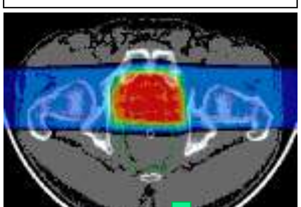
Accelerating ions to beat cancer

Katia Parodi, Ph.D.

Department of Medical Physics,
Ludwig-Maximilians-University Munich, Germany

(also affiliated to Heidelberg Ion Beam Therapy Center, Heidelberg, Germany)

The three columns in the fight against cancer

Surgery	Radiotherapy	Chemotherapy and others
		

Local tumour control,
Palliative treatment

Localised tumour

Survival
Quality of life

Metastatic tumour

The three columns in the fight against cancer

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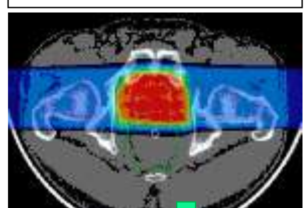

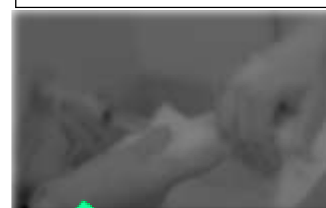

Local tumour control,
Palliative treatment

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The history of radiation therapy

EINE NEUE ART

STRAHLEN.

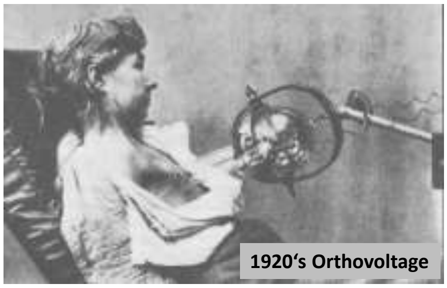
1895: W. C. Röntgen discovers the X-rays at University in Würzburg

1st physics Nobel prize in 1901

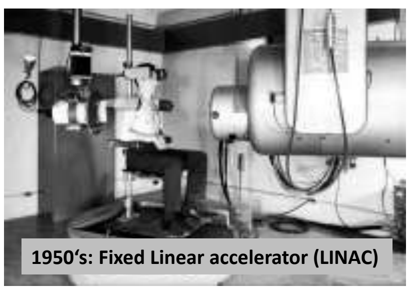
1896: First treatments of tissue with X-rays by L. Freund at University in Vienna

