Cancer therapy with photons, protons and heavy ions

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Overview

- Introduction
- Overview
- Particles in radiation therapy
- Raster scan method
- Summary

Introduction

Motivation

→ tumor therapy requires

→ affected tissues to be removed

→ spreading to get stopped

→ not killing the patient while doing that.

→ chirurgic treatment needs accessibility to tumor

→ chemical treatment stresses the overal body much

→ radiation therapy can target more precisely

History

1895 Wilhelm Conrad Röntgen „a new kind of radiation“

1897 first medical treatment with X-rays

1957, Berkeley, first proton beam therapy

1975, Berkeley, first use of heavy ions.

1979, GSI Darmstadt, SIS12 (SIS18 in 1984) for 1.4 GeV/n

1993, Chiba, carbon beam therapy department founded

1993-97, GSI Darmstadt, carbon beam therapy facility founded

→ development of raster scan procedure

→ development of PET quality control

→ measurements of ion species dependand RBE

2002, Hyogo, carbon beam facility founded

2009, Heidelberg, HIT carbon beam facility, ~ 500 patients per year

2012, Kiel, and 2015 in Marburg, carbon beam facility founded

Overview

Ionizing particles hit Cell

→ Low energy transfer creates oxygen radicals

→ DNA gets damaged beyond repair

→ Cell division is disturbed (mitotic cell death)

→ Cell dies (Apoptosis, blebbing, nucleus fragmentation)

Effectiveness depends on:

→ deposited energy

  → Choice of particles

  → technical application

→ biological reaction to particle

Particle in Radiation Therapy

Particles used for radiation therapy:

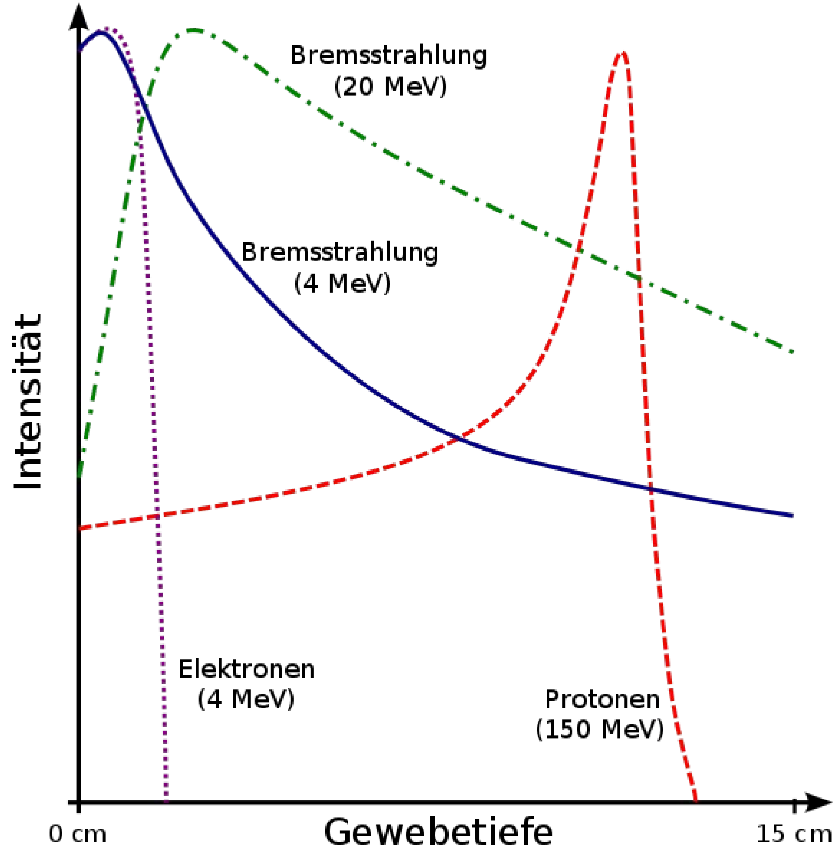
→ Photons

→ Electrons

→ Neutrons

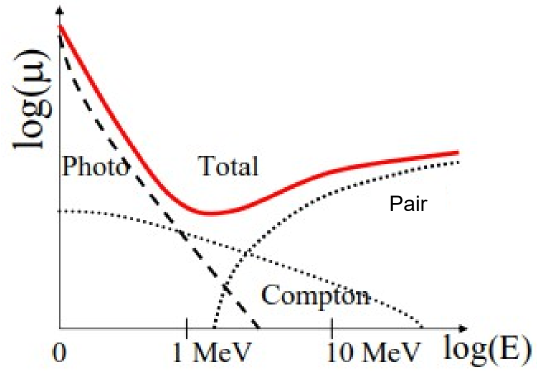
→ Protons

→ Ions



https://de.wikipedia.org/wiki/Tiefendosiskurve

Particle Interaction: Photons



Photons (<23MeV)

→ Easy to produce

→ Xrays (~120 keV) mostly photoeffect

→ energy deposition exponentially decreasing

→ additional energy deposition by secondary electrons

→ healthy tissue before and after target tissue is affected

Photoeffect: bound electron absorbs photon and gets released

$$E_{kin} = h \cdot f - E_{\text{Bindung}}$$

Compton: photon scatters at free electron and looses energy

$$\Delta\lambda = \frac{h}{m_e c}(1 - \cos\phi) = \lambda_C\,(1 - \cos\phi)\ .$$

Pair production: if $E_\gamma > 2m_e c^2$, a electron positron pair can be produced

inside the field of a nucleus

Particle Interaction: Electrons

Electrons

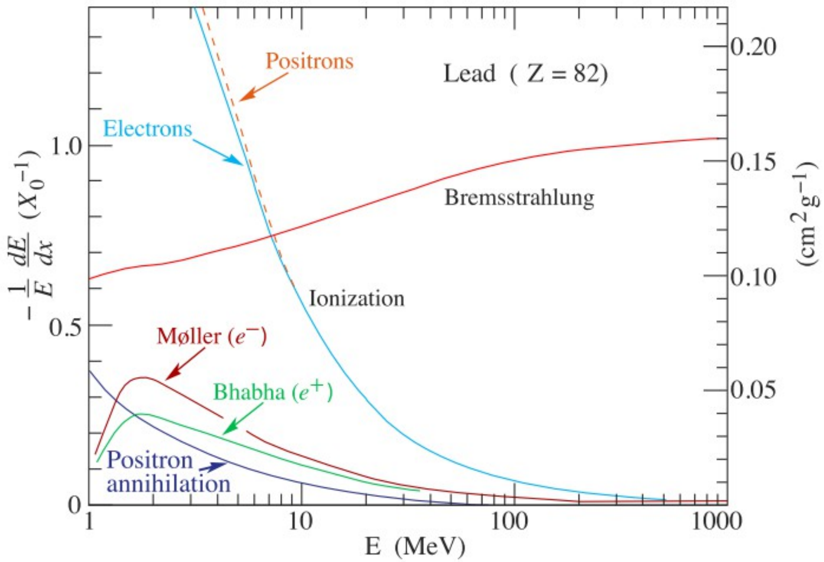
→ high energy: Bremsstrahlung

→ low energy: ionisation and excitation.

→ maximum range (~ 0.5 cm/MeV)

→ less energy deposition per collision than photons

→ elastic collision lead to additional beam spread



http://pdg.lbl.gov/2013/reviews/rpp2013-rev-passage-particles-matter.pdf

Particle Interaction: Protons

Protons

→ produced by particle accelerator

→ high energy: inelastic collisions with target electrons

→ lower energy: inelastic collisions with nuclei

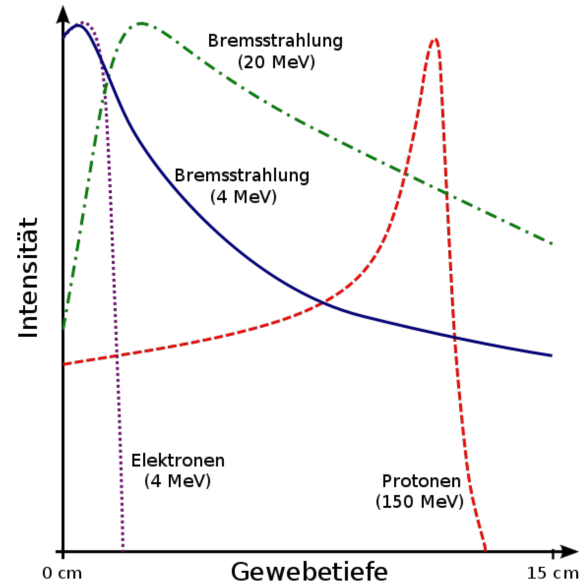
→ elastic scattering at nuclei: beam spread

