *Radiobiology expertise and infrastructure (references)*

Dresden (accelerator) platform (for variable dose rate studies)

research accelerators
development of beam delivery, radiobiological models, dosimetry

clinical machines
establ. methods, models, protocols

Dresden platform

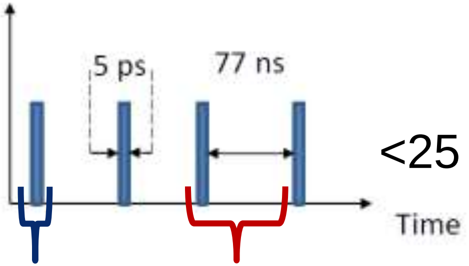
- laser e⁻ (Draco)
- laser ions (Draco + PEnELOPE)
- ELBE electrons
- UPTD protons
- linacs

as | fs | ps | ns | µs | ms | s | h | $t_{Dose\ appl.}$

ultra-high dose rate radiobiology & FLASH

10^{12} Gy/s | 10^{8} Gy/s | 40-100 Gy/s | ~Gy/min

FLASH @ ELBE



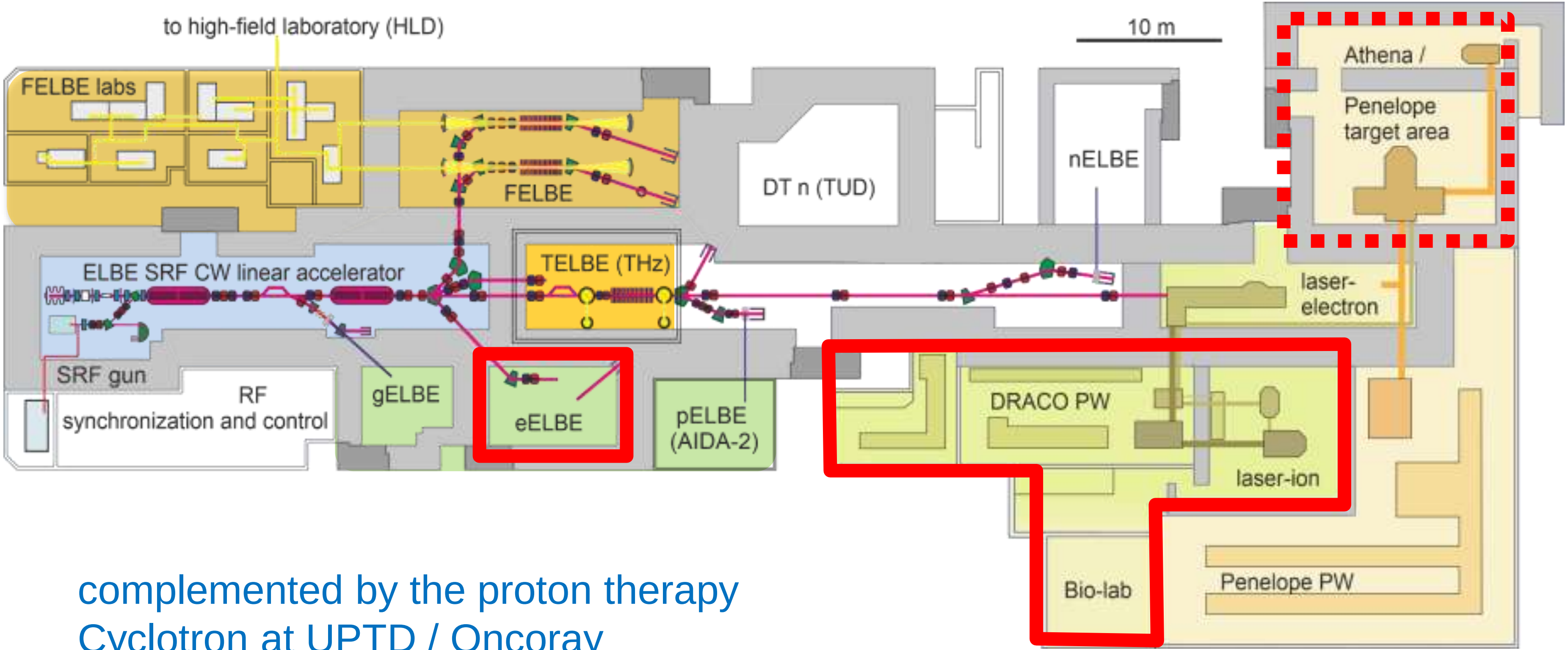
<25 mGy / pulse

~10^{9} Gy/s pulse 3×10^{5} Gy/s mean dose rate

J. Pawelke, et al.,
Radiother. Oncol. 158, P7 (2021)

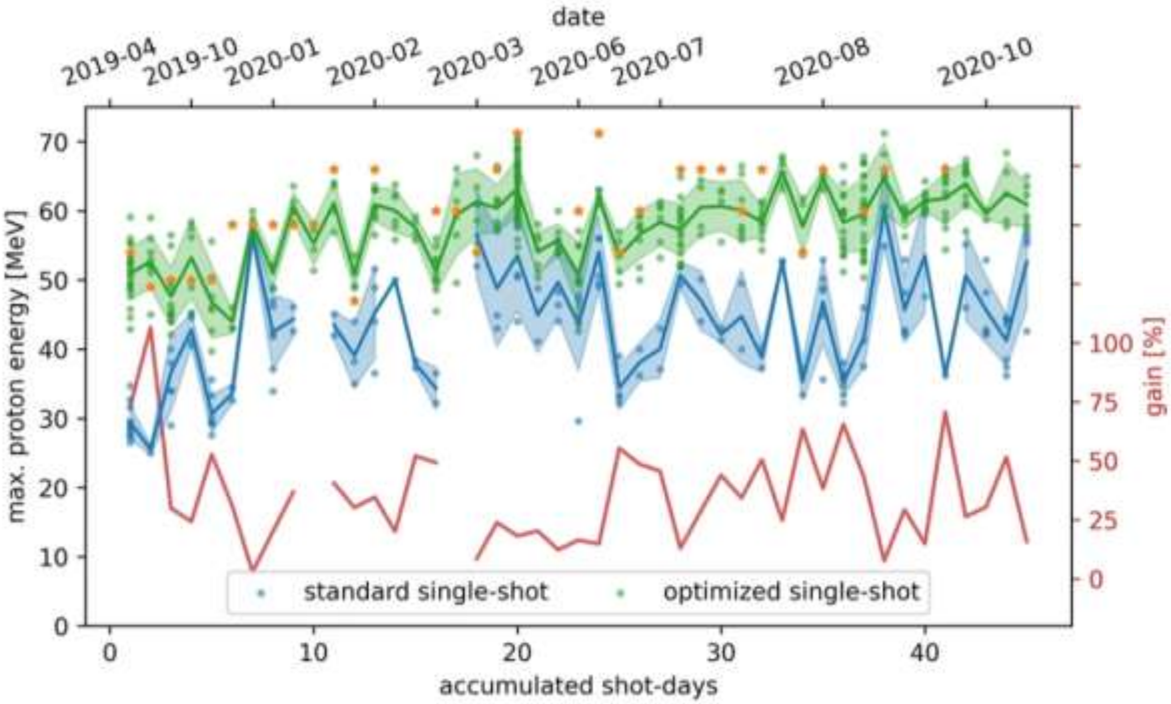
ELBE Center for high power radiation sources

a user facility and advanced accelerator R&D



complemented by the proton therapy Cyclotron at UPTD / Oncoray

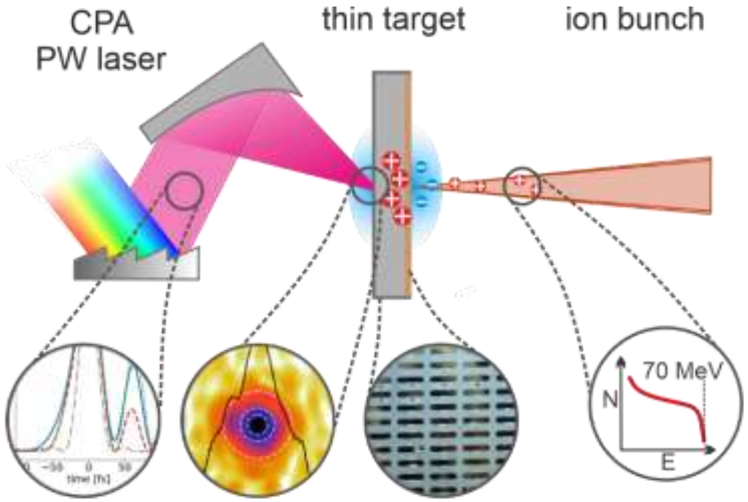
Stable laser proton accelerator operation over month @ >60 MeV through active control of laser pulse parameters