1899: First radiation therapy treatment of a tumour – T. Stenbeck in Stockholm

The evolution of radiation therapy in the 20th century

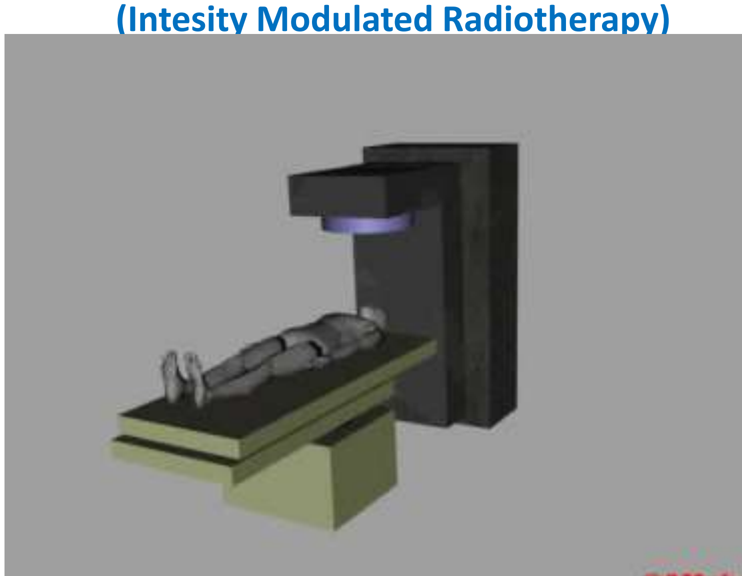

1920‘s Orthovoltage


1950‘s Cobalt source

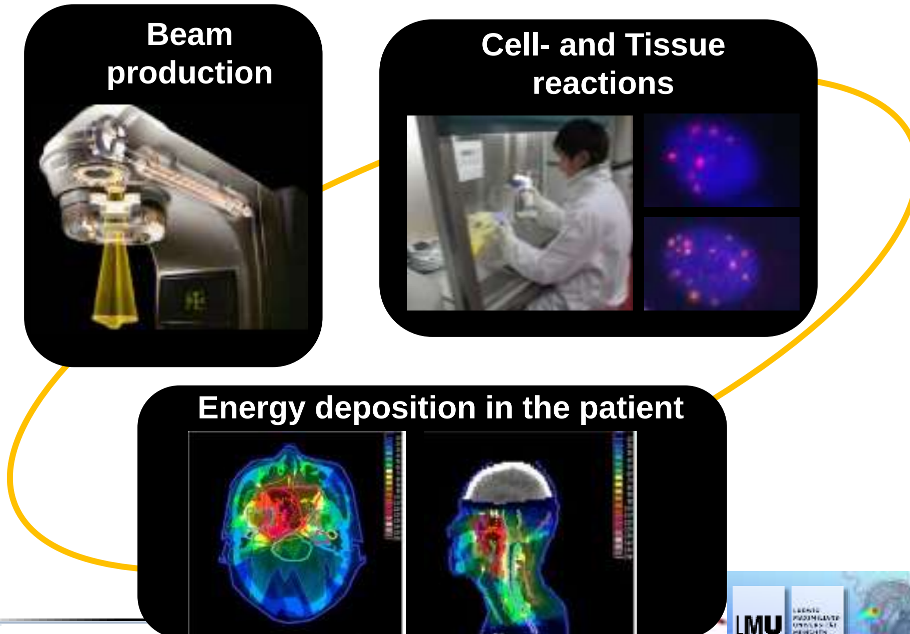

1950‘s: Fixed Linear accelerator (LINAC)


>1960‘s: Rotating LINACs

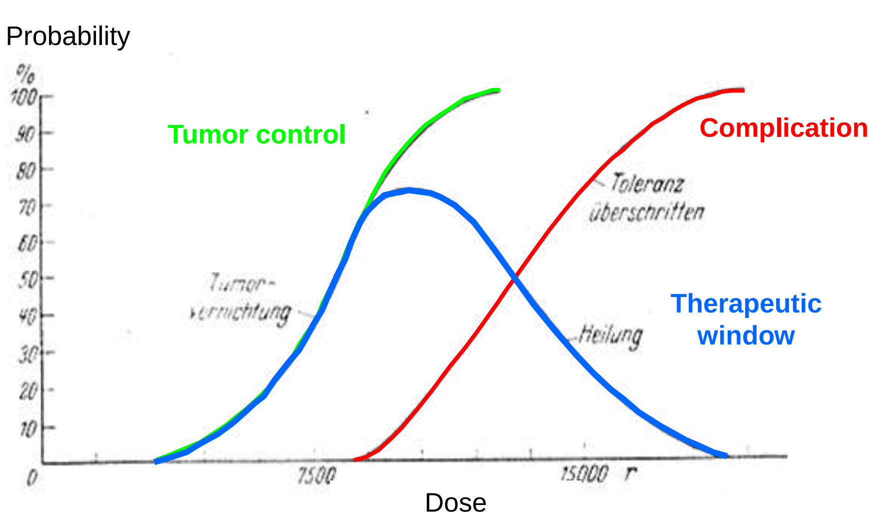
Modern photon therapy (Intesity Modulated Radiotherapy)



Radiation therapy: a highly interdisciplinary science



What is the „Dose"?



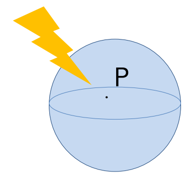
H. Holthusen, Strahlentherapie 57: 254-268, 1936

What is the „Dose"?

The dose (for ionizing radiation)

Average amount of energy absorbed per mass of irradiated volume

[1 Gy = 1 J / 1 kg ≈ 0.24 Calories / 1 Kilogram]



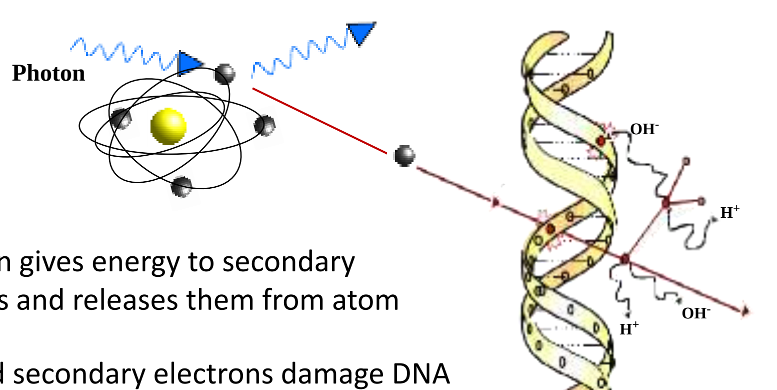
The „dose" of a cup of coffee

Average energy absorbed per mass due to thermal effects would result in „dose" > 20 Gy

