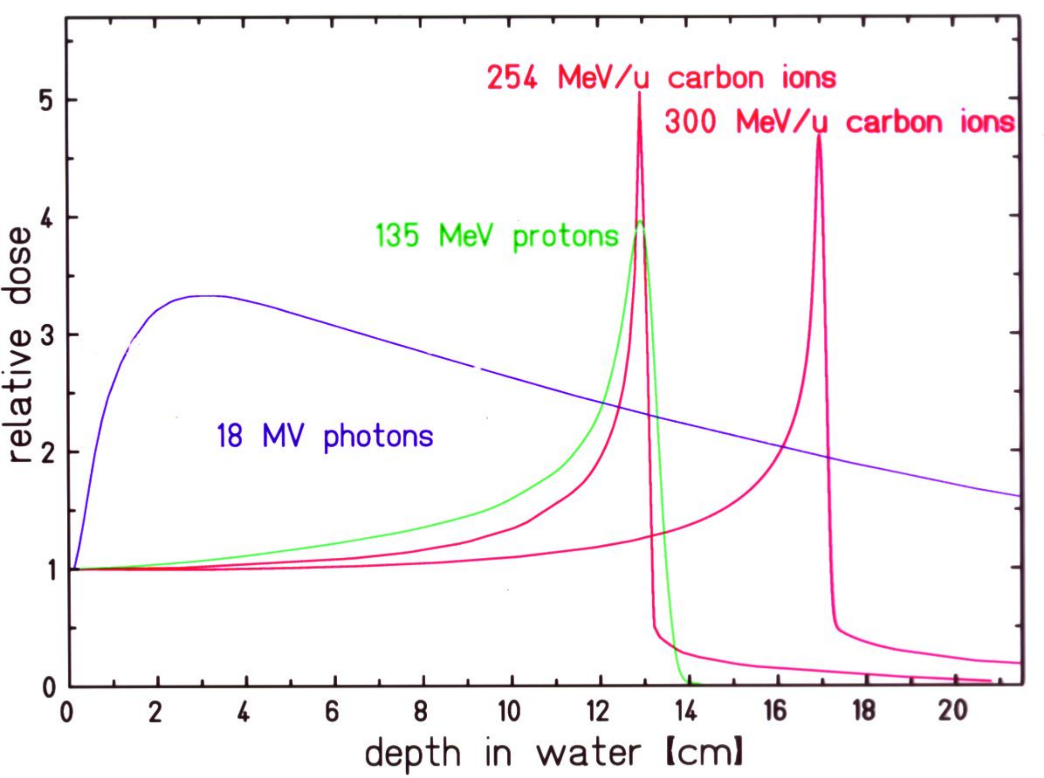
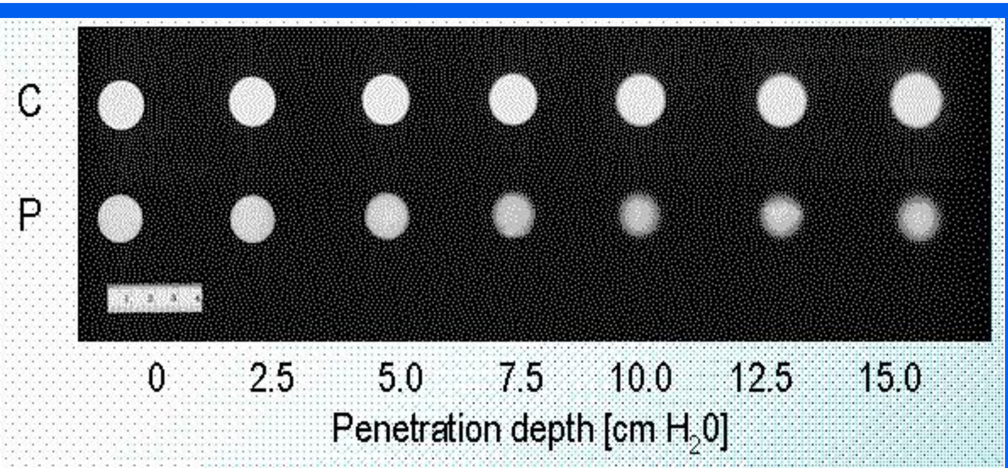
From Fundamental Aspects to the Dedicated Hadron Therapy Facility HIT

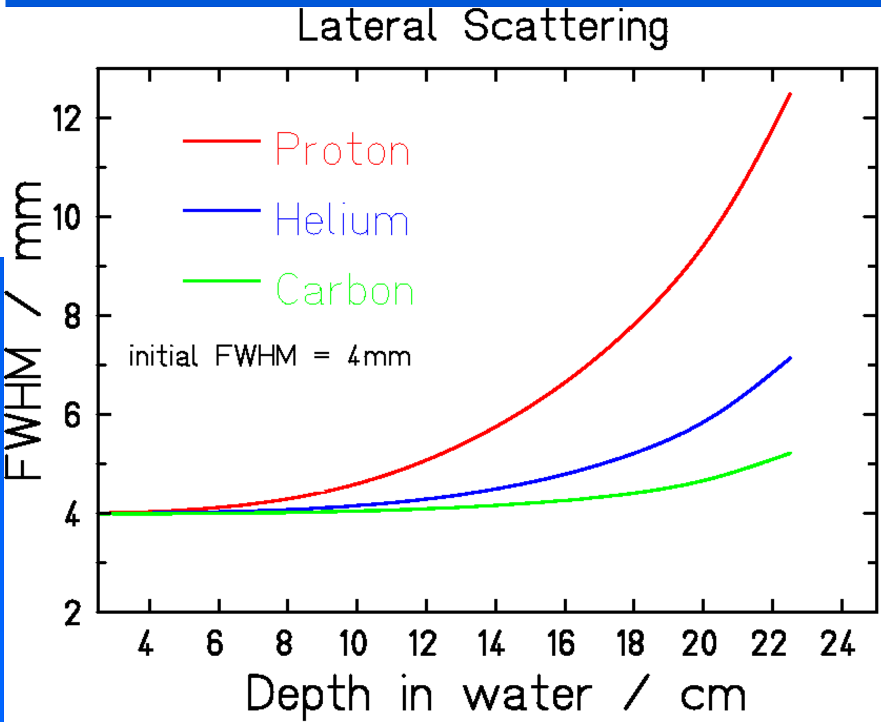
Prof. Dr. Thomas Haberer
Science-Technical Director
Heidelberg Ion Beam Therapy Center

Rationale / Physics

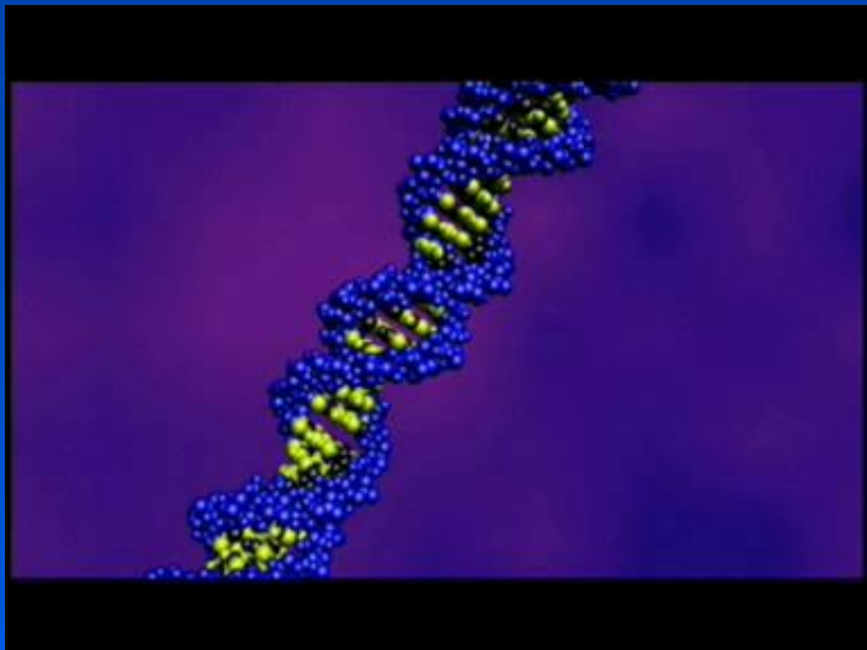


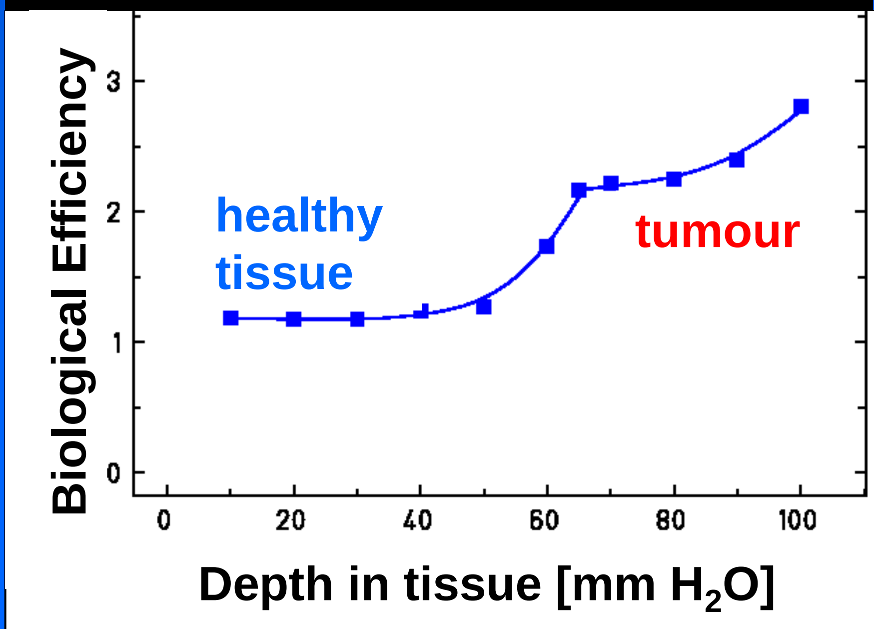
- inverted depth-dose distribution
- mild lateral scattering

