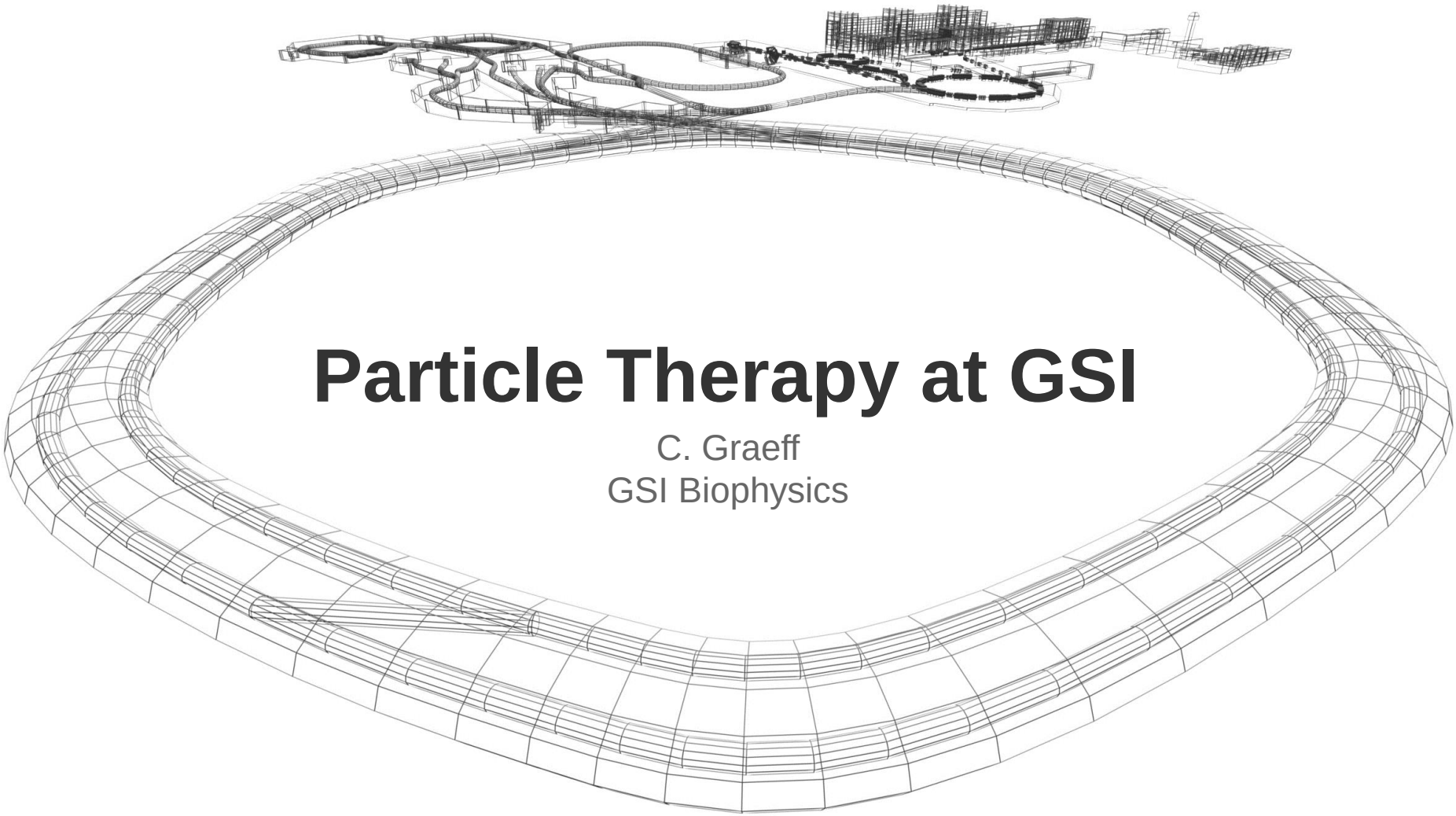
GSI Helmholtzzentrum für Schwerionenforschung GmbH



Particle Therapy at GSI

C. Graeff
GSI Biophysics

GSI Helmholtz Center for Heavy Ion Research

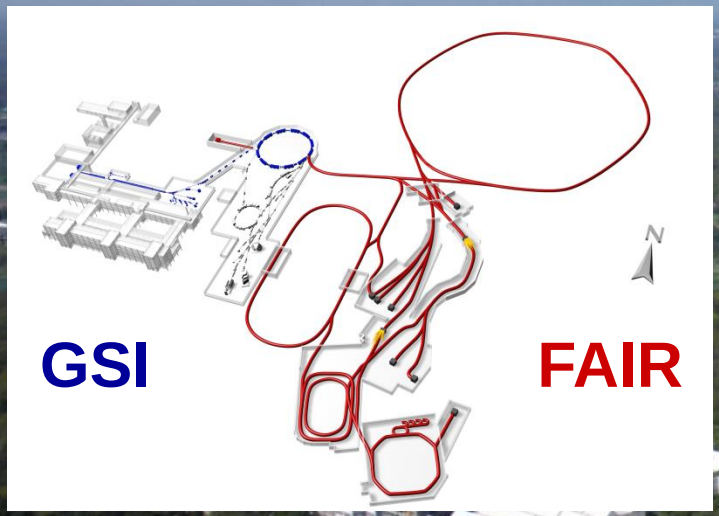
Budget: ~100 M€

Employees: 1350
incl. scientists &
engineers: 750

Visiting scientists: 1000

Large facility equipment: accelerators and experin
1998 – 2008: pilot project of scanned ion therapy

Towards FAIR



- Research continues

  „FAIR Phase 0“

  - regular beam from

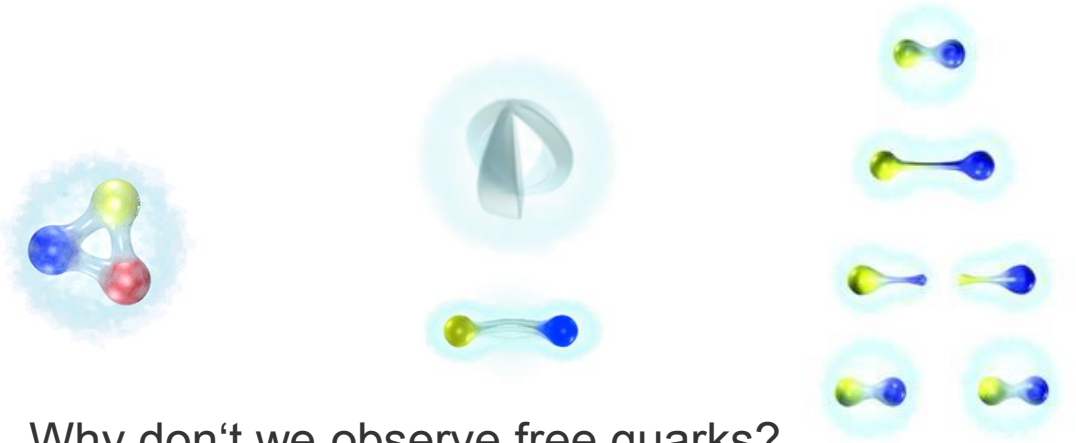
    2018 on (SIS18)

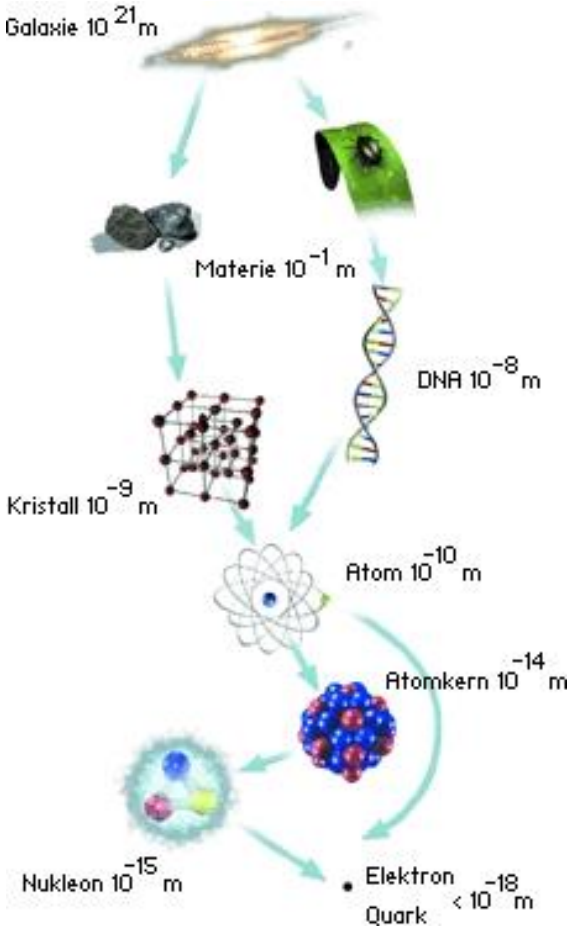
Future Beams:
Intensity: primary HI 100-fold
secondary RIB 10000-fold
Species: Z = -1 – 92
(anti-protons to uranium)
Energies: ions up to 35 - 45 GeV/u
antiprotons 0 -15 GeV/c
Precision: full beam cooling

April 2014

Physics research questions

- Basic components of matter

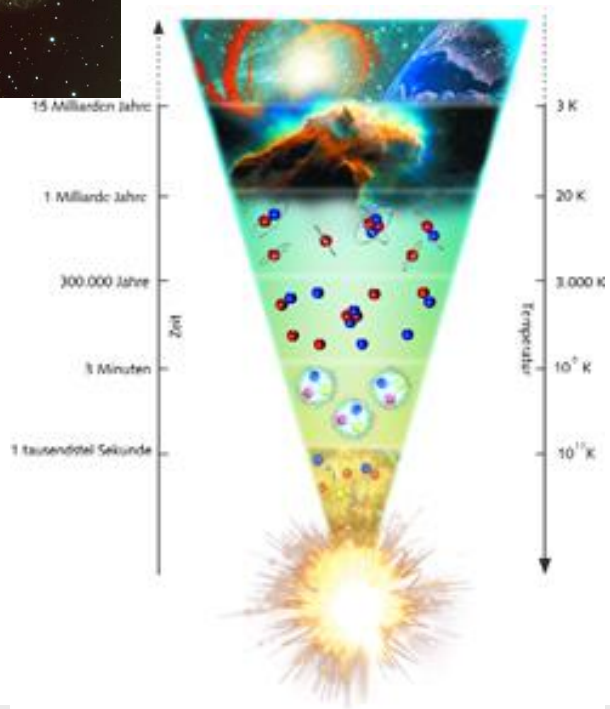




- Why don‘t we observe free quarks?
- Why are protons and neutrons much heavier than their components?
- Which combination of protons and neutrons gives stable nuclei and
  what are properties of non-stable nuclei?
- What are basic symmetries existing in nature and which physics laws do they reflect?