This is **5 times higher** than a whole body dose with only 50% survival probability

A microscopic insight into ionizing radiation interactions

- DNA is sentive target in cell nucleus



M. Hill, MRC, Harwell

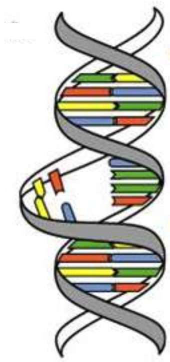
- Radiation gives energy to secondary electrons and releases them from atom
- Released secondary electrons damage DNA

Established Radiation Therapy im 21st Century

The 3 "C's" of Radiation Therapy

1) **"C**ure"
   ~ 50% of cancer cases can be cured
2) **"C**onservative"
   Non-invasive, limited side effects
3) **"C**ost-effective"
   Only ~ 5% of total costs for cancer therapy

(J.P.Gérard)

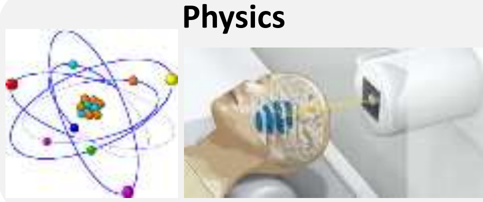


Current challenge:
In ~30% local tumour control fails

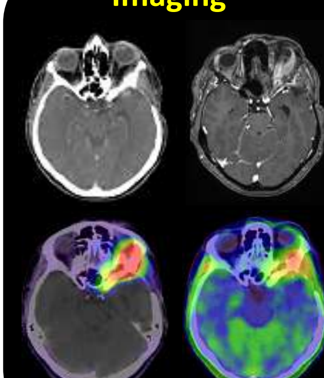
Acta Oncologica, Suppl:6-7, 1996

How to improve treatment outcome?

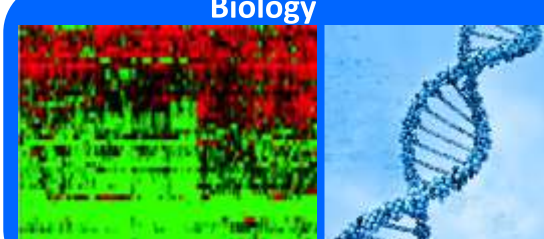
Physics



Imaging



Biology

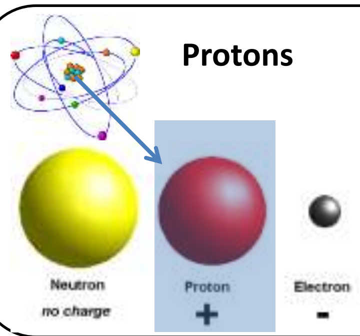


Physics

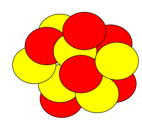
Are other types of radiation more promising than energetic X-rays?

Energetic Ions (protons, carbon)

Protons

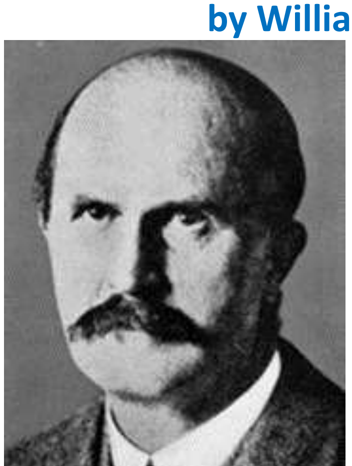


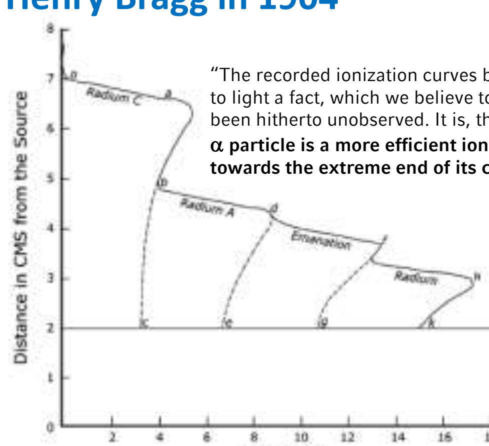
Carbon



6 protons
6 neutrons

The 'Bragg peak' discovery by William Henry Bragg in 1904





"The recorded ionization curves brought to light a fact, which we believe to have been hitherto unobserved. It is, that **the α particle is a more efficient ionizer towards the extreme end of its course.**"