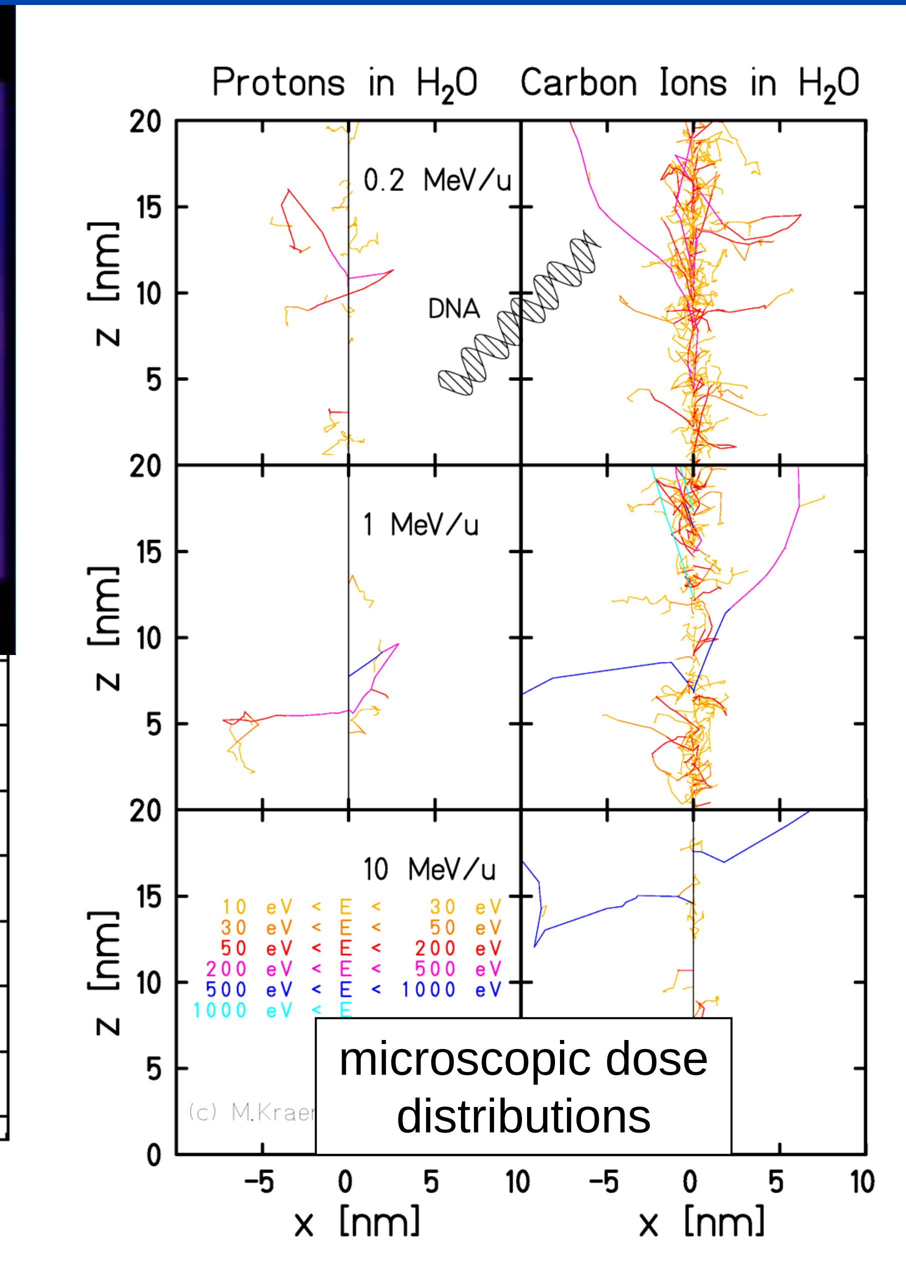




Rationale / Radiobiology







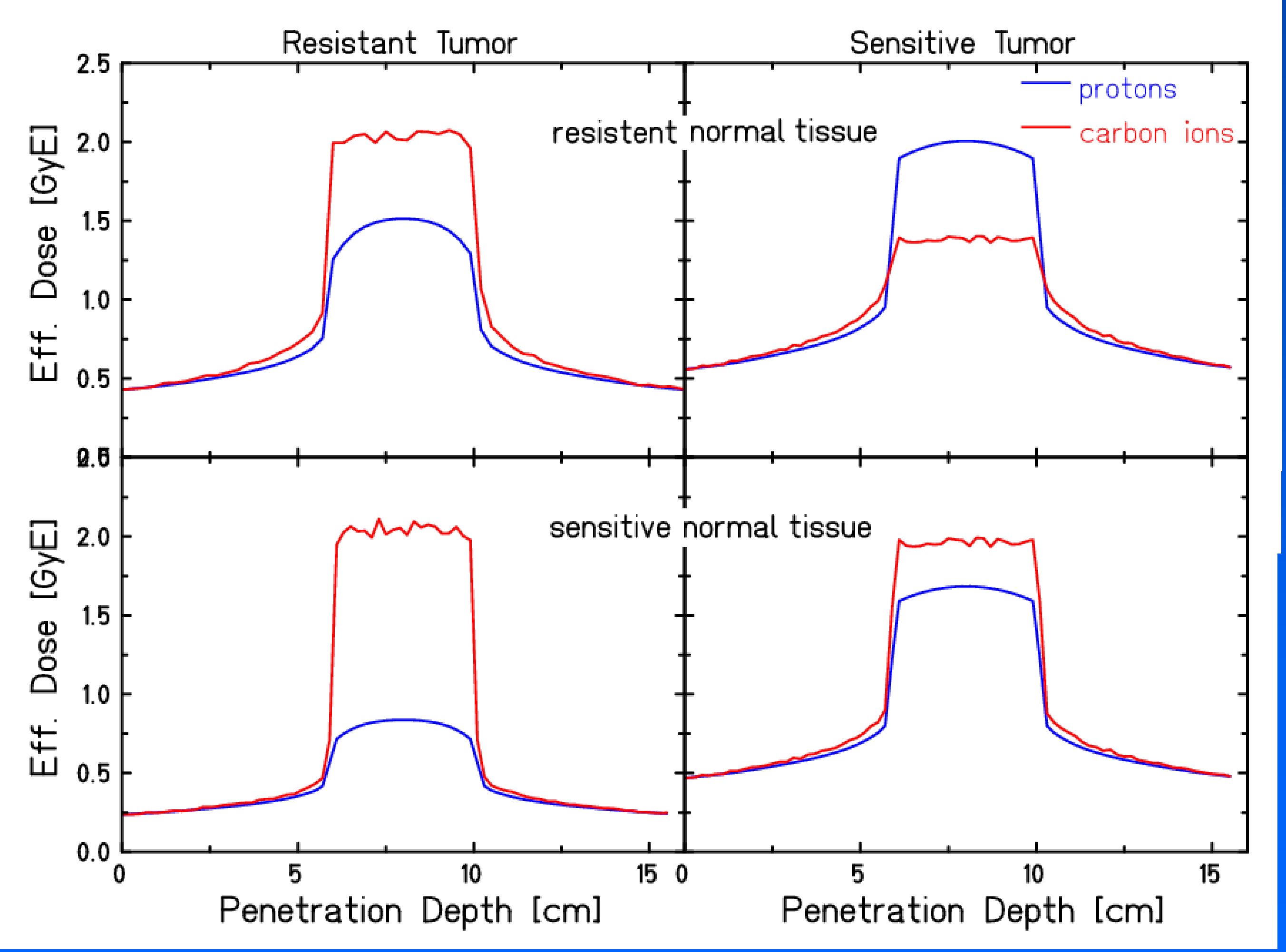
RBE and Tissues

tumour resistant

tumour sensitive

normal tissue resistant

normal tissue sensitive



[LEM IV-Calculation M. Scholz, GSI]

Heavy ions are not in any case advantageous…

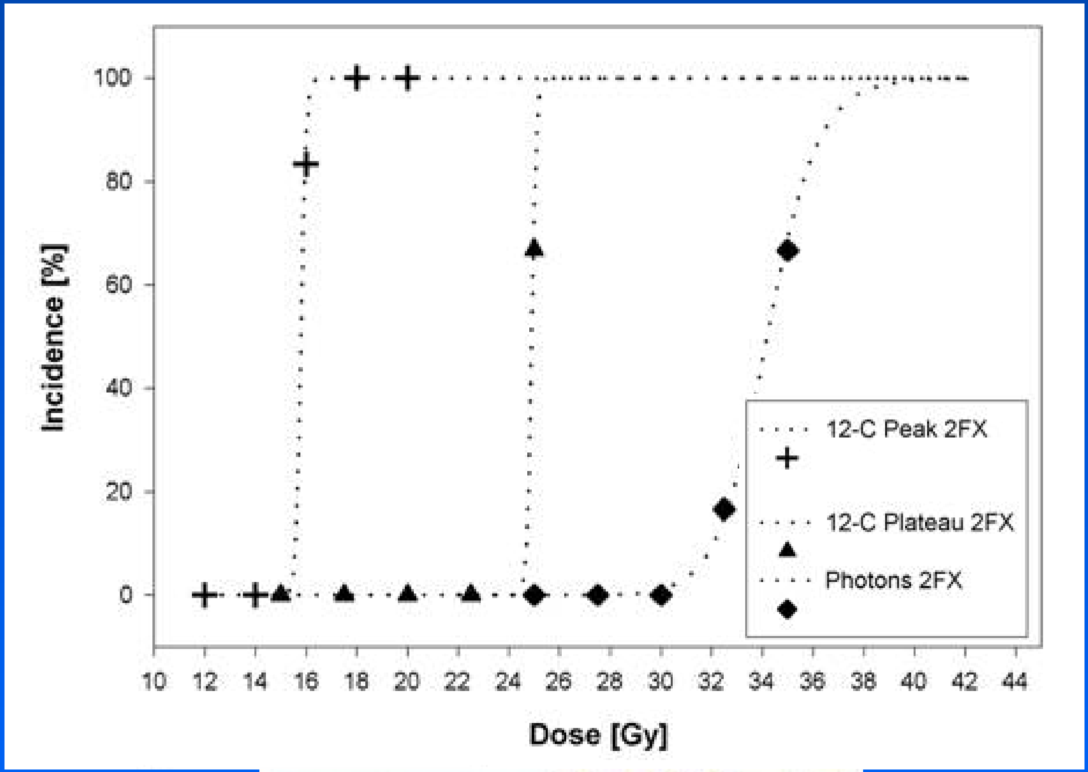
Increased Relative Biological Effectiveness

radiation induced myelopathy in rats after 2 fractions

RBEs:

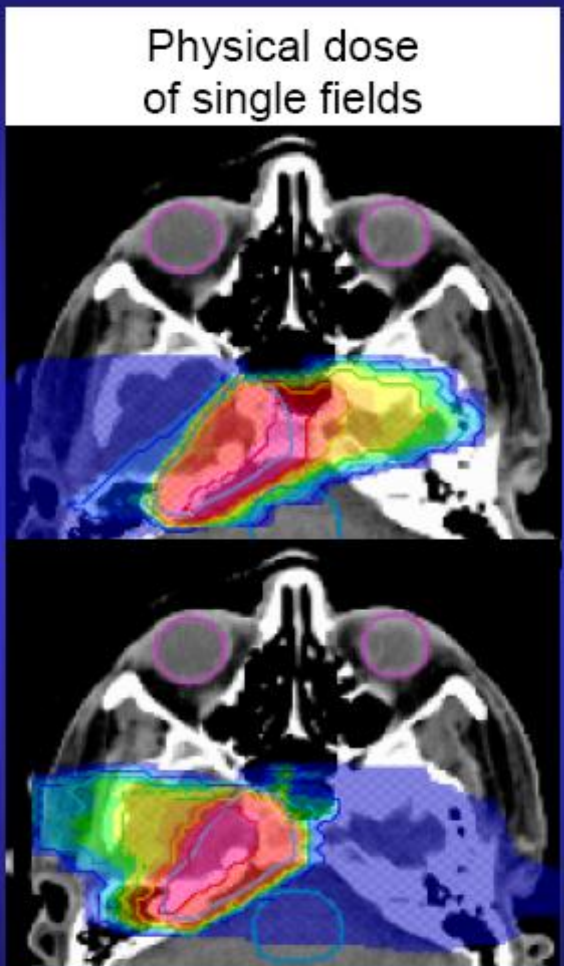
Plateau: ~1.4

Peak: ~ 2.3

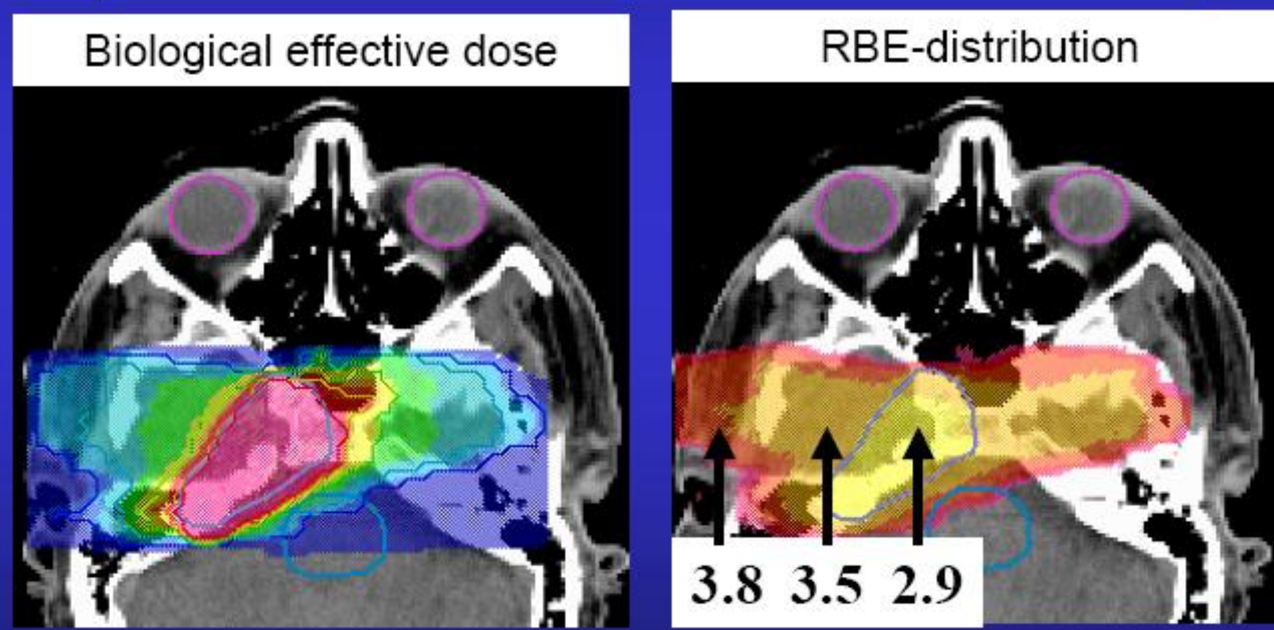


Debus, Karger, Peschke, Scholz, …
Rad. Res. 2003

Biological Treatment Planning Based on Fragment Spectra



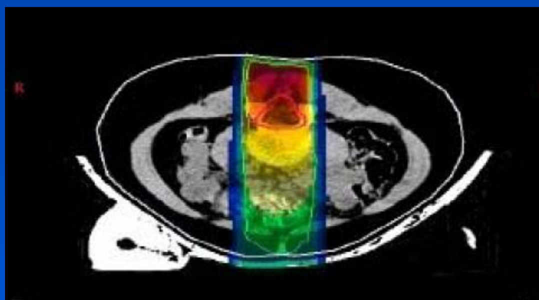
Local effect model of Scholz and Kraft:
Calculation of RBE as a 3D distribution
Input: X-ray survival curves



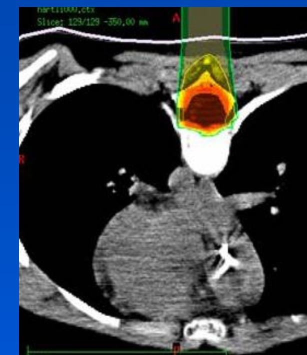
O. Jäkel (HIT) / M. Krämer (GSI)