- routine operation with ≳ 60 MeV cut-off energy over months
- measured / cross-checked with RCF stacks, TP specromter, TOF
- **ready for applications**

T. Ziegler, et al., Scientific Reports 11, 7338 (2021)

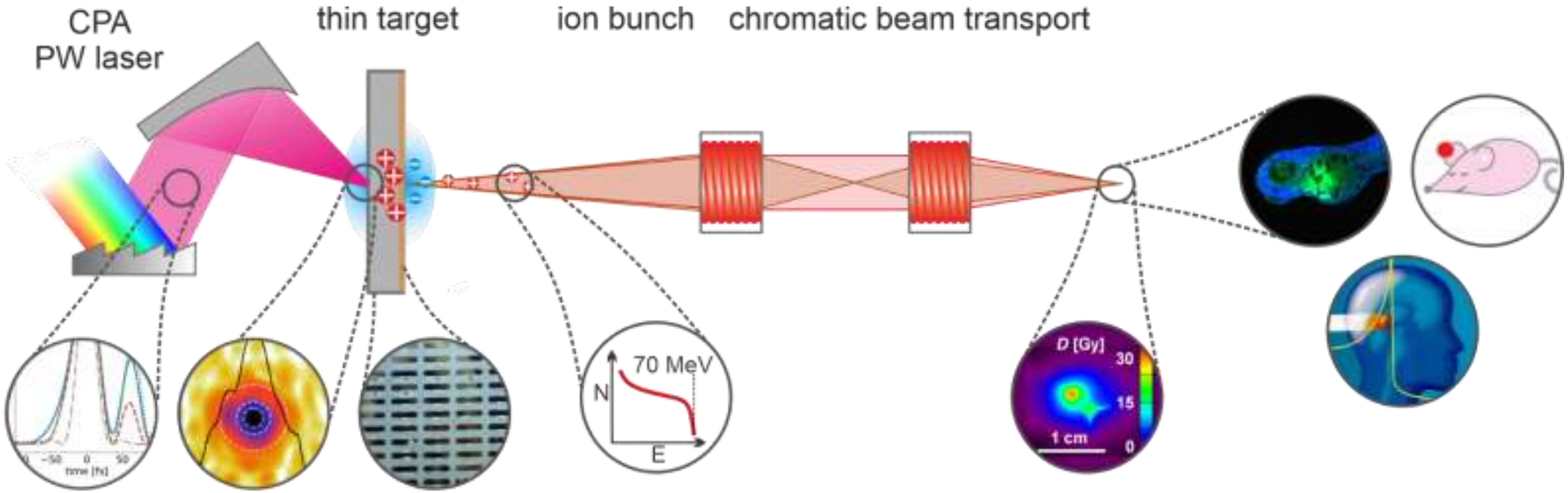
Controlled dose delivery for applications



monitored laser pulse tailoring

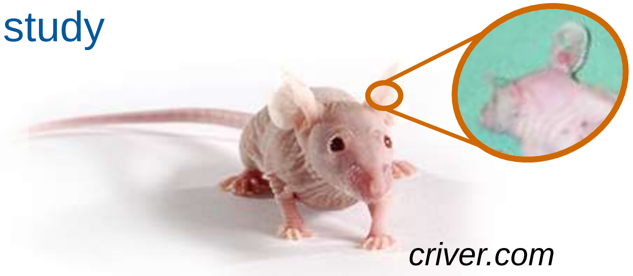
pulsed magnet beamline for
- efficient beam transport
- spectral control
- controlled depth dose delivery