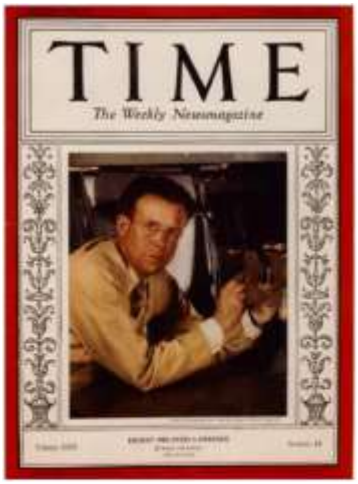
Phil. Mag. 1904; S.6:726–38

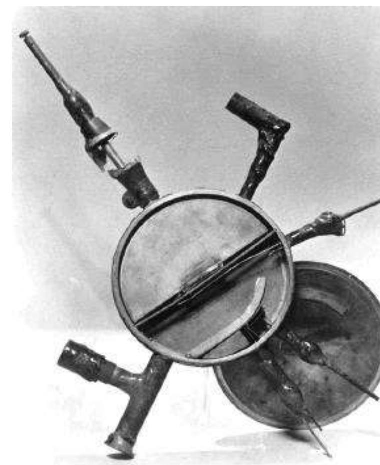
Nobel prize in 1915 together with his son William Lawrence Bragg

Courtesy O Jäkel

The production of energetic protons

- Cyclotron accelerator (1929)
- E. O. Lawrence, Nobel Prize in 1939





The production of energetic heavy ions (incl. Carbon)

- Synchrotron accelerator (1945)
- Independently invented by Edwin M. McMillan in USA and Vladimir I. Veksler in Soviet Union

Edwin Mattison McMillan
Nobel Prize in Chemistry (1951)

Vladimir Iosifovich Veksler

Shared Atoms for Peace Award in 1963

The birth of ion therapy

Radiological Use of Fast Protons
ROBERT R WILSON

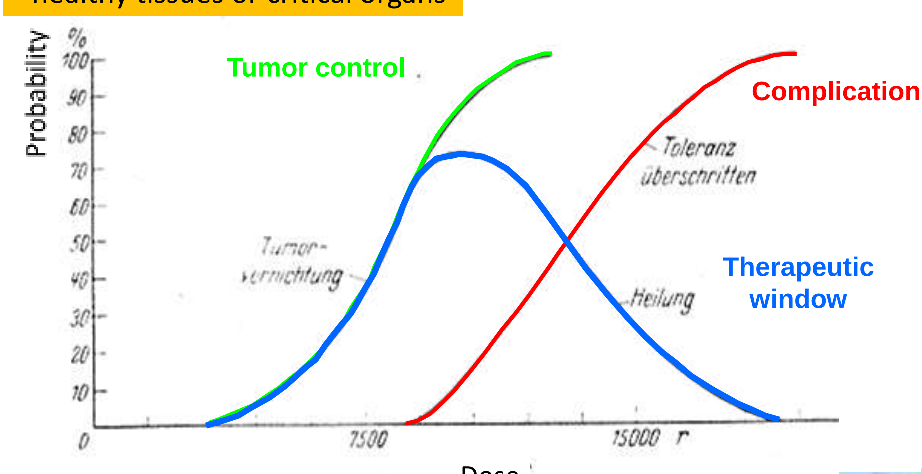
Research Laboratory of Physics, Harvard University Cambridge, Massachusetts
Accepted for publication in July 194

Radiol. 47 (1946) 487-91

- 1946: article by Robert Wilson
  - Protons can be used clinically
  - Accelerators are available
  - Maximum radiation dose can be deposited into the tumour sparing healthy tissues
  - „Heavier nuclei, such as very energetic carbon atoms, may eventually become therapeutically practical“
- 1954: first patients treated in Berkeley with protons
- 1975: first patients treated in Berkeley with heavy ions