→ energy deposition decreases with square of velocity

→ result: proton slows down until stop at energy deposition peak

→ „Bragg peak“

$$\frac{1}{\rho}\frac{dE}{dx} = Kz^2\frac{Z}{A}\frac{1}{\beta^2}\left[\frac{1}{2}\ln\frac{2m_e c^2\beta^2\gamma^2 T_{\max}}{I^2} - \beta^2 - \frac{\delta(\beta\gamma)}{2}\right]$$



https://de.wikipedia.org/wiki/Tiefendosiskurve

→ low dose until maximum bragg peak, afterwards 0 dosage

→ bragg peak position depending on proton energy

→ less lateral scattering than X-Rays or electrons

Particle Interaction: Ions

Ions

→ similar processes as protons

→ higher mass

  → less inelastic scattering per dx

  → less dE/dx until bragg peak

  → little lateral scatter effect

→ higher linear energy transfer (LET) at bragg peak

  → much narrower bragg peak

  → also direkt cell damage effect by nuclear collision

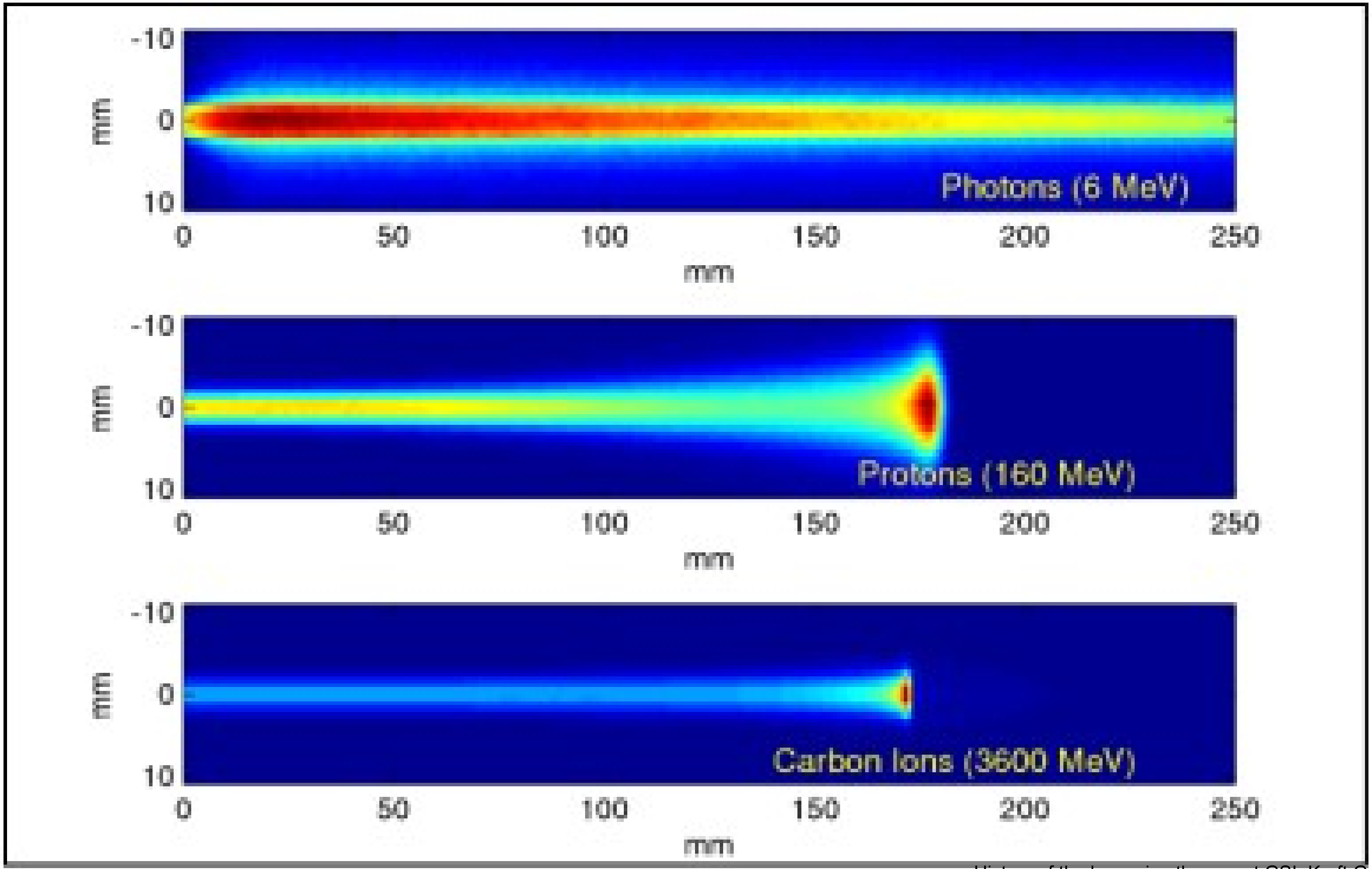
→ nuclear reactions with tissue: dE/dx > 0 behind bragg peak