Medulloblastoma

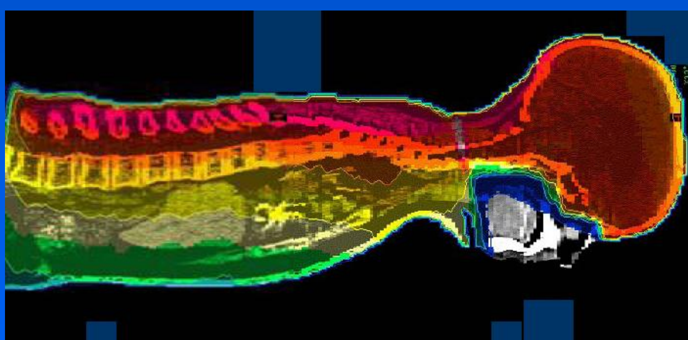
conventional

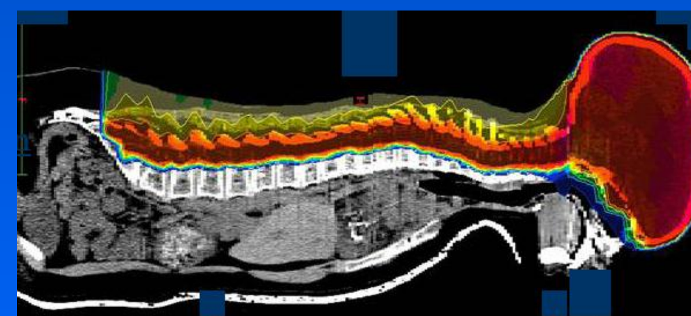


charged particles



Target dose 32 Gy/GyE



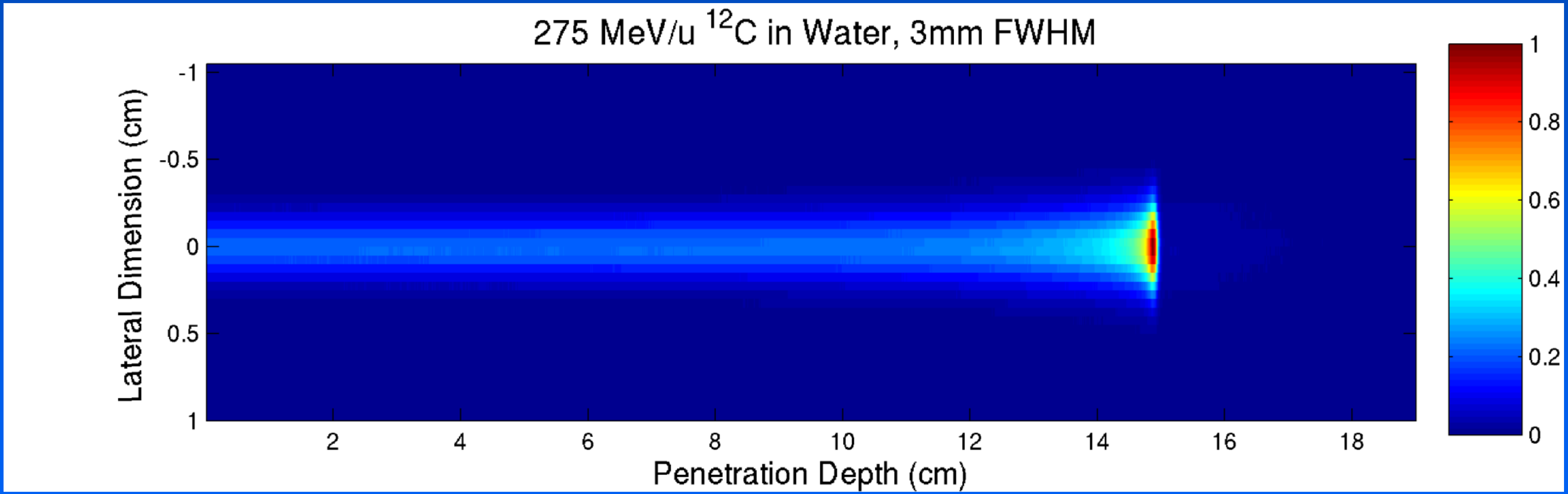


<u>Dose comparison</u>

22 Gy	bone marrow	< 1 GyE
18 Gy	heart	<.5 GyE
20 Gy	intestinal	<.5 GyE

Goal

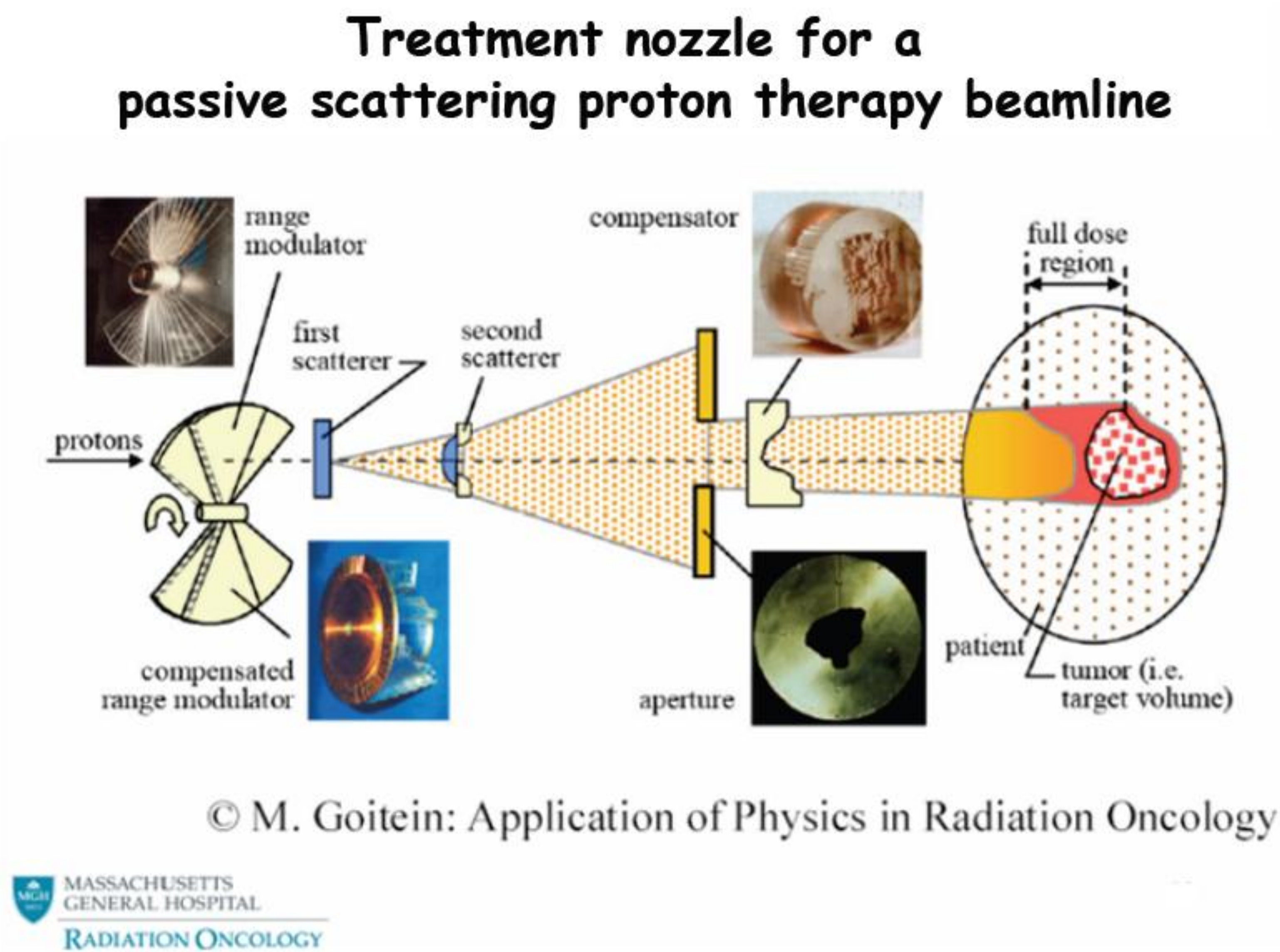
The key element to improve the clinical outcome is **local control!**



entrance channel:
- low physical dose
- low rel. biol. effiency

tumour:
- high physical dose
- high rel. biol. effiency

Passive Dose Delivery

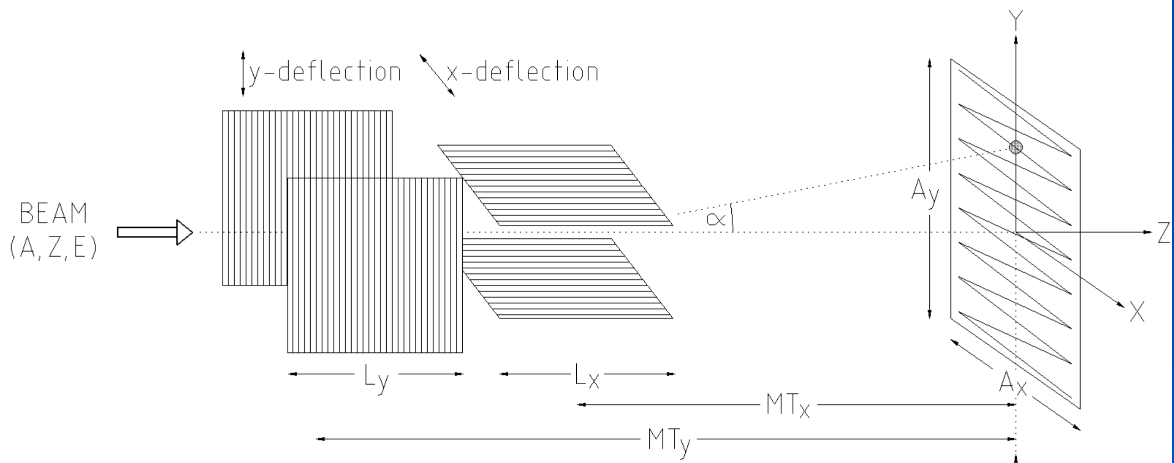


"The major secondary dose contributors are neutrons from the proton treatment nozzle. These external neutrons account for a much higher secondary dose (by about two orders of magnitude) than the internal neutrons."

Jiang, Wang, Xu, Suit and Paganetti (2005)

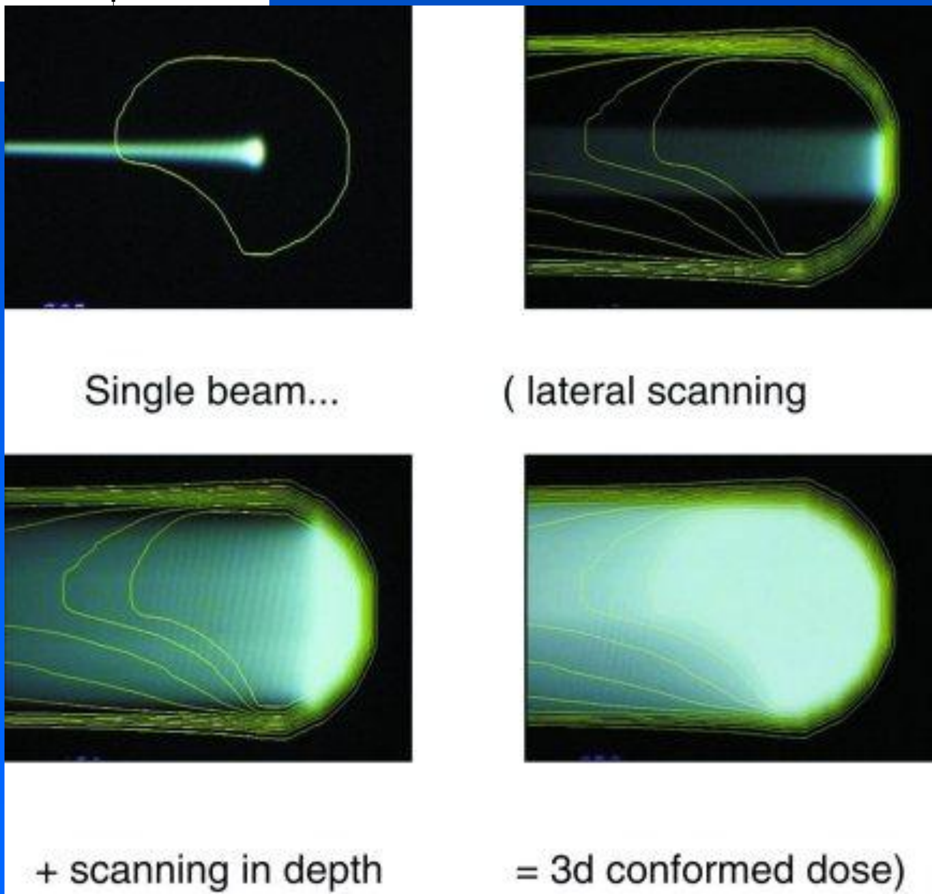
Having spent about $125 million on a proton facility to reduce dose to normal tissues, does it make sense to spray the patient with a total body dose of neutrons, the RBE of which is poorly known, and end up with a second cancer risk similar to IMRT ?