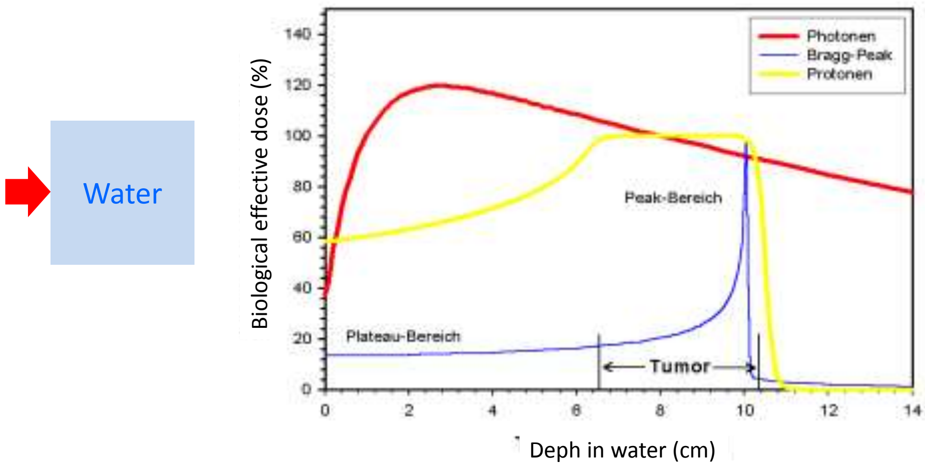
Physics:

- 100% of the dose on target
- 0% of the dose in surrounding healthy tissues or critical organs



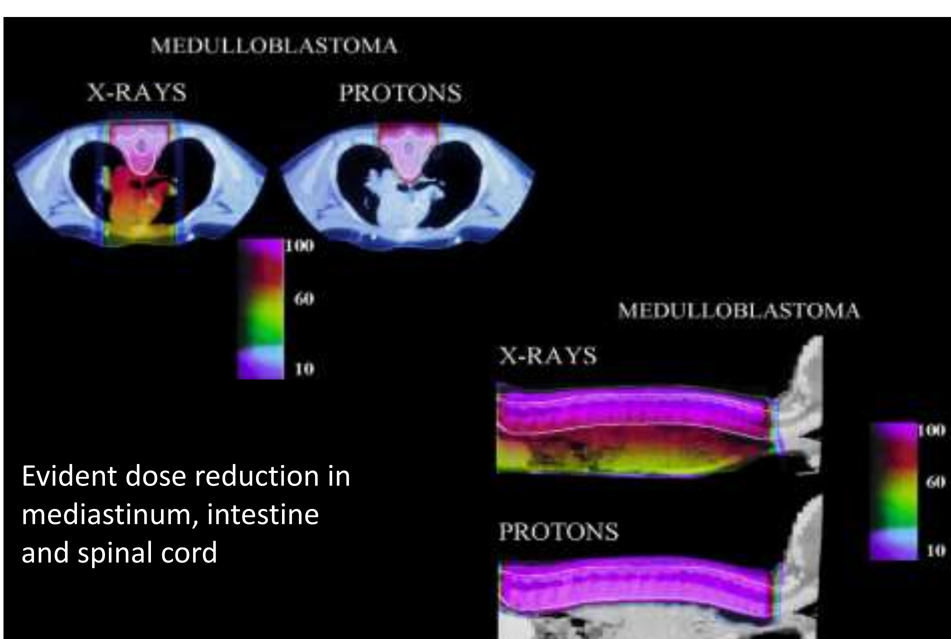
H. Holthusen, Strahlentherapie 57: 254-268, 1936

Advantages of ion beams: depth conformality



- Sparing of normal tissue in entrance channel
- No / low dose in exit channel distal to the tumour

RT for Medulloblastoma: Photons vs. Protons

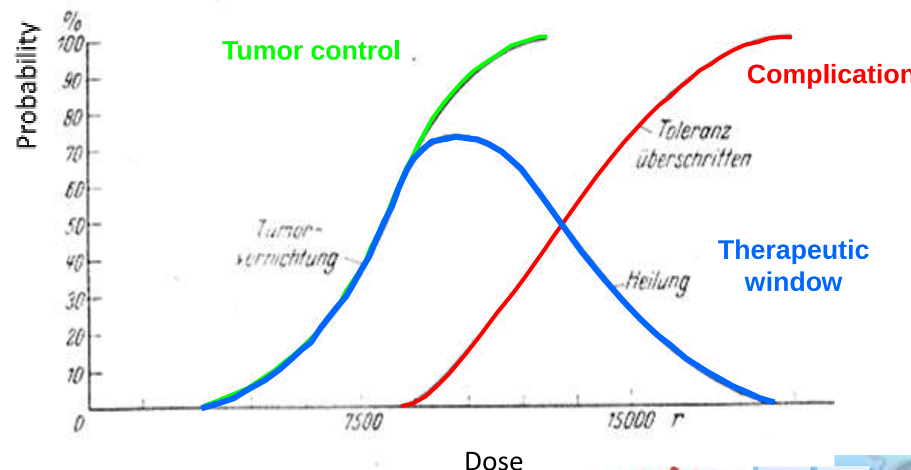


Physics:

- 100% of the dose on target
- 0% of the dose in surrounding healthy tissues or critical organs

Biology :

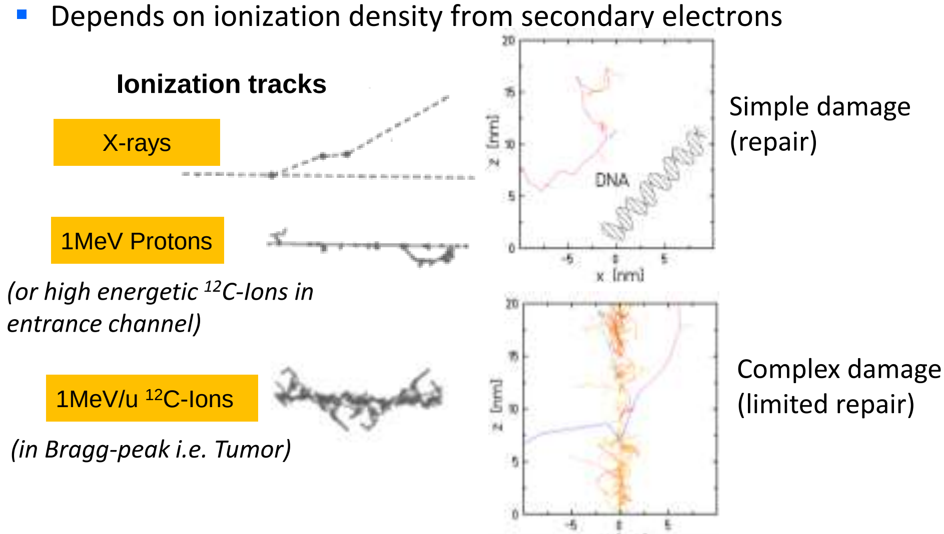
- differential effect
- kill 100% of cancer cells
- "protect" normal cells



H. Holthusen, Strahlentherapie 57: 254-268, 1936

Biological effectiveness

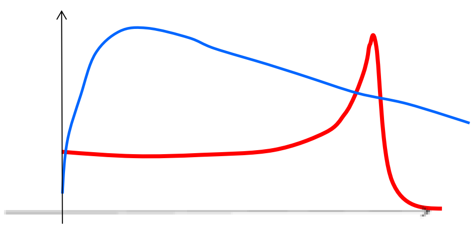
- Is mainly based on double strand breaks of DNA in cell nucleus
- Depends on ionization density from secondary electrons



Ion therapy vs “conventional” radiotherapy

With repect to photons ions offer

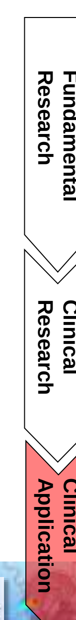
- Improved physical dose deposition
- More complex damage of tumor cells (esp. carbon ions)



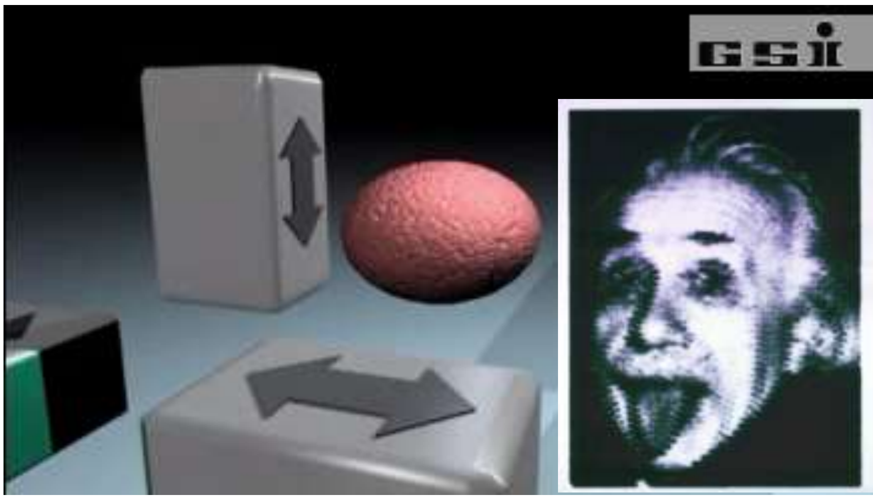
- Tumours close to critical organs
- Tumours in children
- Radio-resistant tumours