→ higher energy needed for same bragg peak distance

→ common: carbon ions

  → highest overlap between biological effectiveness and energy deposition

Particle Interaction: Comparison



History of the heavy ion therapy at GSI. Kraft G

Neutrons

→ need nuclear reaction to produce (reactors, cyclotrons)

→ collisions at low energy produce protons in tumor cell

→ better for low oxygen cells

→ only 1/3 effective dose of protons needed

→ similar deposition curve as X-Rays

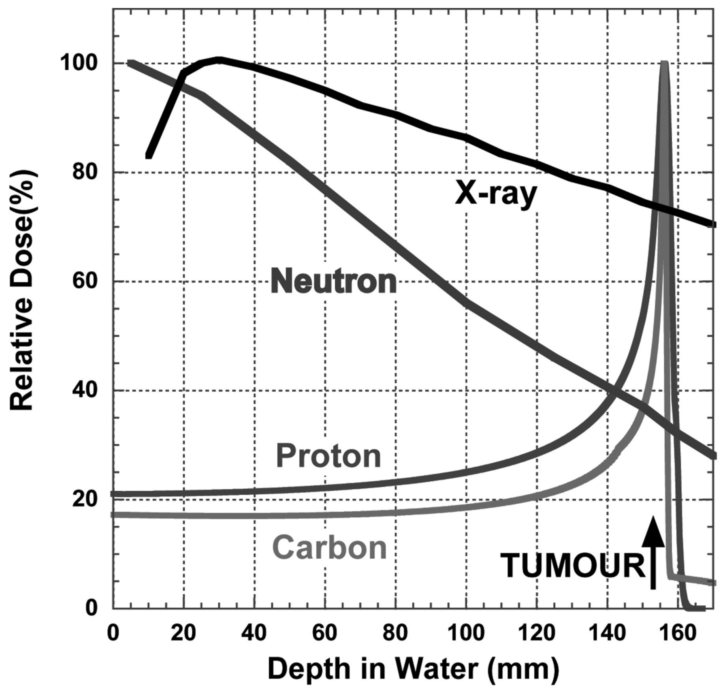
→ using Bor in cell can be more effective:

$$n + {}^{10}\mathrm{B} \longrightarrow {}^{7}\mathrm{Li} + \alpha$$

→ cell gets destroyed directly

→ most dE is at surface

→ high biological effectiveness and bad in depth dose distribution means high damage at healthy cells