Controlled dose delivery for applications



in vivo 3D irradiation (mouse ear tumor)
proof-of-concept study

homogeneous dose
within 5×5×5 mm³
< 10% dose fluctuation
4 Gy in ~minute

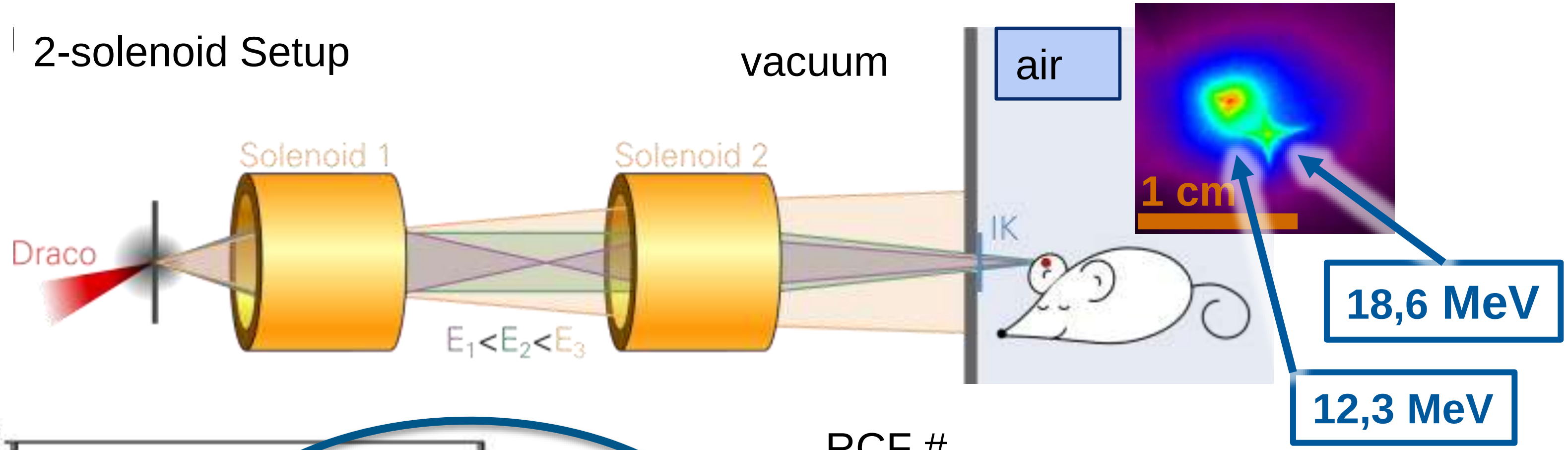


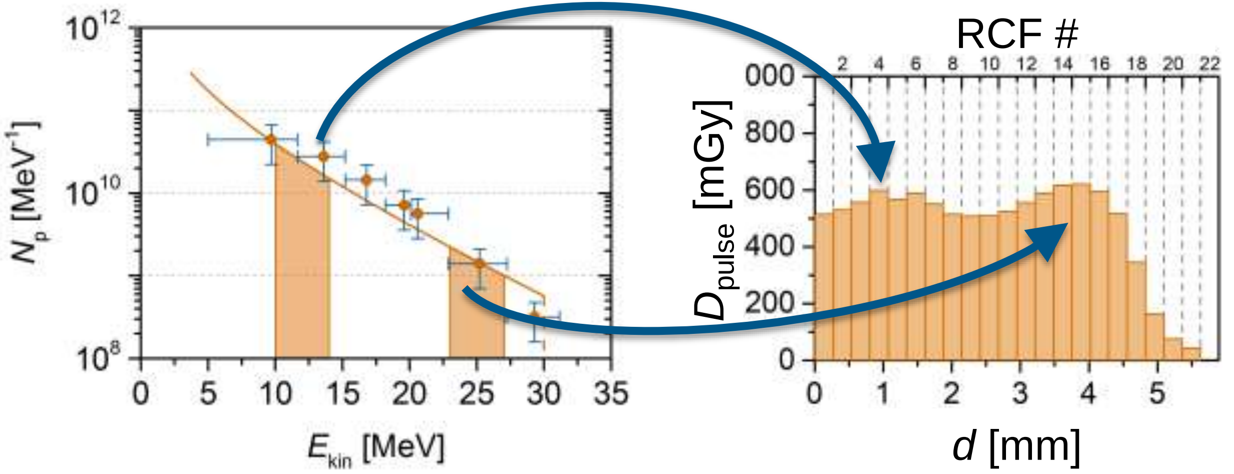
criver.com

F. Brack, et al., Scientific Reports 10, 9118 (2020)
S. Busold, et al., (LIGHT), Sci. Rep. 5, 12459 (2015)
D. Haffa, et al., Sci. Rep. 9, 6714 (2019)
F. Albert, et al., New J. Physics 23, 031101 (2021)