Robert R. Wilson (1914-2000)
Radiotherapy using charged particles

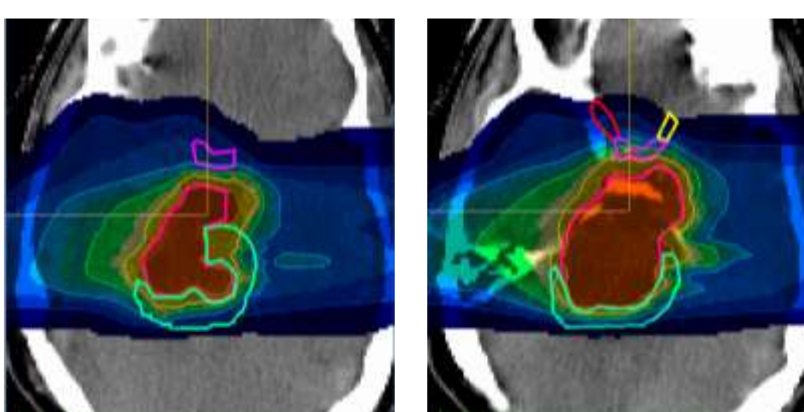
1946	Ion therapy for deep seeted tumors
1954	Lawrence Berkeley Laboratory, USA starts protontherapy
1957	Uppsala starts proton treatment
1975	Lawrence Berkeley Laboratory, USA starts using heavy charged particle
1990	Opening of the Proton Therapy Center in Loma Linda (USA)
1993	Start of Carbon Ion Therapy in Chiba (Japan)
1997	Protonentherapy starts in in Villingen/Schweiz
1997:	**Carbon ion Radiotherapy starts at GSI in Darmstadt**
Today	**Various clinical centers for particle therapy**
2009	**HIT Heidelberg**



Ion beam Scanning

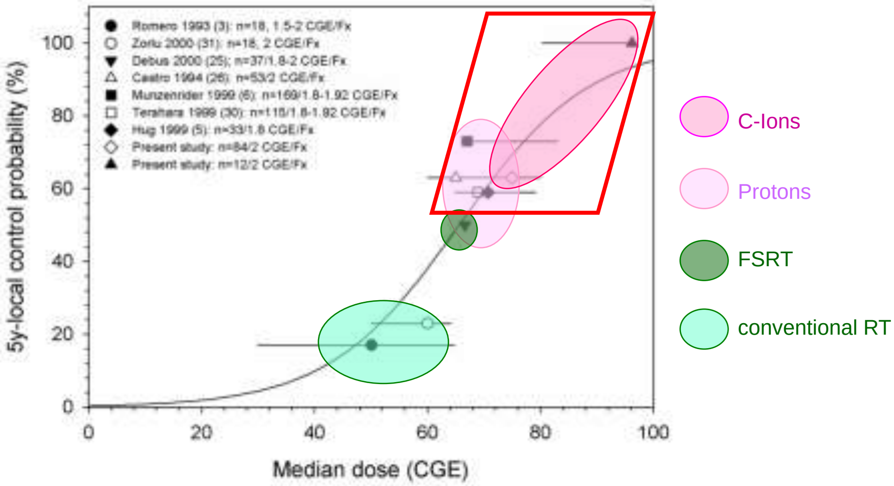


^{12}C-ion therapy for chordoma and chondrosarcoma of the skull base



Source: GSI Darmstadt

Dose Response Relationship
Radiotherapy of Skull Base Chordomas



Needed: Clinical trials

Schulz-Ertner, IJROBP 2007

The growing spread of ion therapy worldwide

- > 47 Proton therapy facilities (5 operational in Germany, 3 planned in UK)
- 8 Carbon ion therapy facilities, of which 4 combined with protons (Germany, Italy, Japan, China)

