RADIOTHERAPY WITH LASER-DRIVEN PARTICLE BEAMS

SZÉCHENYI 2020

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OncoRay – National Center for Radiation Research in Oncology, Dresden

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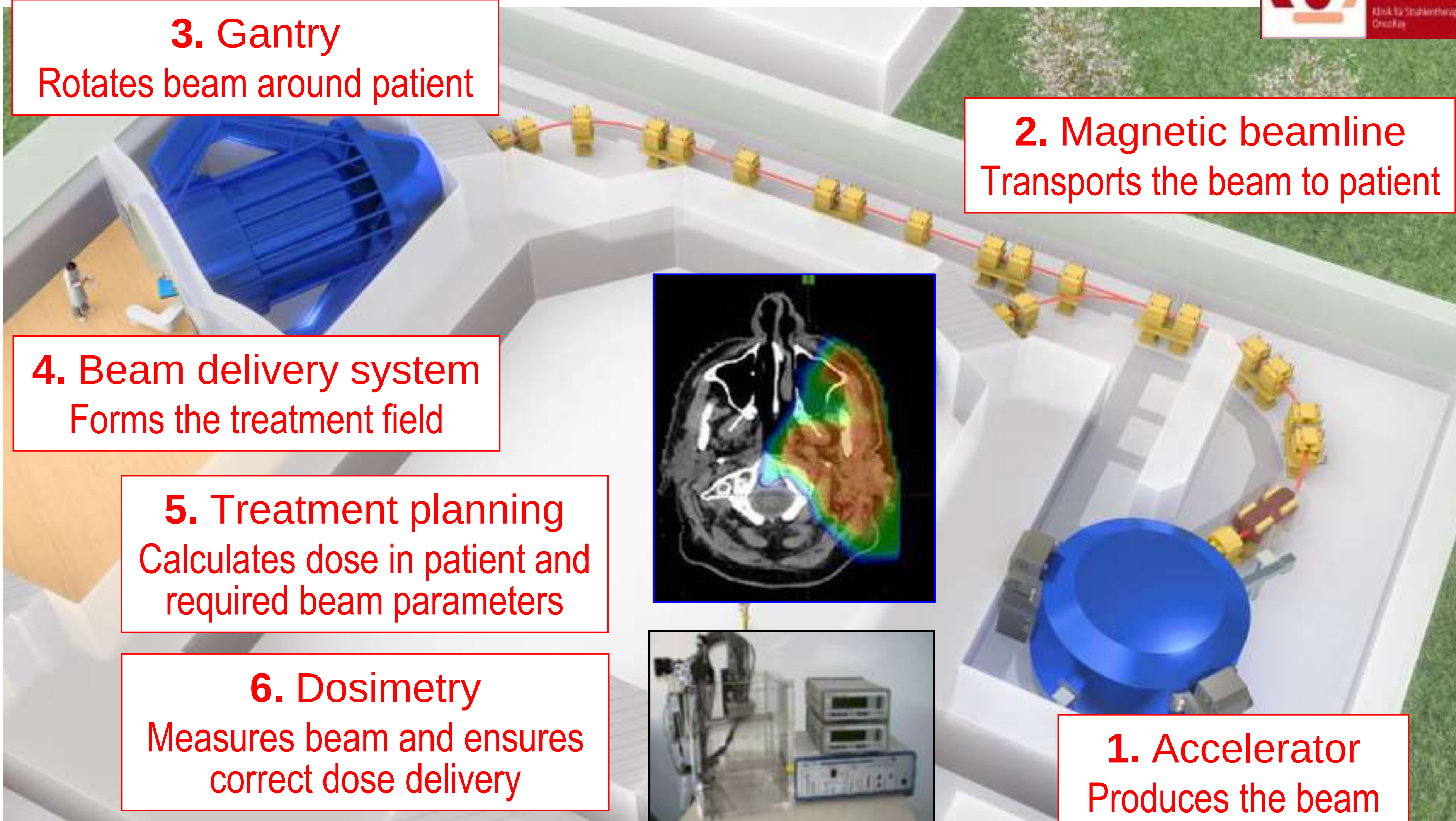
Radiation therapy

External beam therapy (teletherapy) components



3. Gantry
Rotates beam around patient

2. Magnetic beamline
Transports the beam to patient

4. Beam delivery system
Forms the treatment field

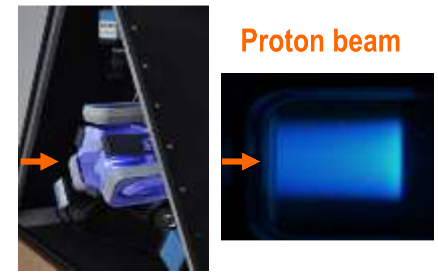
5. Treatment planning
Calculates dose in patient and required beam parameters

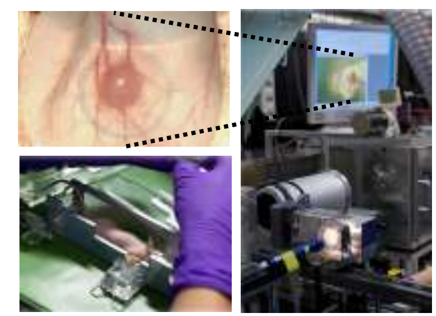
6. Dosimetry
Measures beam and ensures correct dose delivery

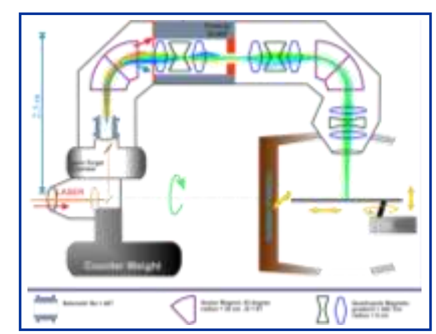
1. Accelerator
Produces the beam

Outline

1. Motivation
2. Laser particle acceleration
3. Research project onCOOPtics
4. Cell and small animal irradiation
5. Towards preclinical prototype
6. Summary

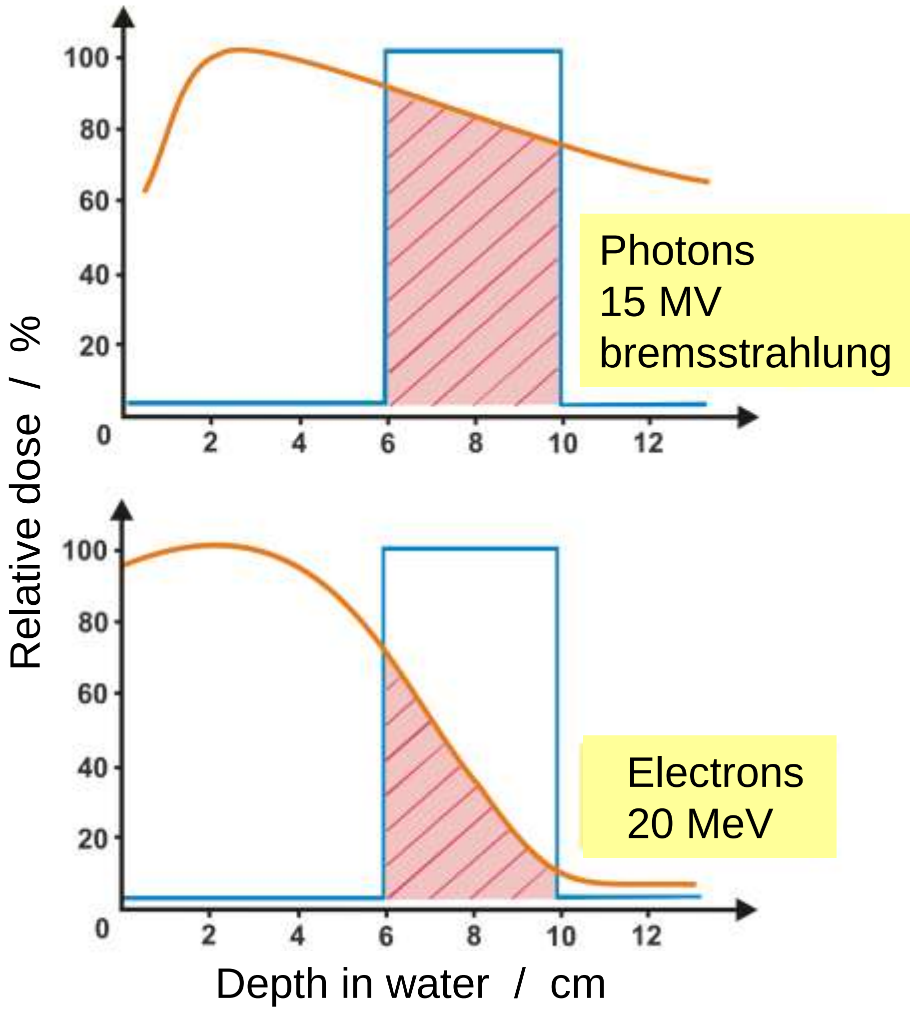


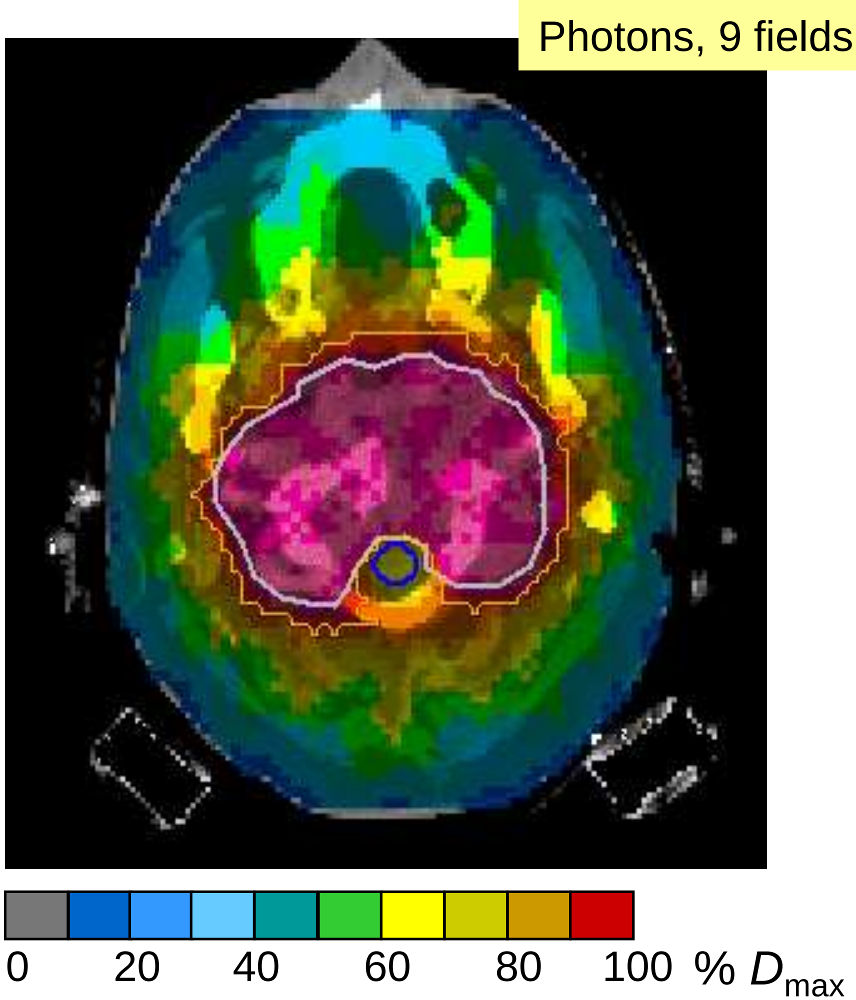




1. Motivation

"Conventional" therapy radiation

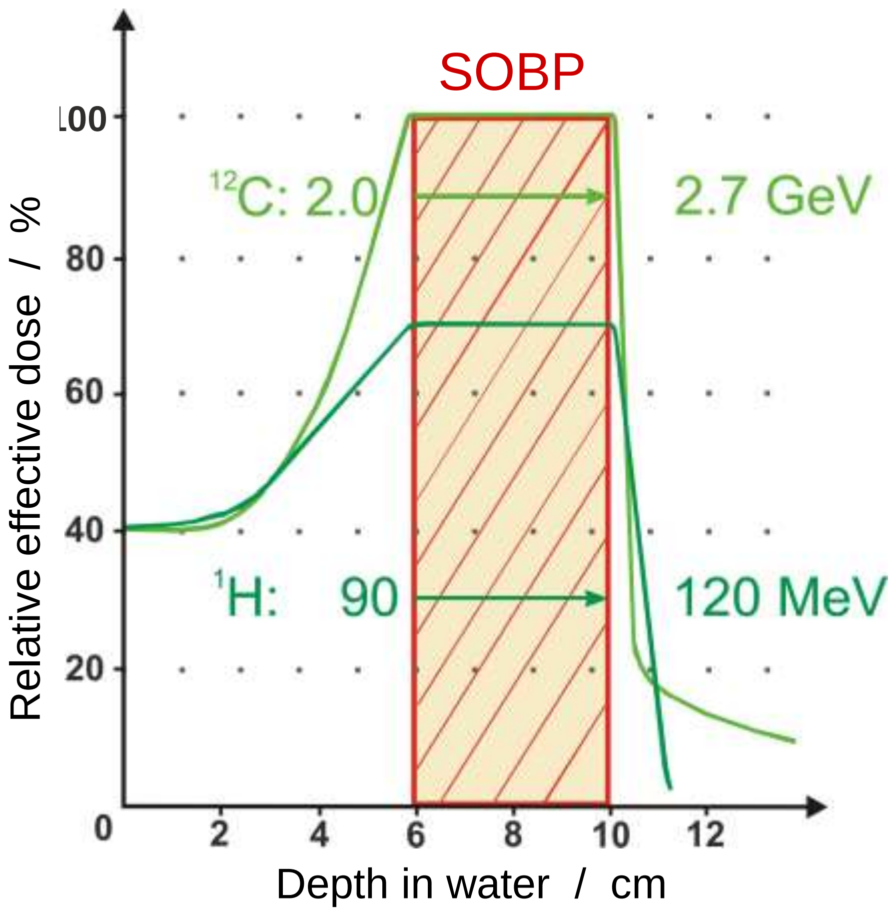


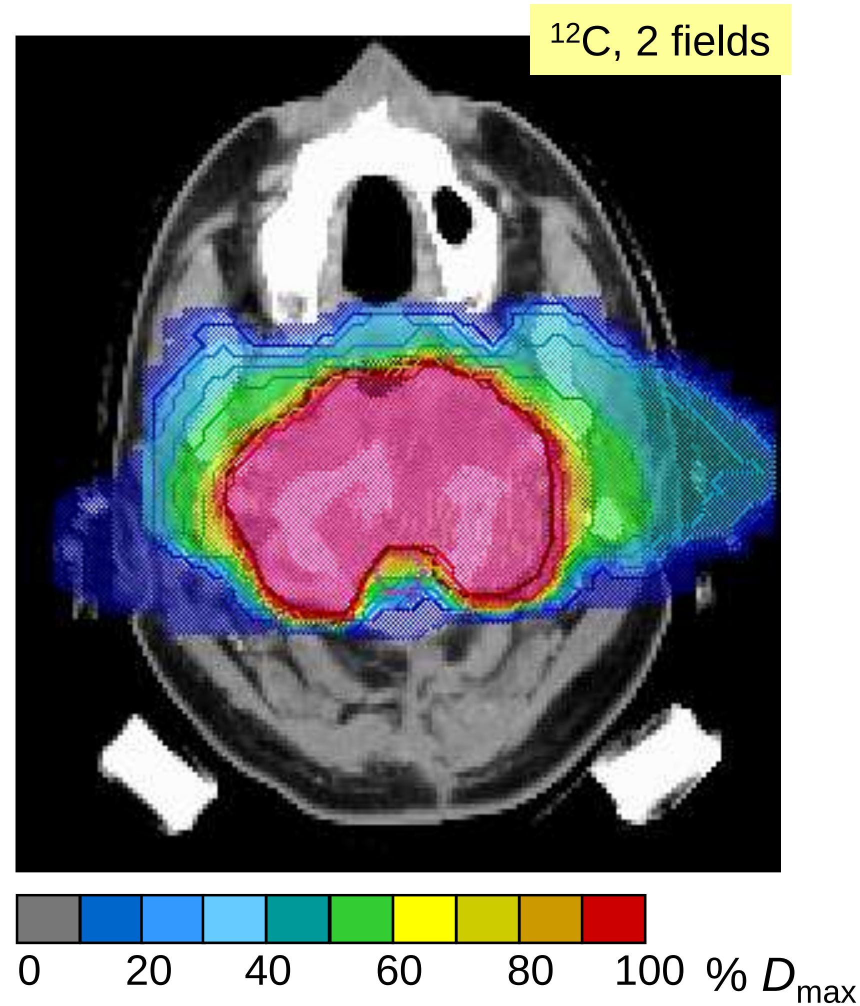


Courtesy Prof. O. Jäkel, DKFZ Heidelberg

1. Motivation

Heavy charged particles
(Ions: ^{1}H ... ^{12}C ... ^{20}Ne)





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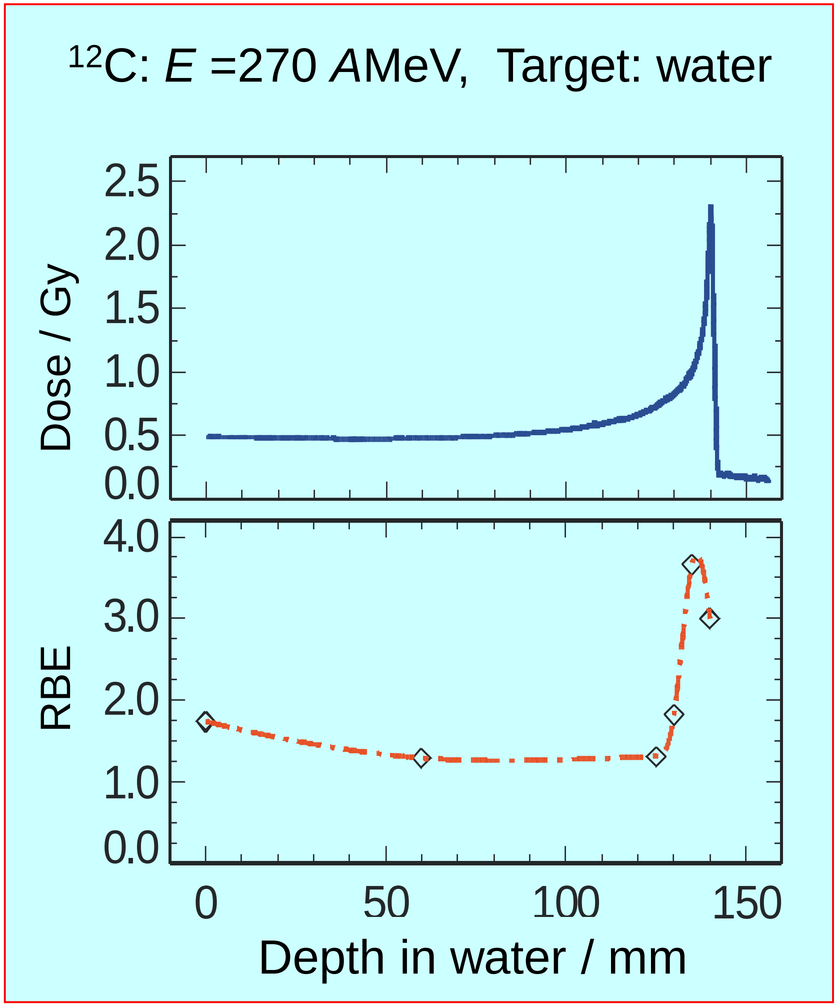
Heavy charged particles (Ions: ^{1}H ... ^{12}C ... ^{20}Ne)



Courtesy W. Kraft-Weyrather, GSI Darmstadt

Advantages of ion beams versus „conventional“ therapy radiation species (electrons and photons):

- Well defined range by beam energy
- Dose growing with depth until the maximum particle range (“inverted depth dose distribution”)
- Elevated RBE in the Bragg-maximum for ions with Z > 2

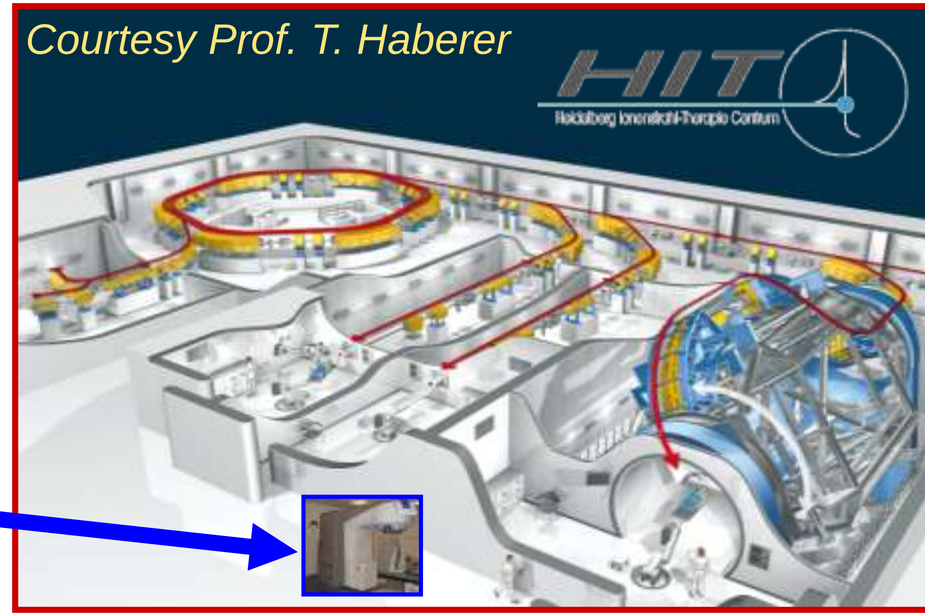
Indications for ion therapy:

- Compact, deep-seated and radiation resistant tumors
- In the vicinity of organs at risk

1. Motivation

Electron LINAC
(20 MeV e^-, 20 MV photons)

Ion Beam Therapy Facility
(430 MeV/Nucleon ^{12}C, synchrotron)



Components: source, accelerator, beamline, gantry

Electron LINAC		Ion Beam Therapy Facility
~ 10 Mill. €	*Investment costs*	~ 100 Mill. €
~ 550 only Germany	*Number of installations*	~50 worldwide

1. Motivation

Electron LINAC

(20 MeV e$^-$, 20 MV photons)

Components: source, acceler

~ 10 Mill. € *Investme*

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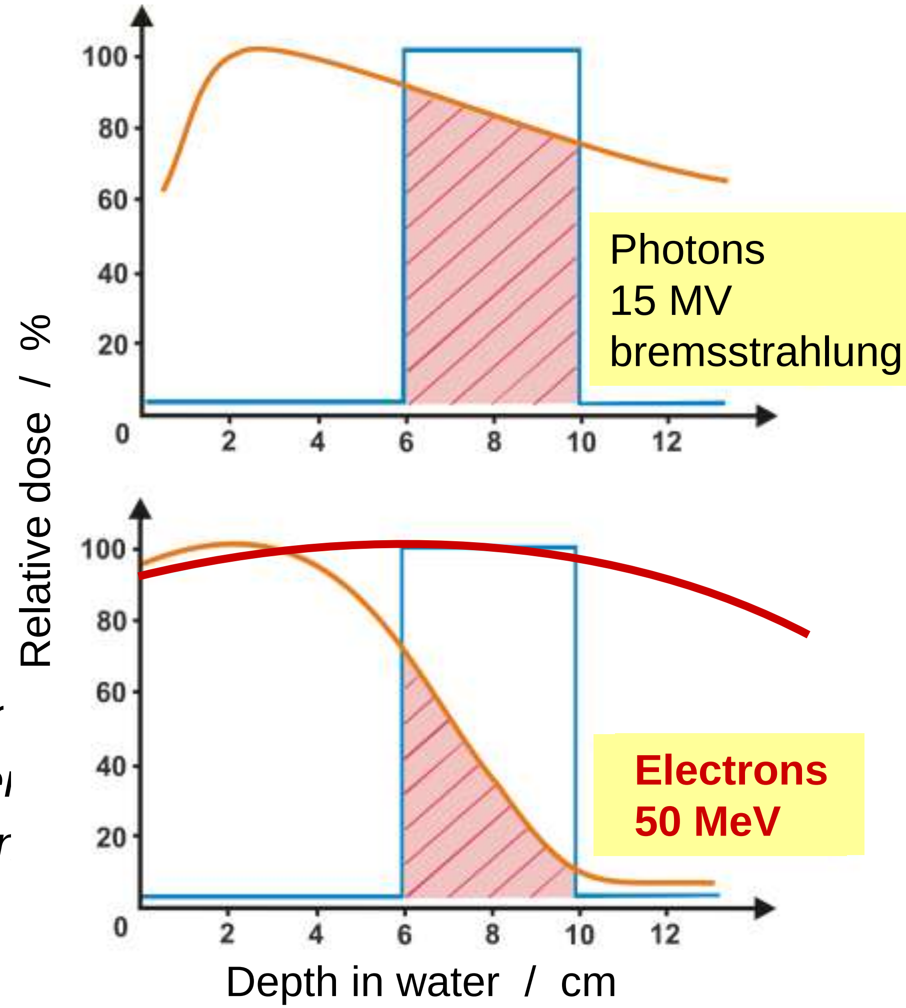
⇨ *Improve dose by very high energy electrons (~ 100 MeV)*

"Conventional" therapy radiation



1. Motivation

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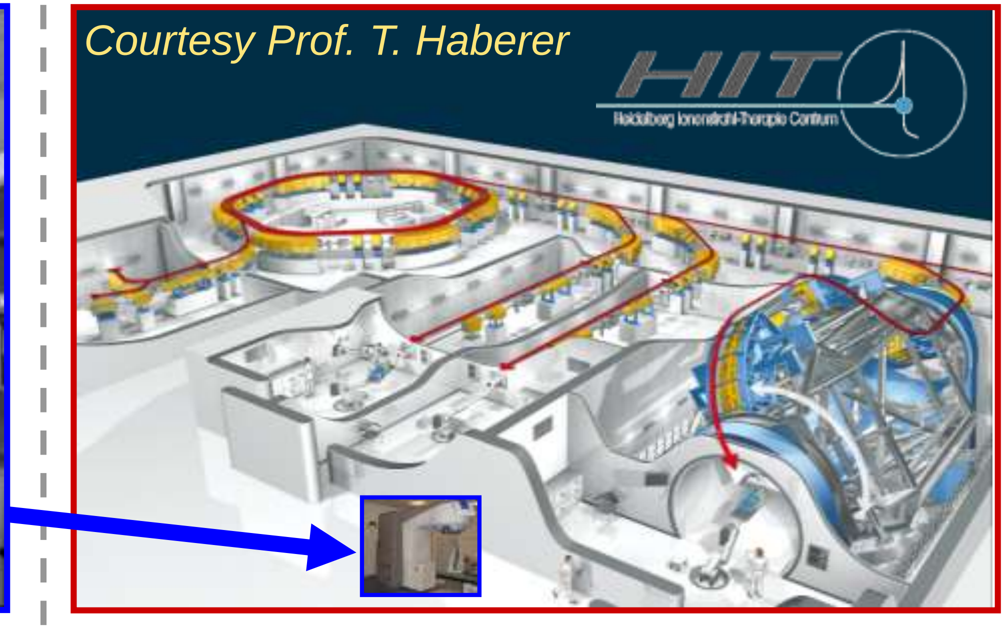
(20 MeV e^-, 20 MV photons)	(430 MeV/Nucleon ^{12}C, synchrotron)