E. Beyreuther et al., PLOS ONE 12 (2017)

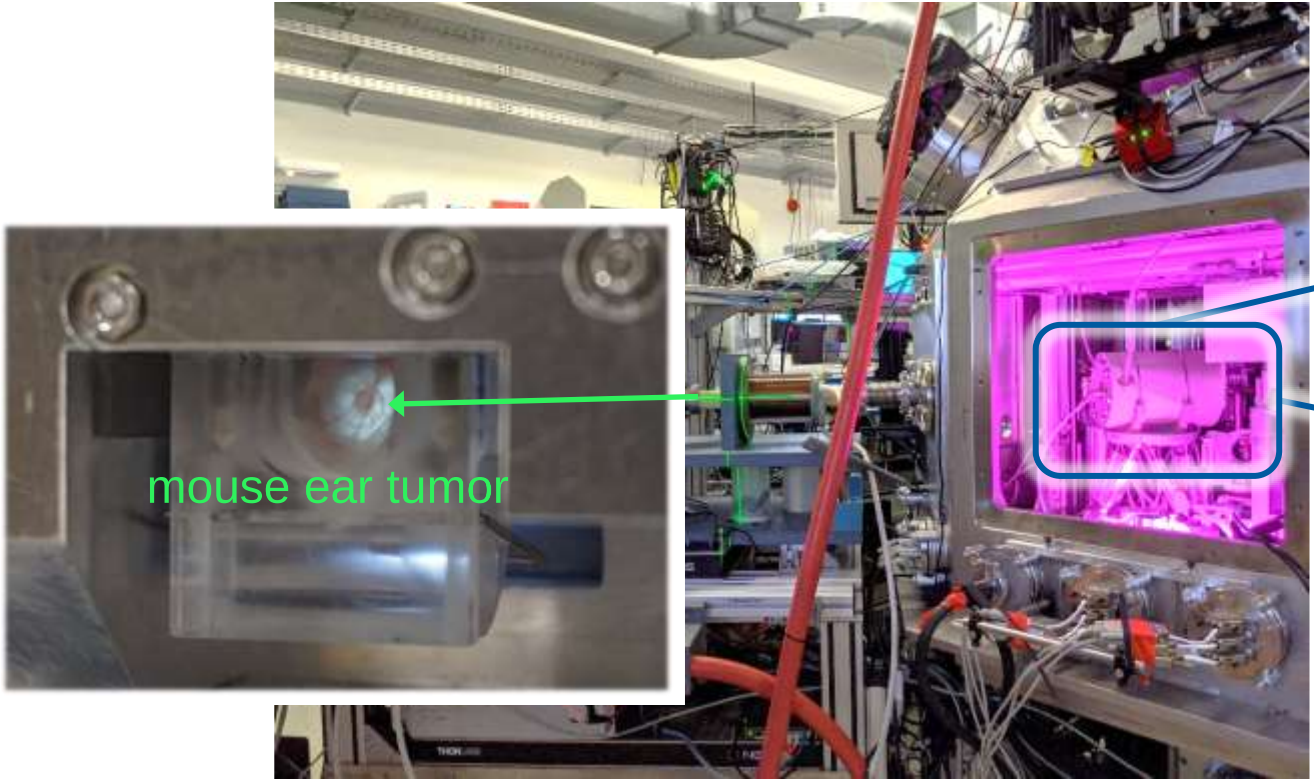
Single pulse depth dose control

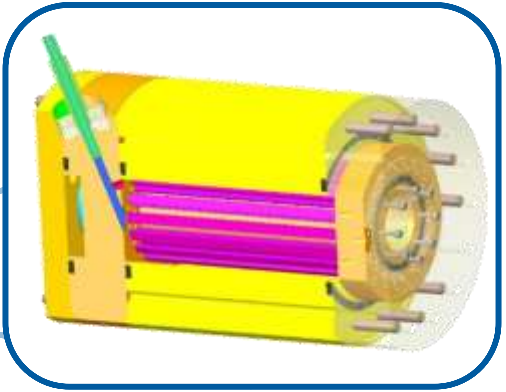




F. Brack, et al., Scientific Reports 10, 9118 (2020)

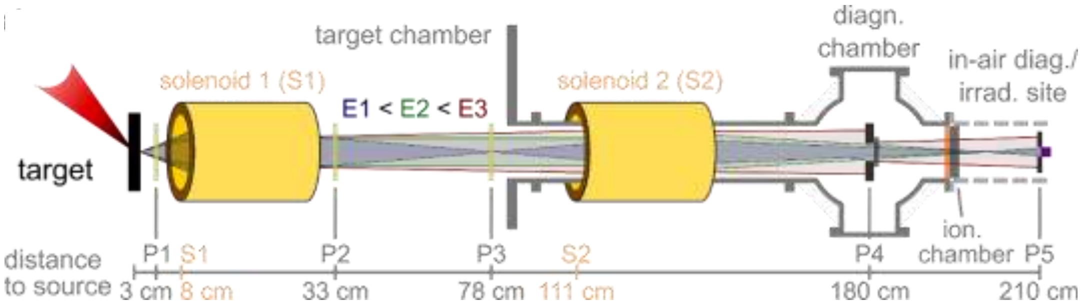
Proton beamline impressions