Worldwide more than 120,000 patients treated with ions

ENLIGHT

The European Network for LIGht ion Hadron Therapy

Several EU-funding for networking and improvement of ion beam therapy

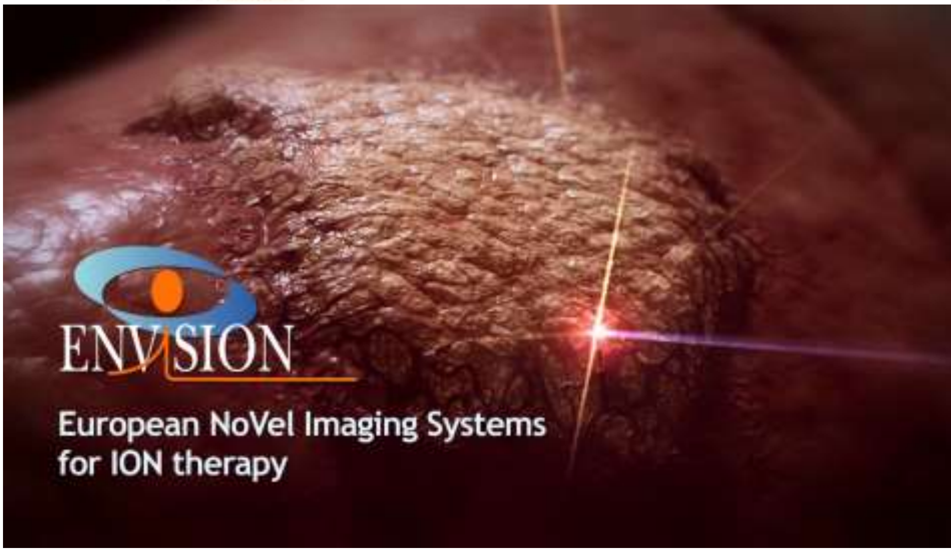
PARTNER 2008-2012

ULICE 2009-2014

ENVISION 2010-2014

ENTERVISION 2011-2015

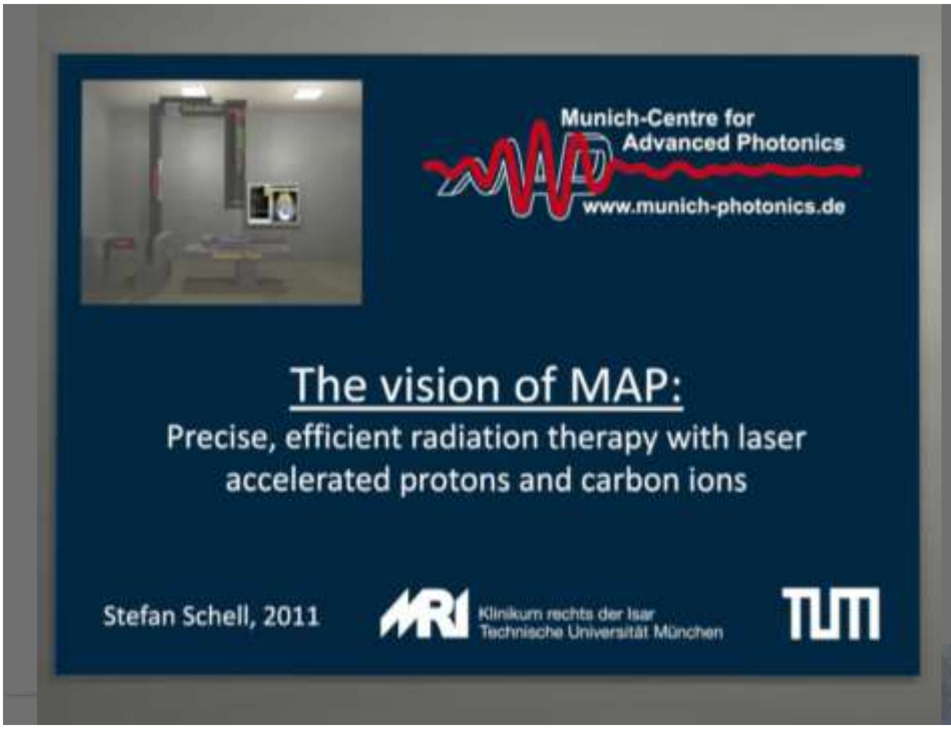
> 150 Institutions
> 400 People
> 25 Countries



A remaining challenge: compact and cost-effective instrumentation

… compared to modern photon LINAC

10 times bigger and costly



The Munich new laser-driven infrastructure

Thanks to …

Former colleagues / team at HIT and Universitätsklinikum Heidelberg

Jörg Schreiber and new team at LMU Munich

MAP, ENLIGHT

Funding (EU, BMBF, DFG)

First patient treatment at HIT, 15.11.2009

www.med.physik.uni-muenchen.de

…and you all for your attention