E.J. Hall, Int J Radiat Oncol Biol Phys 2006;65:1-7



Protons (Pedroni et al., PSI):
spot scanning gantry
1D magnetic pencil beam scanning
plus
passive range stacking (digital range shifter)

Haberer et al., NIM A , 1993

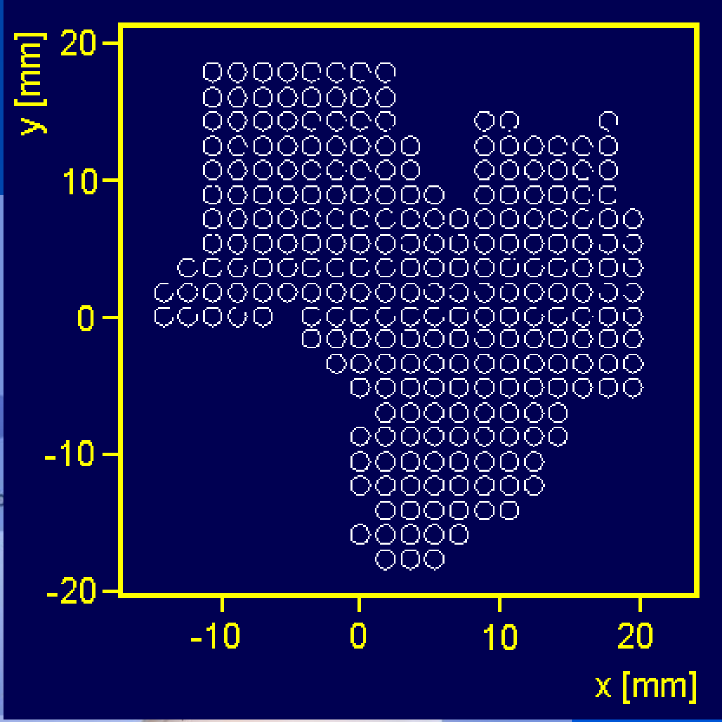


Ions (Haberer et al., GSI):
raster scanning, 3D active,
2D magnetic pencil beam scanning
plus
active range stacking (spot size, intensity) in the accelerator

Beam Scanning

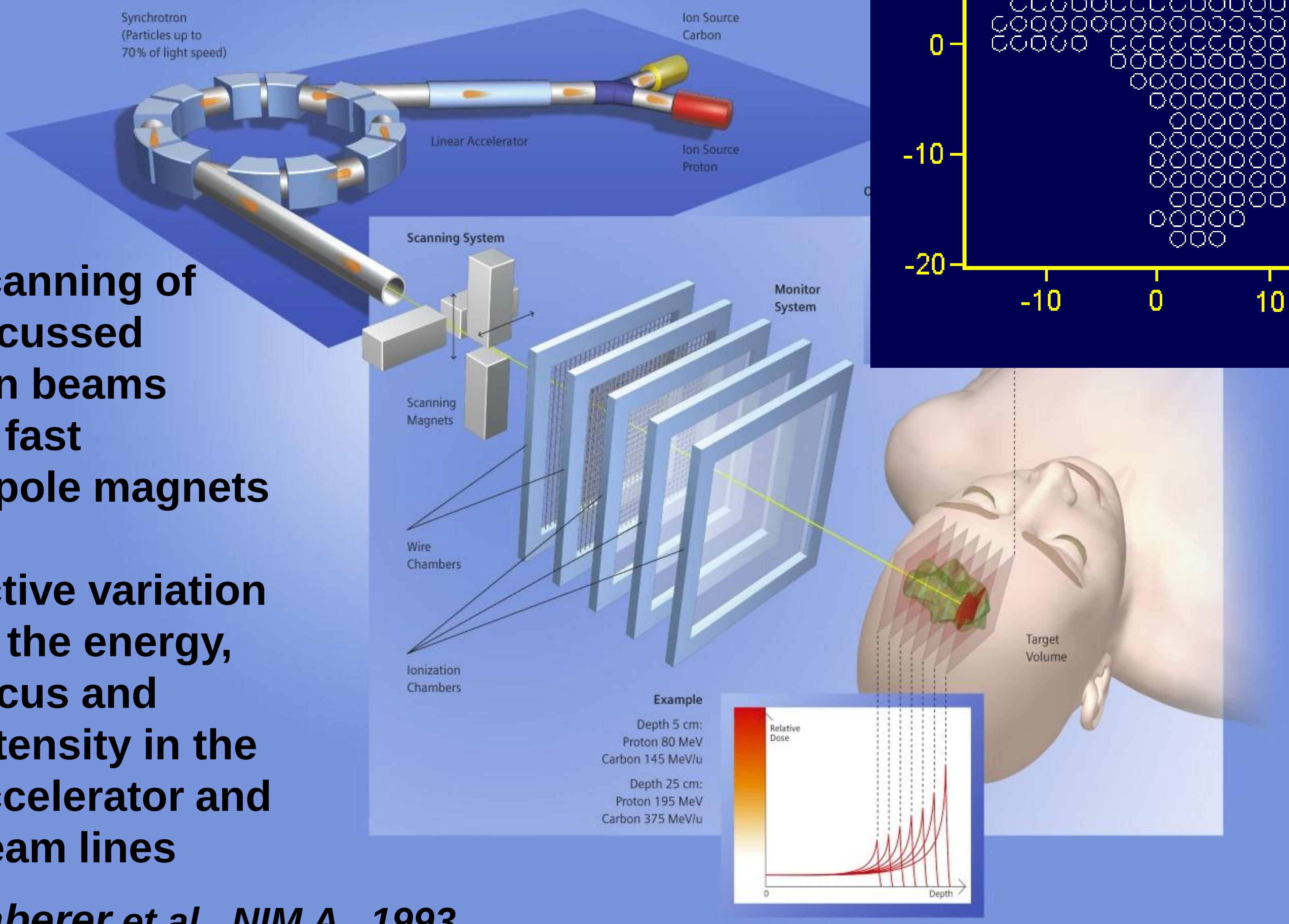
Th. Haberer, Heidelberg Iontherapy Center

Rasterscan Method



scanning of focussed ion beams in fast dipole magnets

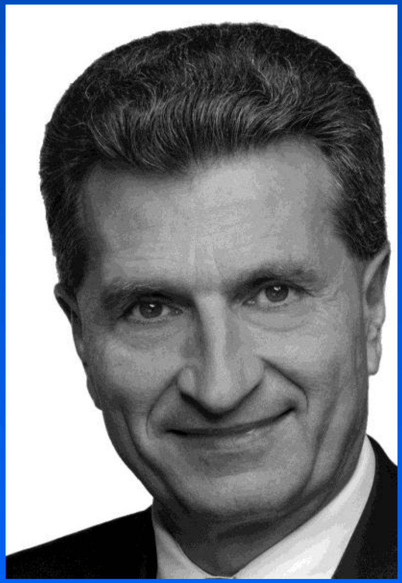
active variation of the energy, focus and intensity in the accelerator and beam lines



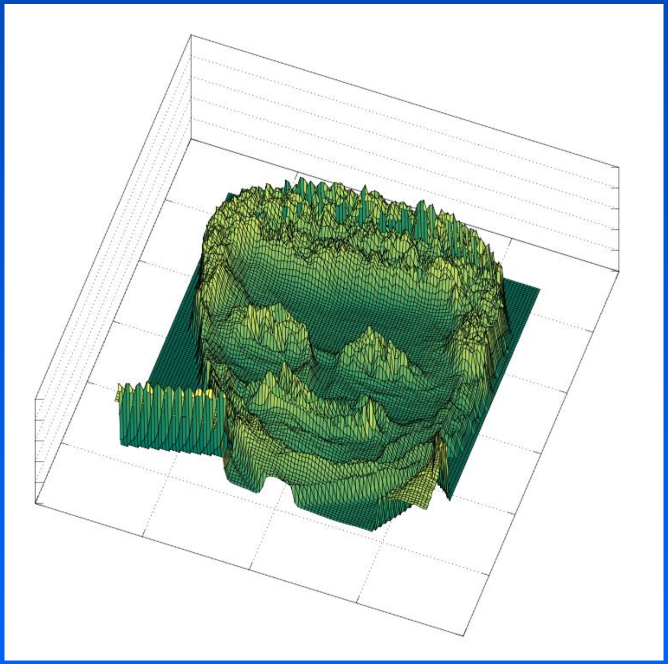
Haberer et al., NIM A , 1993

Beam Scanning!