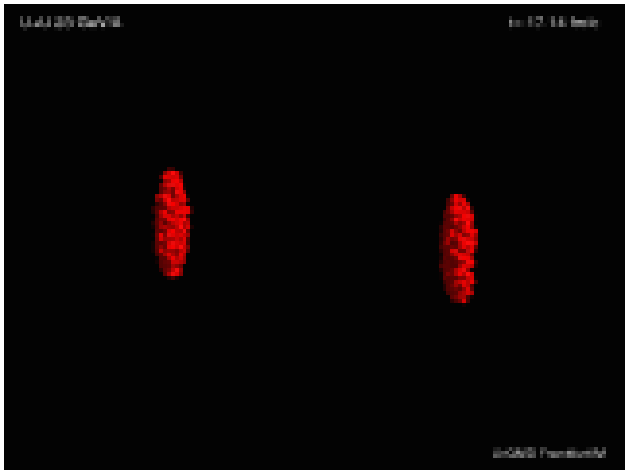
Physics research questions

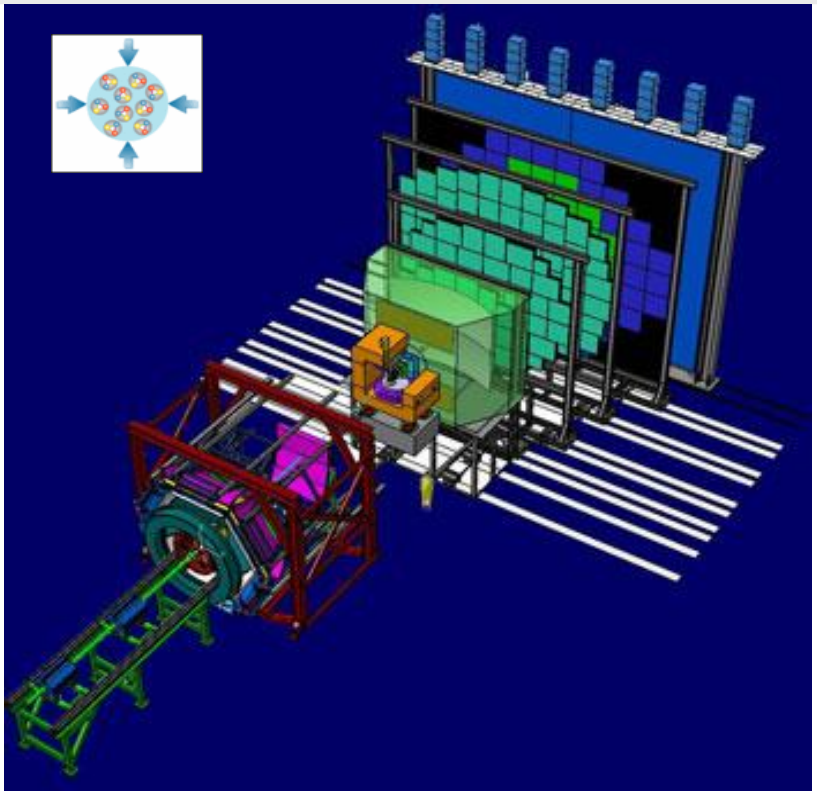
- Evolution of the universe

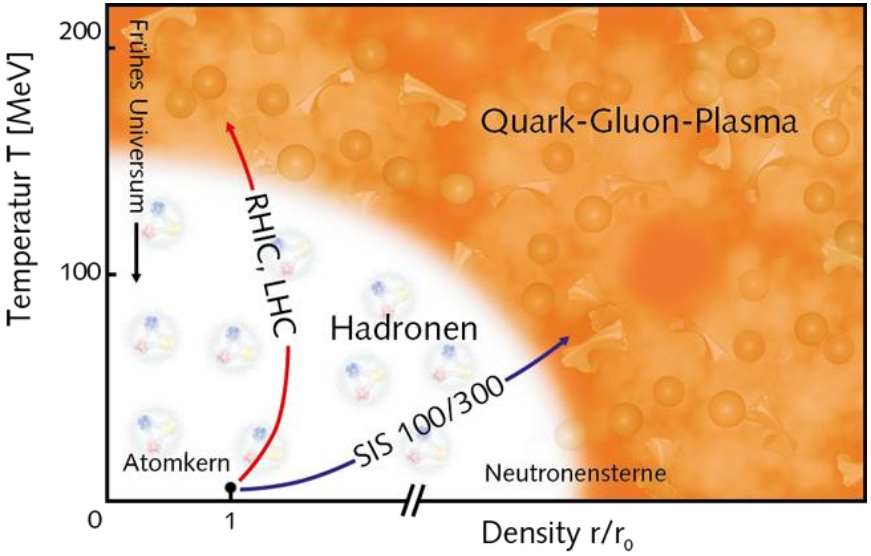


- What came after the Big Bang?
- Can we create quark-gluon pasma in heavy ion reactions?
- Which nuclear reactions are taking place during nuclear fusion? What is the role of non-stable nuclei in fusion?
- In which state occurs nuclear matter under high temperature and pressure?
- What is so called dark matter?
- Why is our universe from matter and not from antimatter? Can we learn more about symmetry breaking in the universe?

One example – CBM experiment







The Biophysics department

8 subgroups from basic biology to applied medical physics

G. Taucher-Scholz (DNA repair)

S. Ritter (chromosome aberrations)

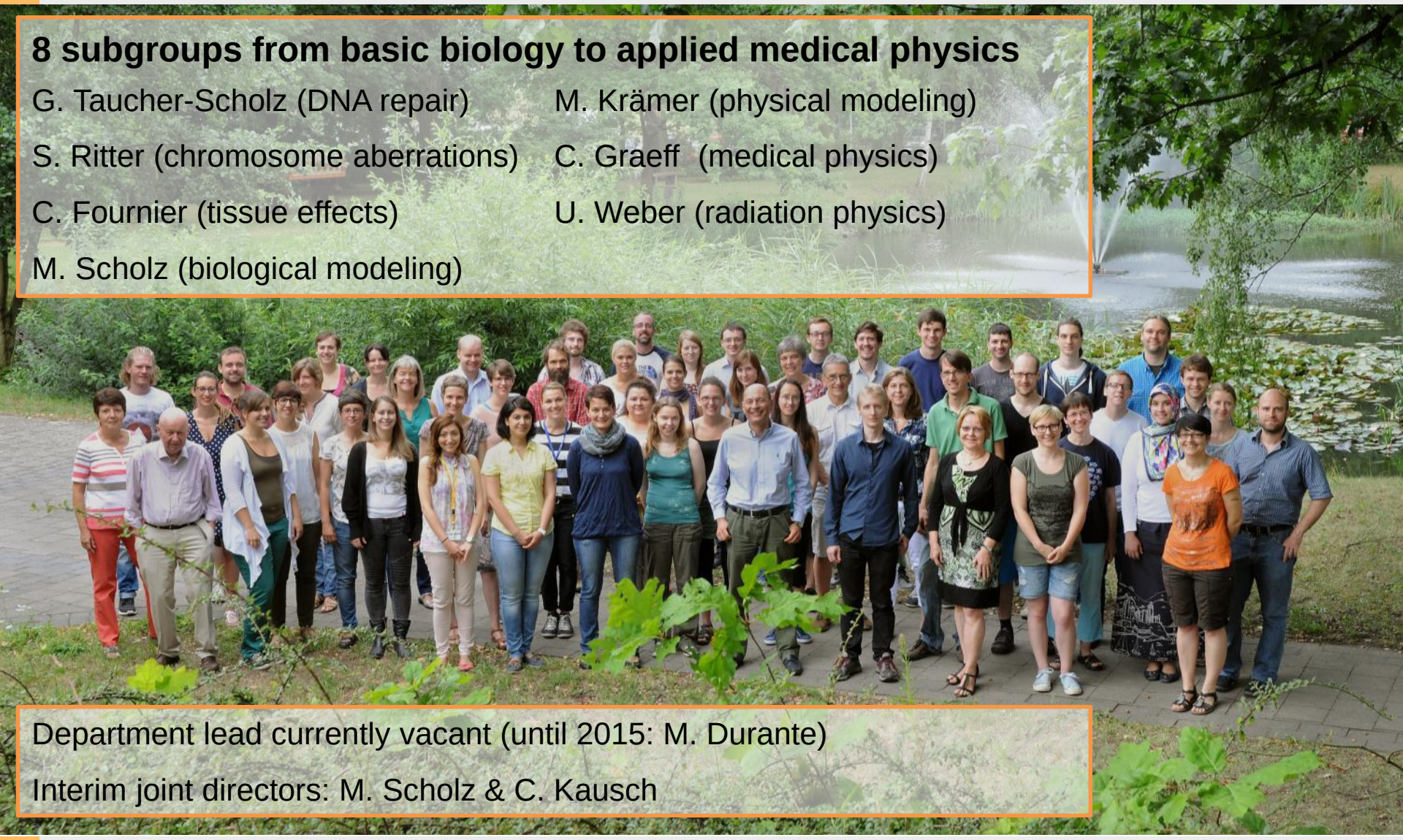
C. Fournier (tissue effects)