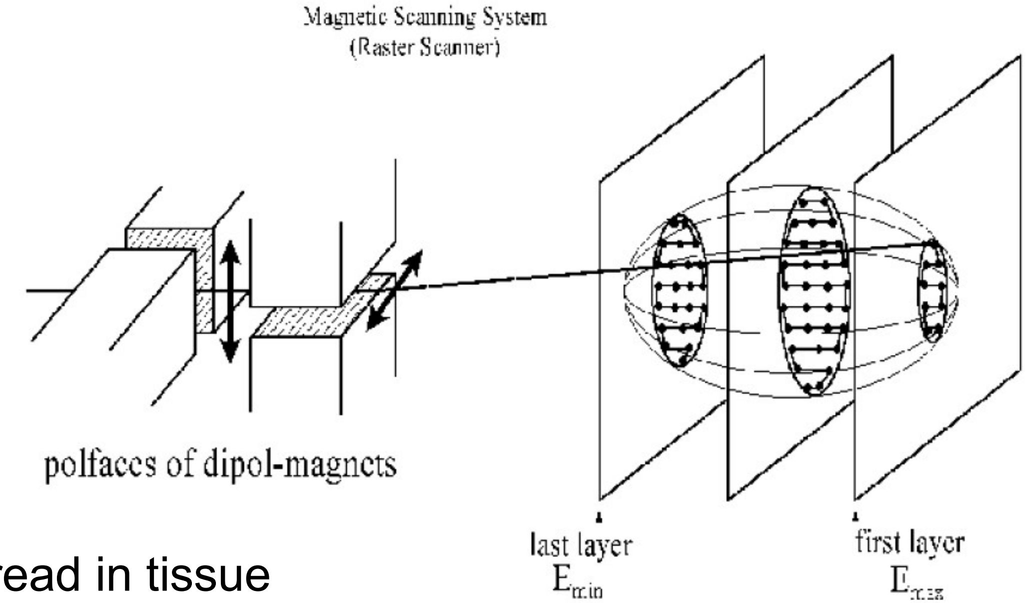
http://rpd.oxfordjournals.org/content/137/1-2/149/F1.large.jpg

Raster Scan Method: Idea

Idea:

→ dipolmagnets scan tissue lateral

→ protons/ions: energy determines depth (bragg peak)



Tumortherapie mit Ionenstrahlen, GSI, Kraft G

Problem:

→ energy deposition spread in tissue

→ minimize energy deposition at healthy tissues

→ tissue species reacts differently to same dosage

→ hard to target moving body parts (e.g. lung, intestines)

Raster Scan Method: RBE

RBE: Relative Biological Effectivenes

→ quotient of dose to a reference type of radiation
with same biological effect.

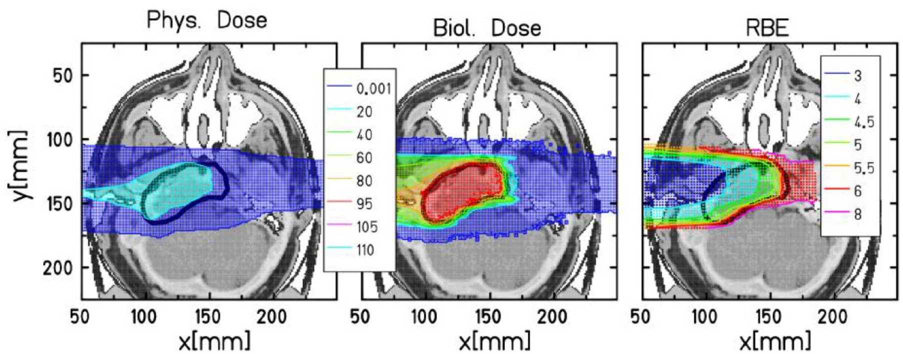
→ increases with LET (DNA double-strand breaks)

→ highly depends on ion species and type of tissue

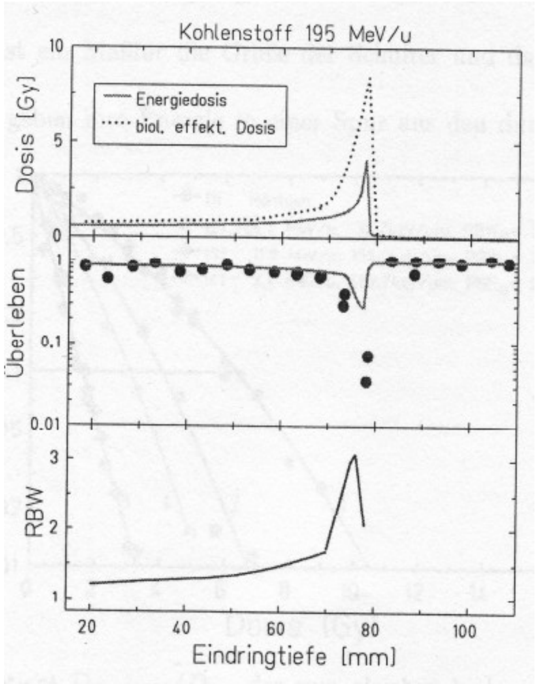
→ biological effective dose = RBE * energy deposition