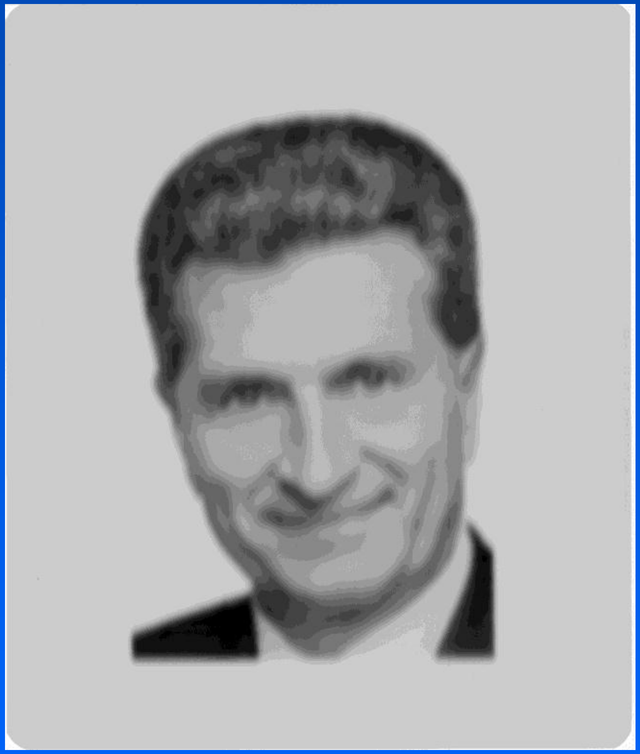
2D-example for dose modulation



original photograph



fluence map

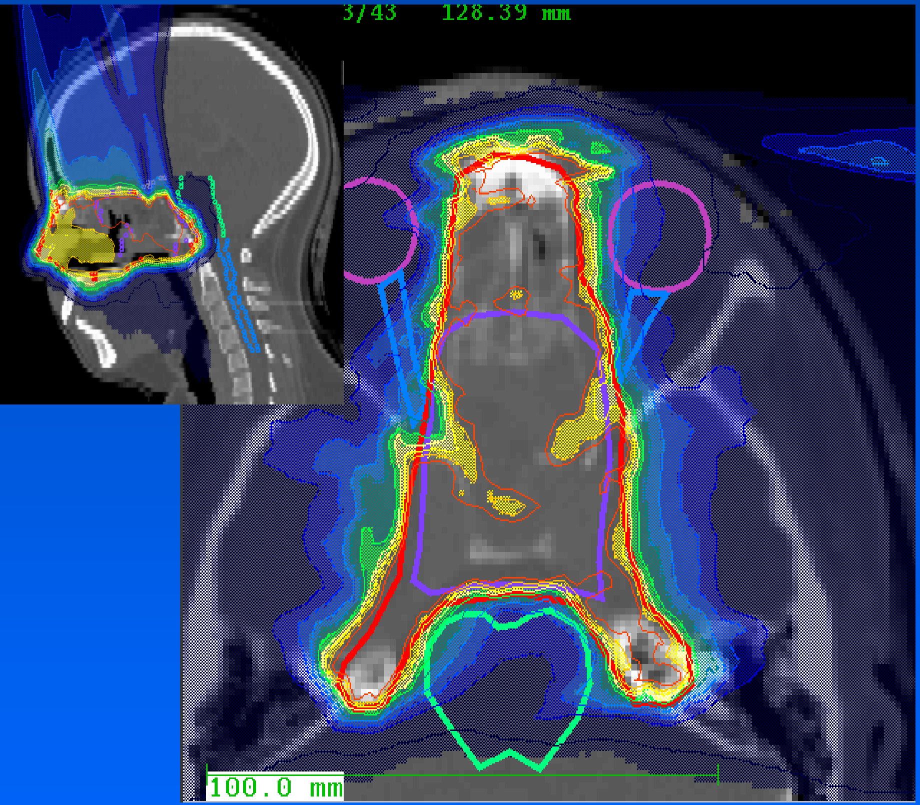


irradiated radiographic film
rasterscan @ HIT

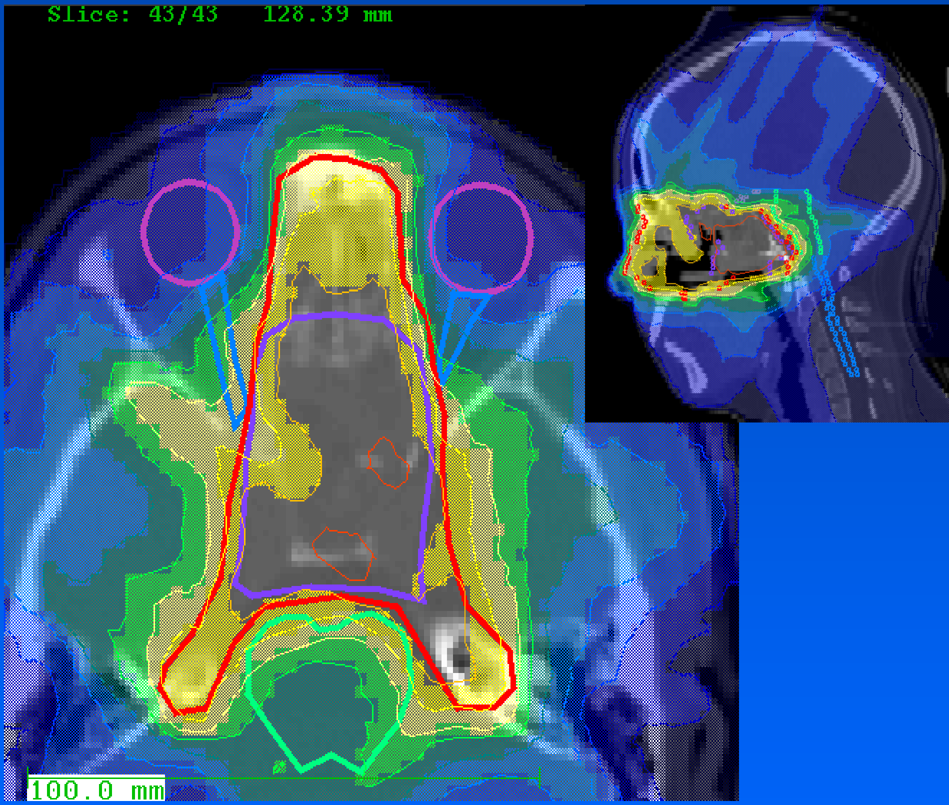
Courtesy Jakob Naumann (HIT), Martin Bräuer (SIEMENS)

Scanned Carbon vs. Intensity Modulated Photons

scanned carbon 3 fields



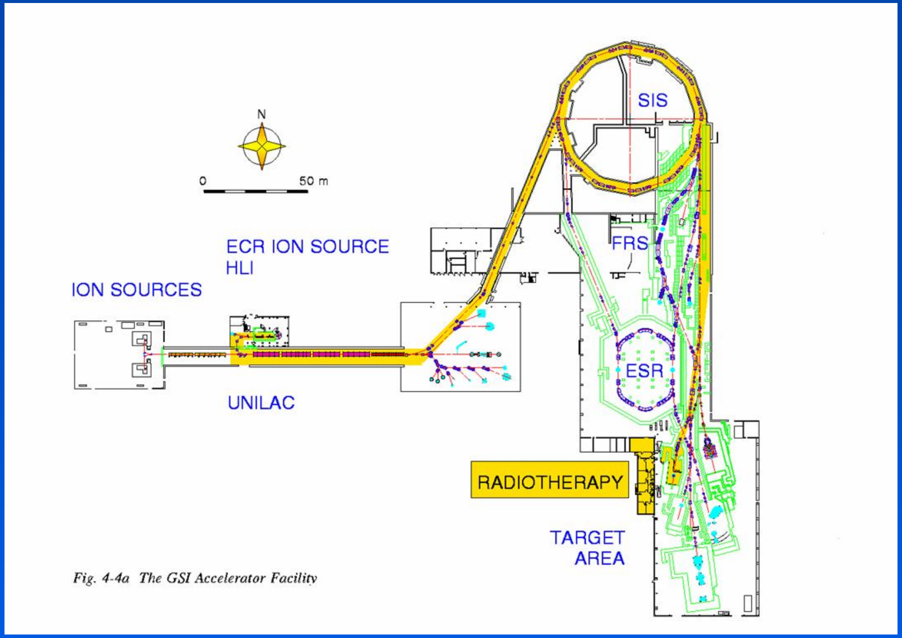
IMRT 9 fields



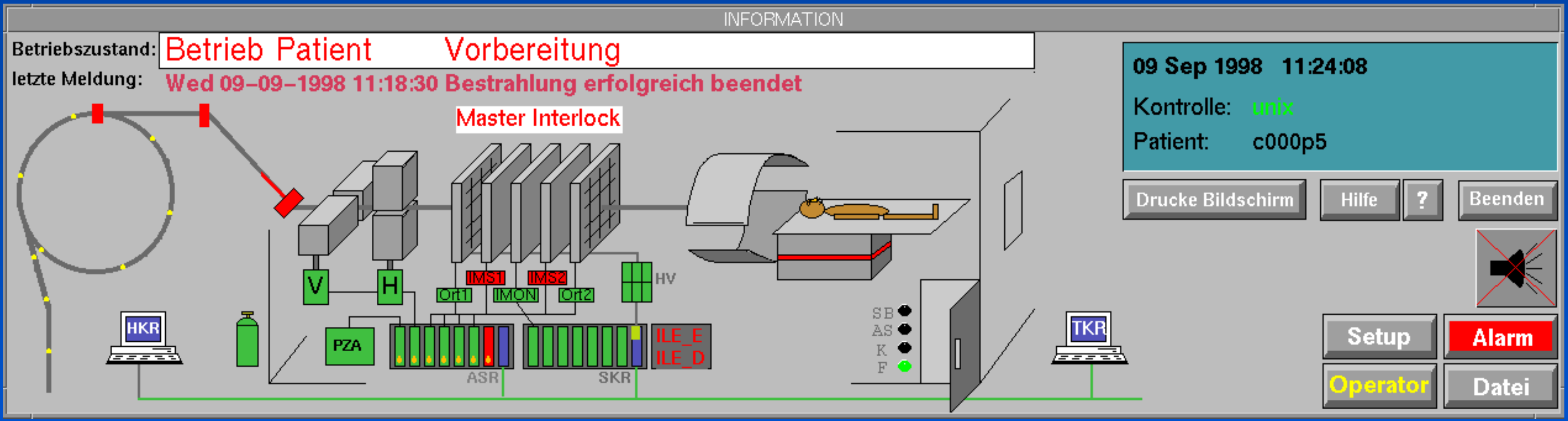
reduced integral dose
steeper dose gradients
less fields
increased biological effectiveness