M. Scholz (biological modeling)

M. Krämer (physical modeling)

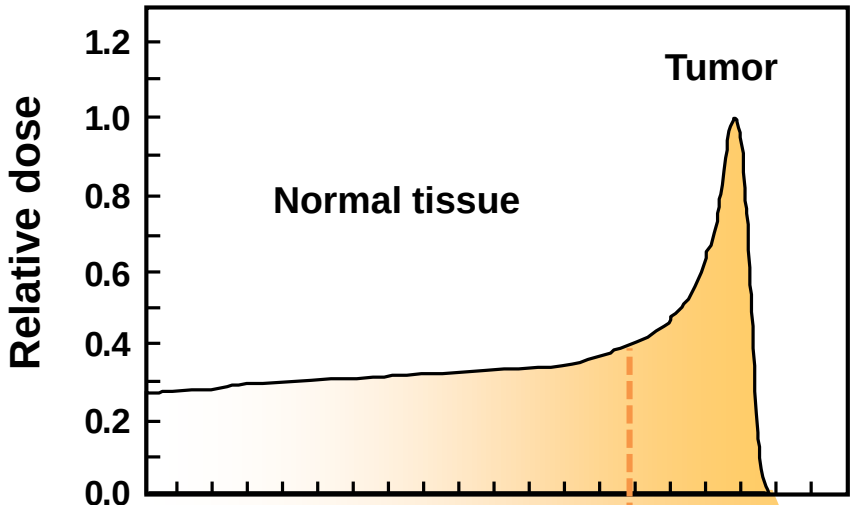
C. Graeff (medical physics)

U. Weber (radiation physics)



Department lead currently vacant (until 2015: M. Durante)

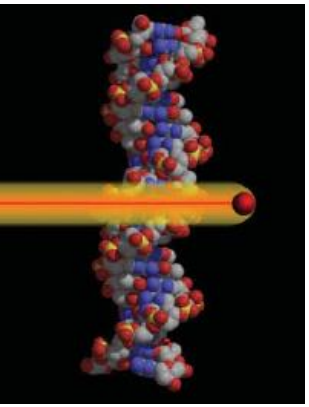
Interim joint directors: M. Scholz & C. Kausch



Durante & Loeffler,

Nat Rev Clin Oncol 2010

	Depth (mm)	
Energy	high	low
LET	low	high
Dose	low	high
RBE	≈ 1	> 1
OER	≈ 3	< 3
Cell-cycle dependence	high	low
Fractionation dependence	high	low
Angiogenesis	Increased	Decreased
Cell migration	Increased	Decreased



Potential advantages of heavy ions

- High tumor dose, normal tissue sparing
- Effective for radioresistant tumors
- Effective against hypoxic tumor cells
- Increased lethality in the target because cells in radioresistant (S) phase are sensitized
- Fractionation spares normal tissue more than tumor
- Reduced angiogenesis and metastatization

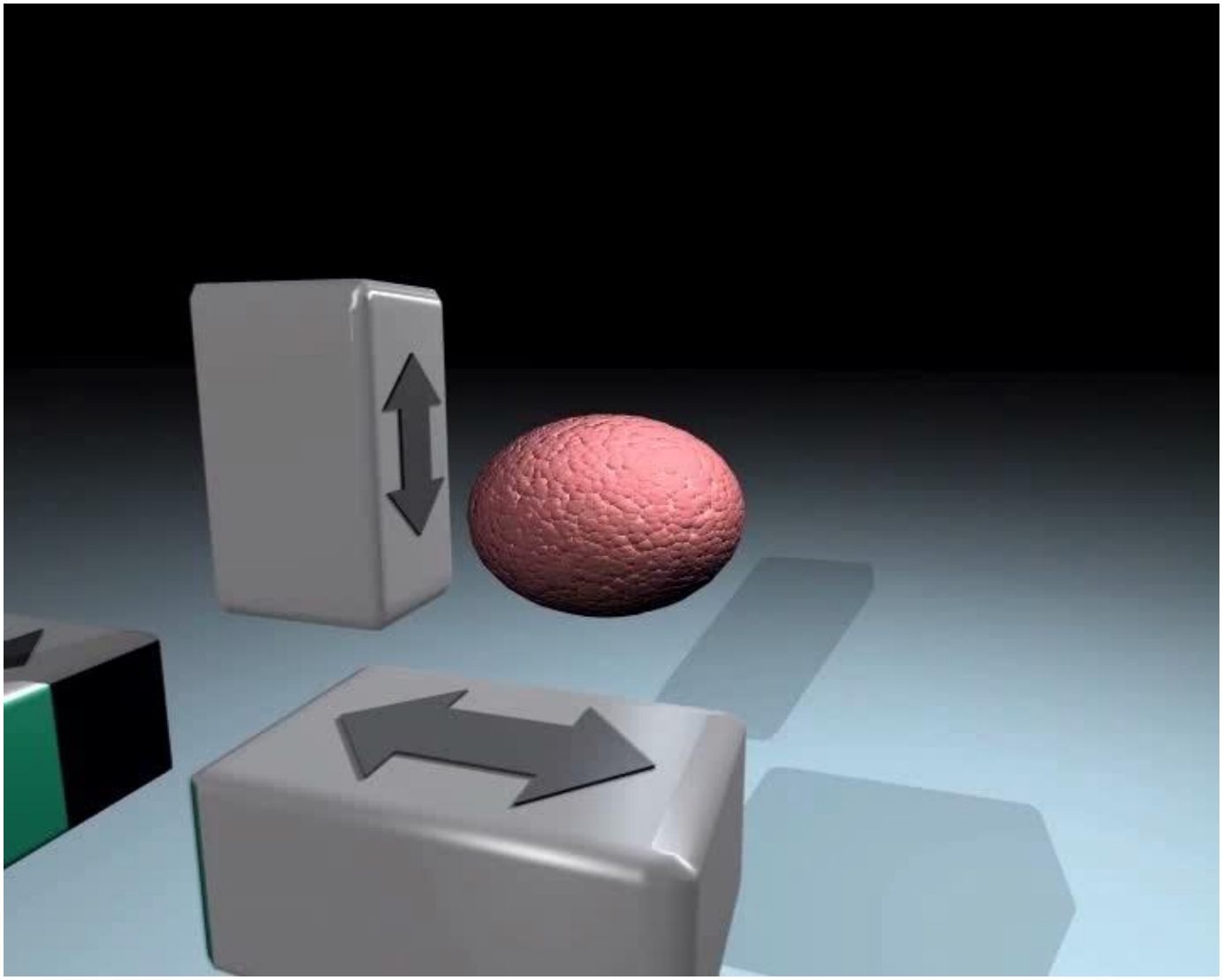
Tumor therapy at GSI – Cave M

- 1997 – 2008: 440 patients treated, mainly chordoma & chondrosarcoma of the skull
- Project partners:
  - GSI, Radiooncology Clinic and DKFZ in Heidelberg, Helmholtz Center Dresden/Rossendorf (former FZR)
- Succeeded in 2009 by Heidelberg Ion Beam Therapy Center (HIT)

Therapy developed at GSI

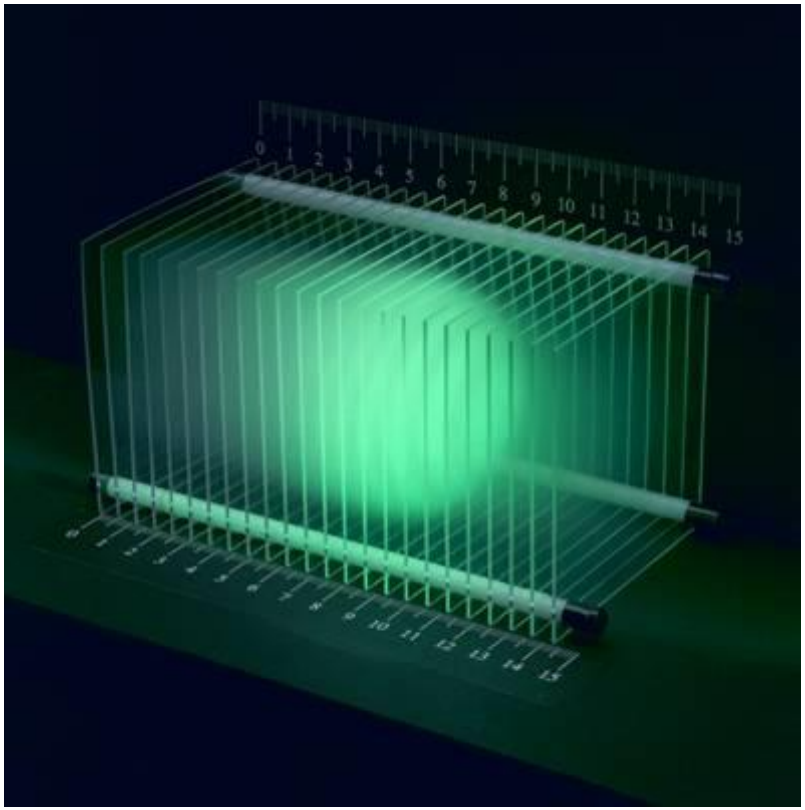
- Accelerator control
  - 255 energies, 7 foci, 15 intensities – different in each spill
- Beam monitoring
  - Precision dose application: PPIC and MWPC still in use today
  - Positron emission tomography: beam range
- Beam scanning
  - First clinical use of full 3D active energy scanning at GSI
- Radiobiology & biological modeling
  - local effect model (LEM I - IV)
- Treatment planning software (TRiP)