Components: source, accelerator, beamline, gantry

~ 10 Mill. €	*Investment costs*	~ 100 Mill. €
~ 550 only Germany	*Number of installations*	~50 worldwide

⇨ *Improve dose by very high energy electrons (~ 100 MeV)*

⇨ *More compact and cost effective facilities*

1. Motivation

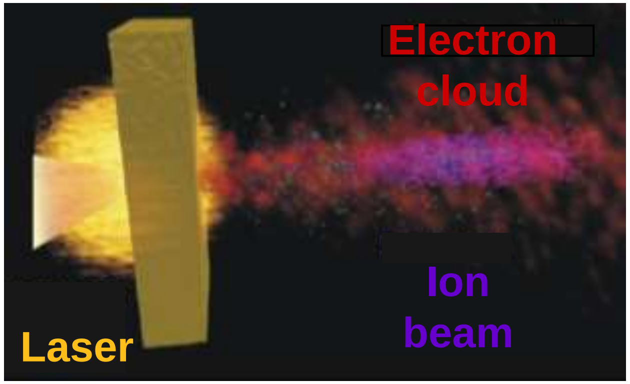
Main focus on:

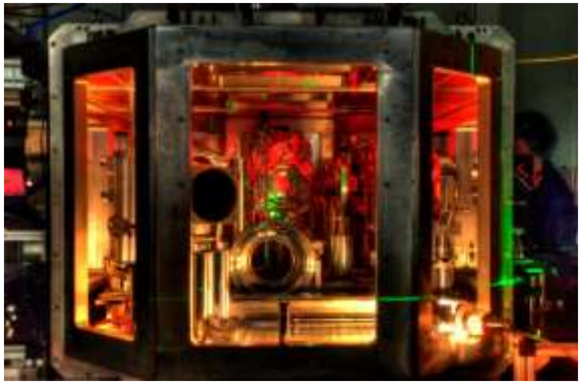
Development of

compact ion therapy facility
based on high-intensity laser

by reducing

- therapy accelerator
- beam transport line and gantry by using
  - ➩ *optical beamline (mirrors) for laser light*
  - ➩ *pulsed magnets for particle beam*





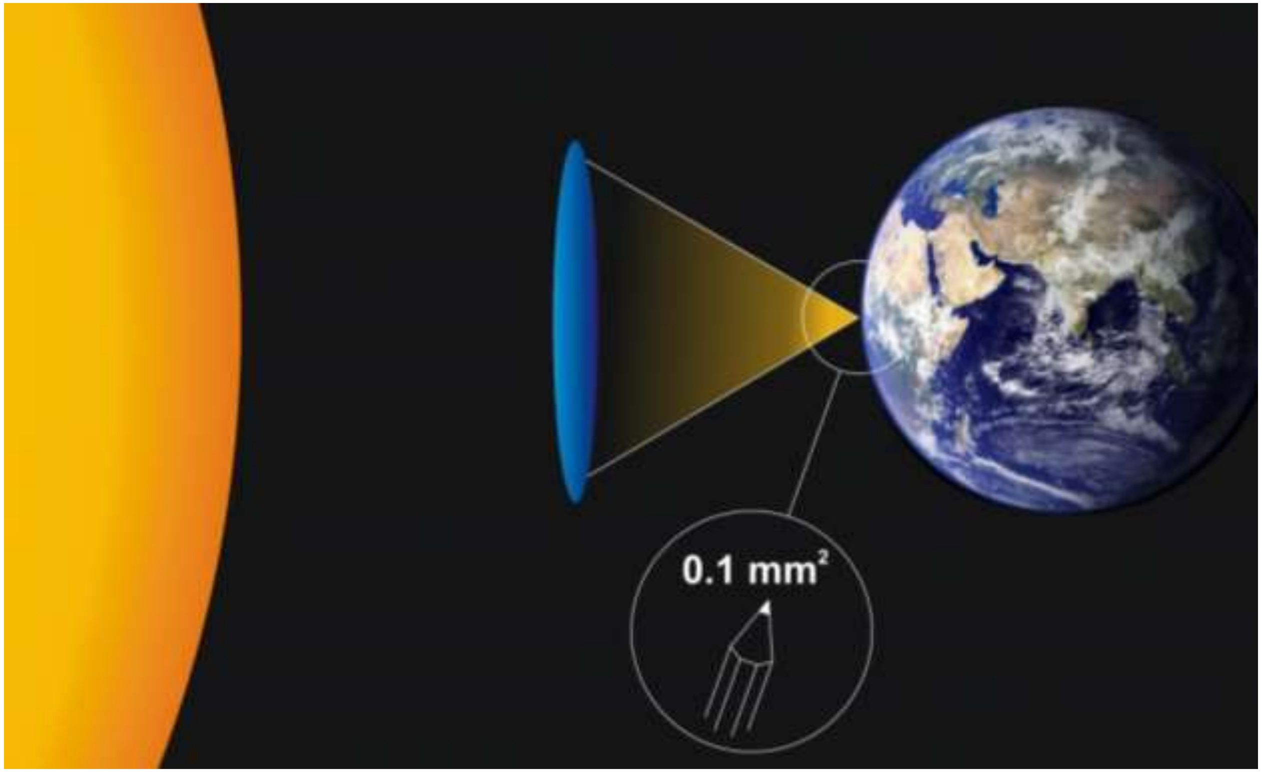
2. Laser particle acceleration

- Ingredients: Light and simple foil

+

2. Laser particle acceleration

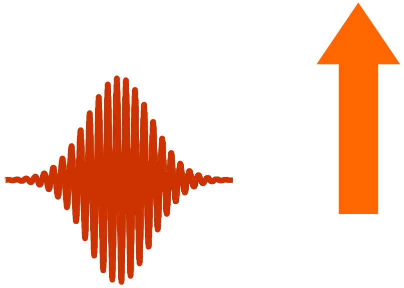
- Light of high intensity: I_{Light} = 10^{20} W/cm²



2. Laser particle acceleration

- Solution: High intensity laser

$I_{Light} = 10^{20}$ W/cm²



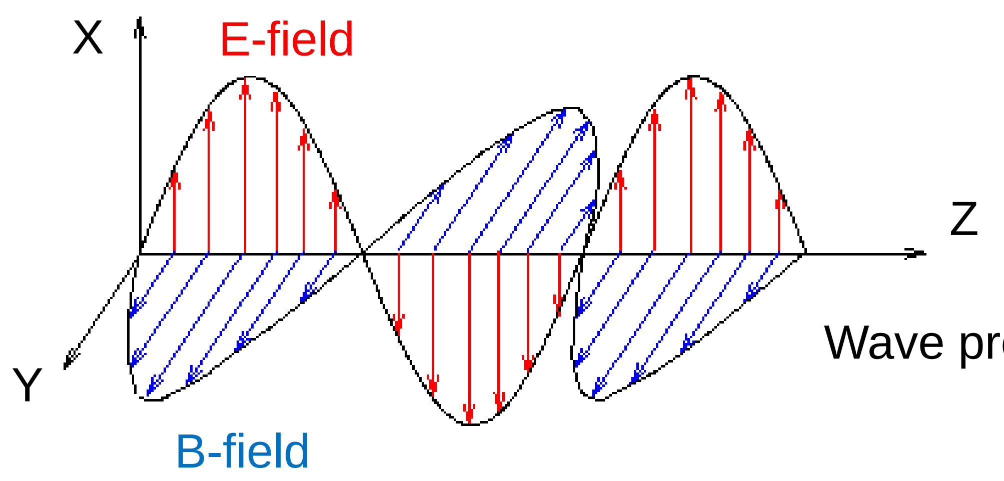
- Focus the laser light
- Very high laser power
- Moderate laser energy, but ultra-short pulse duration

- *10 μm focal spot size*
- *100 TW power*
- *3 J energy*
  30 fs pulse duration

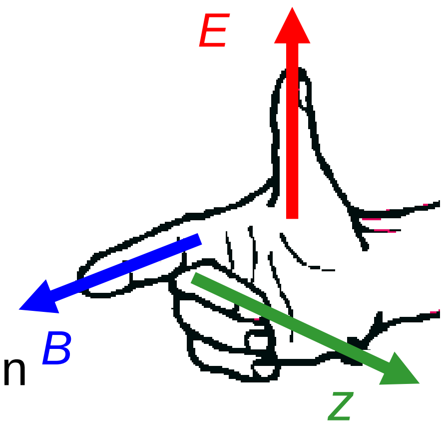
Power: 1 PW = 1000 TW (1 TW = 10^{12} W), Pulse duration: 1 fs = 10^{-15} s

2. Laser particle acceleration

- Light is an electromagnetic wave: $\vec{F}_L = e(\vec{E} + \vec{v} \times \vec{B})$



Wave propagation

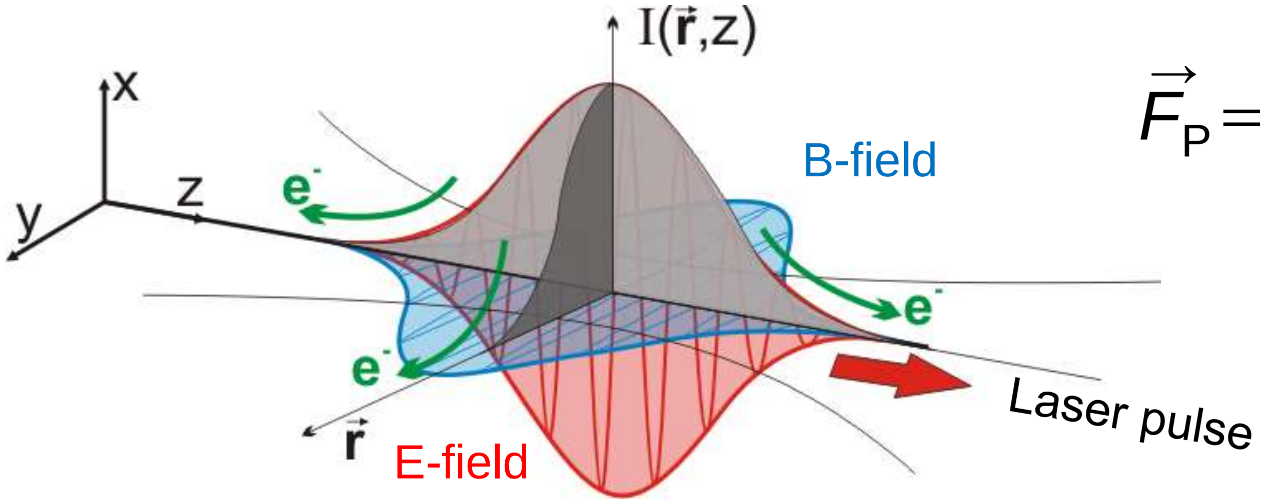


- Low light intensity: Coulomb component dominates
- Higher intensity: Electron acceleration and contribution by magnetic component
- I_{Light} ~ 10^{18} W/cm^2: Electron already reach relativistic energy (v_e ~ c) within half a laser period

Light pulse: wave length ~ 850 nm → frequency ~ $0.3 \cdot 10^{15}$ Hz (= 300 THz)

2. Laser particle acceleration

- Ponderomotive acceleration by intensity gradient:



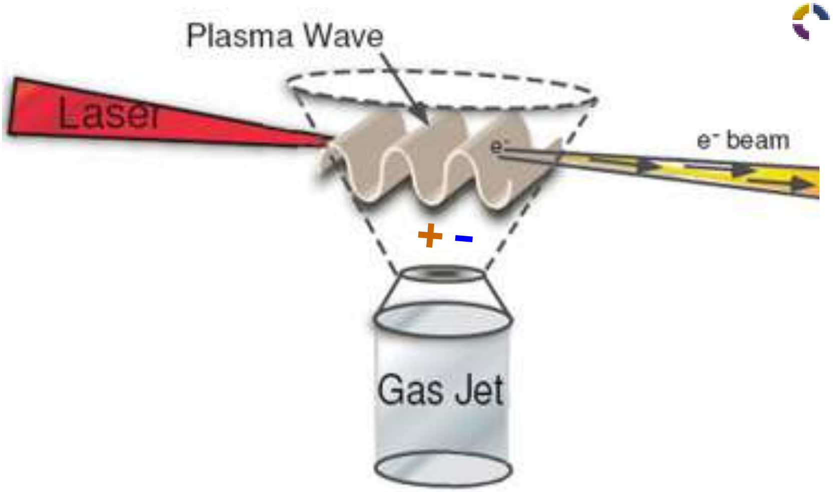
$$\vec{F}_P = -\frac{e^2}{4m\varpi^2}\nabla E^2$$

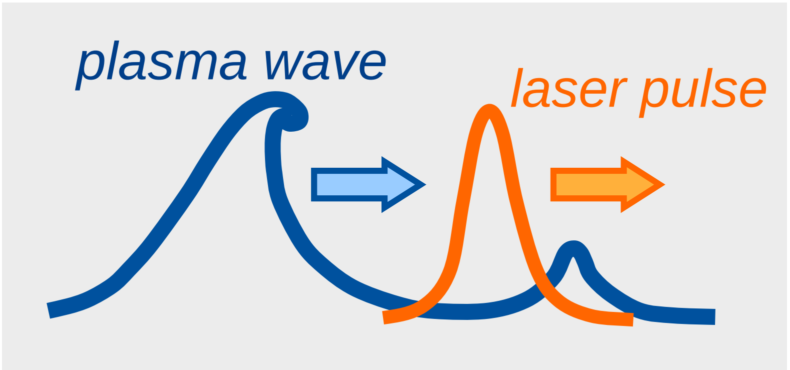
- I_{Light} ~ 10^{24} W/cm² for direct proton acceleration ($m_p = 1000 \cdot m_e$)

⇨ ***For acceleration of a beam pulse (very many particles), collective effect is necessary!***

Light pulse: duration ~ 30 fs → length ~ 9 mm

2. Laser electron acceleration

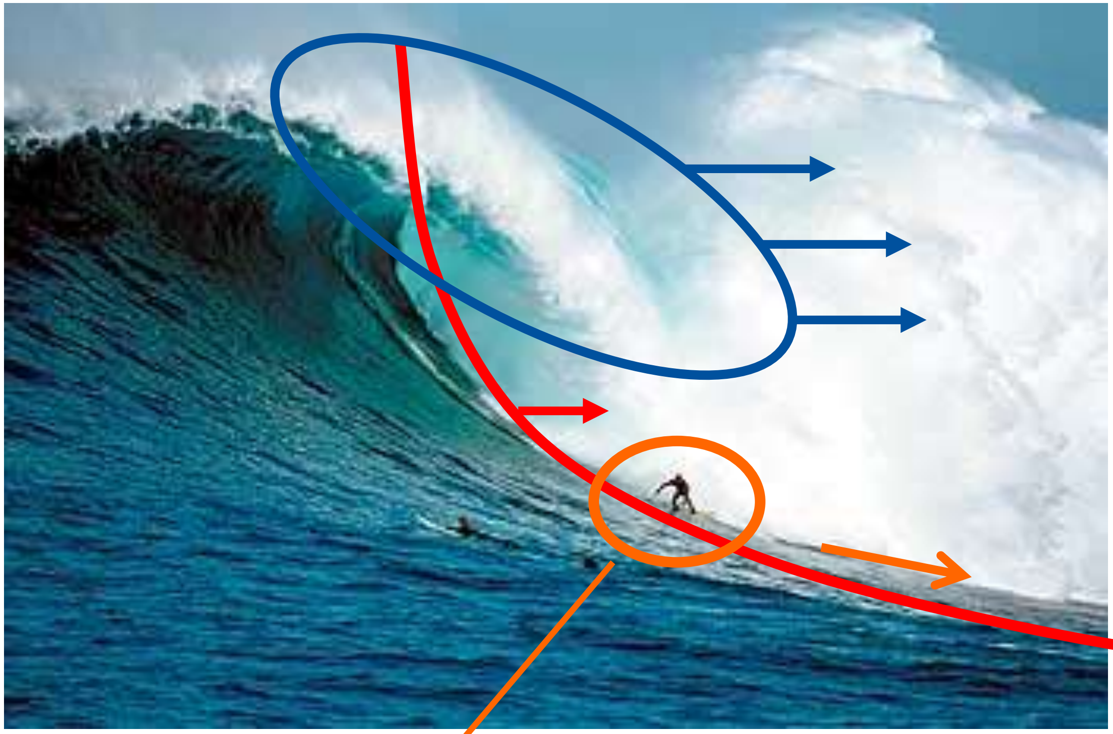


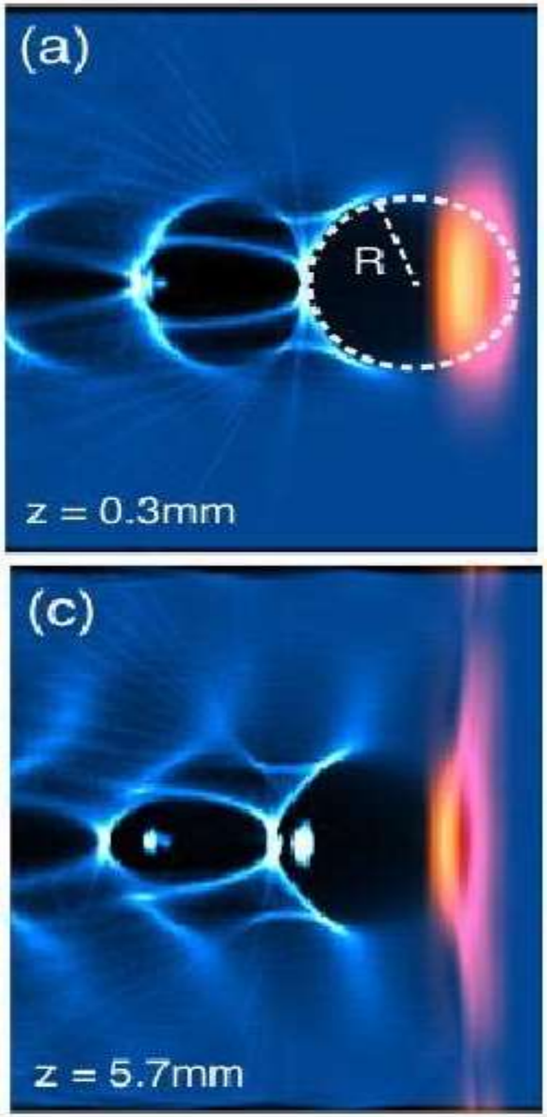


- Laser wakefield acceleration (LWFA):
  - Laser pulse generates an electron density modulation: plasma wave
  - Support gradients of GeV/cm for $5x10^{18}$ e/cm^3

2. Laser electron acceleration

- Non-linear wave-breaking (self-injection) $v > v_{ph}$





- Test particle (external injection) $v_e > v_{ph}$

2. Laser electron acceleration

… effective, but rather hard to control

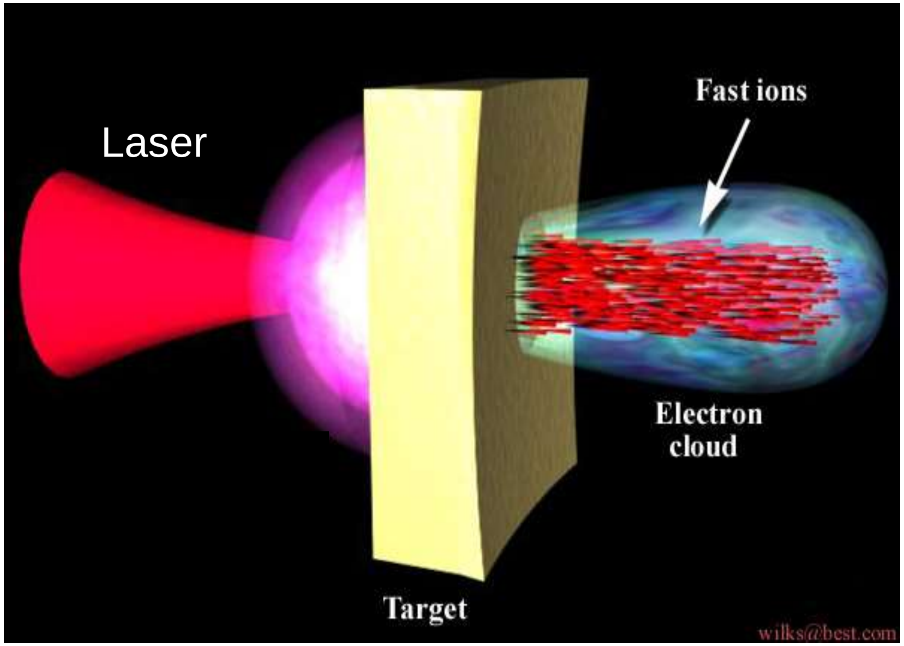
and normally destructing the accelerating wave (or wake)

2. Laser ion acceleration

- Ions to heavy for direct acceleration

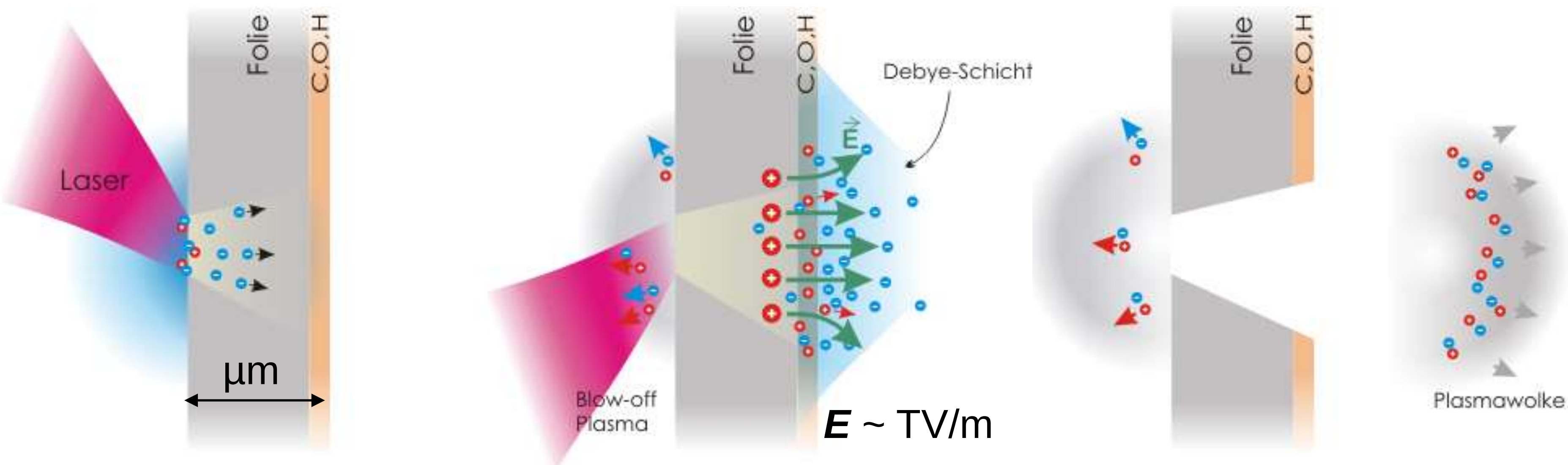
  ⇨ *quasi-static fields required*

  ⇨ *overdense plasmas (solid density, opaque)*



2. Laser ion acceleration

- Target Normal Sheath Acceleration (TNSA)



The laser light:

- **is absorbed and creates a plasma in the foil**
- **accelerates electrons**

fs - time scale

The electrons:

- **propagate through the foil and form Debye sheath**
- **build up a quasi-static electric field**

The electric field:

- **ionizes the rear surface and accelerates the ions**
- **expanse plasma into vacuum**

ps - time scale

2. Laser particle acceleration

Laser target:

$I_{Light} \geq 10^{18}$ W/cm^2

Interaction with matter

Gas (high density) — *transparent* ⟷ *opaque* — **Solid (foil)**

LWFA — **Electron acceleration**

TNSA — **Ion acceleration**

$m_{Electron} \ll m_{Ion}$

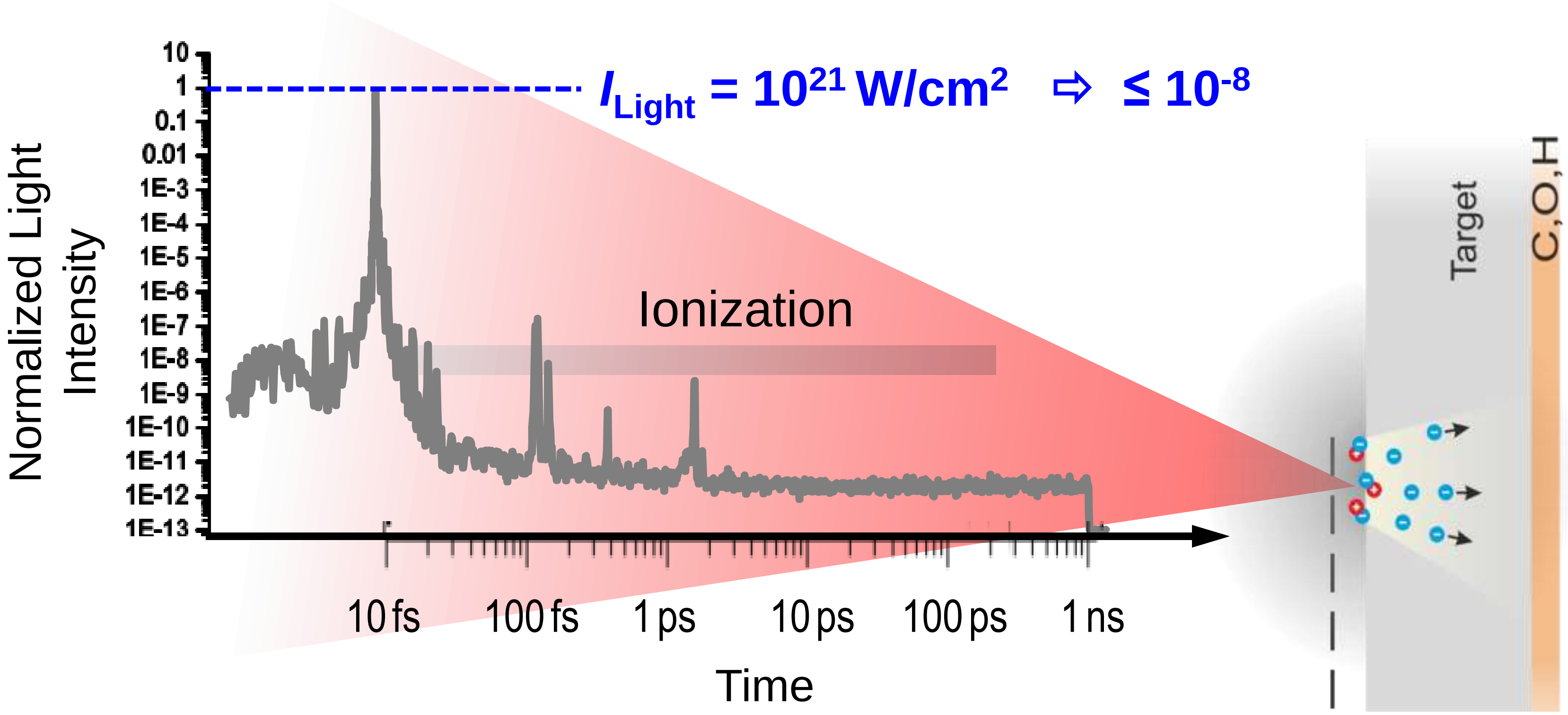
2. Laser particle acceleration

Laser system characteristics:

- Pulse duration
  - ultra-short pulse (~ 1 fs … ~ 100 fs)
  - short pulse (~ 100 fs … ~ ps)
  - long pulse (~ ns)
- Energy per pulse (laser peak power)
  - ~ J   (~ Terawatt)
  - ~ kJ … ~ MJ (~ 1 Petawatt)
- Pulse repetition rate
  - > Hz
  - few shots per day / hour
- Temporal pulse contrast
  - $\leq 10^{-6}$ (ionization threshold: 10^{13} W/cm^2, no preplasma)

Amplifier chain of the SHIVA laser at LLNL, late 1970's (Nd:Glass 10 kJ, 1 ns)

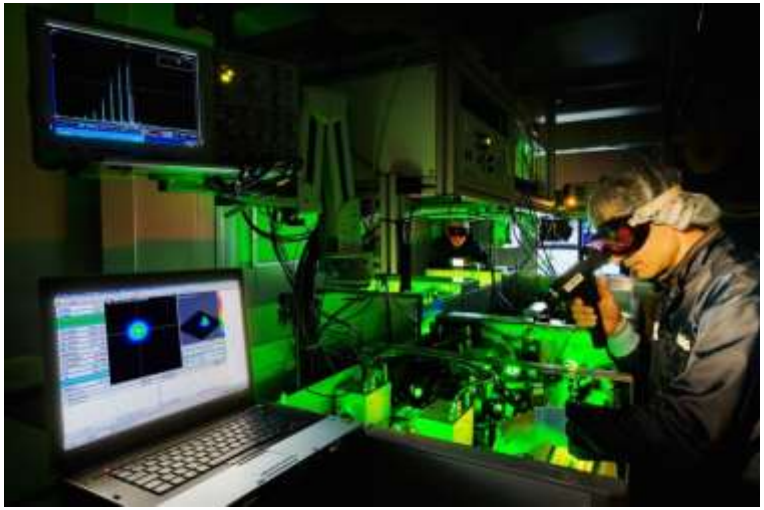
Laser system characteristics:



- **Temporal pulse contrast**
  - ≤ 10^{-6} (ionization threshold: 10^{13} W/cm², no preplasma)

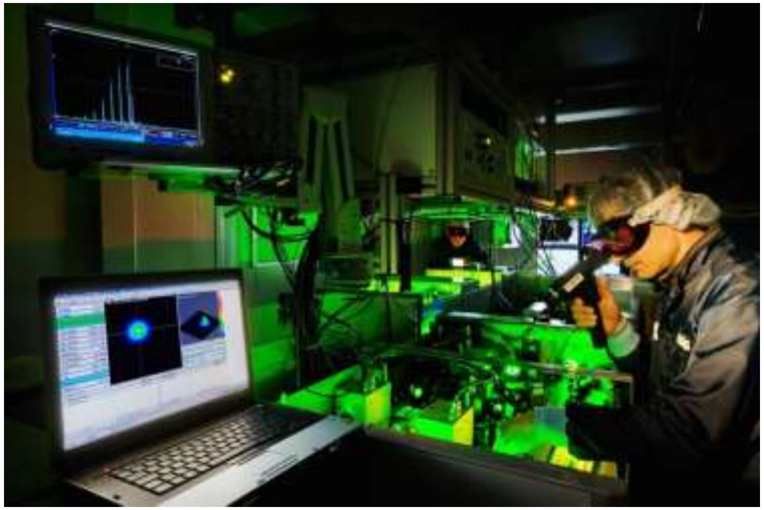
Laser system for electron therapy:

- Pulse duration
  - **ultra-short pulse (~ 1 fs … ~ 100 fs)**
  - short pulse (~ 100 fs … ~ ps)
  - long pulse (~ ns)
- Energy per pulse (laser peak power)
  - **~ J (~ 10 Terawatt)**
  - ~ kJ … ~ MJ (~ 1 Petawatt)
- Pulse repetition rate
  - **> Hz**
  - few shots per day / hour
- Temporal pulse contrast
  - **~ 10^{-6}** (ionization threshold: $10^{12 \ldots 13}$ W/cm^2, no preplasma)



Laser system for ion therapy:

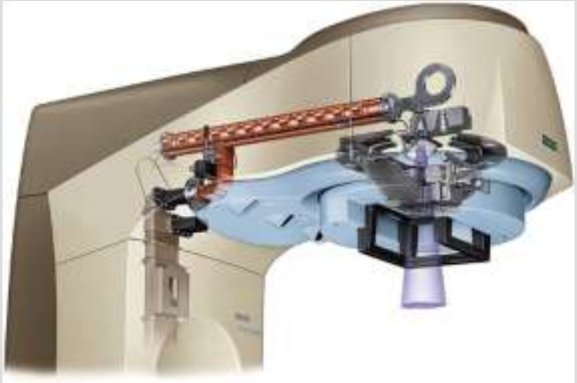
- Pulse duration
  - ultra-short pulse (~ 1 fs … ~ 100 fs)
  - **short pulse (~ 100 fs … ~ ps)**
  - long pulse (~ ns)
- Energy per pulse (laser peak power)
  - ~ J (~ Terawatt)
  - **~ kJ … ~ MJ (~ 1 Petawatt)**
- Pulse repetition rate
  - **> Hz**
  - few shots per day / hour
- Temporal pulse contrast
  - **≤ 10^{-8}** (ionization threshold: $10^{12 \dots 13}$ W/cm^2, no preplasma)



2. Laser particle acceleration

Conventional therapy accelerators:

Electron LINAC	Proton Cyclotron	Carbon Synchrotron
20 MeV e^-	230 MeV p	430 MeV/Nucleon ^{12}C



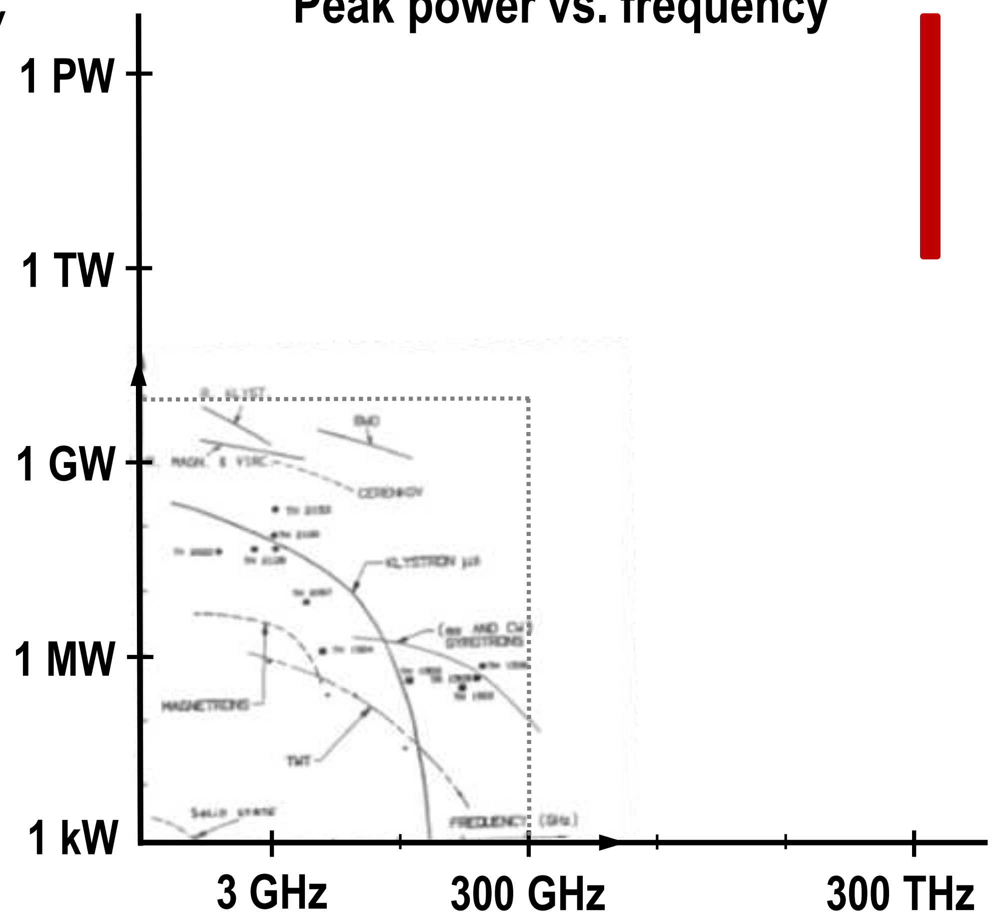
20 MV/m	1 MV/m	0,01 MV/m

Laser Particle Accelerator: 1.000.000 MV/m
(⇨ 1000 MeV at 1 mm)

Rational of light as power source for accelerators:

- Increasing the driver frequency has been key in accelerator development
- Offering large peak power and frequency, **laser pulses** represent the natural extent of this strategy
- Plasma is one promising medium for converting laser energy in **ion kinetic energy over short distance / time**
    - Compactification
    - Particle bunch properties

Peak power vs. frequency



R.G. Carter: http://cds.cern.ch/record/865919/files/p107.pdf

2. Laser particle acceleration

Conventional therapy accelerators:

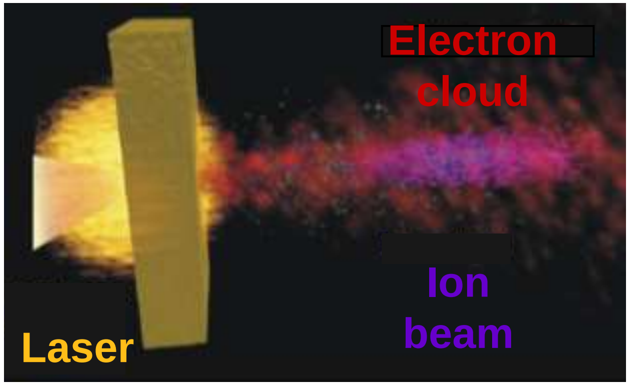
Electron LINAC	Proton Cyclotron	Carbon Synchrotron
20 MeV e^-	230 MeV p	430 MeV/Nucleon ^{12}C

20 MV/m	1 MV/m	0,01 MV/m

- Deliver monoenergetic, pencil-like, (quasi) continuous particle beams

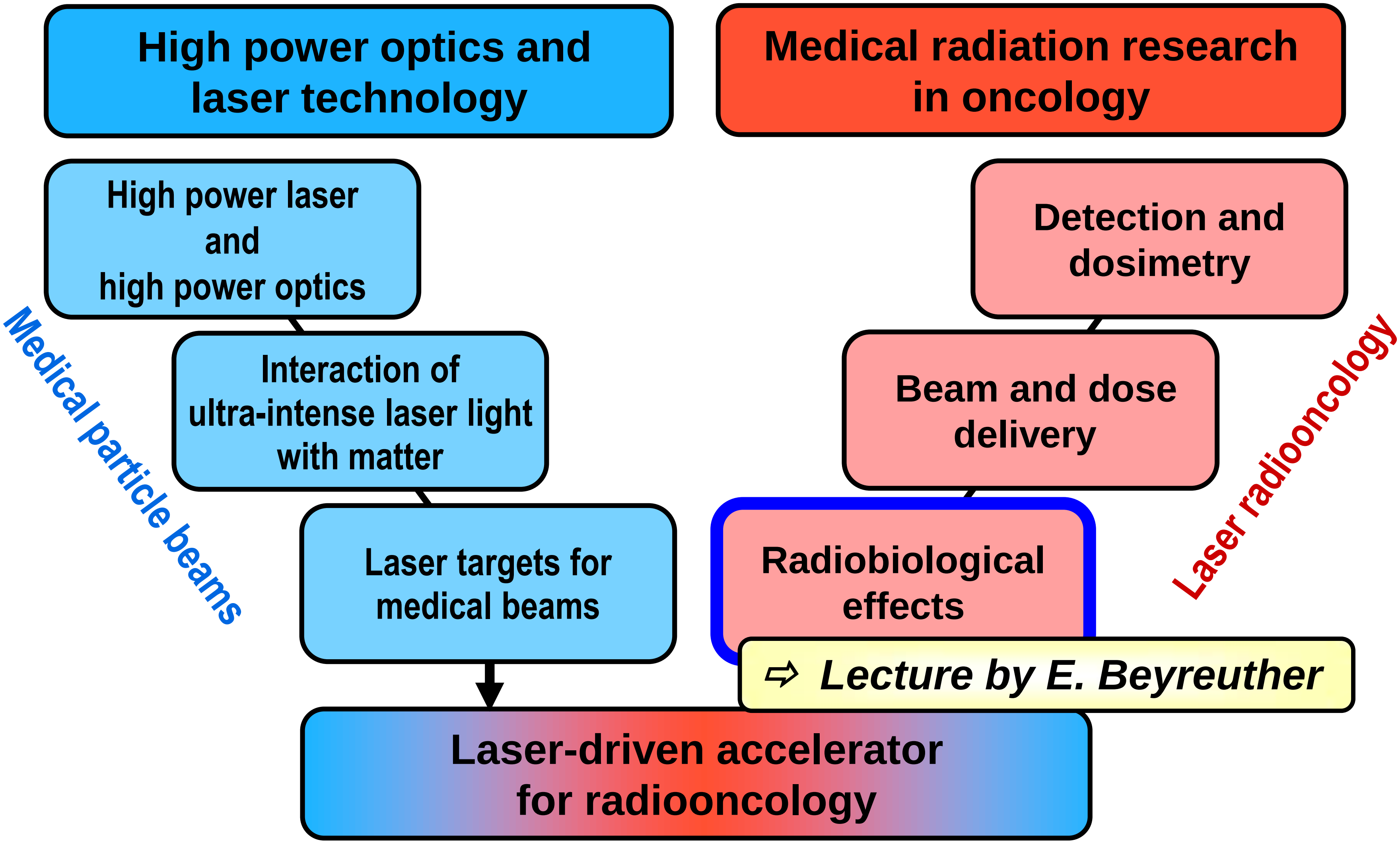
Specific properties of laser-accelerated particle beams compared to conventional accelerator beams:

- Ultra-short beam pulses (~ 1 ps)
- Low pulse repetition rate (~ 10 Hz)
- High single pulse dose (~ 1 Gy) and ultra-high pulse dose rate (> 10^{12} Gy/s)



- Broad energy spectrum
- Large beam divergence (~ 10 degrees)
- Contaminated beams (e^-, γ, X, other ions, n)
- Instable beams due to non-linear acceleration process

2. Laser particle acceleration



2. Laser particle acceleration

History:

- 1979: First theoretical description (electrons)
  T. Tajima and J.H. Dawson: Laser electron accelerator. Physical Review Letters 43, 267-270
- 1985: Introduction of chirped pulse amplification (CPA) and generation of high-intensity laser pulses
  D. Strickland & G. Mourou: Optics Communications 56 (1985) 219-221
  P. Maine et al.: IEEE Journal of Quantum Electronics 24 (1988) 398-403
- Since 2000:
  - Tremendous progress in experimental generation of intense electron and proton/ion pulses (single-pulse experiments!)
  - Proposal for medical application (based on theoretical study and simulation!)

  ⇨ ***Main focus on laser-driven ion therapy***

2. Laser particle acceleration

History:

- Since 2005: Establishment of national research network consortia
  - USA: FCCC (**F**ox **C**hase **C**ancer **C**enter) ✗
  - Japan: PMRC (**P**hoto-**M**edical **R**esearch **C**enter) ✗
  - France: SAPHIR **(S**ource **A**ccéléreé de **P**rotons par laser de **H**aute **I**ntensité pour la Radiologie) ✓
  - UK: LIBRA (**L**aser **I**nduced **B**eams of **R**adiation and their **A**pplication) ✓
  - Germany: MAP (**M**unich-centre for **A**dvanced **P**hotonics) ✓
  - Germany: onCOOPtics (OncoRay + ultra optics) ✓
  - Italy: PROMETHEUS (**PRO**tons, ions and coherent x-rays facility based on high power laser for **ME**dical research, oncological **THE**rapy, bio-imaging and radiobiological **US**es) ?
  - Europe (Czech Republic / Hungary): ELI-MED / ELI-ALPS ✓

3. Research project onCOOPtics

LAMELIS | OncoRay






oncooptics

TECHNISCHE UNIVERSITÄT DRESDEN

University Hospital Carl Gustav Carus Dresden

HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

OncoRay
National Center for Radiation Research in Oncology Dresden

+

ultra optics

IOQ Jena

Friedrich Schiller University of Jena

Fraunhofer Institute for Applied Optics and Precision Engineering
IOF

Supported by Bundesministerium für Bildung und Forschung

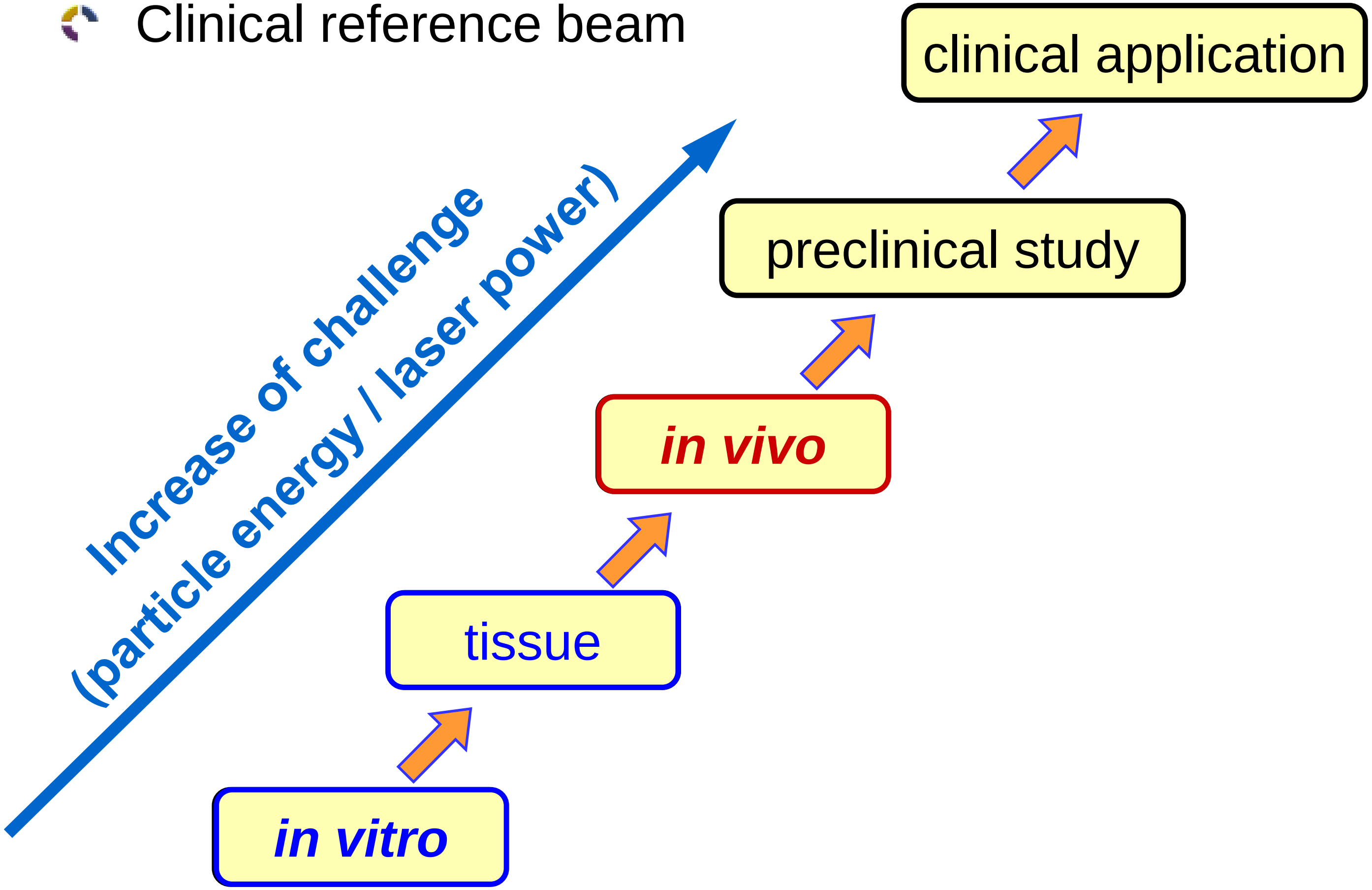
2007-2012, 11.5 Mill. €
(grant no. 03ZIK445)

2012-2017, 6.7 Mill. €
(grant no. 03Z1N511)

3. Research project onCOOPtics

Implementation of new technology:

- Translation research
- Clinical reference beam



3. Research project onCOOPtics

Precondition: Sufficiently intense laser system

- Stable and reliable operation with reproducible beam properties
- From laser-accelerated electrons …
  … to laser-accelerated proton beams

Available laser systems:

- 2007: **10 TW laser** JETI (10 Hz, 80 fs, 1 J), Jena
  - **Electron acceleration up to 50 MeV**
  - Proton acceleration up to 2.5 MeV
- 2010: **150 TW laser** DRACO (10 Hz, 25 fs, 4 J), Dresden
  - Commercial system (Amplitude Technologies, France)
  - **Proton acceleration up to 25 MeV**

4. Cell and small animal irradiation

Laser-based irradiation technology:

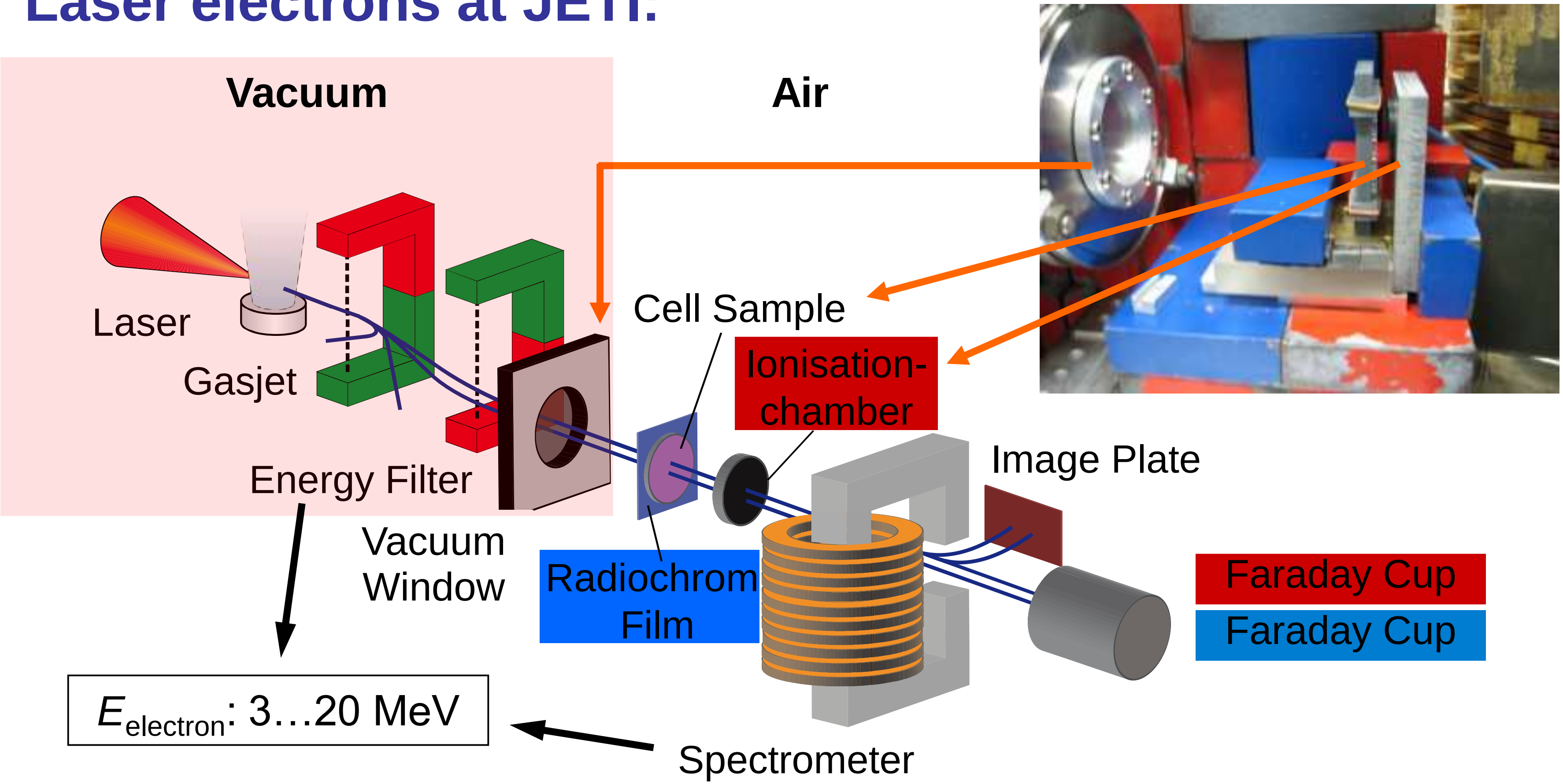
- Established with all necessary key components like
  - Laser accelerator
  - Precise real-time and absolute dosimetry
  - Suitable irradiation field formation including energy selection
  - Simple treatment planning
  - Controlled delivery of prescribed dose
- For laser electrons and laser protons
- Used for systematic radiobiological experiments