courtesy O. Jäkel, HIT

Carbon Ion Therapy @ GSI 1997 - 2008

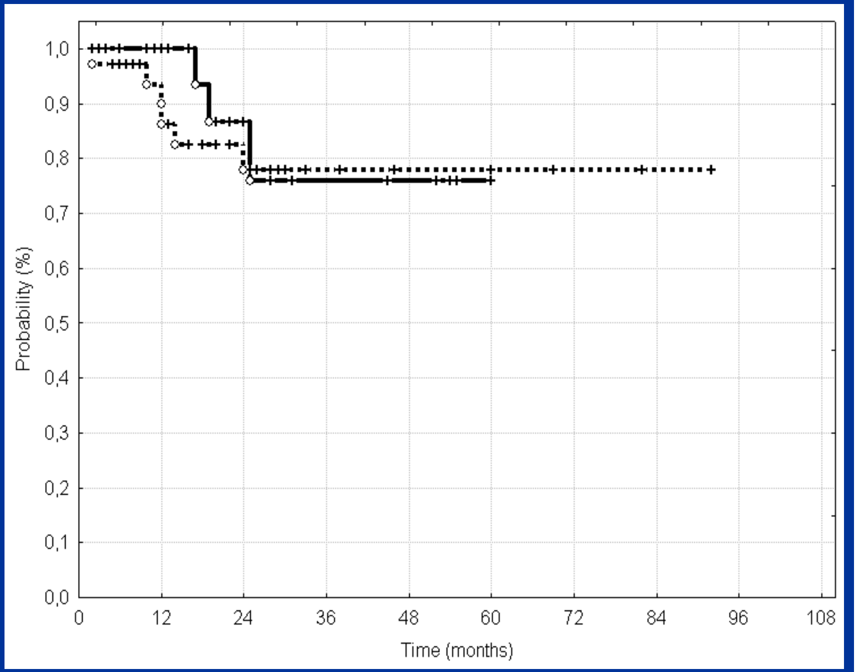


Key Developments @ GSI

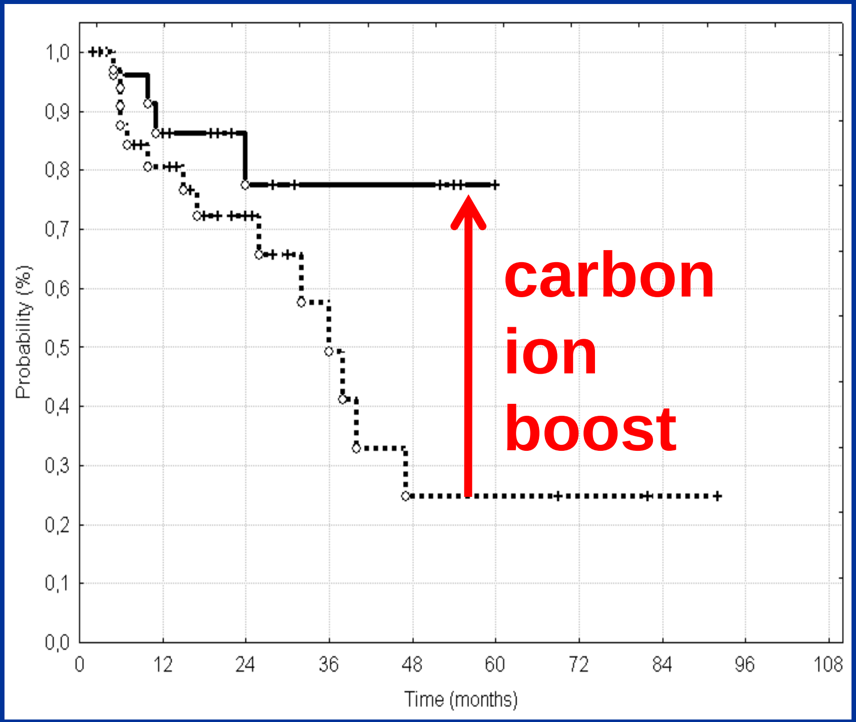


- Scanning-ready **pencil beam library** (25.000 combinations): 253 energies (1mm range steps) x 7 spot sizes x 15 intensity steps
- **Rasterscan method** incl. approved controls and safety
- **Beammonitors** follow the scanned beams (v <= 40 m/s) in real-time
- **Biological interactionmodel** (LEM) based on 25 years of radiobiological research
- Physical beam **transportmodel**
- **Planningsystem** TRiP
- **In-beam Positron Emission Tomography**
- **QA system**
- Prototype of **the scanning ion gantry**

IMRT (photons) vs IMRT (photons) +C12 : locally advanced adenoid-cystic carcinoma



survival



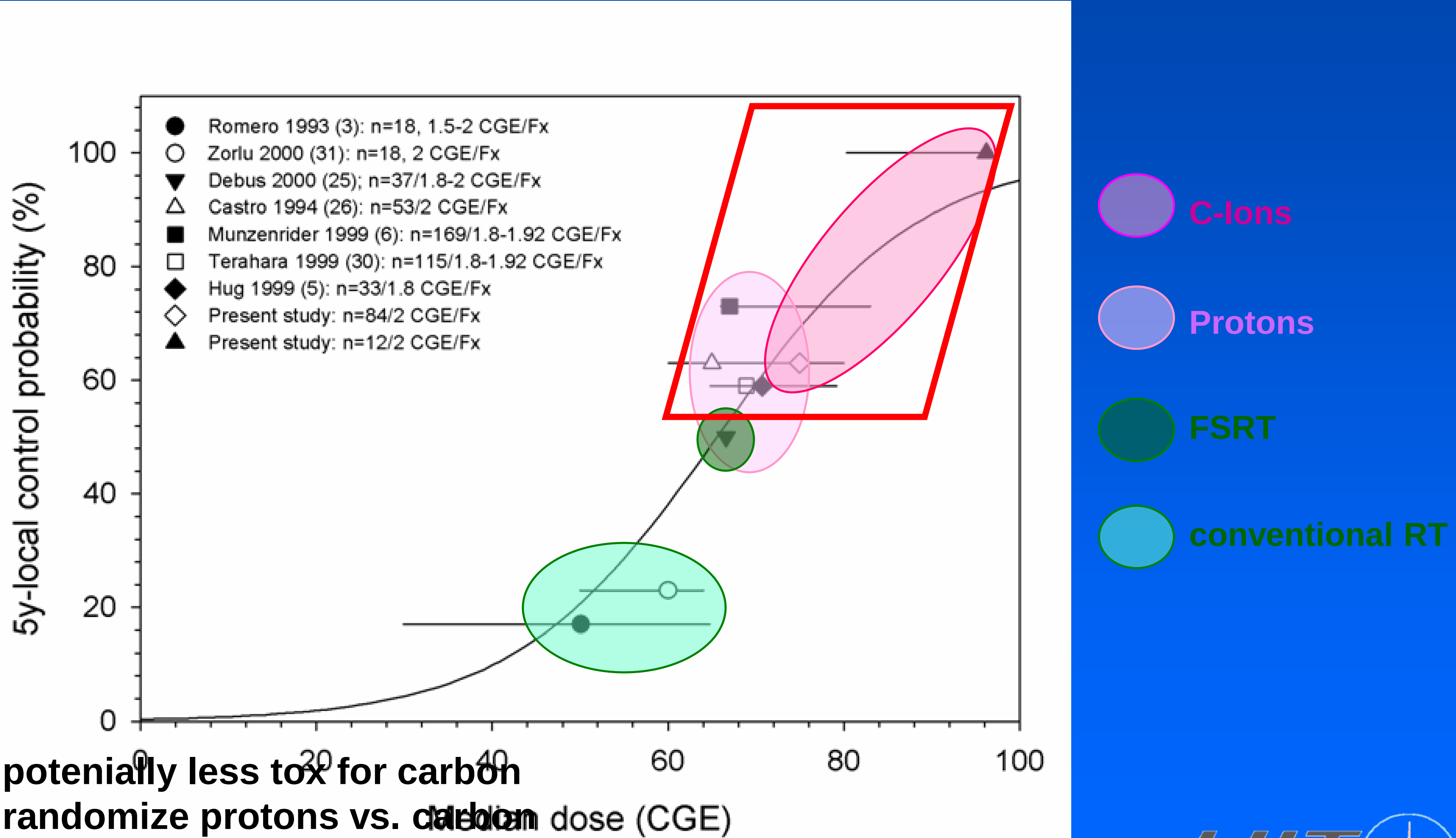
local control

- acute toxicity acceptable
- late toxicity > CTC Grad 2 < 5%

Schulz-Ertner, Cancer 2005

Th. Haberer

Motivation: Dose Response Relationship Radiotherapy of Skull Base Chordomas

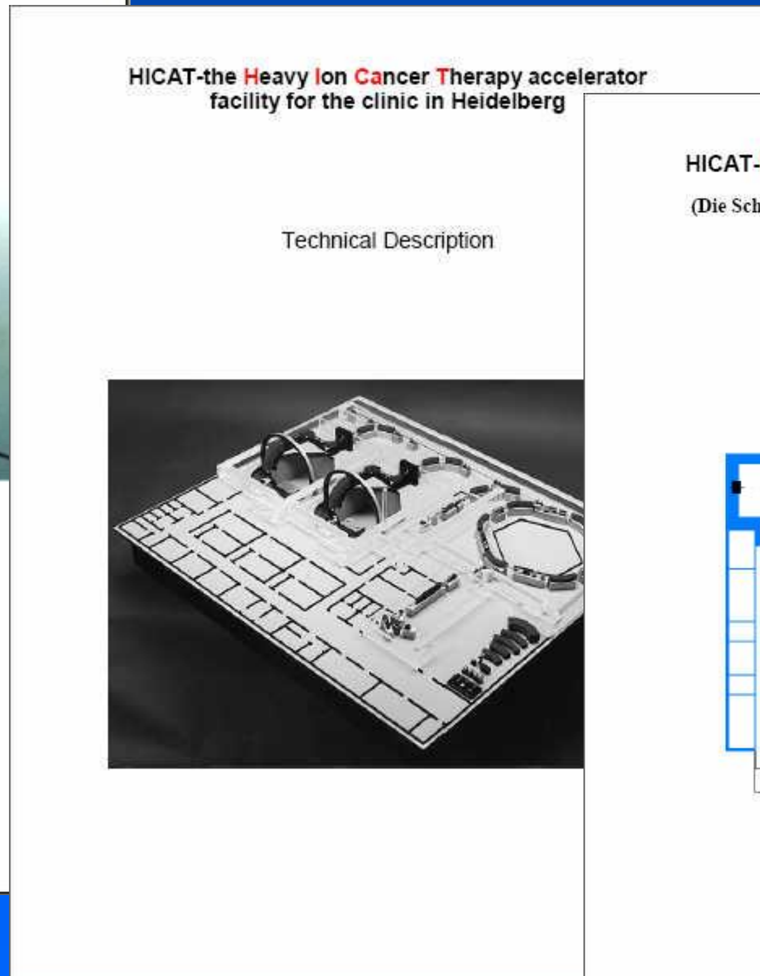


potenially less tox for carbon
randomize protons vs. carbon

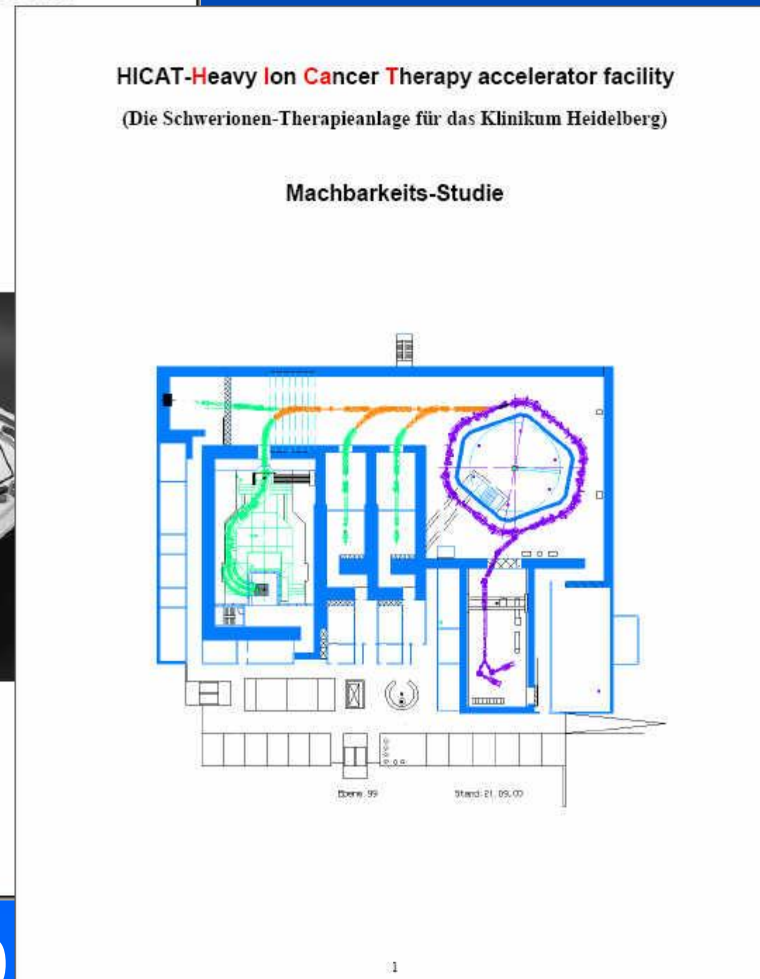
[Schulz-Ertner, IJROBP 2007]