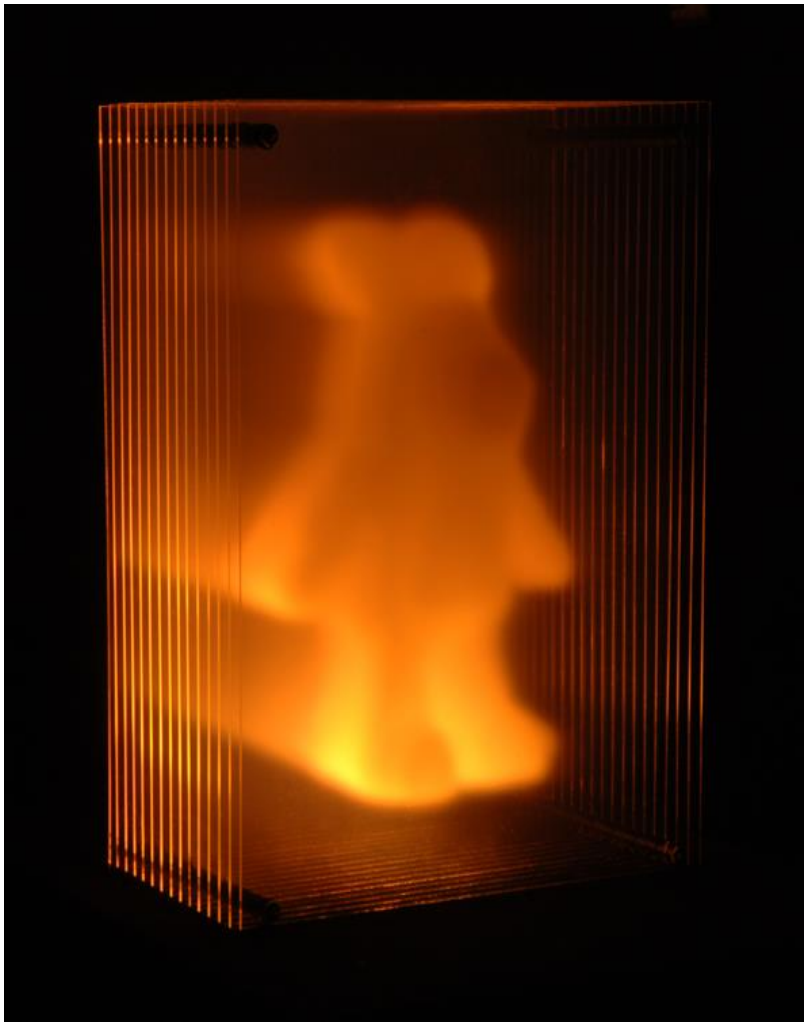
Rasterscanning



Haberer et al. 1993

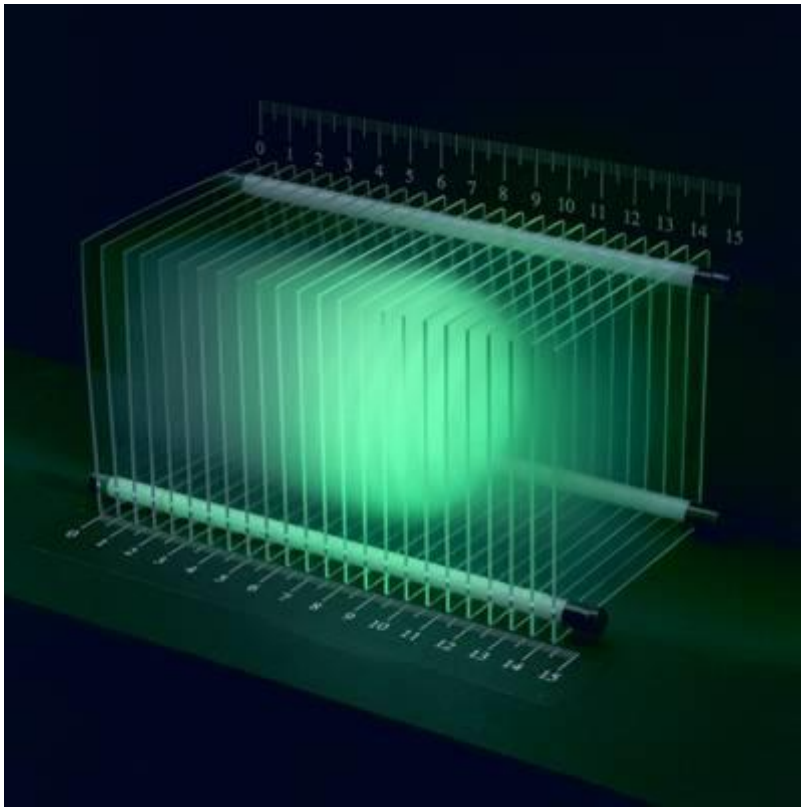
Scanned beam examples / CR-39 stack

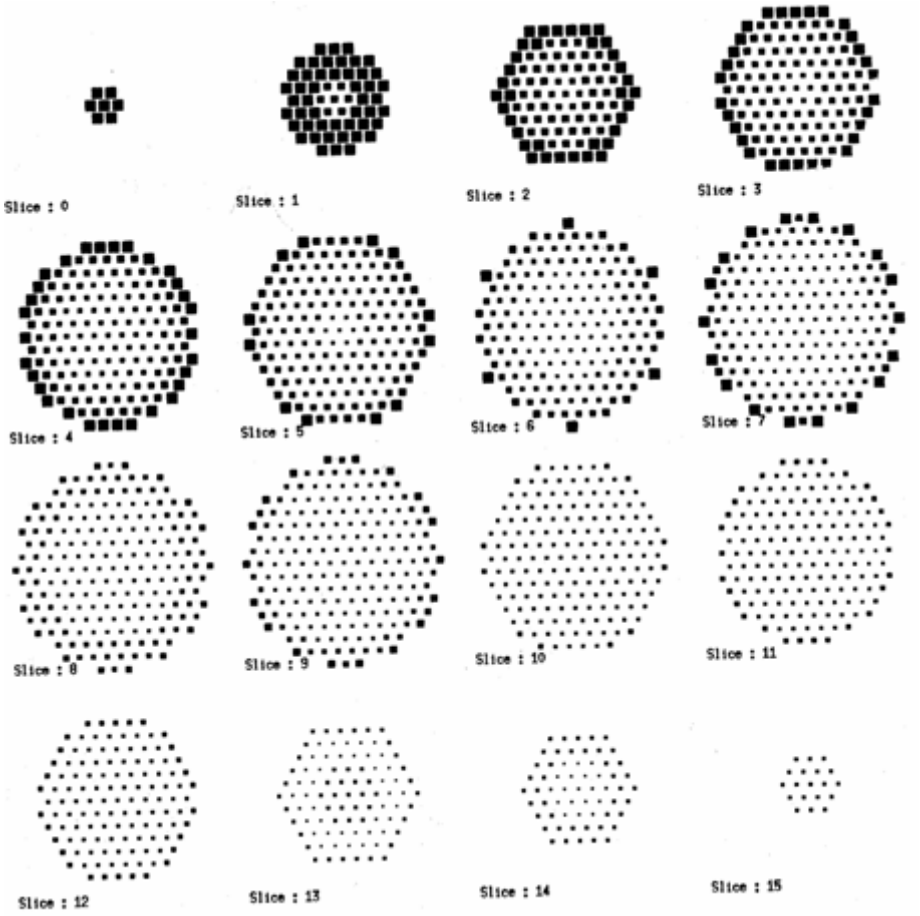




[M. Krämer, U. Weber, GSI and Phys. Med. Biol. 2000]

The treatment plan - example





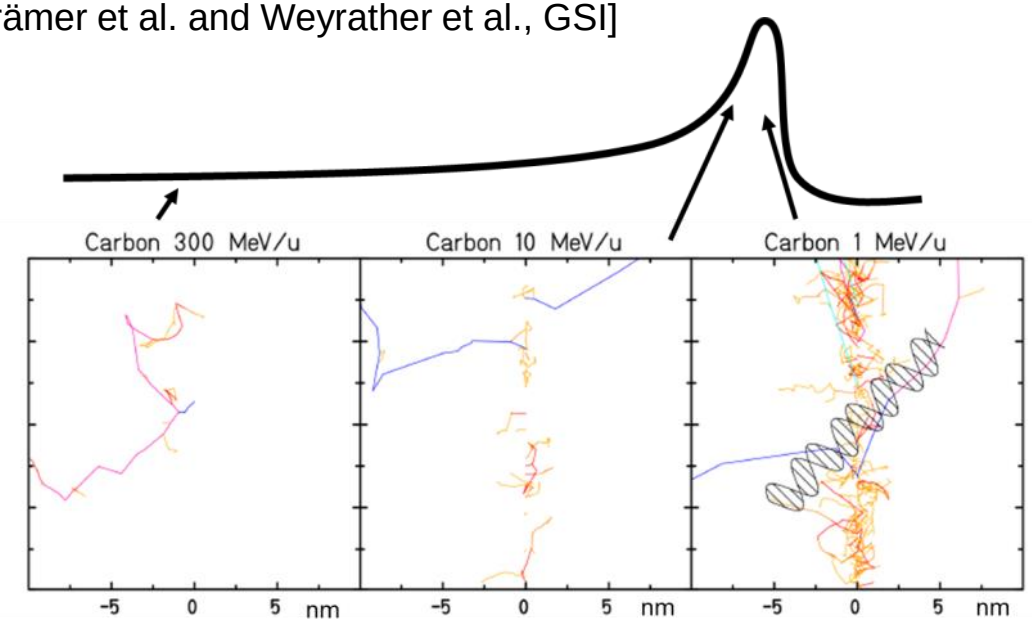
[M. Krämer, U. Weber, GSI and Phys. Med. Biol. 2000]