→ determined experimental

→ carbon has RBE maximum at bragg peak



History of the heavy ion therapy at GSI. Kraft G, courtesy Michael Kraemer, GSI



Wilma K. Ewyrather, Gerhard Kraft, GSI
Darmstadt – Abt. Biophysik

Raster Scan Method: Spread Out Bragg Peak

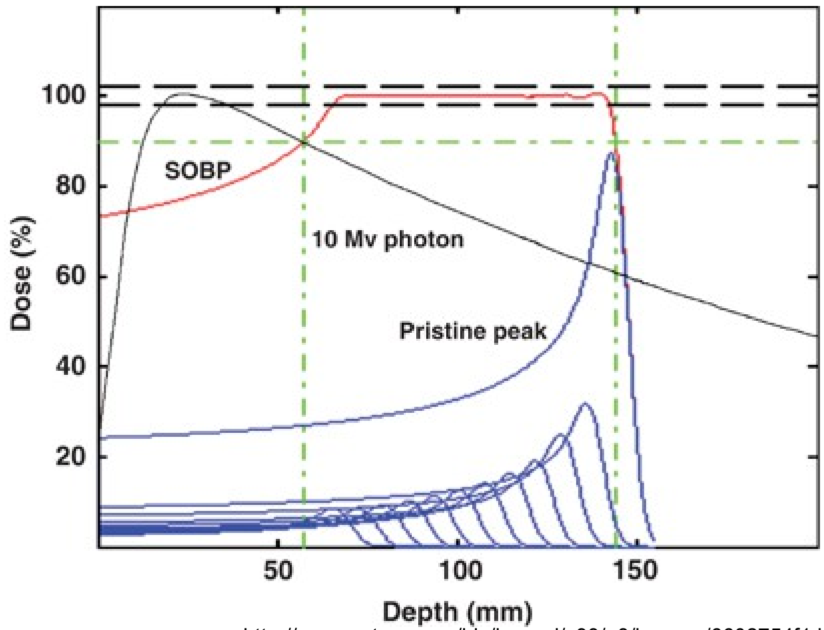
Spread out bragg peak:

→ overlaying ion beams with different energies

→ spreading bragg peak longitudinal

→ keeping target-dose constant

→ minimizing collateral dose



http://www.nature.com/bjc/journal/v93/n8/images/6602754f1.jpg

Raster Scan Method: Application

Raster Scan procedure

→ tumor division into slices

~ 100 slices

→ each slice is divided into raster cells

~ 10 - 30000 raster cells per slice

→ beam diameter ~ 3 raster cells

→ from RBE & energy deposition,

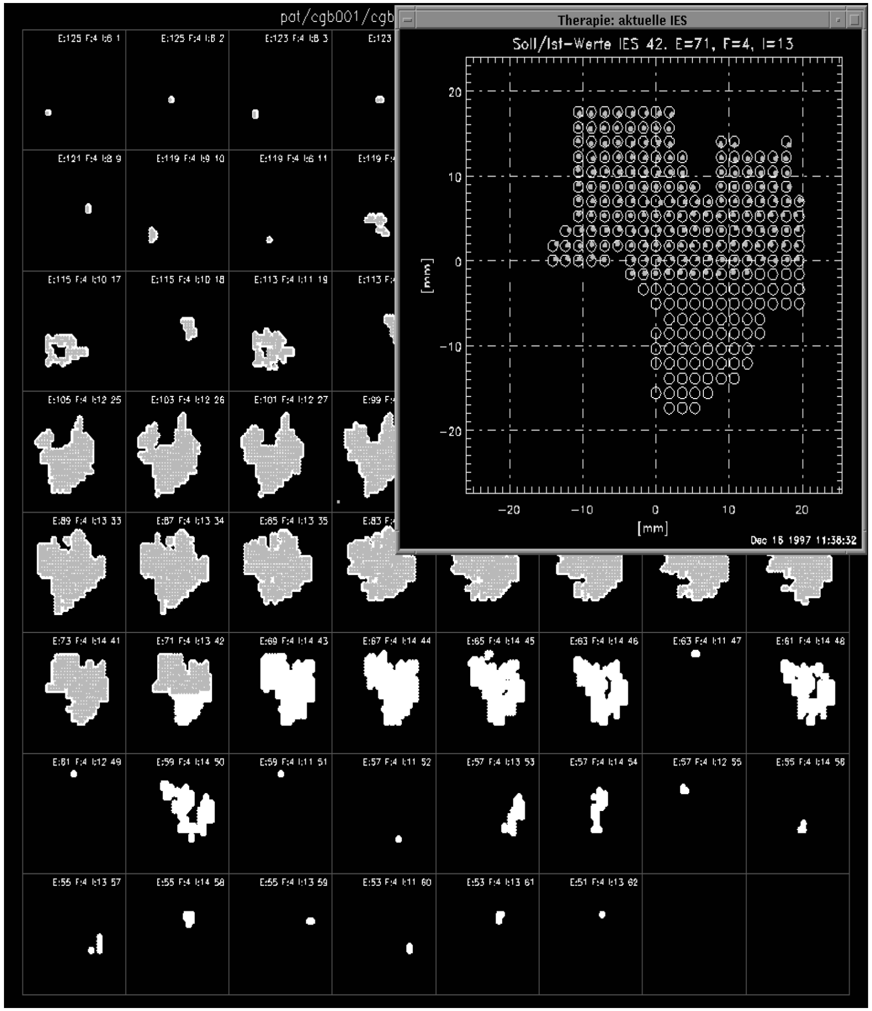
to be applied energy is computed

Example:

→ complete application time: 5-10 min

→ daily application for 20 days

→ beam size ~ 6 mm



Tumortherapie mit schweren Ionen, GSI, Gerhard Kraft

Raster Scan method: PET

PET (Positron Emission Tomography) Verification:

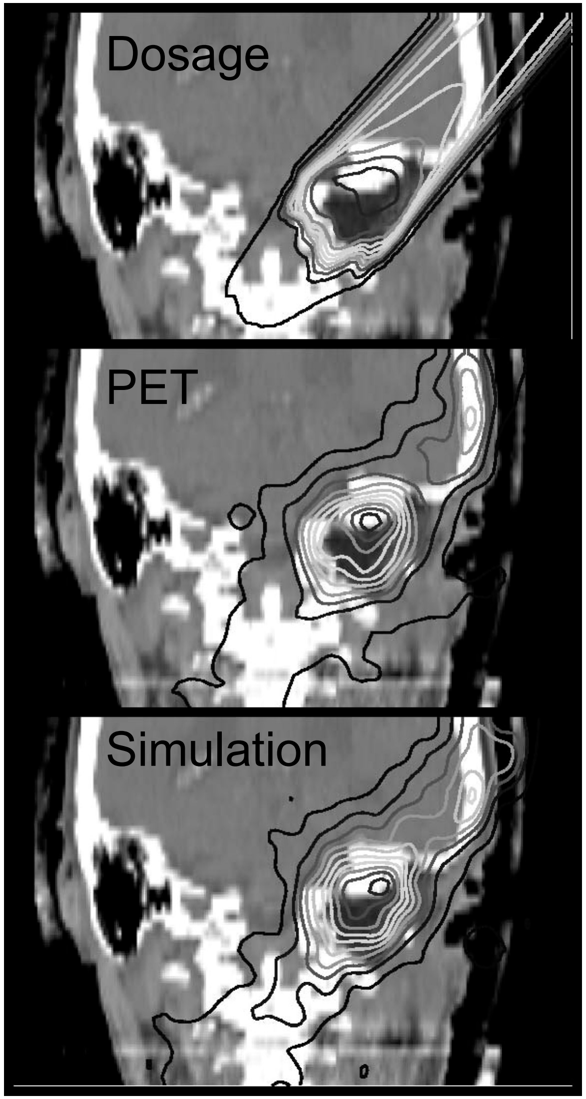
→ quality control: which dosage was applied where

→ nuclear collisions produce instabile atoms.