Limitation:

- Irradiation at fixed horizontal beams (no rotating gantry)
- Dose delivery to small target volumes (~ cm size)
- Beam transport by conventional (permanent) magnets

4. Cell irradiation

Laser electrons at JETI:

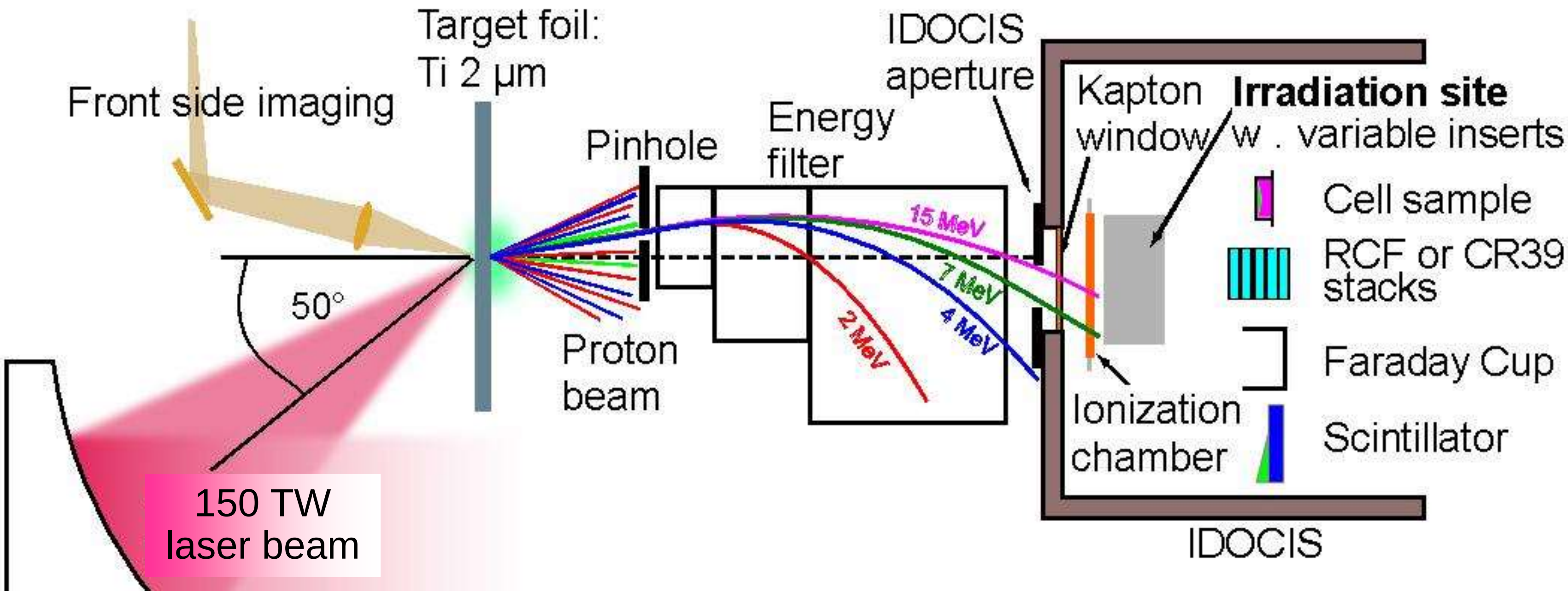


Online dosimeter ⇨ Beam monitoring, irradiation control

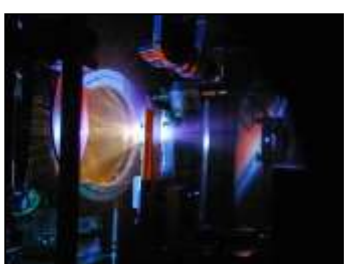
Offline dosimeter ⇨ Absolute dosimetry @ cell monolayer

Laschinsky et al.: Radiother Oncol 92(2009)89, Beyreuther et al.: Med Phys 37(2010)1392, Richter et al.: Radiat Meas 46(2011)2006

Laser protons at DRACO: E_p = 6-18 MeV; f = 0,1 Hz



Kraft et al.: NJP 12 (2010) 085003, Zeil et al.: RSI 81 (2010) 013307 & NJP 12 (2010) 045015, Richter et al.: Med Phys 36 (2009) 5506 & PMB 56 (2011) 1529, Metzkes et al.: NIM A 653 (2011) 172, Zeil et al.: Nature Comm 3 (2012) 874 & Appl Phys B 110 (2013) 437, Karsch et al.: Z Med Phys 21 (2011) 4

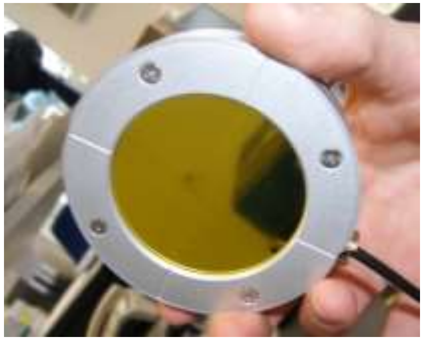




4. Cell irradiation

Proton dosimetry:

Transmission ionization chamber

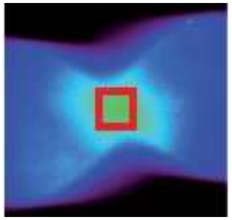


- Relative dose per pulse
- Online

- Dose rate independent absolute dose per pulse
- Online

Faraday cup

- Dose rate independent absolute dose
- Spatial dose distribution
- Retrospective



Radiochromic film

- Energy distribution
- Online

Scintillator

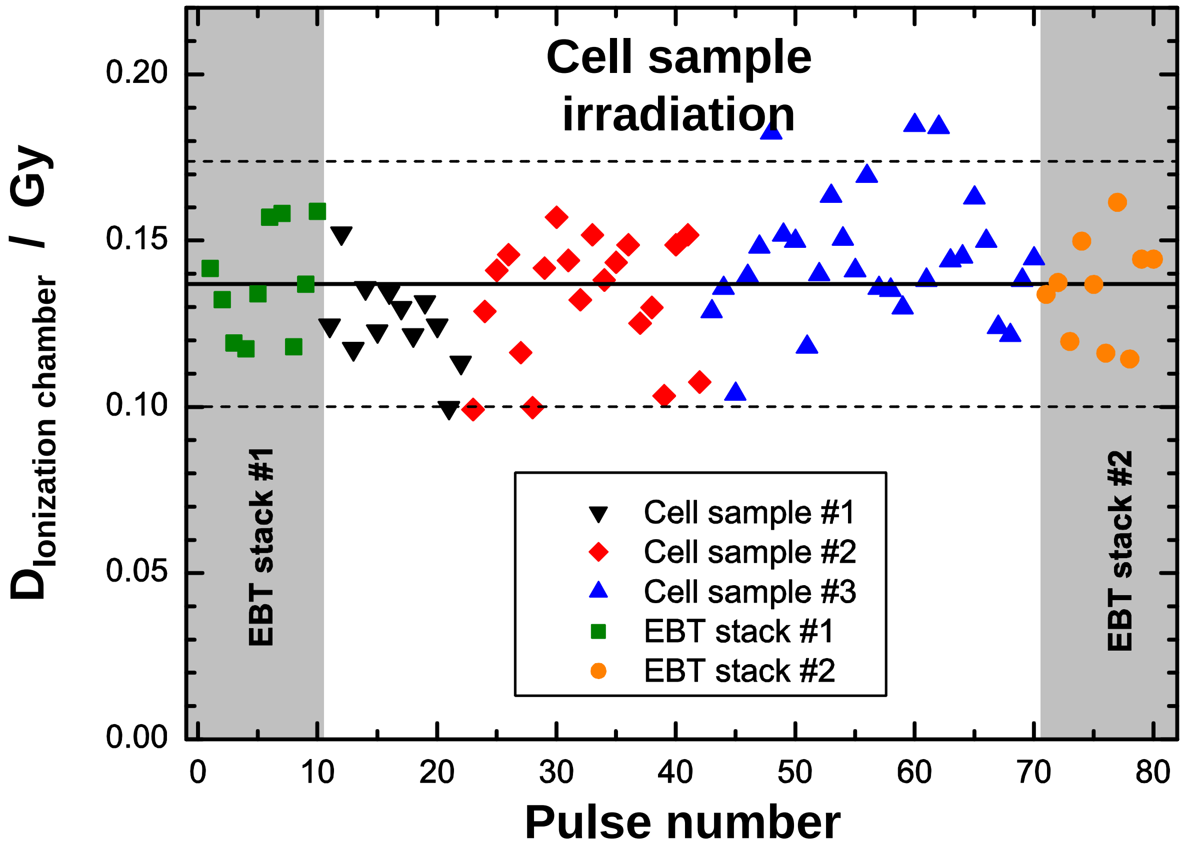
Monitoring of all cell and dosimeter irradiation

Measuring before and after cell sample irradiation

➩ ***Two independent absolute as well as online dosimetry systems***

Richter et al.: Med Phys 36(2009)5506 & Phys Med Biol 56(2011)1529, Karsch et al.: Z Med Phys 21(2011)4 & Med Phys 39(2012)2447

Proton pulse dose measurement:



150 TW DRACO laser

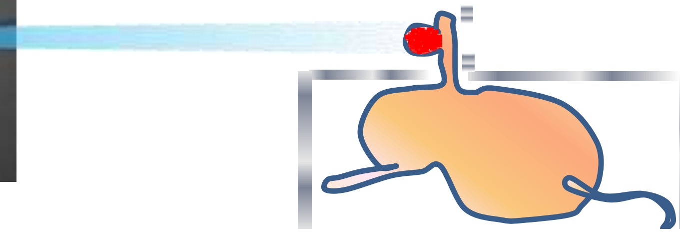
0.14 Gy ± 28% per pulse

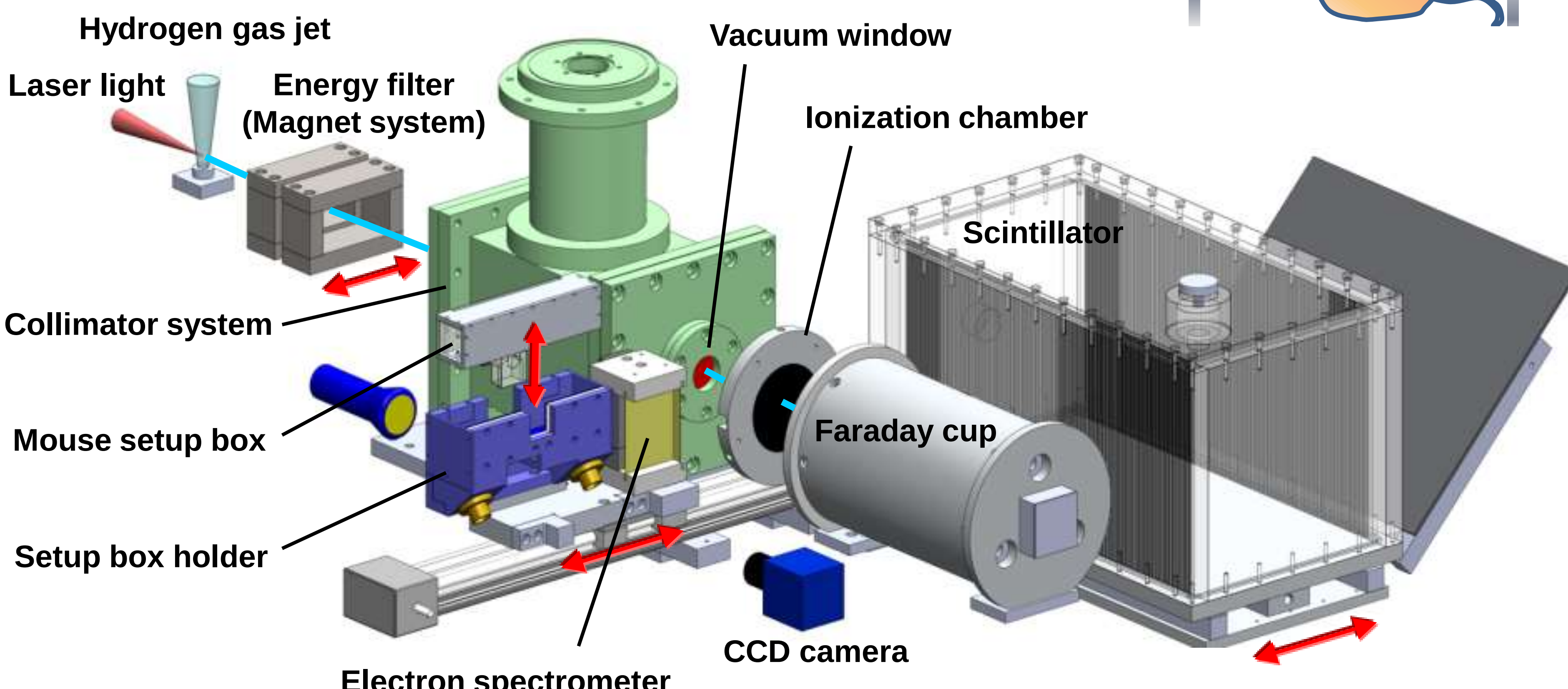
➪ ***Stable and online monitored pulse-to-pulse operation for controlled irradiation of cell samples***

Kraft et al.: NJP 12 (2010) 085003

4. Human tumor irradiation on mice

Laser electrons (JETI)

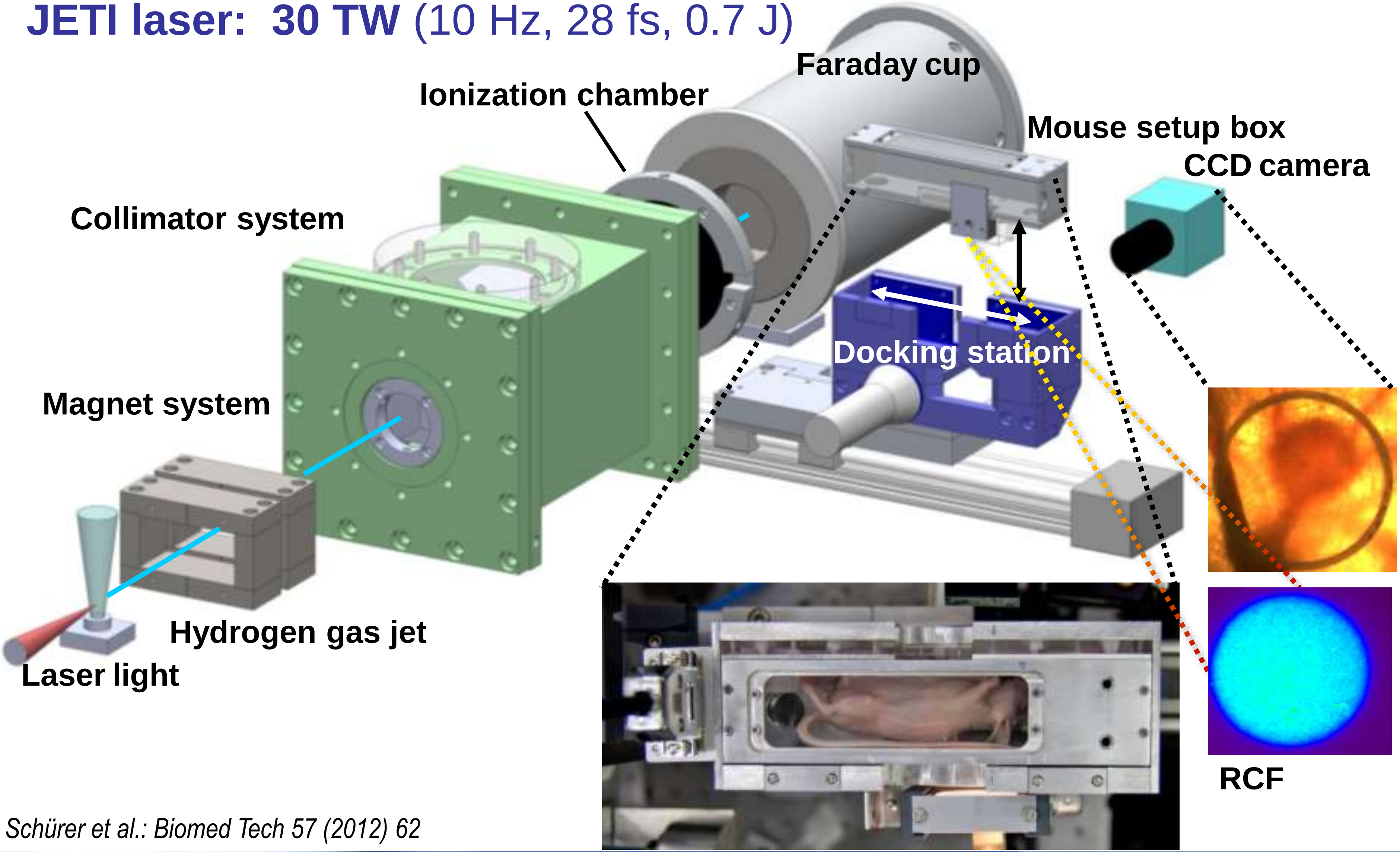




Schürer et al.: Biomed Tech 57 (2012) 62

4. Human tumor irradiation on mice

JETI laser: 30 TW (10 Hz, 28 fs, 0.7 J)

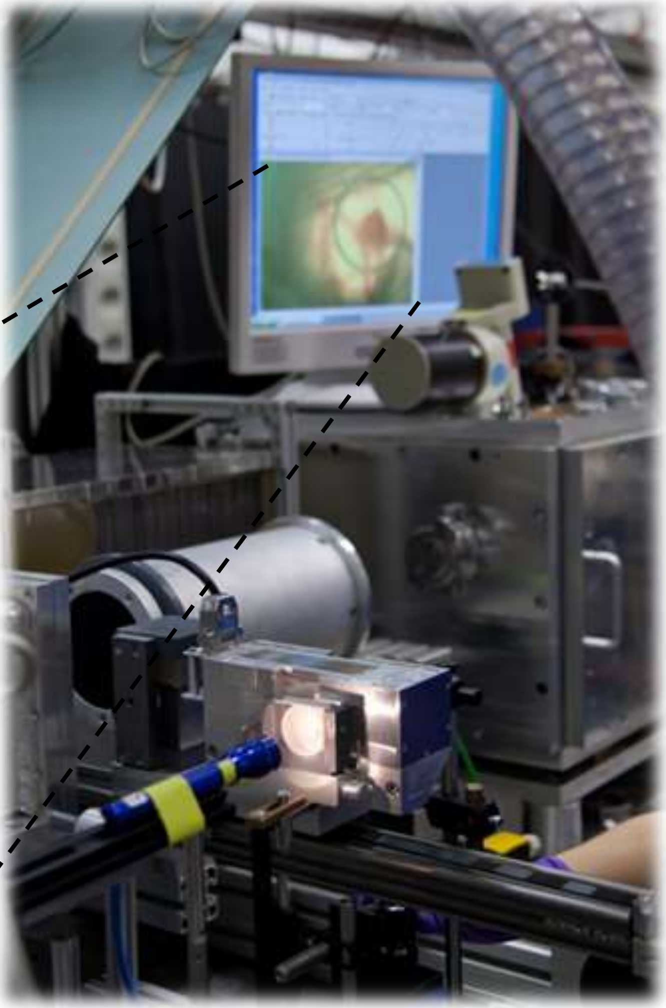


Schürer et al.: Biomed Tech 57 (2012) 62

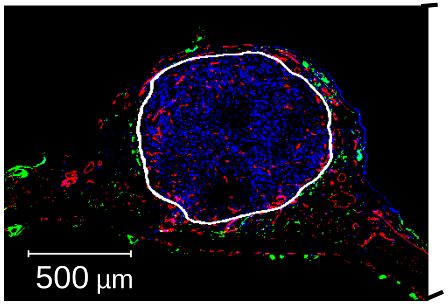
4. Human tumor irradiation on mice

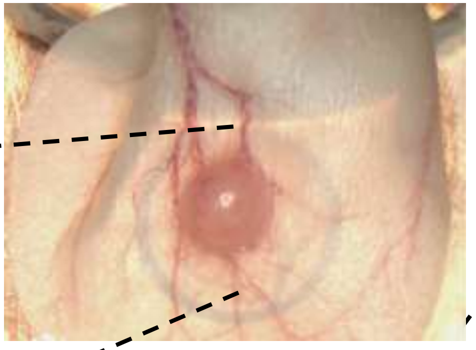
Laser electrons (JETI):

- Preparation and fixation of mouse



- Tumor histology (perfusion, hypoxia, blood vessels)





- Verification of tumor position before irradiation

Schürer et al.: Biomed Tech 57 (2012) 62, Brüchner et al.: Radiat Oncol 9 (2014) 57

5. Towards preclinical prototype

Laser-based technology established for irradiation of cells and small animals with:

- High energy electrons (~ 50 MeV)
- **Low energy protons (~ 25 MeV)**

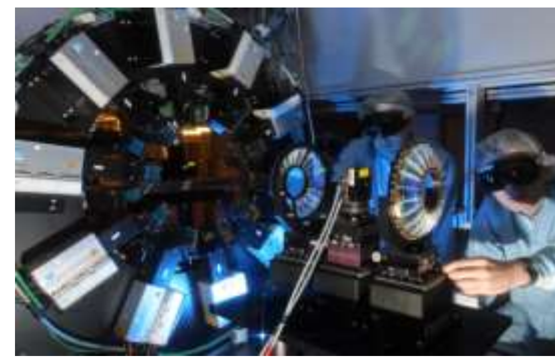
Developing laser-based medical beam delivery unit:

- Increase proton energy from ~ 25 MeV to ~ 250 MeV
- Irradiation of large tumor volumes
- From fixed beam irradiation to dose delivery by rotating gantry

5. Towards preclinical prototype

Increase of proton energy to ~250 MeV by petawatt laser power:

- **DRACO laser upgrade**
  - 150 TW → 1 PW (~30 J, ~30 fs, 10 Hz)
- **Diode pumped laser system POLARIS**
  - 1 PW; >100 J; 120 fs; 0,03 Hz
  - 100 TW amplifier stage in operation
- **Diode pumped laser system PENELOPE**
  - 1 PW; ~150 J; 150 fs; 1 Hz
- **ELBE center for high power radiation sources**

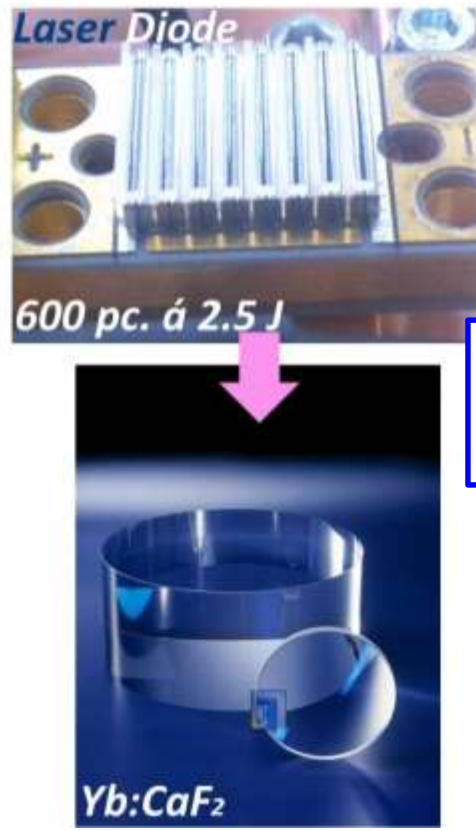


5. Towards preclinical prototype

Two alternative technologies of petawatt laser:

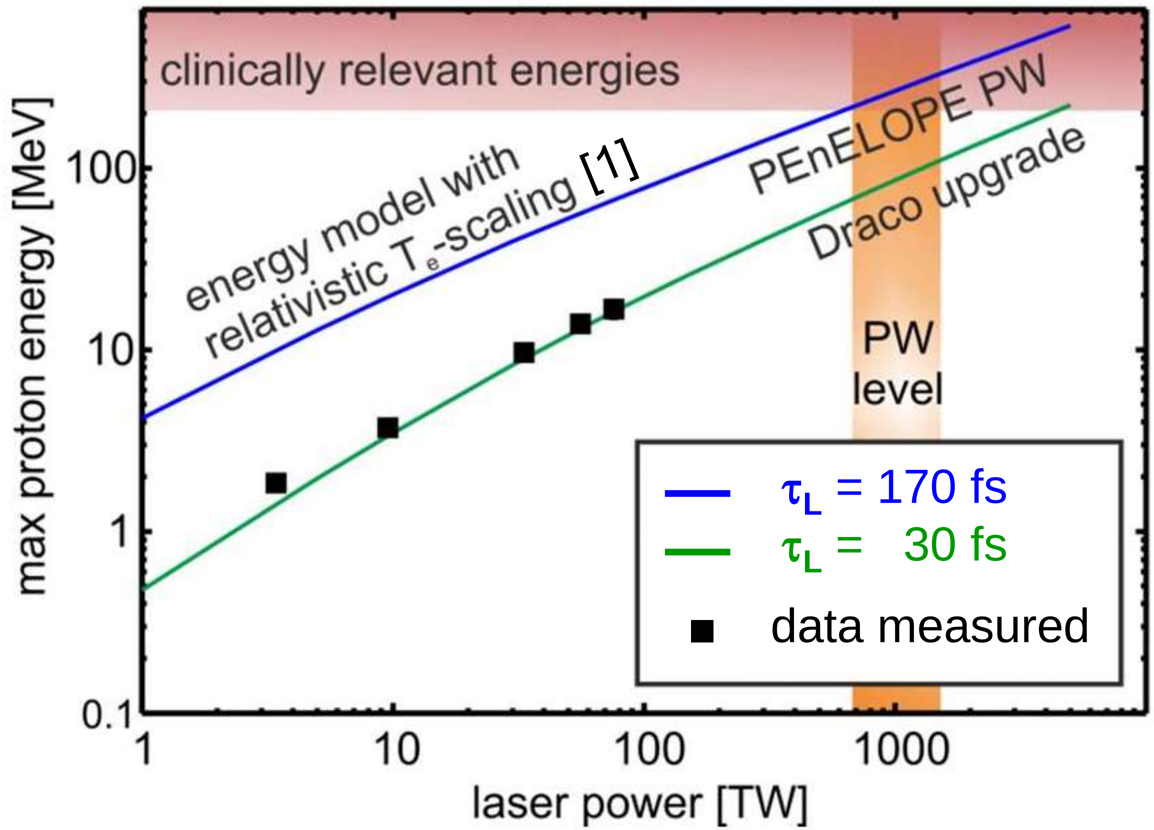
- Ultra-short pulse laser (Ti:Sa, flash lamp pumping, ~30 fs)
- Short pulse laser ($Yb:CaF_2$, laser diode pumping, ~150 fs)