The Local Effect Model

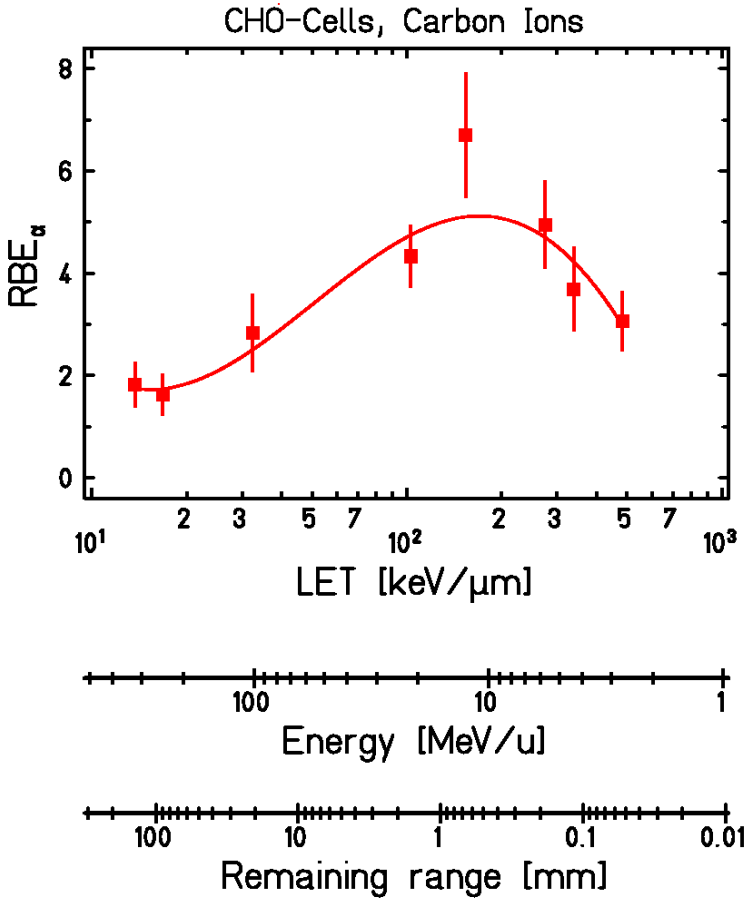
- Current version: LEM IV
  - Slightly different modeling approach
  - Supports multiple particles
  - Proton RBE!
- LEM I in clinical use in Siemens Syngo TPS
  - Heidelberg, Marburg, Pavia, Shanghai
- LEM IV licensed to RaySearch
  - Will be used at MedAustron
- Main investigator: Michael Scholz

Relative Biological Effectiveness RBE

[Krämer et al. and Weyrather et al., GSI]

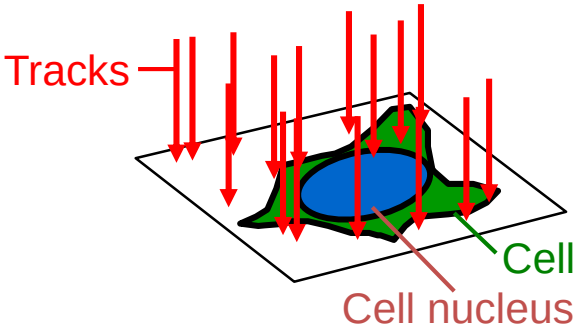


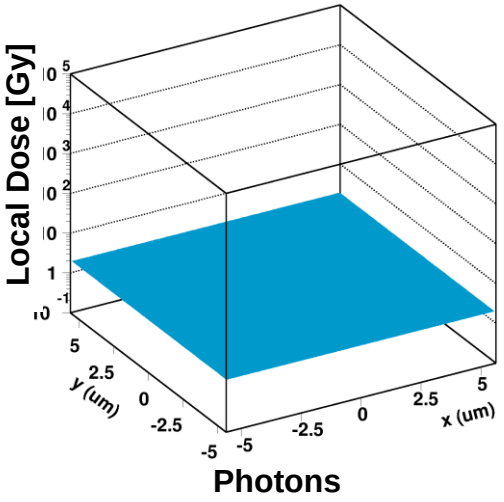
$$RBE = \frac{Dose_{X-ray}}{Dose_{ions}}$$

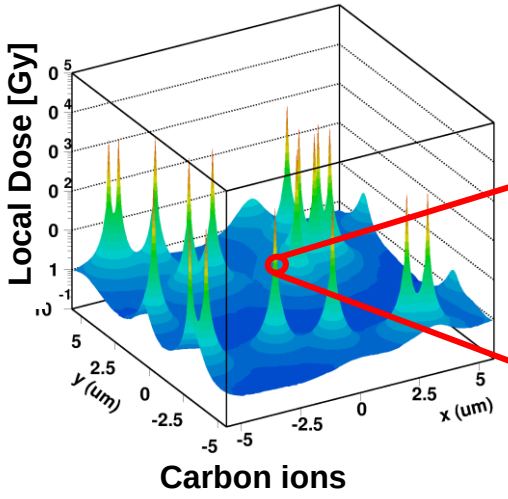


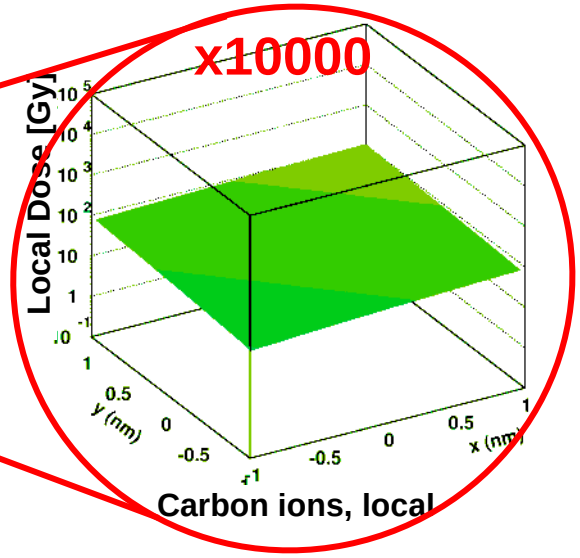
- Linear Energy Transfer ~ stopping power
- Modeling required to determine RBE!

Basis of the local effect model





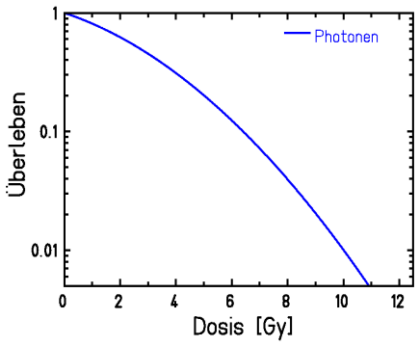




Local Effect Model LEM

Basic Assumption:
Increased effectiveness of particle radiation
can be described by a combination of the
photon dose response and microscopic dose distribution

Local Effect (Photons) = Local Effect (Ions)