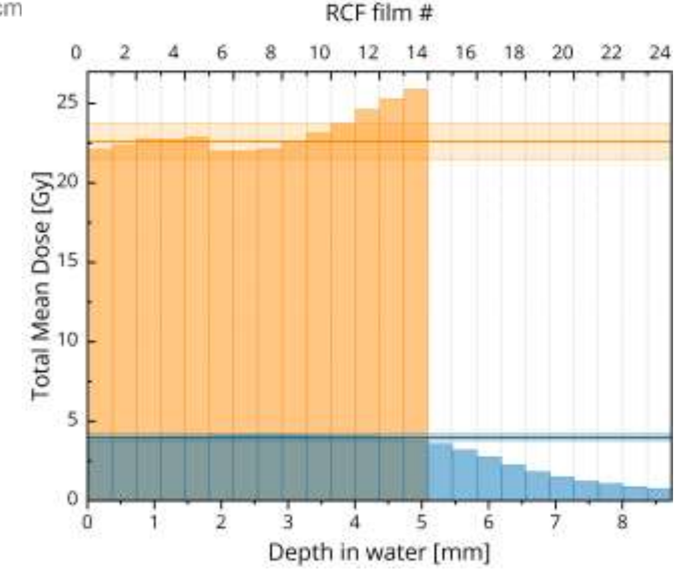


pulsed solenoid lense
(actively air cooled,
few pulses / min)

First in-vivo proton irradiation study



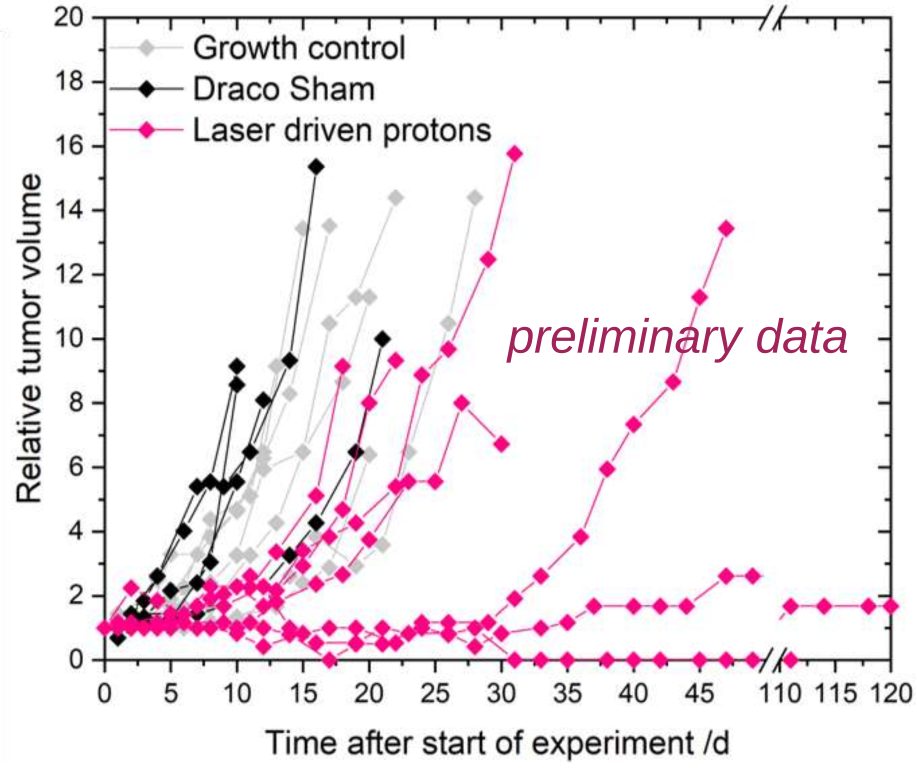
transfering intense poly-chromatic proton pulse into flat and laterally homogeneous depth-dose