- *JETI*
- *DRACO*



- *POLARIS*
- *PEnELOPE*

5. Towards preclinical prototype

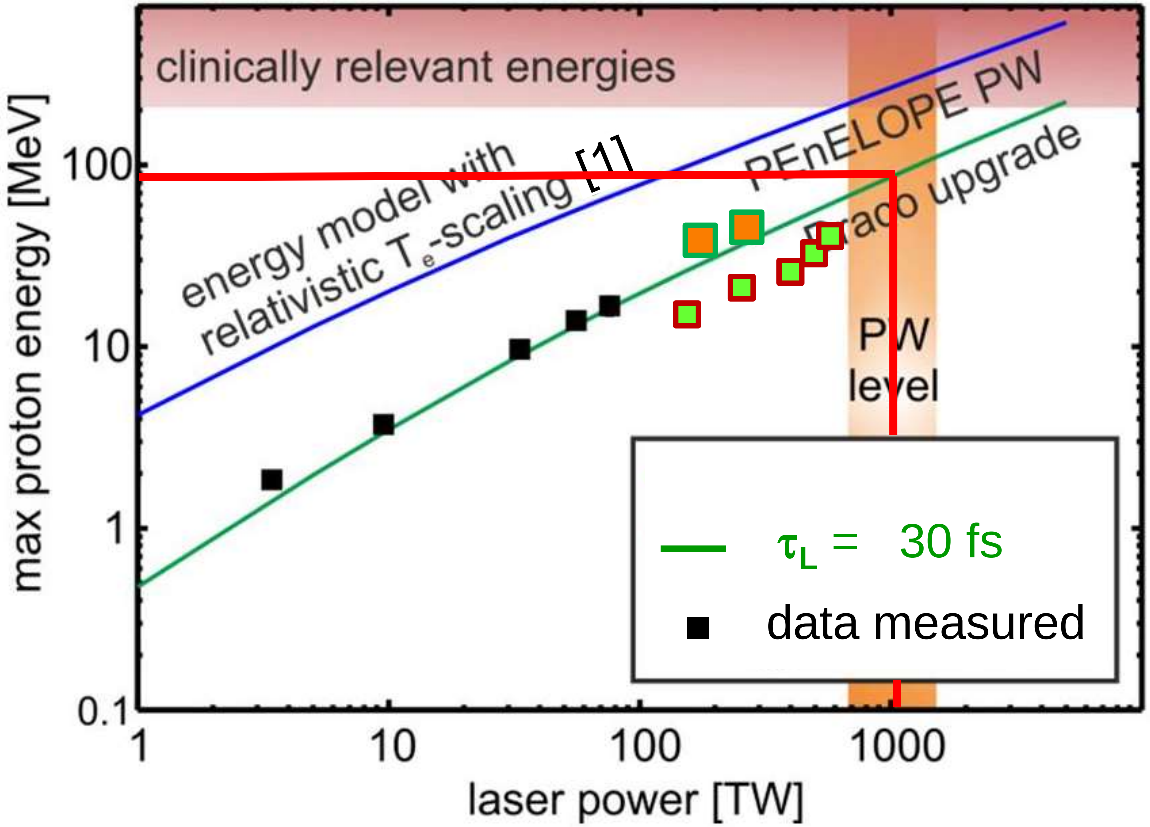


Two alternative technologies of petawatt laser:

- Ultra-short pulse laser (Ti:Sa, flash lamp pumping)
- Short pulse laser ($Yb:CaF_2$, laser diode pumping)

[1] *Kluge et al.: PRL 107 (2011) 205003*

5. Towards preclinical prototype



Very preliminary laser conditions on target

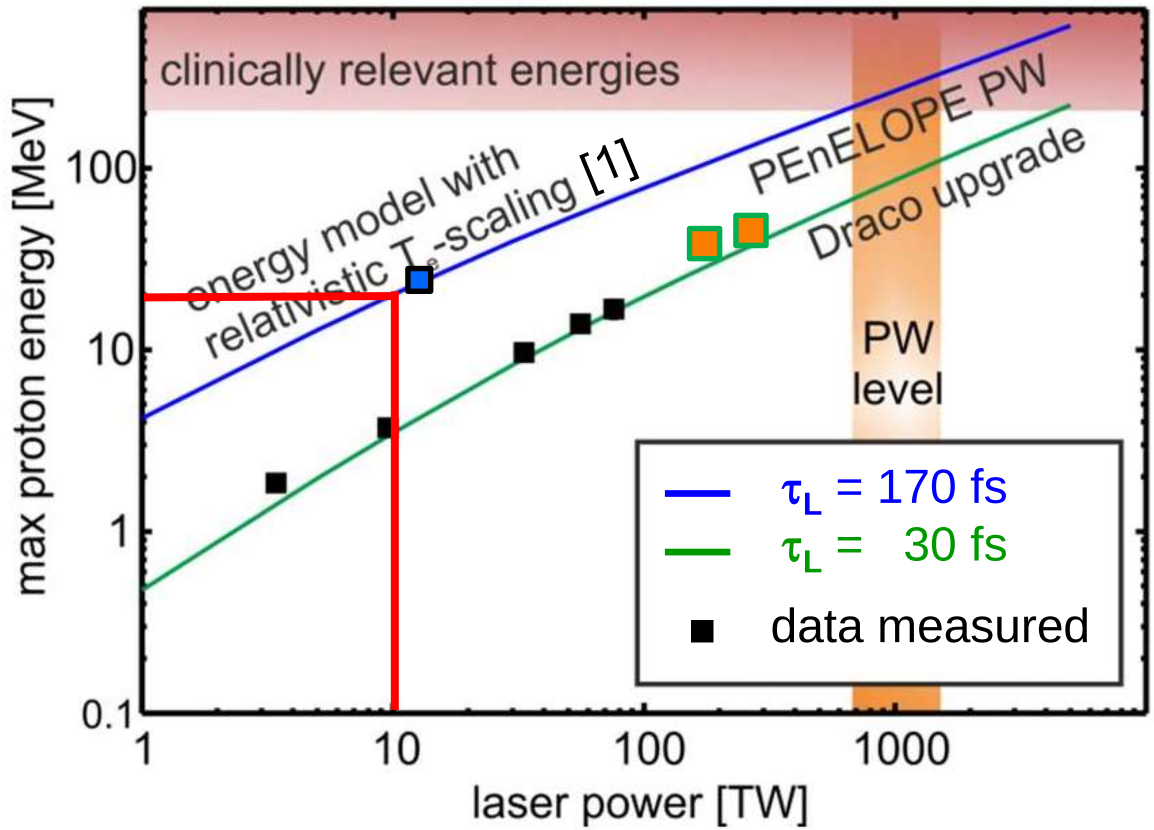
Other systems:

Ogura et al.: Opt Lett 37 (2012) 2868

Jong Kim et al.: PRL 111 (2013) 165003

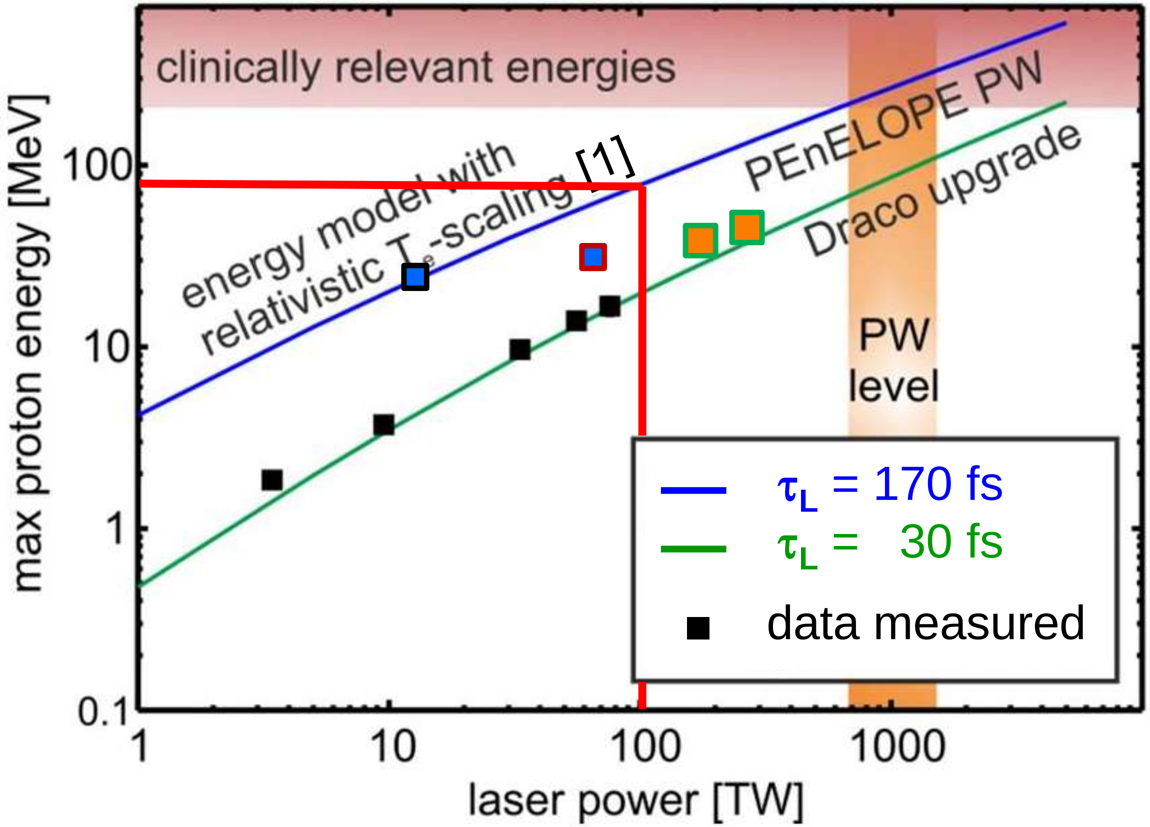
- 2016: **Petawatt class laser DRACO upgrade** (10 Hz, 30 fs, 30 J)
  - In cooperation with Amplitude Technologies, France
  - Proton acceleration up to ~90 MeV
  - In vivo experiments in progress

5. Towards preclinical prototype



- 2013: Petawatt class **laser POLARIS** (0.03 Hz, 120 fs, 120 J)
  - In-house development
  - **10 Terawatt amplifier** stage in operation

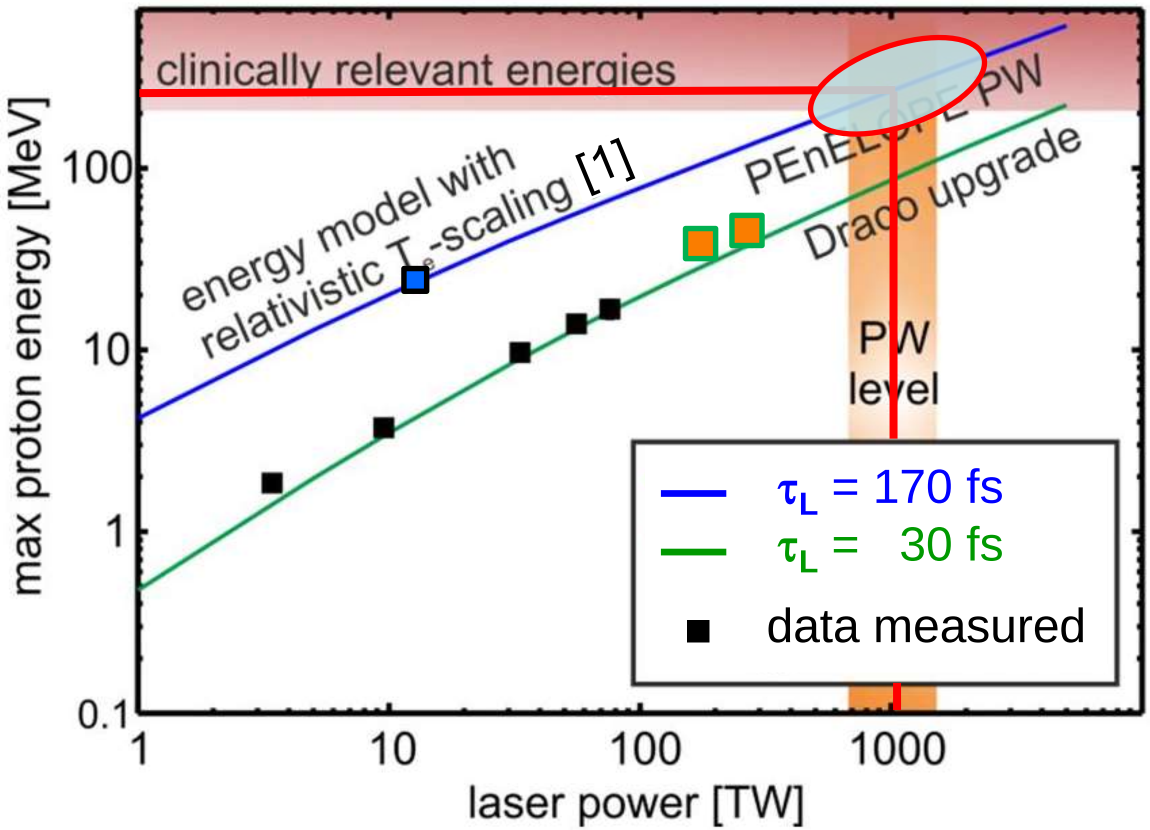
5. Towards preclinical prototype



Temporal pulse contrast problems

- 2016: Petawatt class **laser POLARIS** (0.03 Hz, 120 fs, 120 J)
  - In-house development
  - **100 Terawatt amplifier** stage in operation

5. Towards preclinical prototype

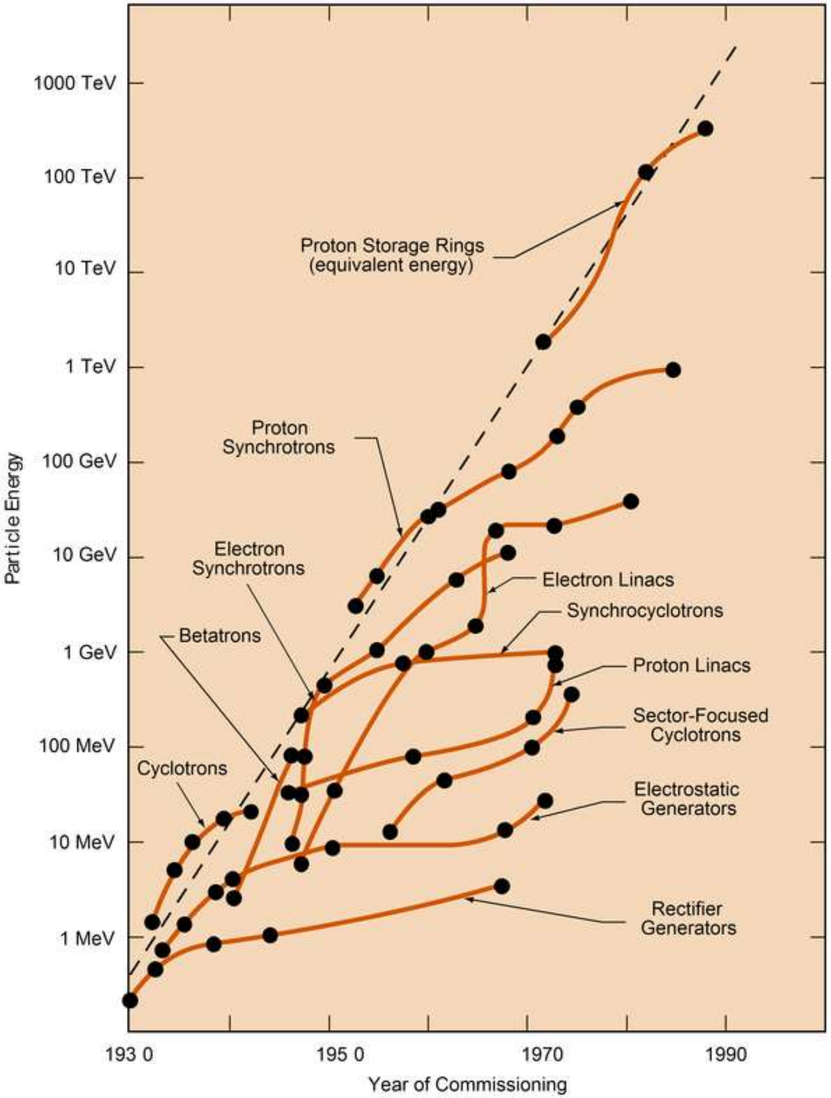


- 2017: **Petawatt class laser PENELOPE** (1 Hz, 150 fs, 150 J)
  - In-house development, optimized for pulse contrast
  - Under construction

5. Towards preclinical prototype

Livingstone chart:

- Achieved maximum particle energy for different accelerators
- Energy increases on average by a factor of ~33 within 10 years (almost independent from the acceleration principle)
- 10 Hz Ti:Sa laser systems: Maximum proton energy from 2 MeV in 2006 to 45 MeV in 2013 (factor 23 within 7 years)

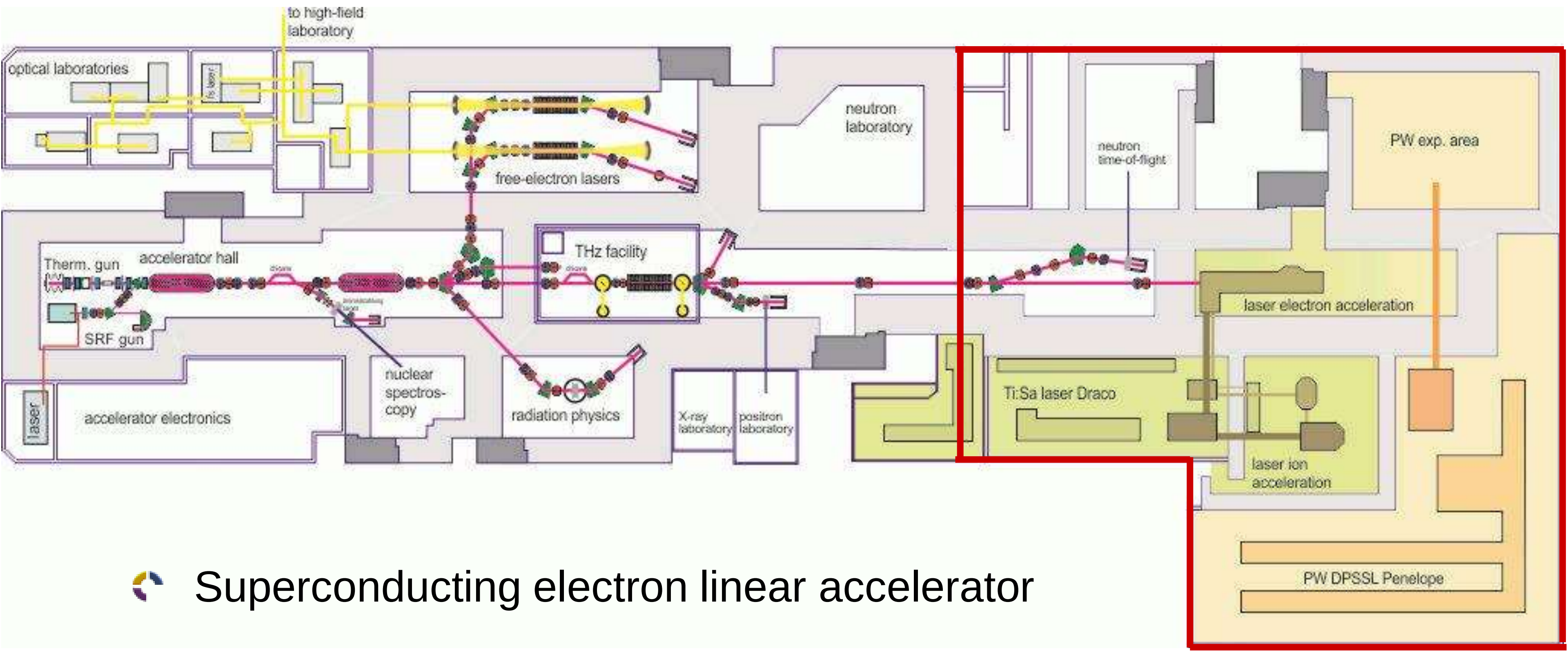


Courtesy to R. Ischebeck who adapted it from A. Chao et al., Proc. Snowmass 2001 Conf., eConf C010630, SLAC-R-599

http://www.ischebeck.net/media/Accelerator%20Physics/Advanced%20Accelerator%20Concepts/Livingston%20Plot/Livingston%20Plot%201.png (12.04.2017)

5. Towards preclinical prototype

ELBE center for high power radiation sources:

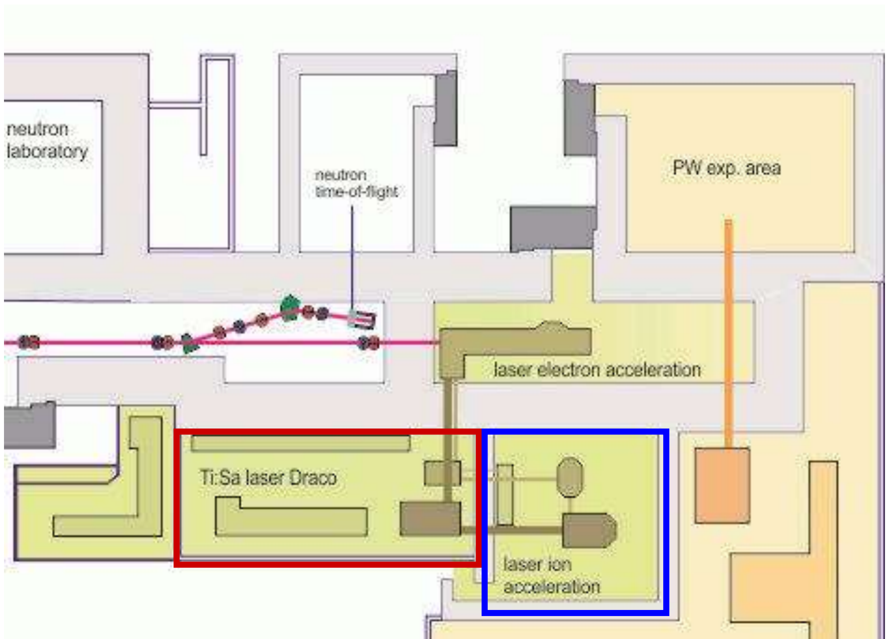


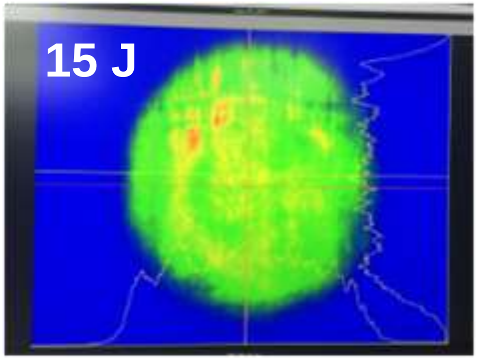
- Superconducting electron linear accelerator
- 1 PW DRACO upgrade & 1 PW PEnELOPE

Funded by Free State of Saxony, 20 Mill. €

ELBE center for high power radiation sources:

- 1 PW DRACO upgrade installed
- 700 TW in routine operation





Dosimetry:

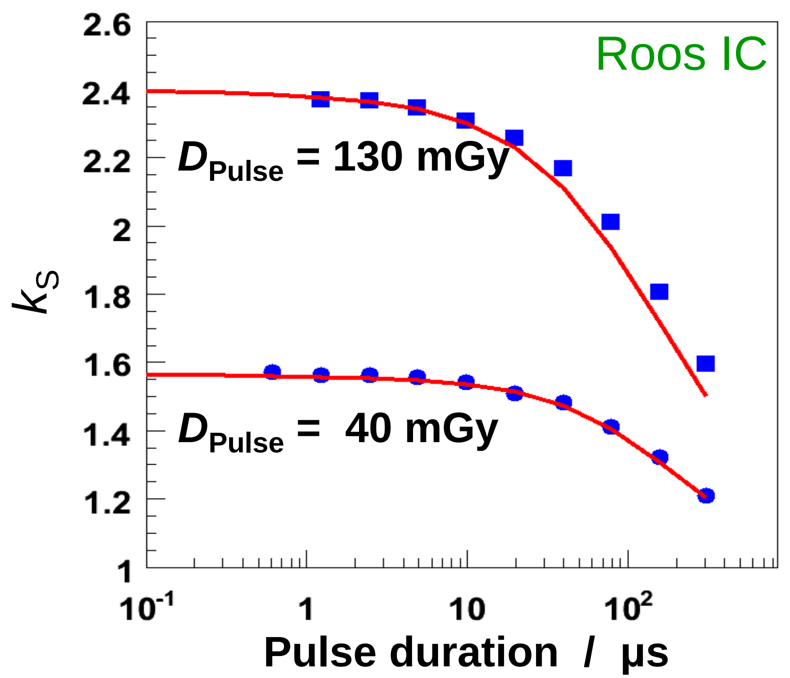
- Clinical standard: absolute dose measurement by (air-filled) ionization chambers
- Requires recombination correction

$$k_S = \frac{\text{released charge}}{\text{collected charge}}$$

- Established for continuous beams and low-dose single pulse exposure
- For pulsed radiation fields of arbitrary pulse duration and repetition rate:

  Experimental determination *

  Theoretical description *



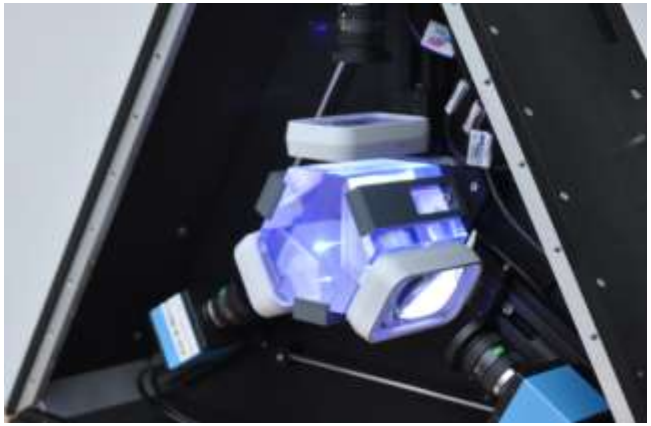
* *Karsch et al.: Z Med Phys 21 (2011) 4*
  Karsch et al.: Med Phys 39 (2012) 2447

* *Karsch and Pawelke: Z Med Phys 24 (2014) 210*
  Karsch: Phys Med Biol 61 (2016) 3222 & Med Phys 43 (2016) 6154