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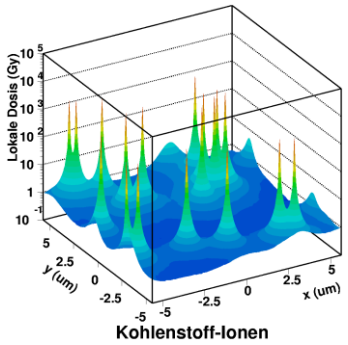
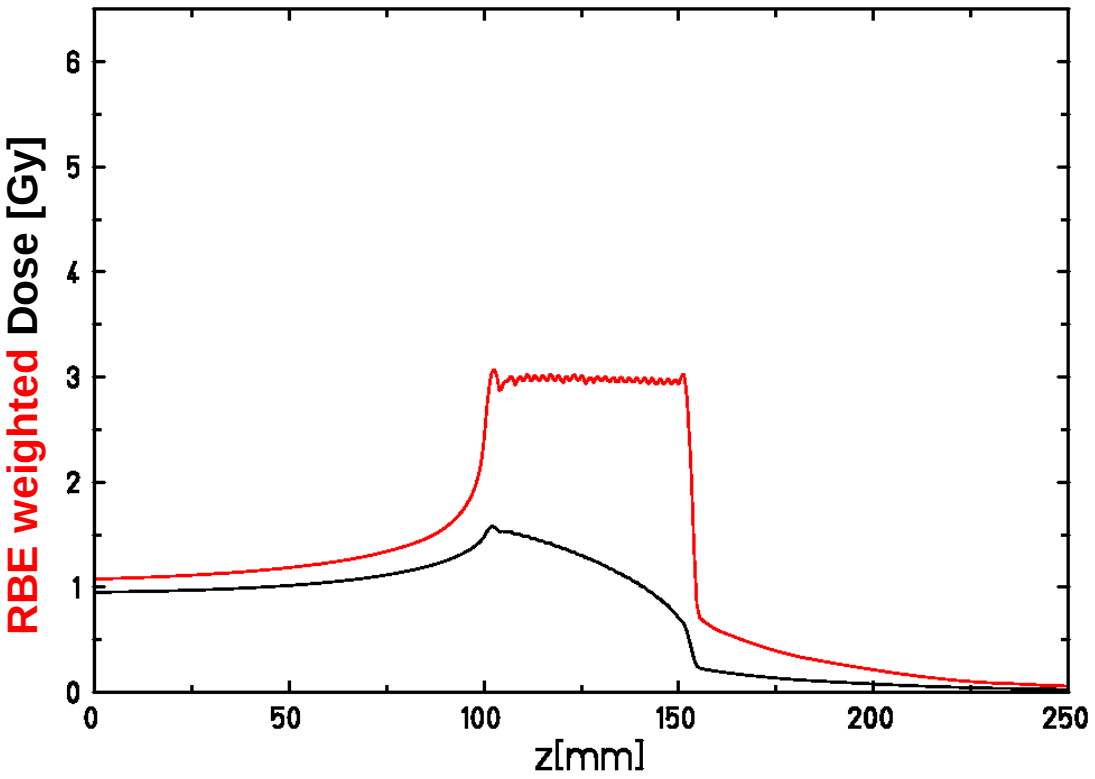
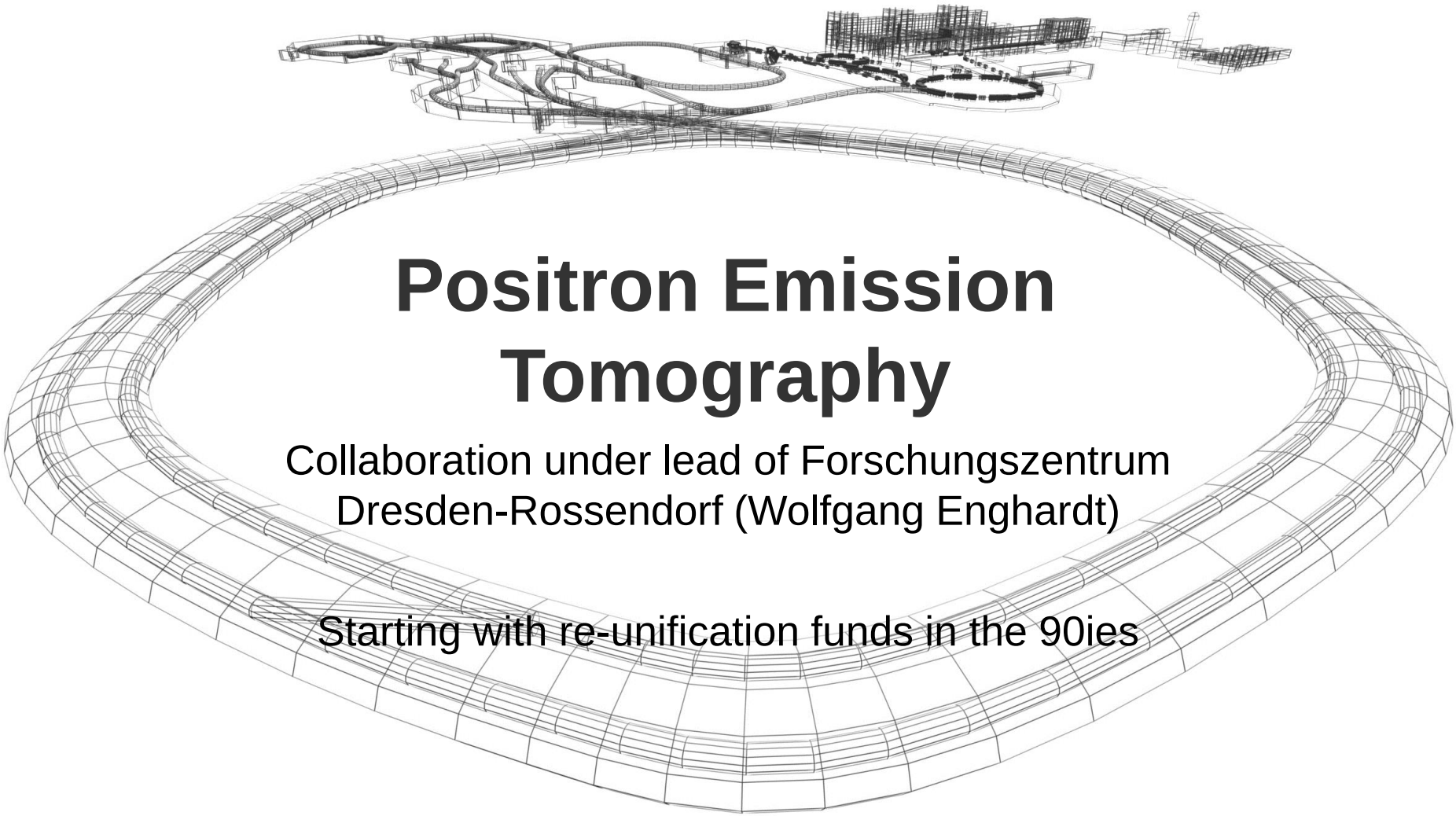


➡ RBE !

LEM: Transfer of low-LET experience to high-LET

Depth Dependence of RBE



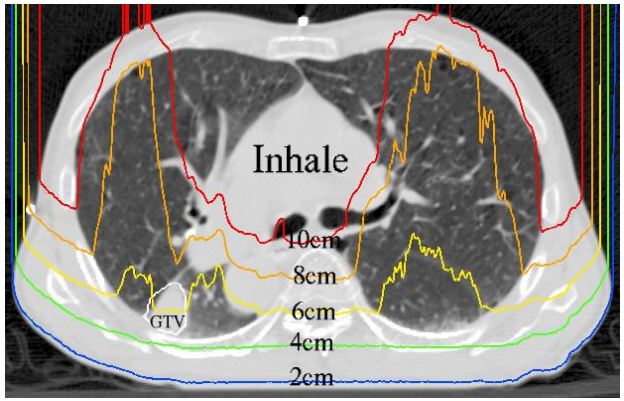


Positron Emission Tomography

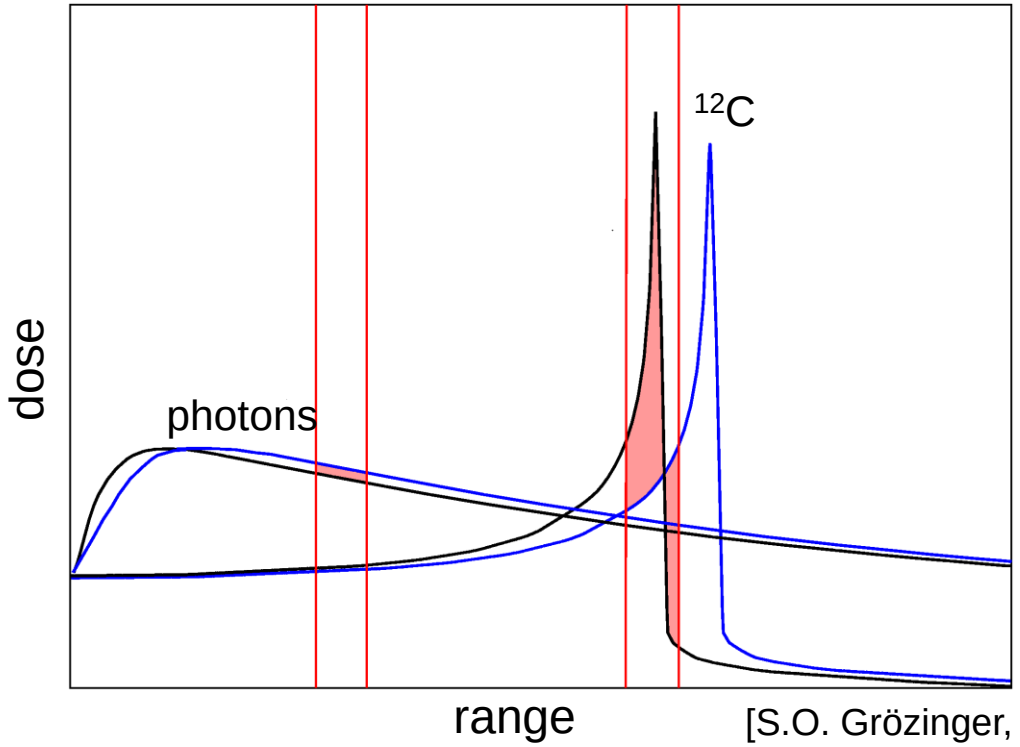
Collaboration under lead of Forschungszentrum Dresden-Rossendorf (Wolfgang Enghardt)