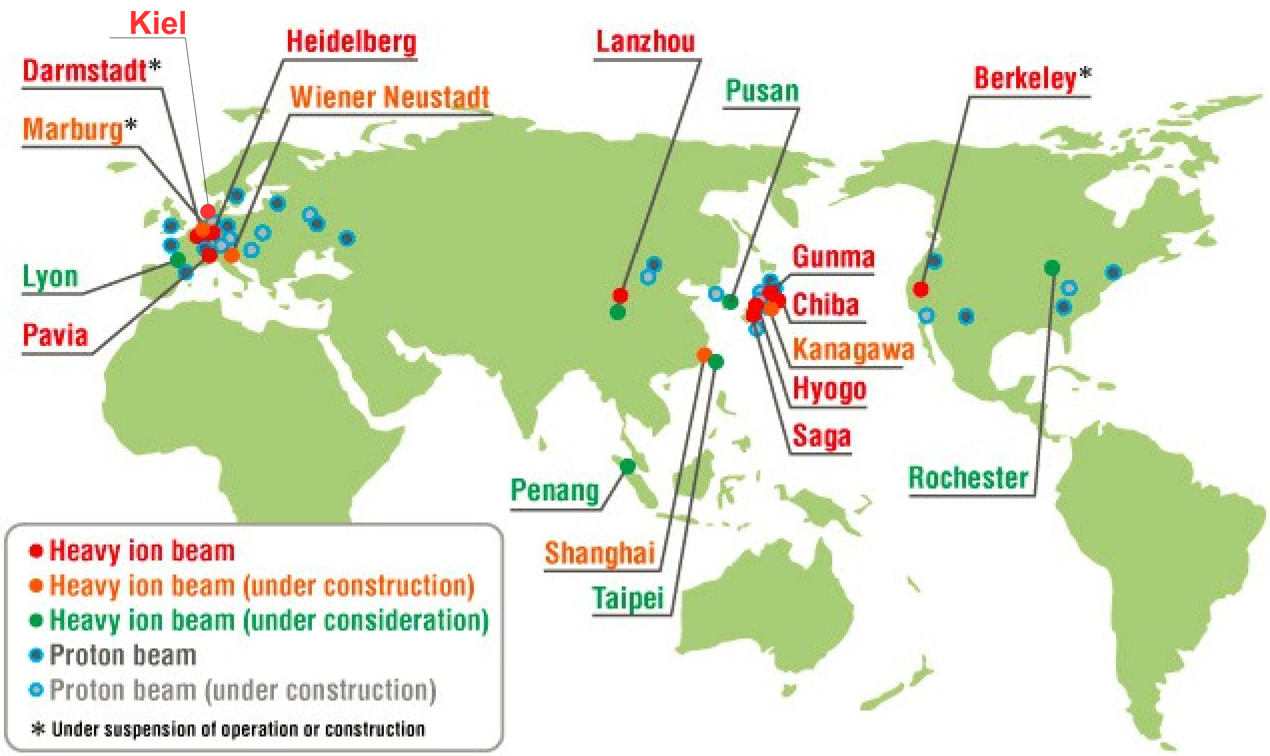
→ ^{10}C, ^{11}C and ^{15}O decay emitting positrons

→ positrons decay into 2 gamma ~ 511 keV

→ detection gives estimate of beam particle reach



Facilities



http://www.hirt-japan.info/en/what/japan.html

→ during 2013 105.000 patients successfully treated with protons

→ 13.000 patients per year treated by heavy ions

→ ~ 49 working proton beam facilities

→ ~ 10 working ion beam facilities using carbon

Summary

→ radiation therapy is nowadays established cancer therapy method

→ photons, electrons, neutrons, protons and ions

→ heavy ion beams promise to be most effective method (situational)

→ RBE, raster scan method and PET further increases precision

→ facilities for heavy ion beam production are still expensive,

but centers are build all over the world

Papers and references

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