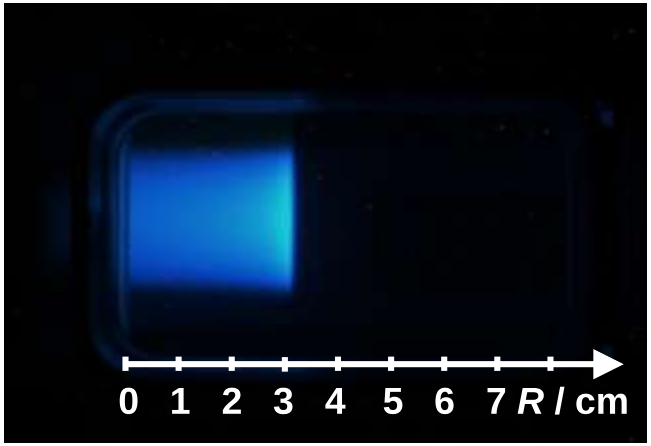
5. Towards preclinical prototype

Dosimetry:

- Online measurement of 3D dose distribution for single pulses
- Scintillator block and optical tomography
- First small-scale prototype
- Proof-of-principle irradiation tests (γ, e^-, p)
- Promising dosimetry method
- Prototype sufficient for development of laser-driven proton therapy at current stage



Proton beam (60 MeV)



Kroll et al.: Med Phys 40 (2013) 082104-1

5. Towards preclinical prototype

Dose delivery to large tumor volumes:

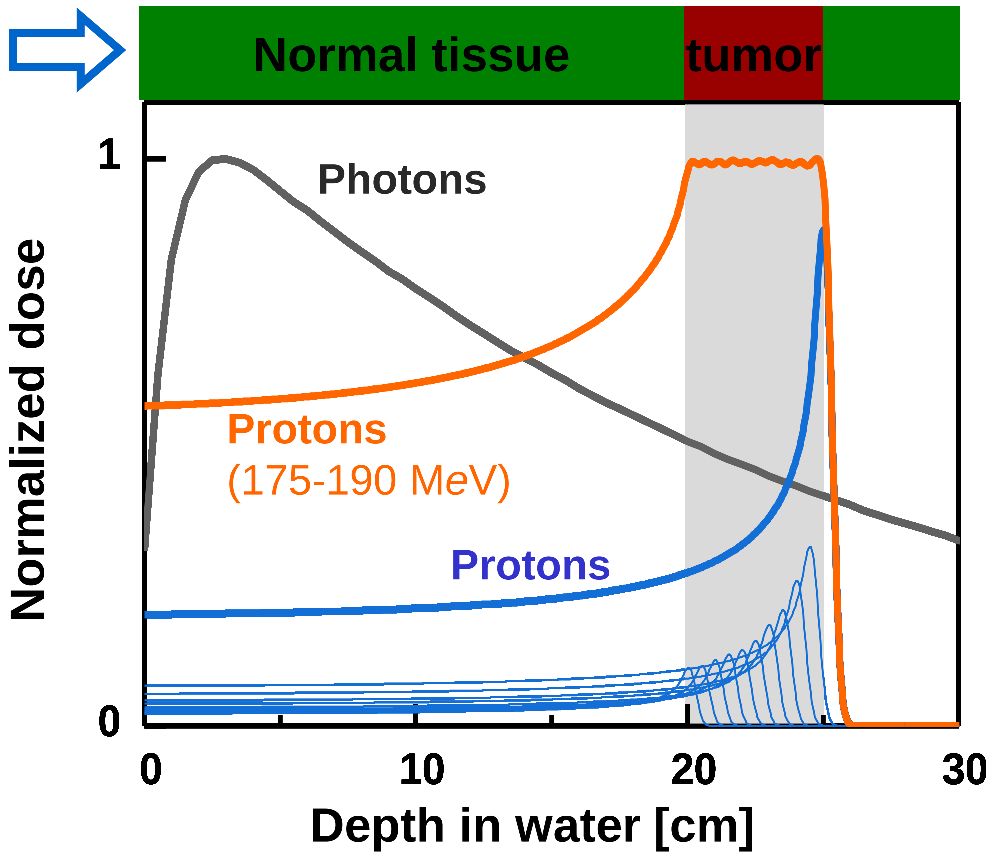
- Laser-driven beams:
  - broad energy spectrum,
  - large beam divergence
  - limit of low number of pulses (10 min@10 Hz → 6000 pulses)

- Straightforward approach:
  - Apply conventional dose delivery systems

    ⇨ *Select monoenergetic, pencil-like beams*

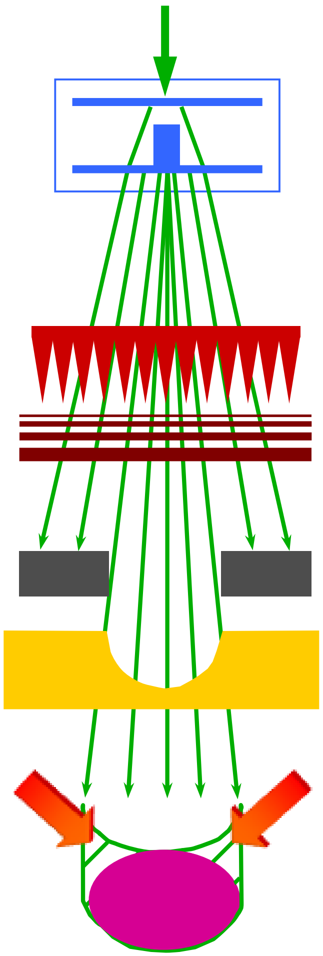
Dose delivery: Spread-out Bragg peak (SOBP) formation

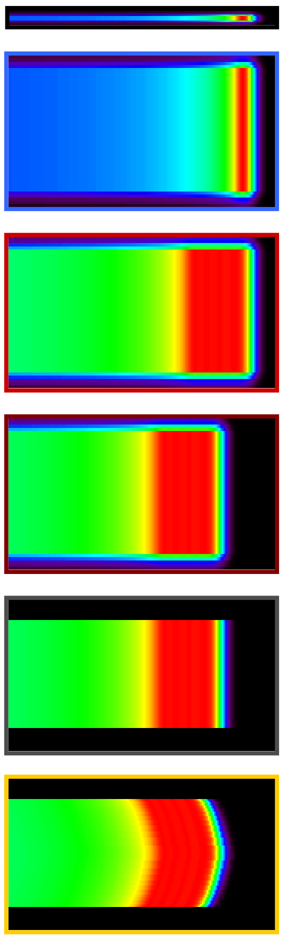
- Monoenergetic beams



5. Towards preclinical prototype

Dose delivery: Passive irradiation field formation





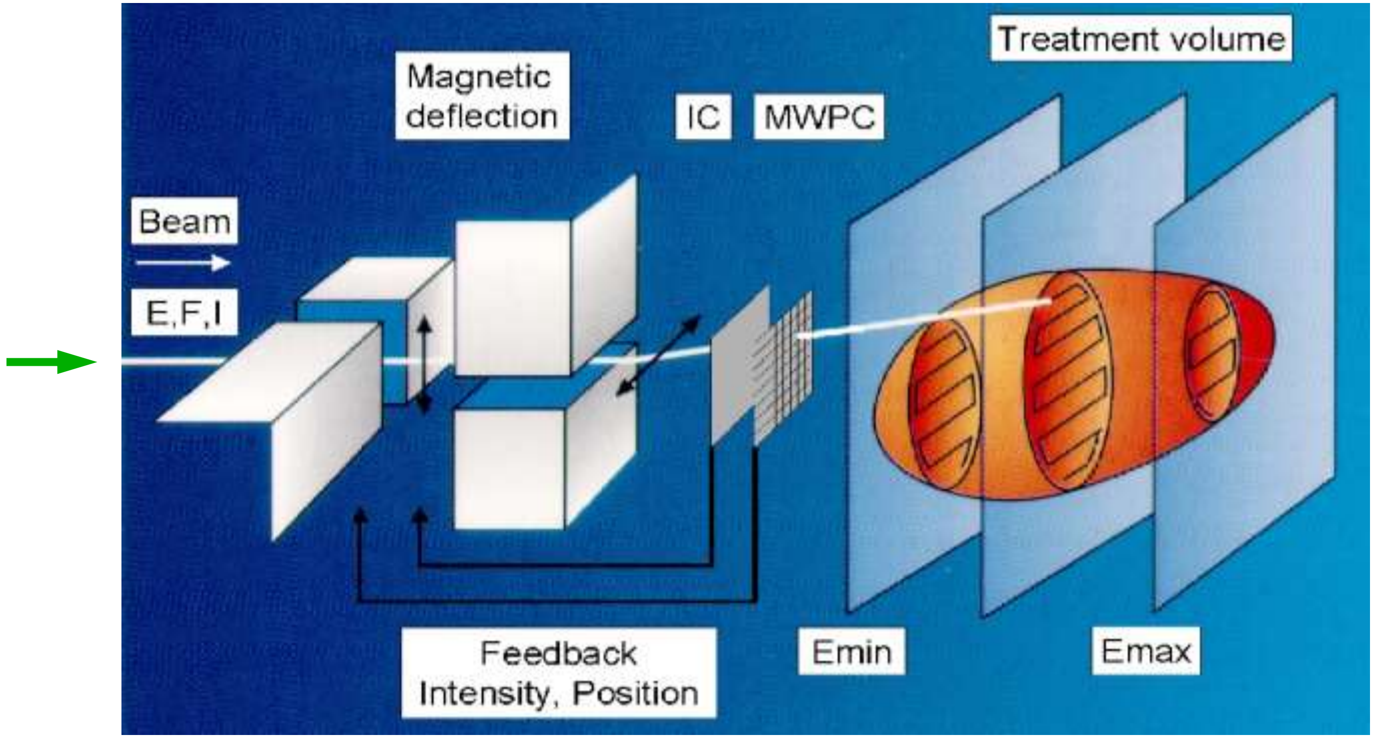
- Adapt monoenergetic pencil-like ion beam to 3D tumor contour
- 2D lateral beam widening by scatterer / scanning magnets
- Beam widening in beam direction by range modulator (⇨ SOBP)
- Shift of SOBP in beam direction by range shifter
- Adapt irradiated area to tumor contour: lateral by collimator
- distal by range compensator
- **High dose region (healthy tissue)**

D. Schardt et al.: Rev. Mod. Phys. 82 (2010) 383

5. Towards preclinical prototype

Dose delivery: **Pencil beam scanning** (GSI)

T. Haberer et al.: Nucl. Instrum. Meth. A330 (1993) 296

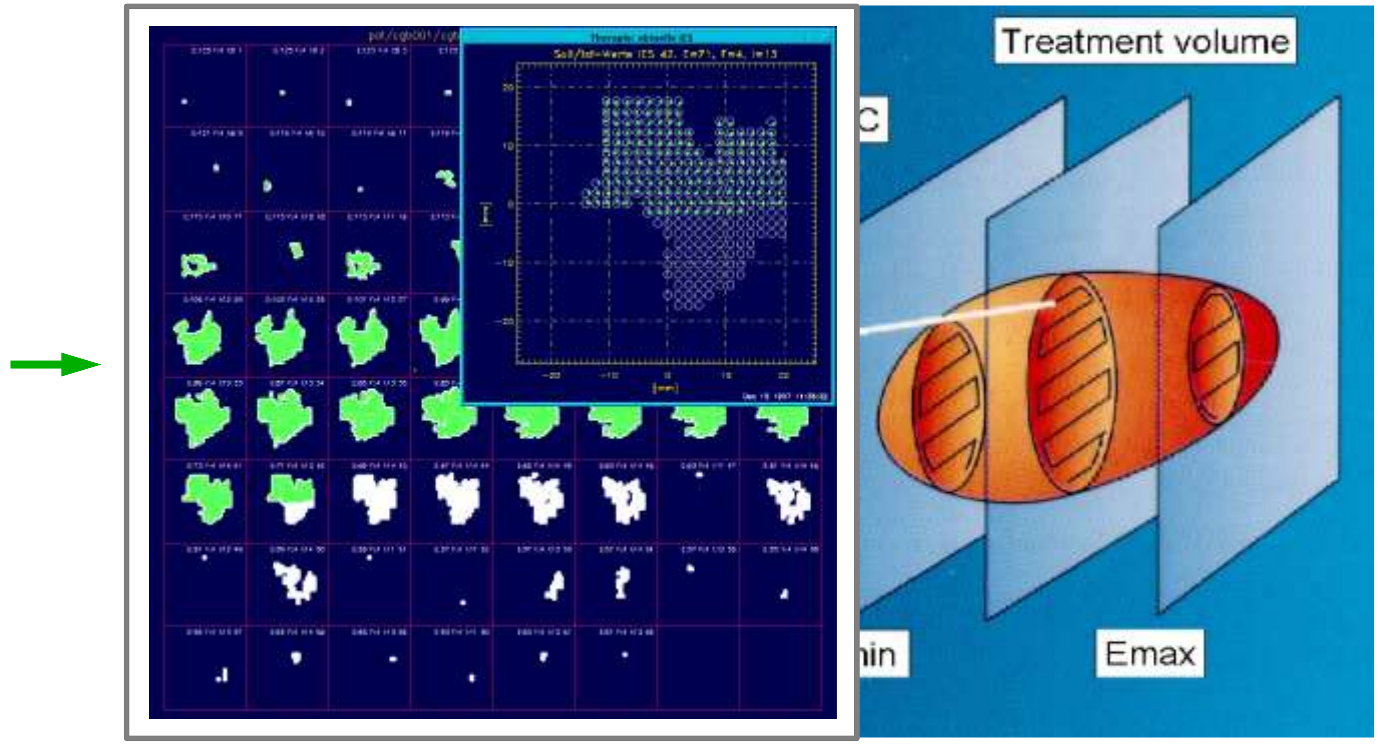


- Monoenergetic pencil beams from accelerator (*F* = 4 – 10 mm ø)
- Magnetic deflection (horizontal, vertical)
- Range modulation by energy variation (E_{12C} = 1 – 5 GeV)
- Intensity controlled scanning ($I = 10^6 – 10^8$ ^{12}C/s)

5. Towards preclinical prototype

Dose delivery: **Pencil beam scanning** (GSI)

T. Haberer et al.: Nucl. Instrum. Meth. A330 (1993) 296



- Monoenergetic pencil beams from accelerator (*F* = 4 – 10 mm ø)
- Magnetic deflection (horizontal, vertical)
- Range modulation by energy variation (E_{12C} = 1 – 5 GeV)
- Intensity controlled irradiation of up to ~27000 spots (30·30·30)

5. Towards preclinical prototype

Dose delivery to large tumor volumes:

- Laser-driven beams:
  - Broad energy spectrum,
  - Large beam divergence
  - Limit of low number of pulses (10 min@10 Hz → 6000 pulses)

- Straightforward approach:
  - Apply conventional dose delivery systems (pencil beam scanning)

    ⇨ *Select monoenergetic, pencil-like beams*

    ⇨ *Dump a large number of protons (~95%)*

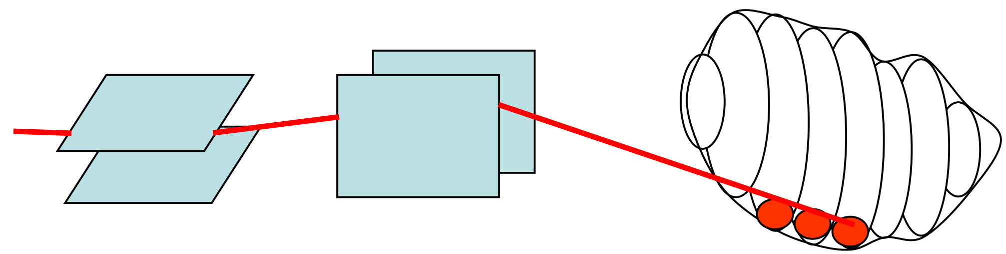
    ⇨ *Production of a high level of secondary radiation*

Dose delivery to large tumor volumes:

- New concept:
  - Deliver as much particles as available and useful

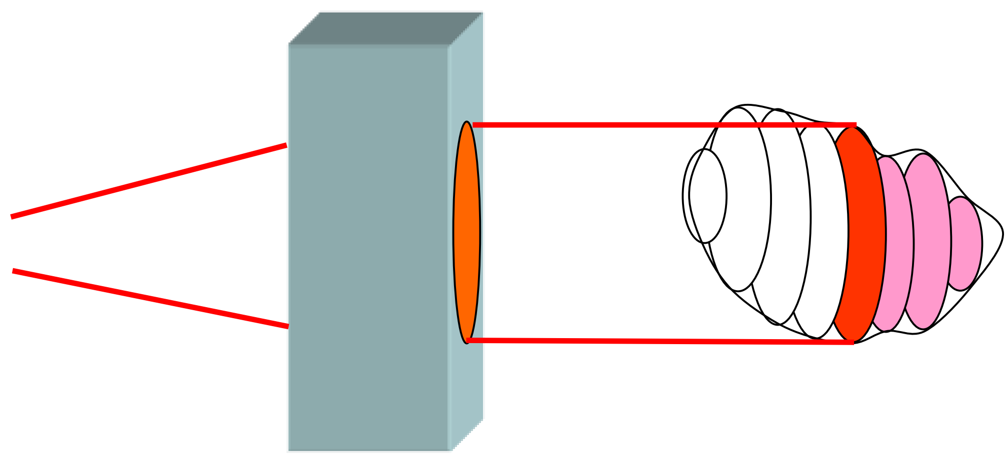
1. Approach

Pencil beam +
defined broad energy spectrum

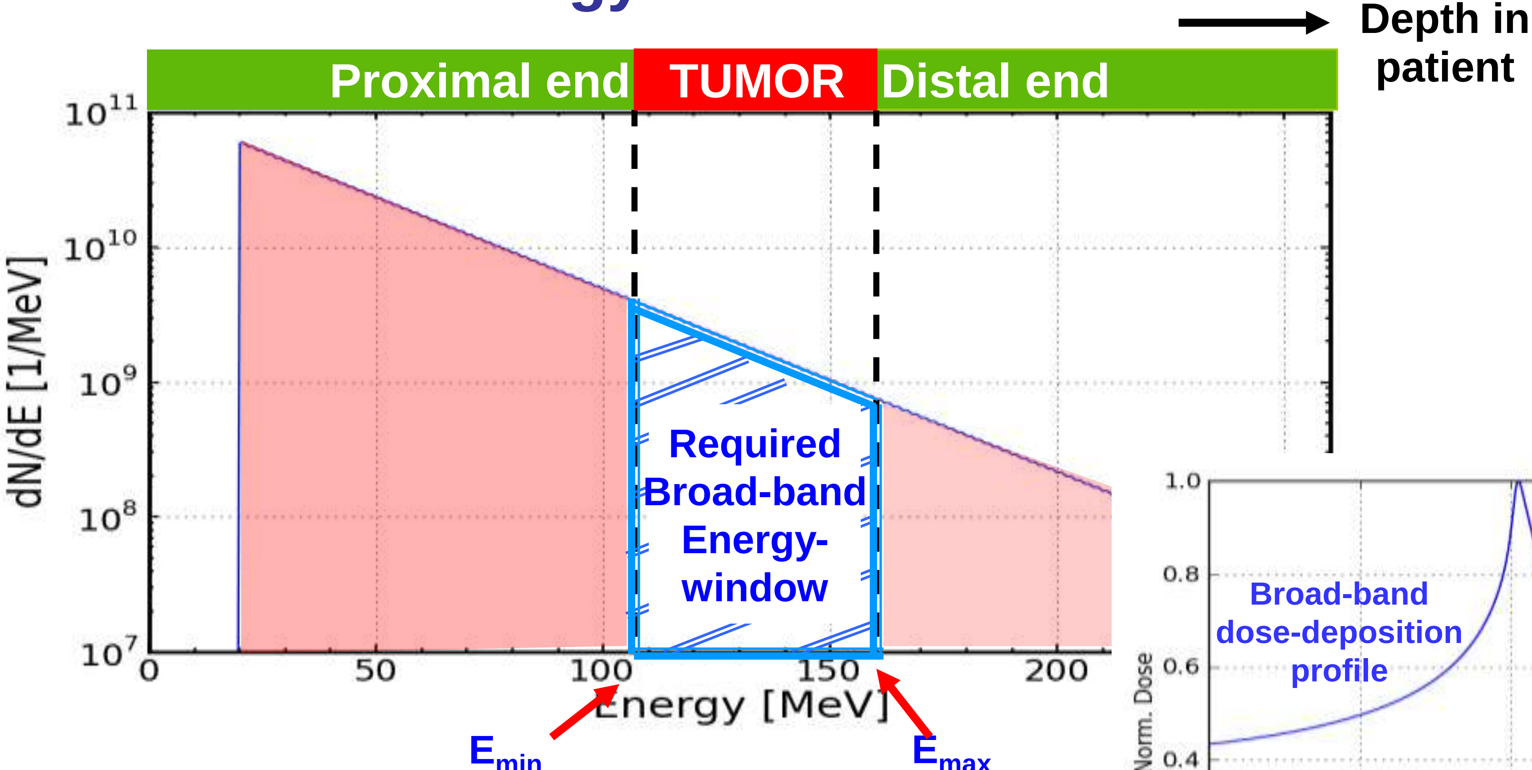


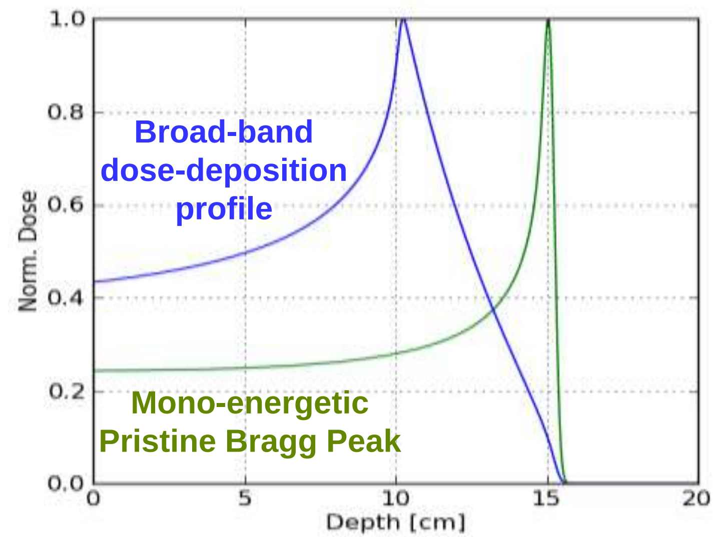
2. Approach

Wide beam +
quasi-monoenergetic



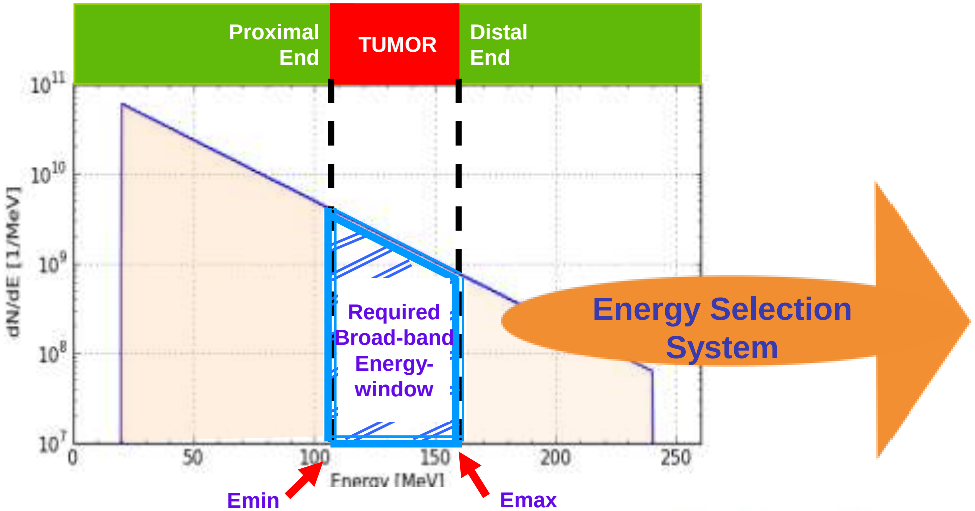
Broad-band energy selection:

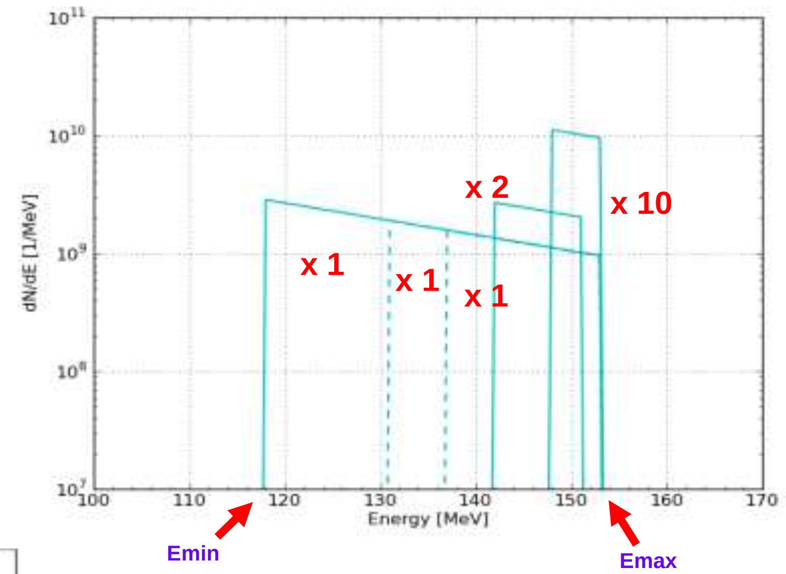


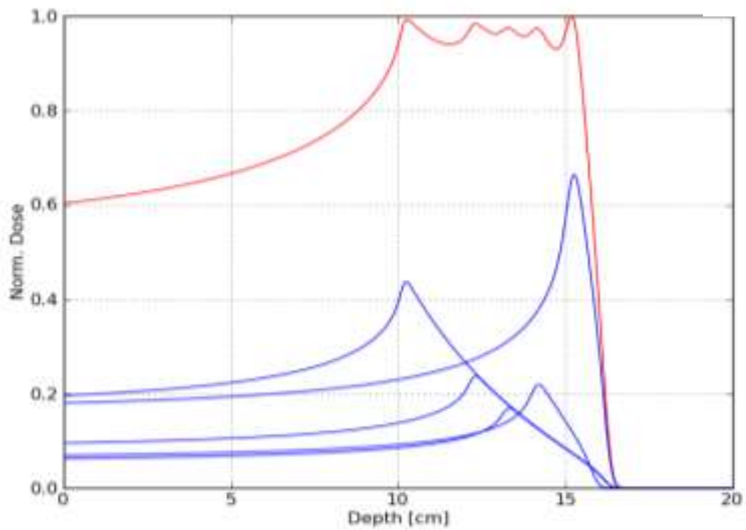


- Scaled spectrum from experimental data, for therapeutical energy range
- Assume arbitrary energy selection system capable to filter Broad-band Energy-window