Two modes of operation:

- Controlled dose at highest precision (mouse experiment, accumulated shots)
- Maximum dose rate (up to 25 Gy/shot) enabling FLASH irradiation studies (zebra fish experiment)

First in-vivo proton irradiation study with laser accelerated protons

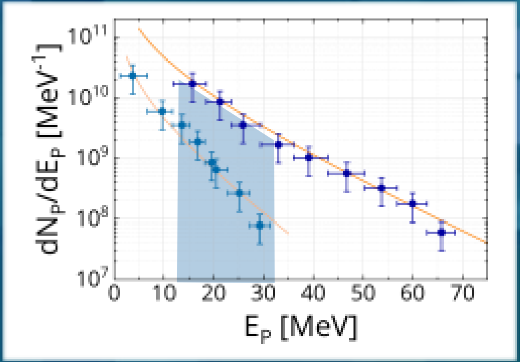


- Full-scale pilot study in a small animal model with a laser proton beam
- Radiation induced (4 Gy) effect observed
- In total 47 mice at HZDR (Draco 4 Gy | Draco 0 Gy | X-ray 4 Gy | X-ray 0 Gy | Controll) + same number for reference at clinical beam
- Long-term survival unexpected, yet requiring higher statistics …

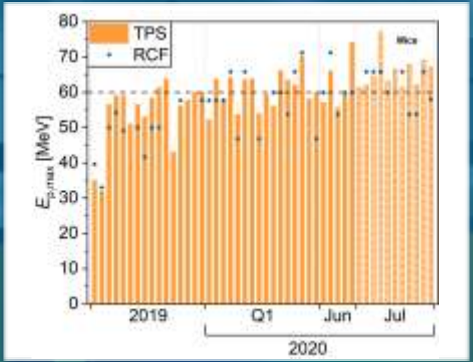
F. Kroll, E. Beyreuther, et al., on arxive soon

High dose-rate in-vivo proton irradiation at DRACO-PW pilot study demonstrates system readiness

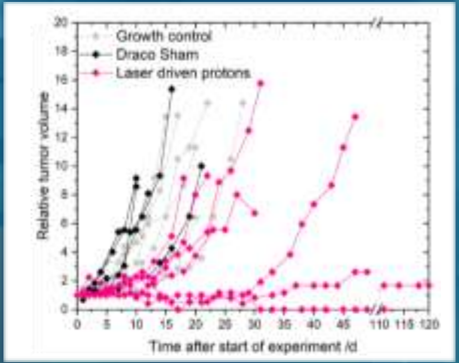
- energy to penetrate volume



- stability



- model – growth delay



- beam transport, energy selective shaping, monitoring, online and absolute dosimetry
- capability to handle ~100 mice with reference irradiation (x-ray, proton)
- FLASH performance demonstrated and Zebra-fish studies ongoing

HZDR

- **K. Zeil**, **J. Metzkes-Ng**, C. Bernert, F. Brack, S. Kraft, **F. Kroll**, L. Obst-Huebl, M. Rehwald, M. Reimold, H.P. Schlenvoigt, T. Ziegler, et al.
- **A. Irman**, J. Couperus, J. Krämer, A. Köhler, T. Kurz, S. Schöbel, O. Zarini, et al.,
- **T. Kluge**, **A. Debus**, M. Bussmann,R. Pausch, K. Steiniger, A. Hübl, M. Garten, et al.
- **J. Pawelke, E. Beyreuther, L. Karsch, M. Krause, et al.,**
- M. Siebold, D. Albach, S. Bock, R. Gebhardt, U. Helbig, M. Löser, T. Püschel, et al.

- U. Schramm, T. Cowan, R. Sauerbrey

KPSI

WEIZMANN INSTITUTE OF SCIENCE

European XFEL

SLAC