Starting with re-unification funds in the 90ies

Range uncertainties



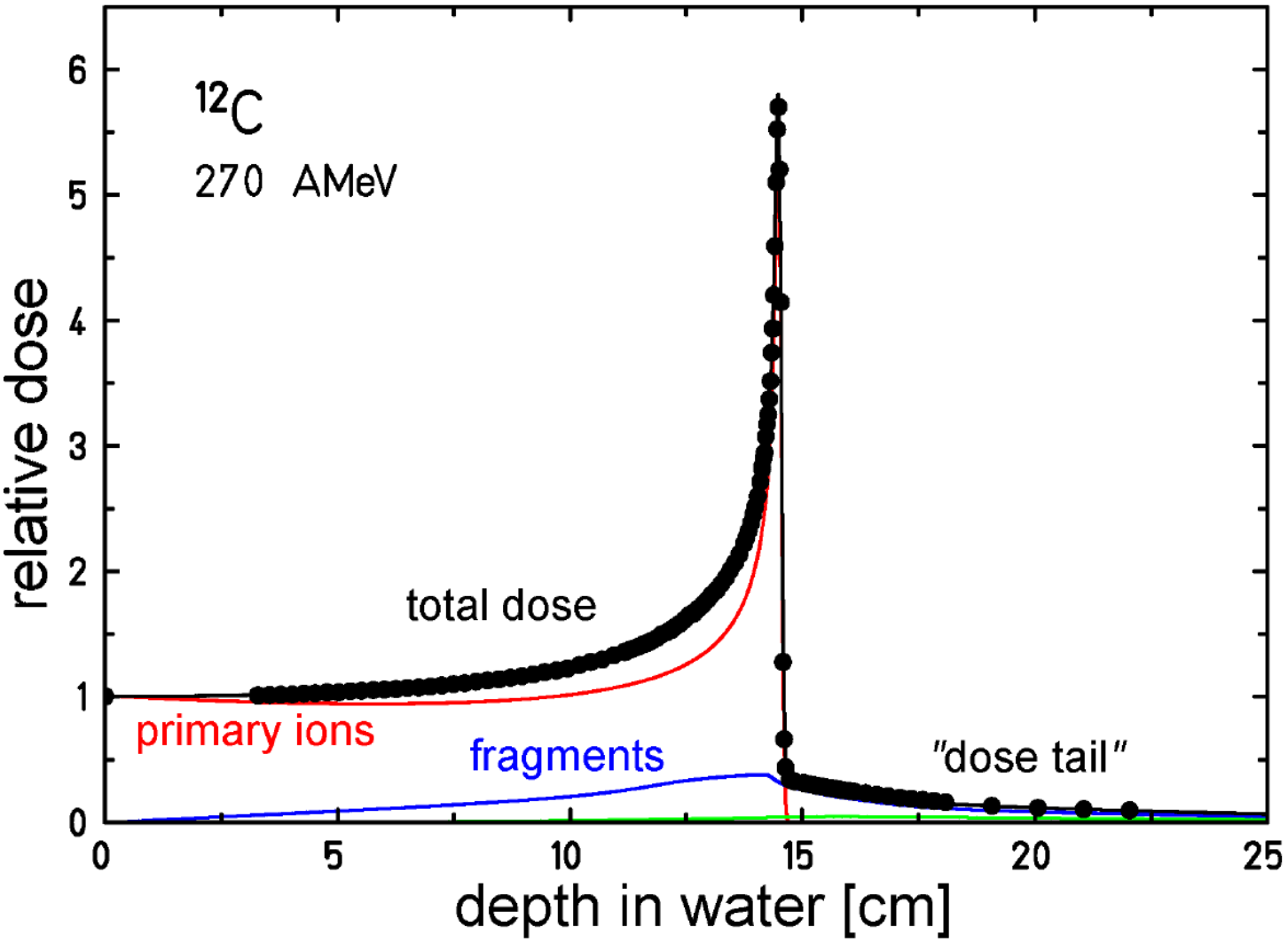
- (Mostly) controllable for regions with defined bone structure: ~ 1 mm in head & neck



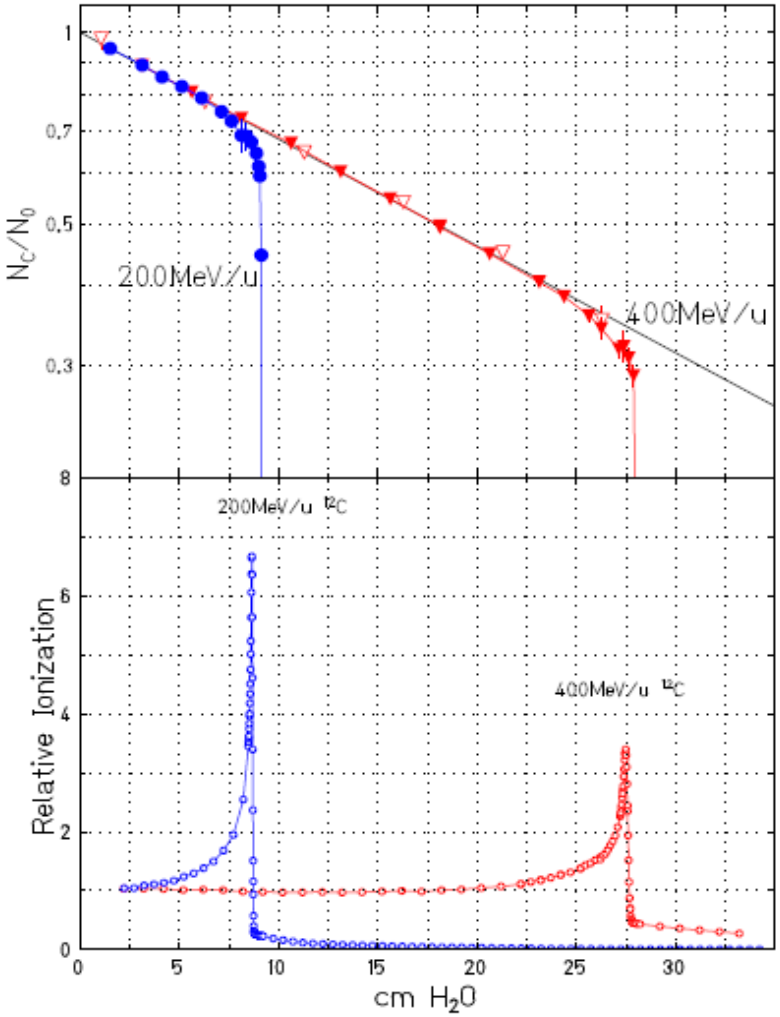
[S.O. Grözinger, GSI]

- Much more difficult in chest / abdomen: deformable tissue, breathing & heart beat