Broad-band energy selection:







— Superimposed dose profile

— Individual broad-band dose profile

Total: 15 pulses

Masood et. al.: Appl Phys B 117 (2014) 41

5. Towards preclinical prototype

Dose delivery by rotating gantry:

New Concept:

- Pulsed nature of laser-driven beams
- Use pulse powered magnets
  - Higher magnetic field for more compact designs
  - Lower weight
- Conventional (iron-core) magnets:
  - B_{max} ~ 2 T (iron magnetization limit)
- Pulse powered (air-core) magnets:
  - B_{max} > 10 T (current limit)

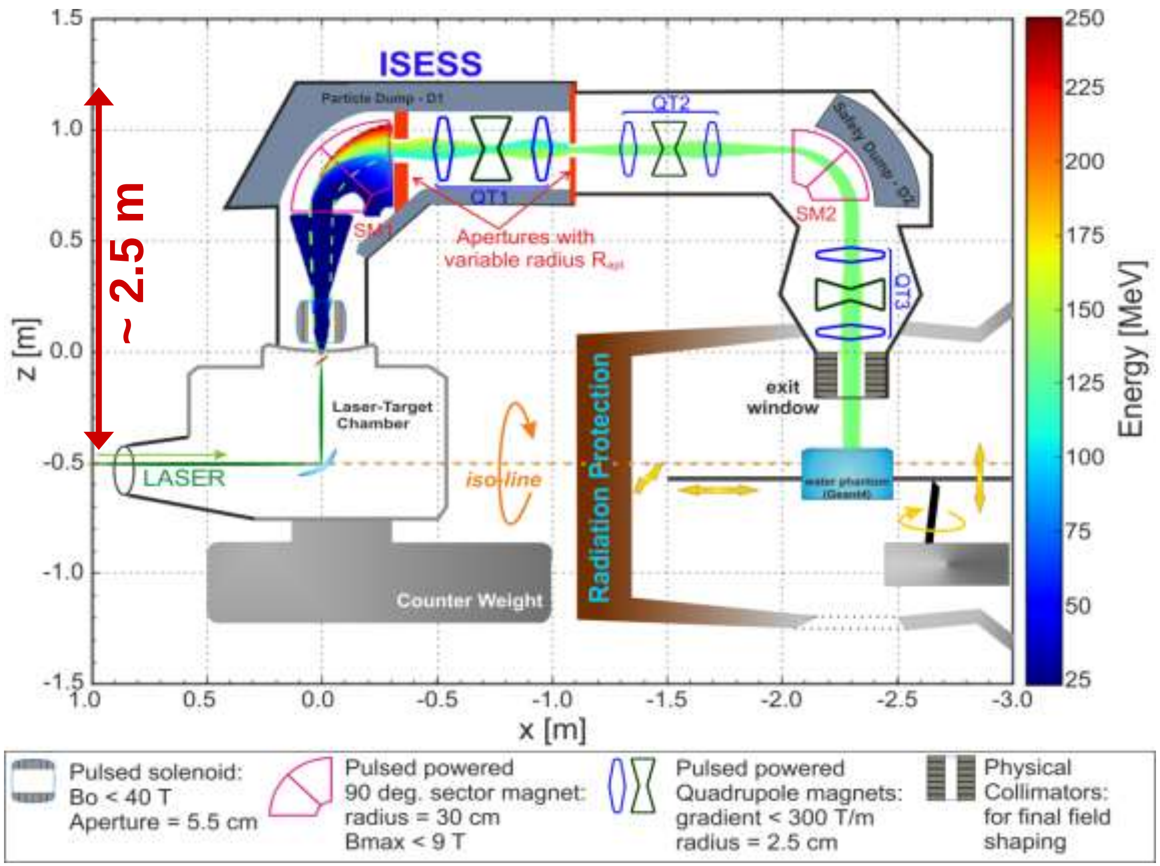
⇨ *Mechanical strength for intense magnetic pressure (high current pulses)*

Masood et. al.: Appl Phys B 117 (2014) 41

5. Towards preclinical prototype

Gantry design:

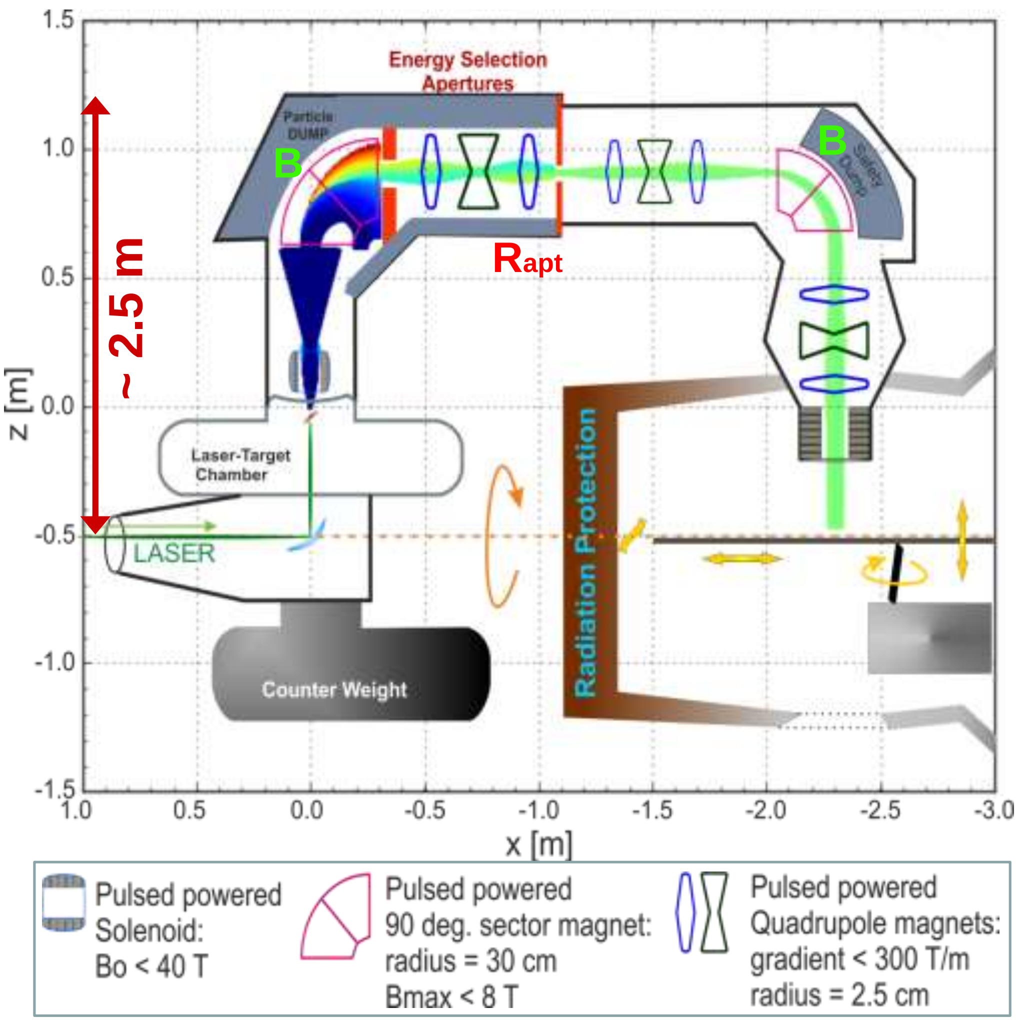
- Laser target chamber integration
- Broad energetic beam delivery (3 – 20%)
- High beam transport efficiency (20 – 97%)
- Variable beam spot size
- High-field pulse powered magnets
- More compact (only half size)

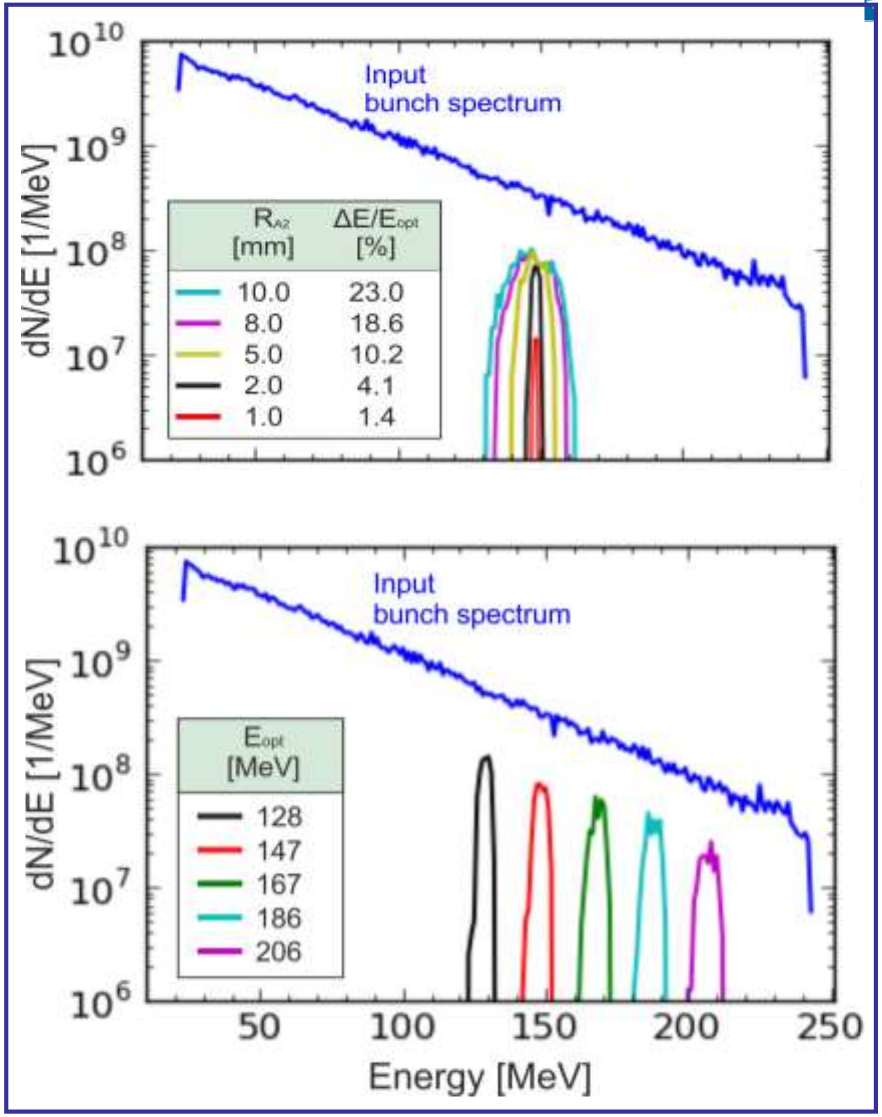


Masood et. al.: Appl Phys B 117 (2014) 41 & Phys Med Biol 62 (2017) 5531

5. Towards preclinical prototype

Gantry design:

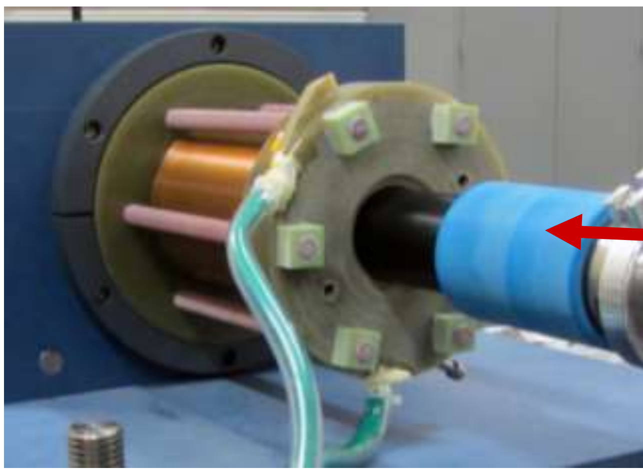


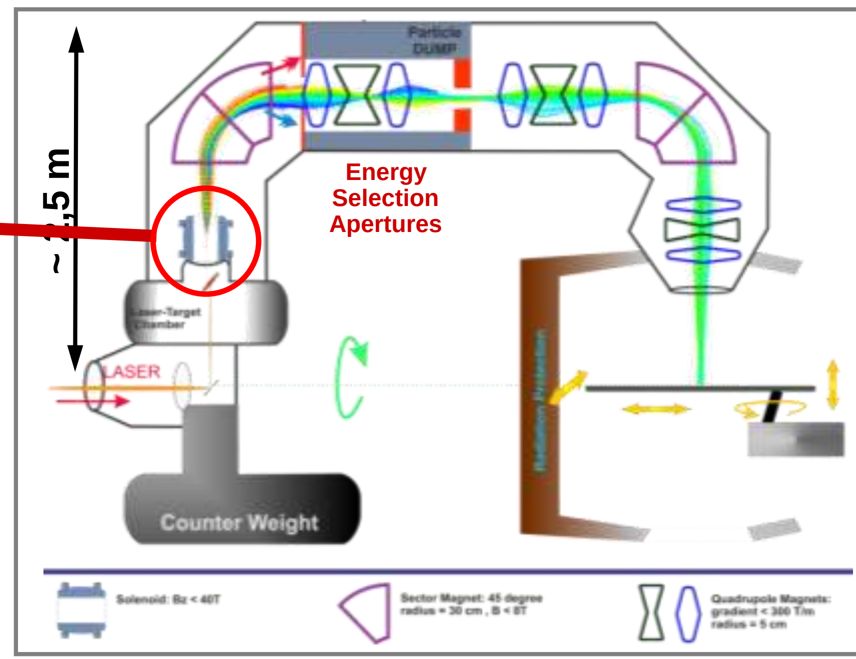


5. Towards preclinical prototype

Pulse powered solenoid:

- Beam capture and focusing
- Several prototypes (B_0: ~50 T) developed
- Tested and applied at laser-driven proton beams

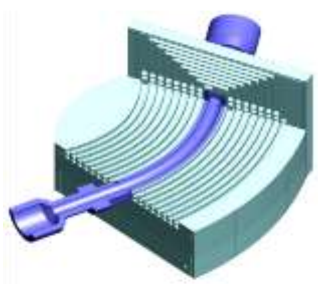


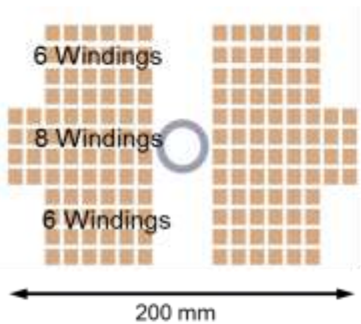


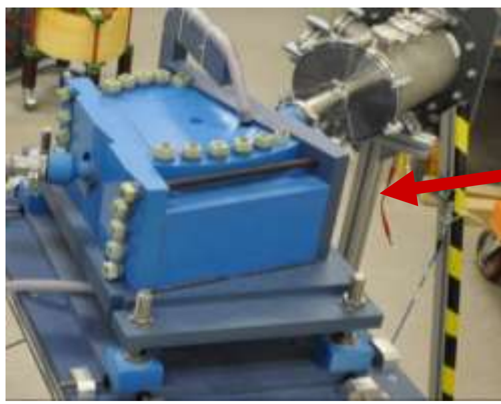
Burris-Mog et al.: PR STAB 14 (2011) 121301, Busold et al.: PR STAB 16 (2013) 101302

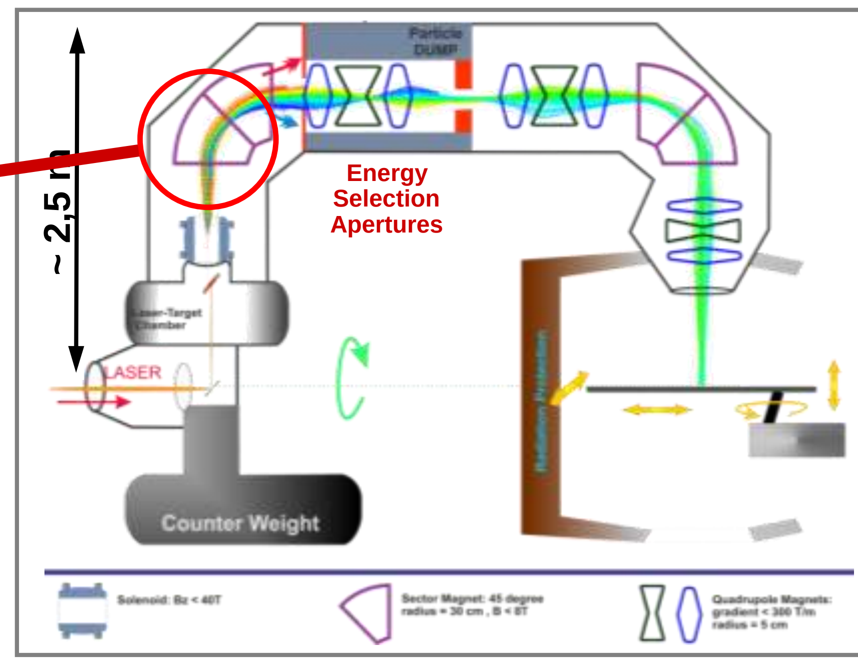
Pulse powered dipole:

- Beam bending and energy selection
- Designed (magnetic strength ~10 T, 45º bending → ~200 MeV)
- Manufactured and characterized at pulsed proton beams







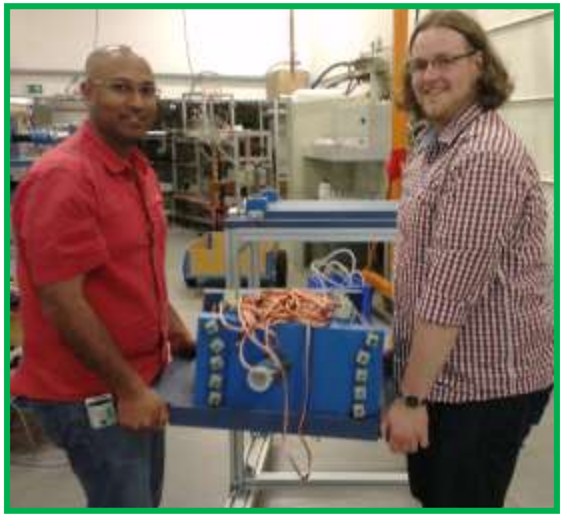


Schürer et al.: Patent application DE 10 2015 200 213.6 (9.1.2015)

5. Towards preclinical prototype

Pulse powered dipole:

- Beam bending and energy selection

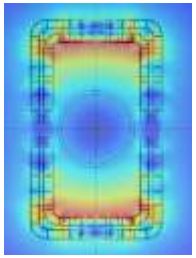


Schürer et al.: Patent application DE 10 2015 200 213.6 (9.1.2015)

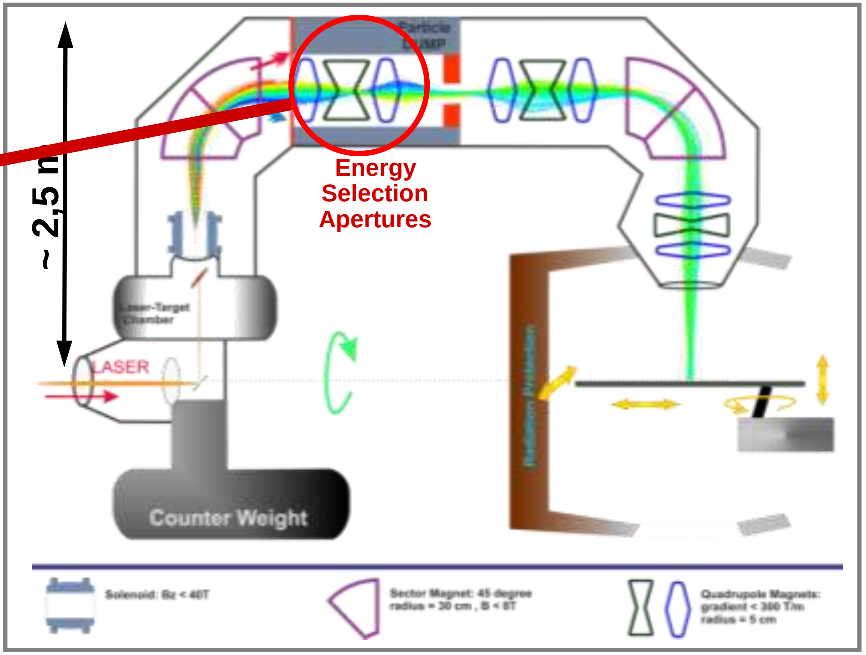
Pulse powered quadrupole:

- Beam shaping and correction
- Multi layer design: High gradient ~250 T/m → ~6 T at poles
- Manufactured


Winding design

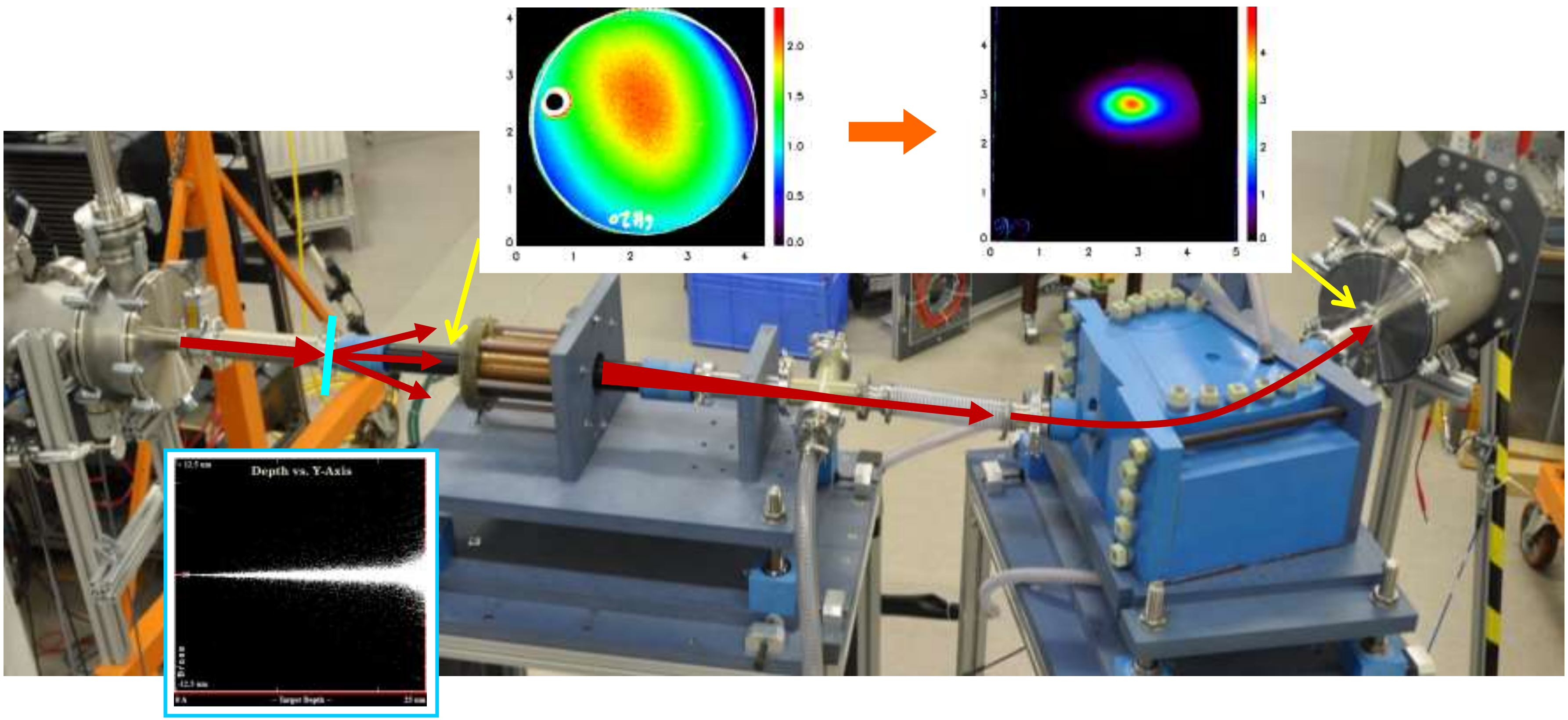

3D magnetic field simulation

Prototype



Pulse magnet beamline section:

- Tested at conventional pulsed proton beam (tandem, 10 MeV)



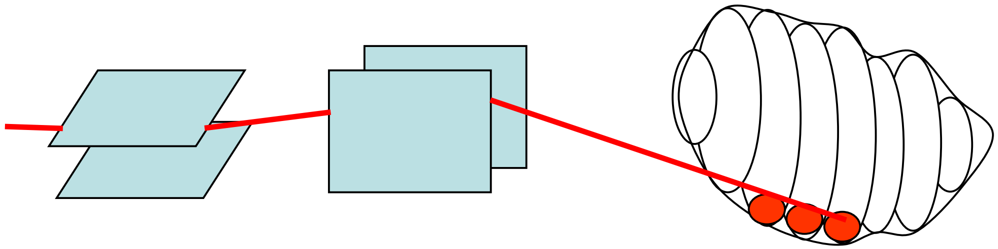
Scatter foil (25 µm brass)

Dose delivery to large tumor volumes:

- Tumor conform dose delivery:
  - Dosimetric quality of treatment plans

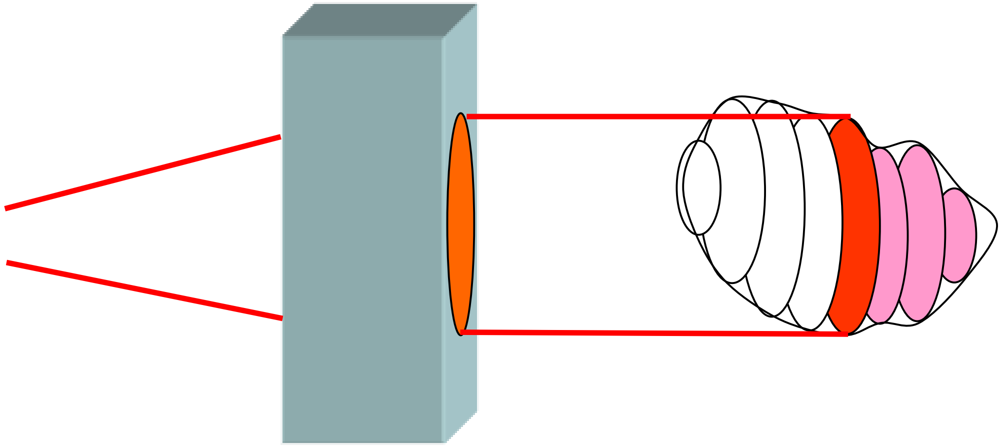
1. Approach

Pencil beam +
defined broad energy spectrum



2. Approach

Wide beam +
quasi-monoenergetic



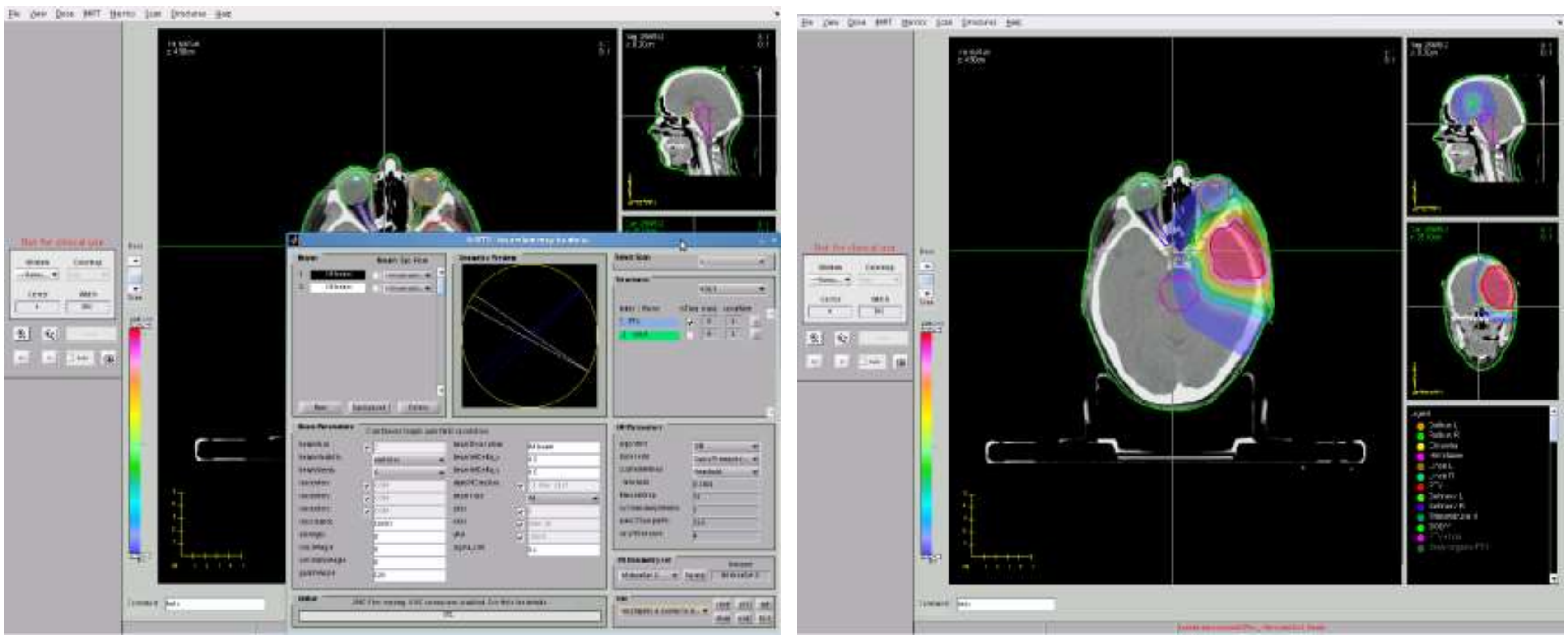
5. Towards preclinical prototype

Dose delivery to large tumor volumes:

- Treatment planning in collaboration with Prof. J. Wilkens
- Application of 3D TPS - CERR-LAP with our Gantry

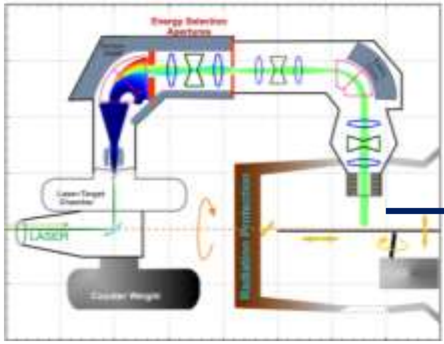
Munich-Centre for Advanced Photonics

Technical University Munich



K. M. Hofmann, U. Masood, J. Pawelke, J. J. Wilkens, AAPM & DGMP Conference 2014

5. Towards preclinical prototype



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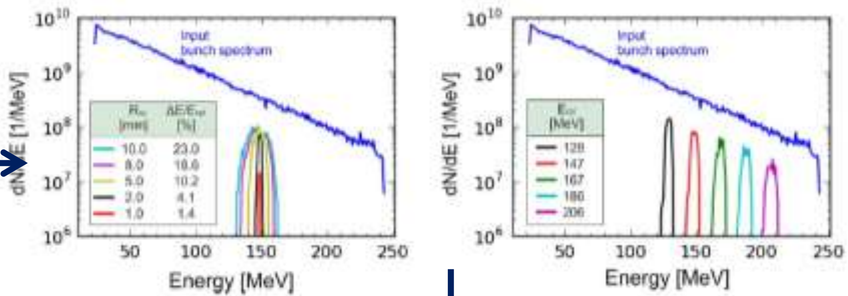

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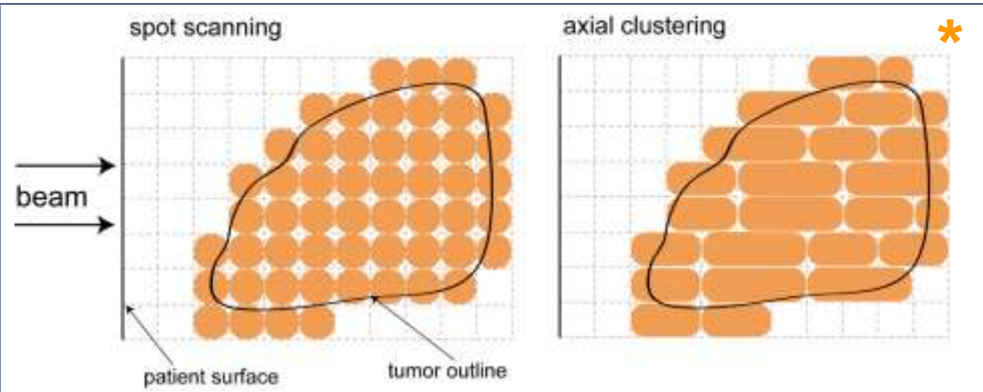
Treatment Planning System (TPS)

a) Vary lateral width of beam

b) Vary proton number in input spectrum



1. Only integer shots possible

2. Modulate proton intensity from shot-to-shot

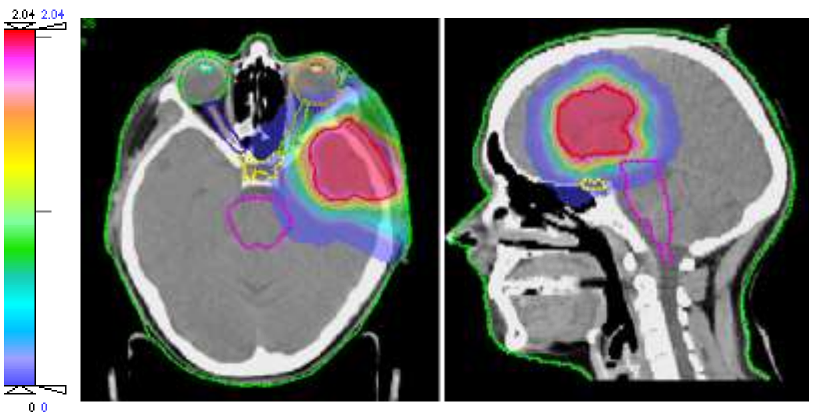
Multiple 3D proton plans

- Clinically interesting plans
- Plans which need detailed review
- Not acceptable plans

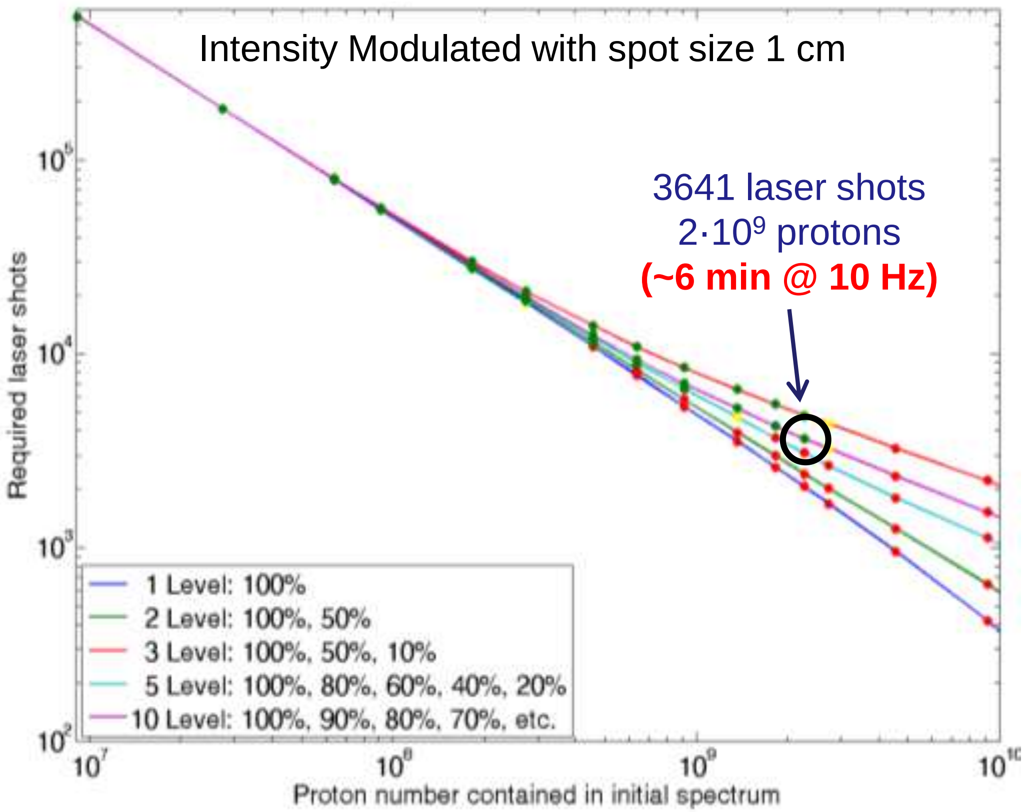
* *S Schell, JJ Wilkens: Med Phys 37 (2010) 5330*

Dose delivery to large tumor volumes:

- Hundreds of treatment plans varying beam spot size, proton number and intensity modulation in input spectrum
- Treatment plans of high clinical quality

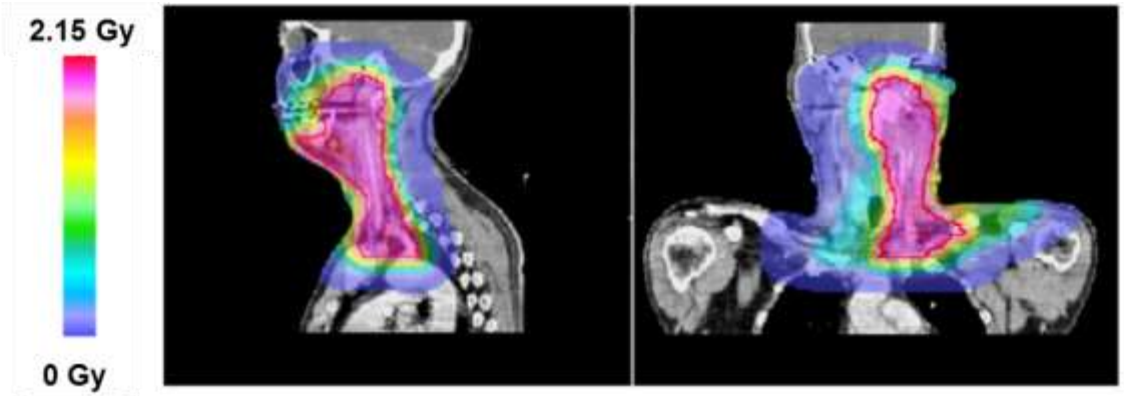


Astrocytoma, V_{PTV} = 274 cm^3, Gantry: $50^o/120^o$



Hofmann et al.: Med Phys 42 (2015) 5120
Masood et al.: Phys Med Biol 62 (2017) 5531

5. Towards preclinical prototype



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Treatment planning evaluation:

Tumour volume	600 cm^3
Beam directions	50° and 300°
Beam spot size	2 cm (FWHM)
Energy widths	3 – 19%
Proton bunches	12326
No. of protons/bunch	3.75×10^6
Irradiation time (@ 10 Hz)	8 – 10 min *But: 5x conventional times!*

Hofmann et al.: Med Phys 42 (2015) 5120 & Masood et al.: Phys Med Biol 62 (2017) 5531

5. Towards preclinical prototype

University Proton Therapy Dresden:

History

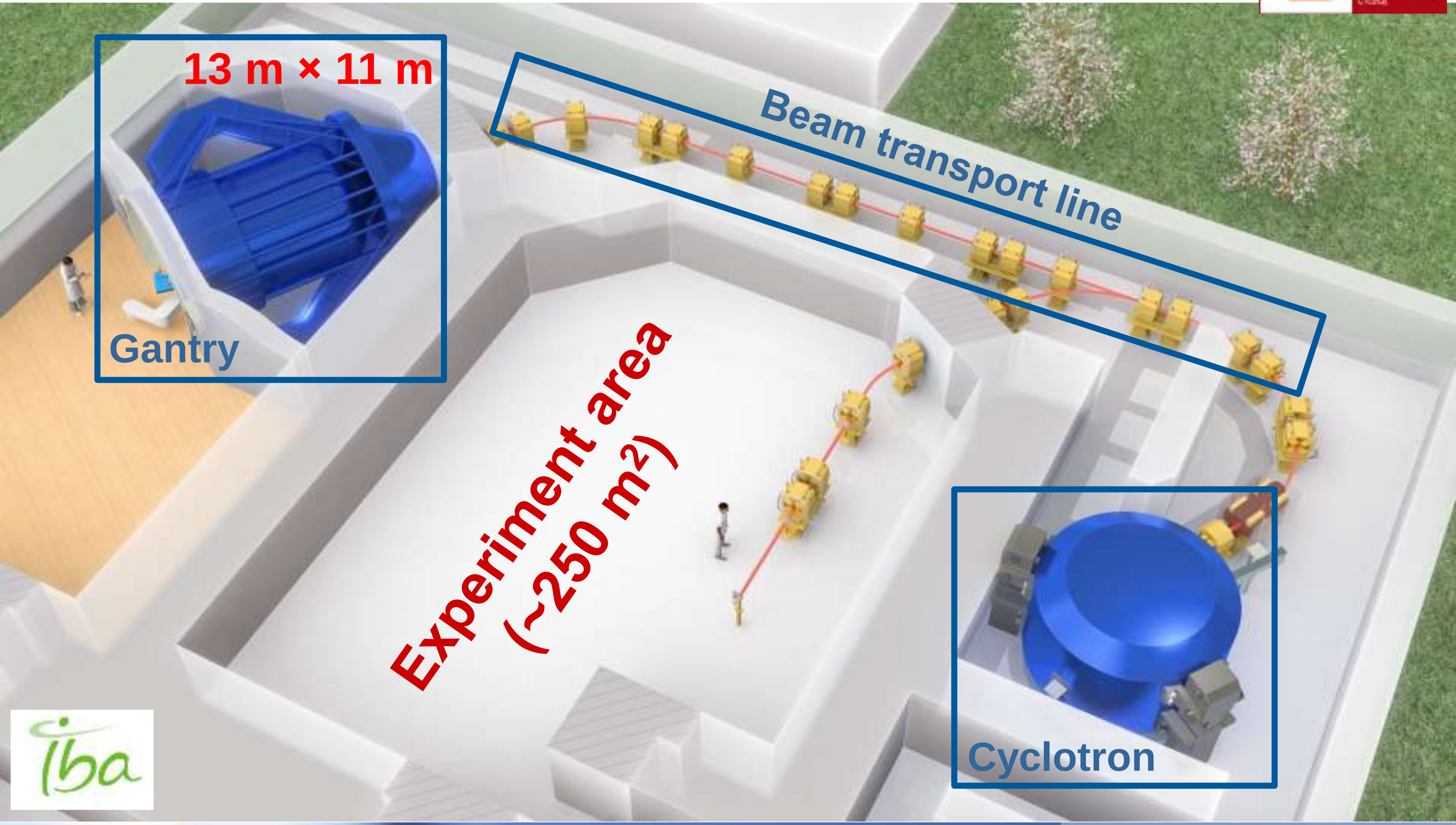
- Layout conclusions: 2007
- Financing: 2009
- Start construction: May 2011
- Roofing ceremony: May 2012
- Inauguration: Sep. 2013
- 1st patient: Dec. 2014
- 1st experiment: Feb. 2015

Present

- Increase number of patients (aiming for >270 patients in 2019)
- Experiments in parallel to patient treatment

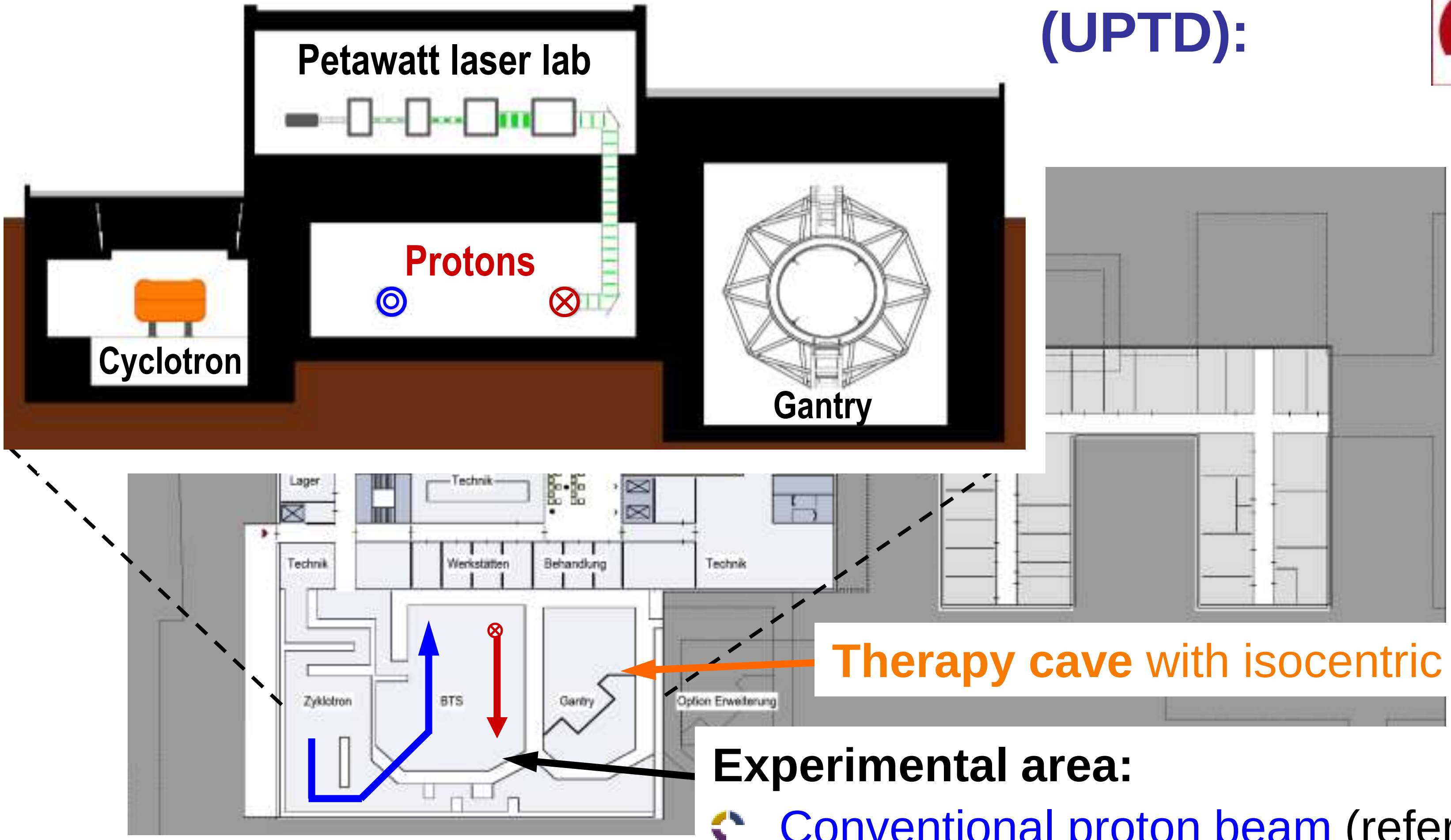
5. Towards preclinical prototype

University Proton Therapy Dresden (UPTD):



5. Towards preclinical prototype

(UPTD):



Experimental area:

- Conventional proton beam (reference)
- Laser-driven protons (prototype system)

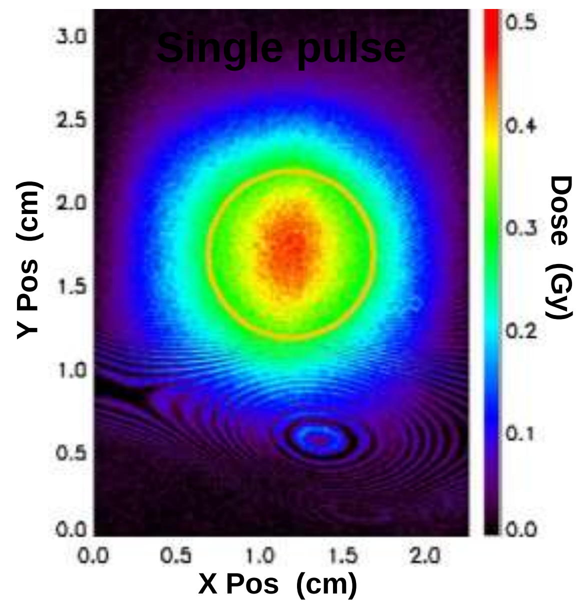
⇨ ***Integrating prototype laser accelerator into clinical setting***

5. Towards preclinical prototype

Experimental area:

- Conventional proton beam
  - Horizontal
  - Monochromatic
  - *d* = 10 mm (FWHM)
  - *E* = (70 – 230) MeV
  - *I* = (0.1 – 10) nA
- Flexible beam pulsing
  - *T*, Δ*t* = 100 ms … min
  - DPP = mGy …Gy
- Pulse magnet tests

Single pulse



Summary

Laser-based irradiation technology is established for cell and small animal irradiation with electrons and protons.

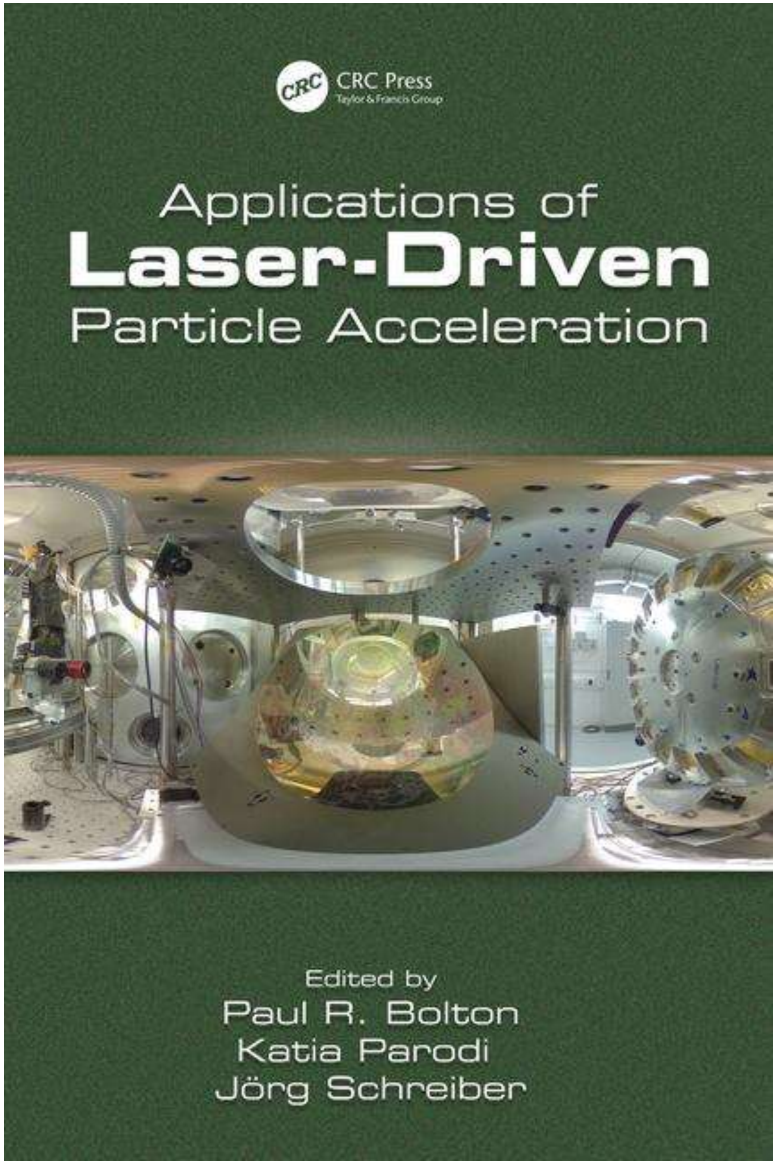
Medical proton beam units require new approaches for efficient and tumor conform irradiation of large target volumes by a rotating gantry.

Laser system and acceleration process improvement are crucial for providing therapy relevant proton beams (increase of proton energy, pulse repetition rate, stability, reproducibility, …).

Development of a preclinical prototype still needs a lot of research and will take years!

Read more ....

- June 5th, 2018 by CRC Press
  ISBN 9781498766418, also eBook
  388 pages, 166 illustrations, 24 chapters
- Part I: Acceleration mechanisms and capabilities
  - Laser-driven electron & ion acceleration
  - Associated photon & neutron generation
- Part II: Applications of laser-driven beams for
  - 8: radiobiological experiments
  - 10: fast radiobiological processes
  - 11: ion beam therapy (LIBRT)
  - 12: radiography & tomographic imaging
  - ......



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  T. Cowan, U. Schramm (laser particle acceleration, beam transport)
  W. Enghardt (medical radiation physics), F. Fiedler (radiation physics)
  G. Pausch (*in vivo* dosimetry), K. Zuber (detectors), J. Henniger (dosimetry)
  M. Baumann, N. Cordes, A. Dubrovska, M. Krause, L. Kunz-Schughart, J. Steinbach (*in vitro* and *in vivo* experiments)
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- **Network and contacts on proton/ion radiotherapy**
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Please visit Dresden !

THANK YOU FOR YOUR ATTENTION!

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