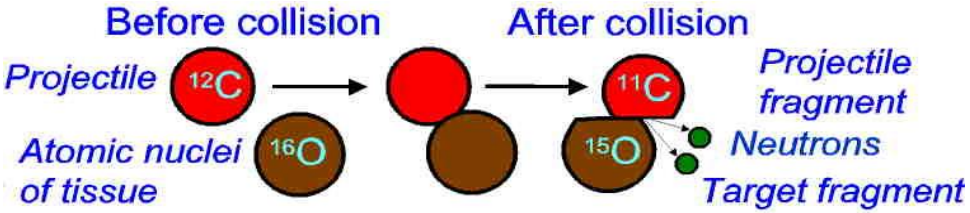
Bragg curve – fragment contribution



Loss of initial particles

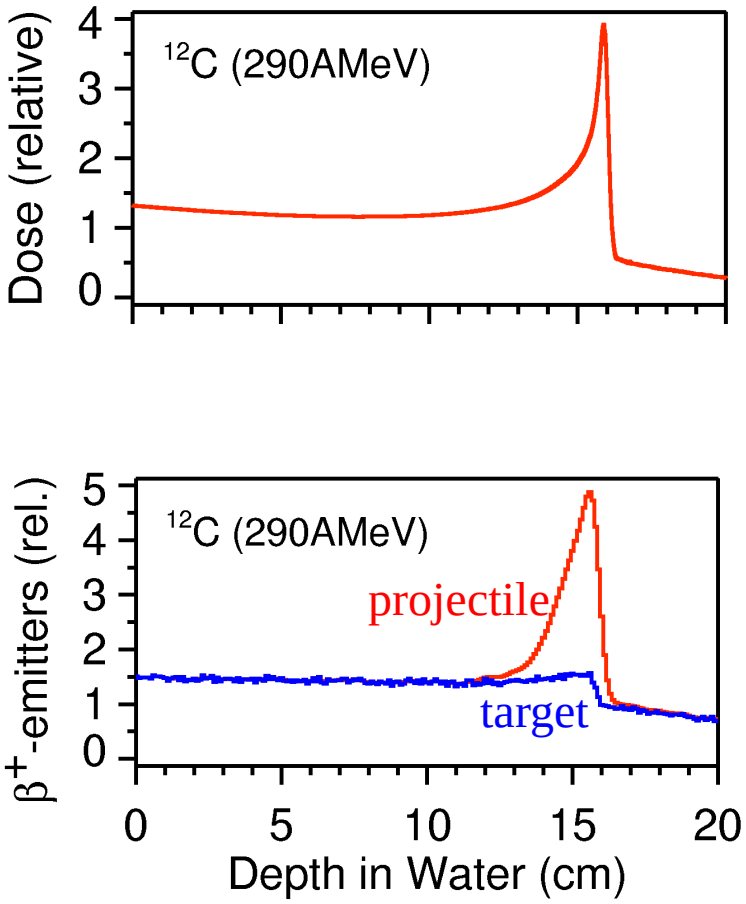


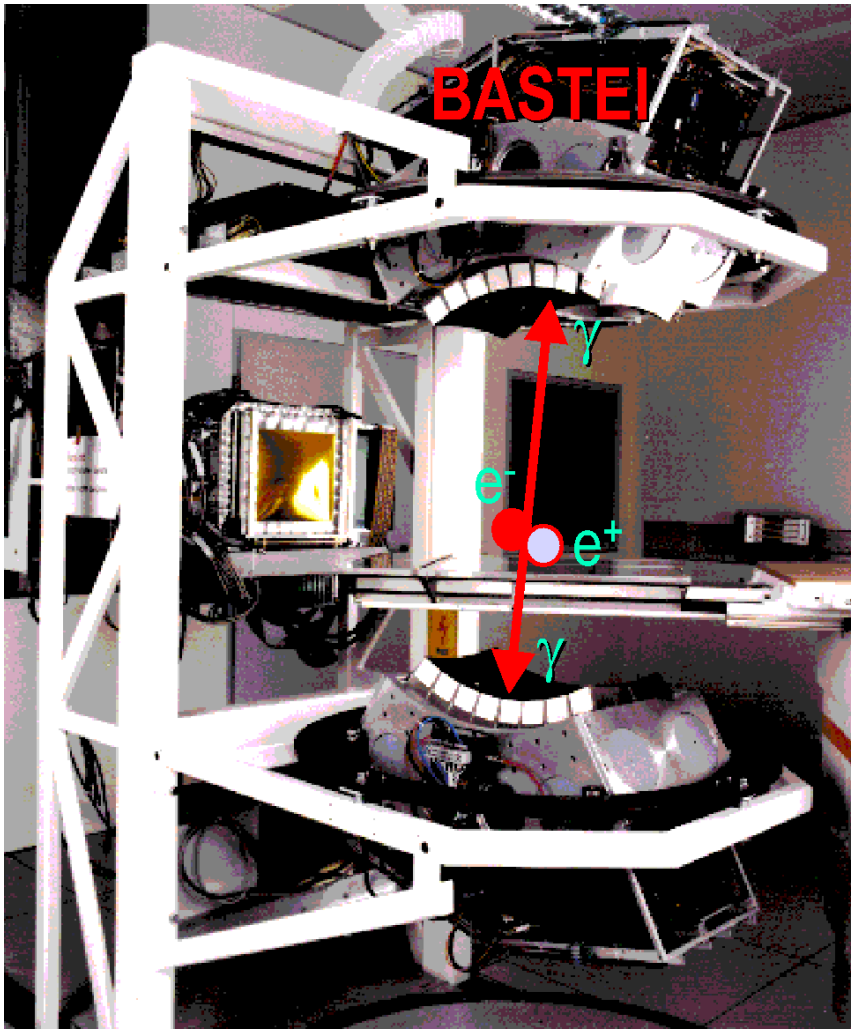
[E. Haettner, MSc-Thesis]



- Some projectile fragments are positron emitting isotopes, e.g. ^{11}C and ^{10}C (half-lifes: 20 min and 20 sec)
- Can be used for Positron Emission Tomography (PET)

PET-control of treatment

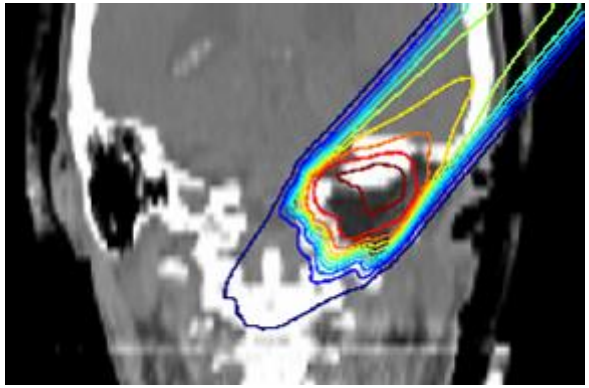




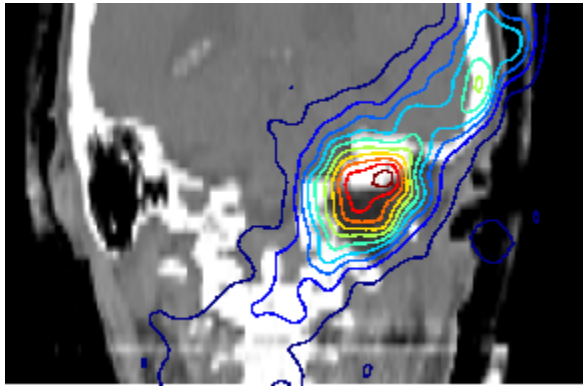
[Enghardt et al. Rossendorf]

Dose verification with PET

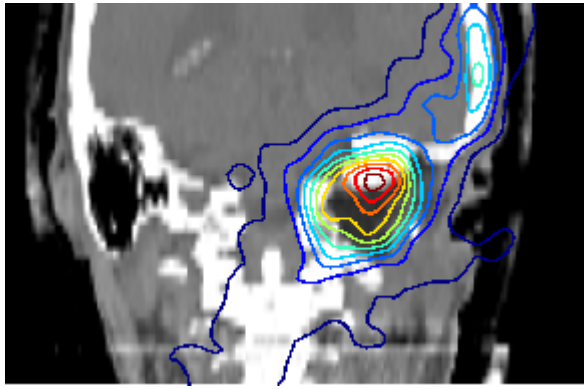
- 3D reconstruction by back projection
- Positron emitter distribution neither proportional nor equivalent to the dose distribution
- Comparison with expected positron emitter distribution



Treatment plan



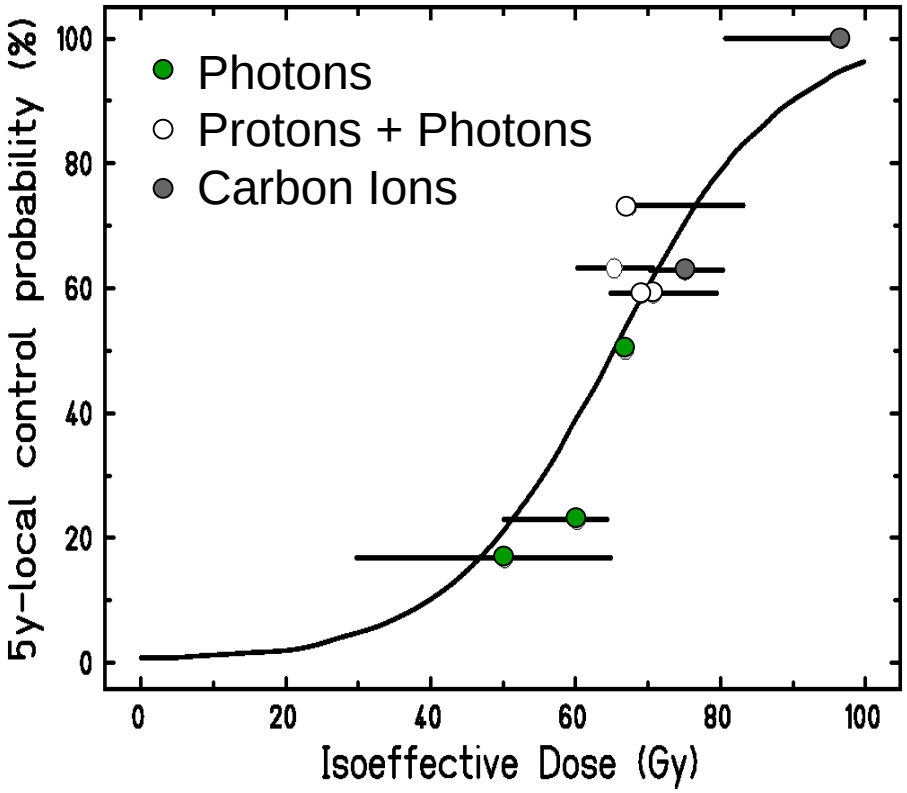
Predicted β^+-activity



Measured β^+-activity

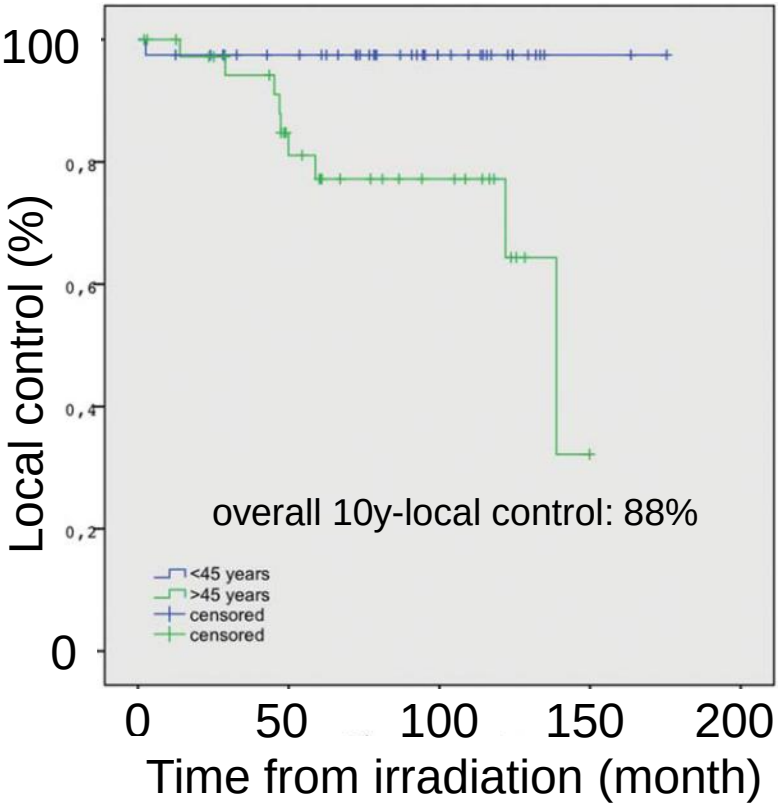
[Enghardt et al. Rossendorf]

Clinical outcome of the pilot project



Chondrosarcoma

Schulz-Ertner et al., IJROBP 2007



Chordoma

Uhl et al., Cancer 2014

Future research topics

- FAIR-specific
  - Space irradiation (C. Schuy, Tuesday)
  - Particle imaging / theranostics (M. Schanz, Wednesday)
- Tissue-level effects / adverse events
- Radio-Immunology
- Licensed for human stem cells
  - Radiotoxicity in embryonal development
  - Radiotoxicity for neuronal / cardiac tissue
- Different ion species: He, O
- Effect-based optimization: Kill painting
- Moving targets (C. Graeff, Wednesday)