Design Phase

Proposal 1998



Technical Design 2000



Feasibility Study 2000

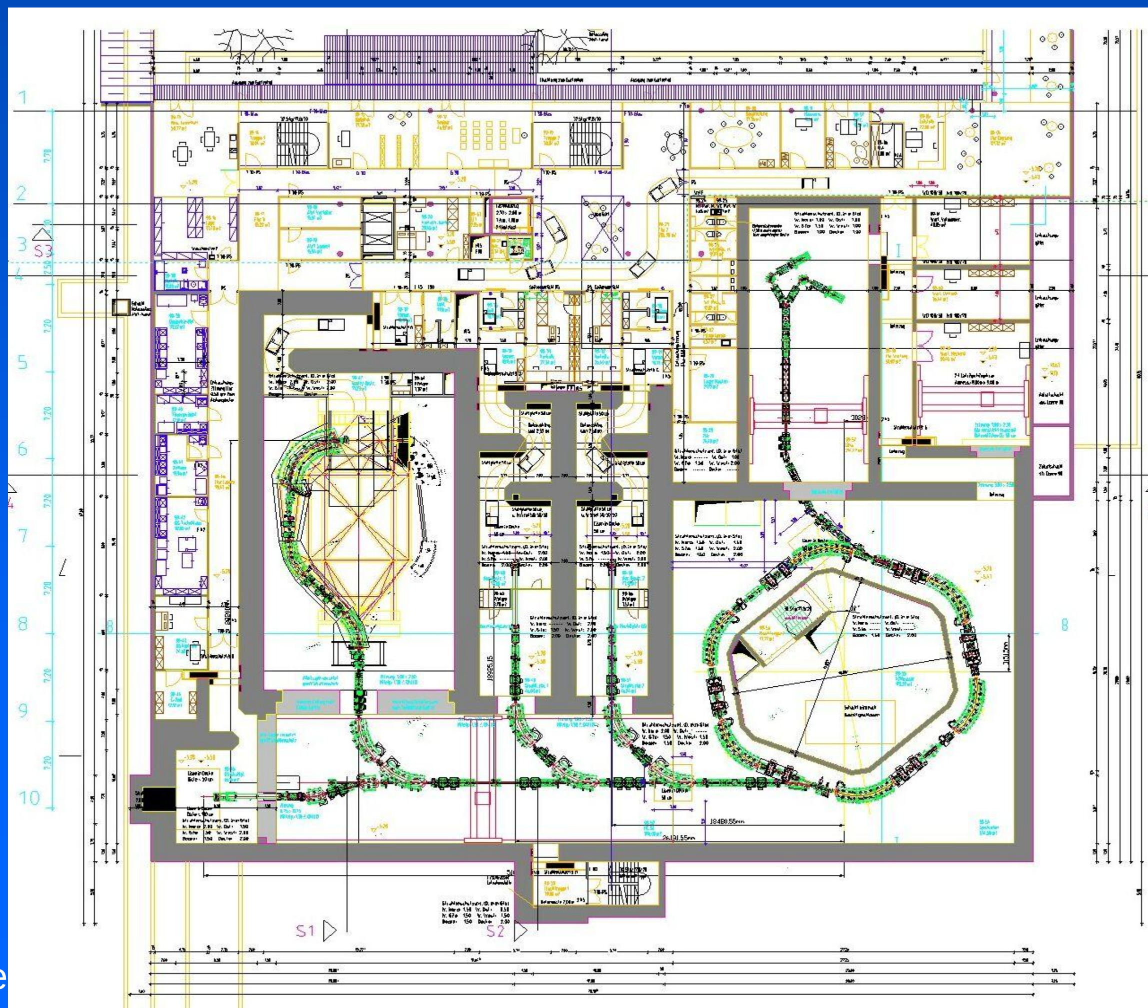
Heidelberg Ion Therapy Center (HIT)

Clinical Integration

Children's Hospital

National Center for Tumour Diseases

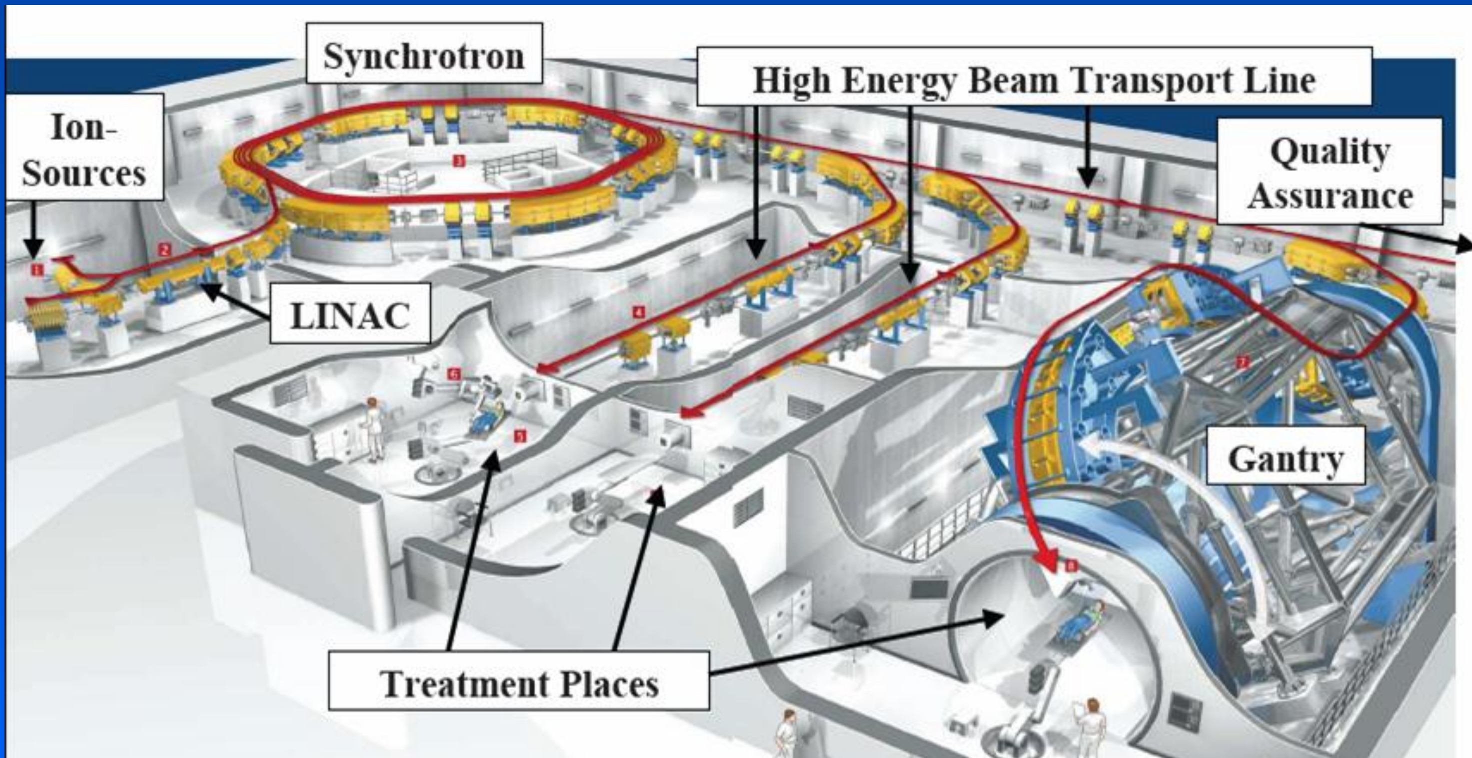
Women's Hospital



Radio-Oncology

Neuro-surgery

Heidelberg Ion Therapy Center
„Flexibility and Precision“



- compact design 60m x 70m
- full clinical integration
- rasterscanning only
- world-wide first ion gantry
- > 1000 patients and
  > 15.000 fractions/yr

- low-LET modality:
  Protons (Helium)
- high-LET modality:
  Carbon (Oxygen)
- ion selection within minutes
- R+D in a broad range

Some Facts

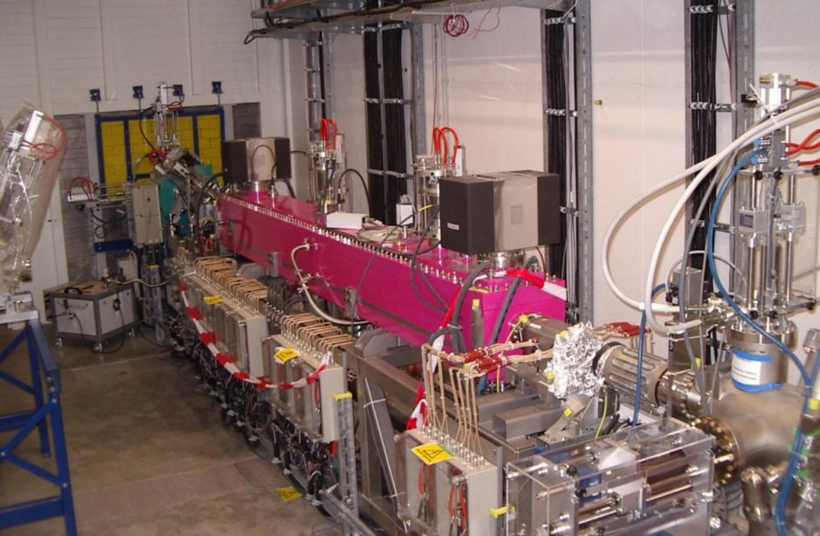
- Effective area 5.027 m²
- Concrete 30.000 tons
- Constructional steel 7.500 tons
- Capital Investment 120 M€

Start of construction: November 2003
Completion of building and acc.: June 2006
First patient treated: Nov. 15th, 2009

Project Partners:

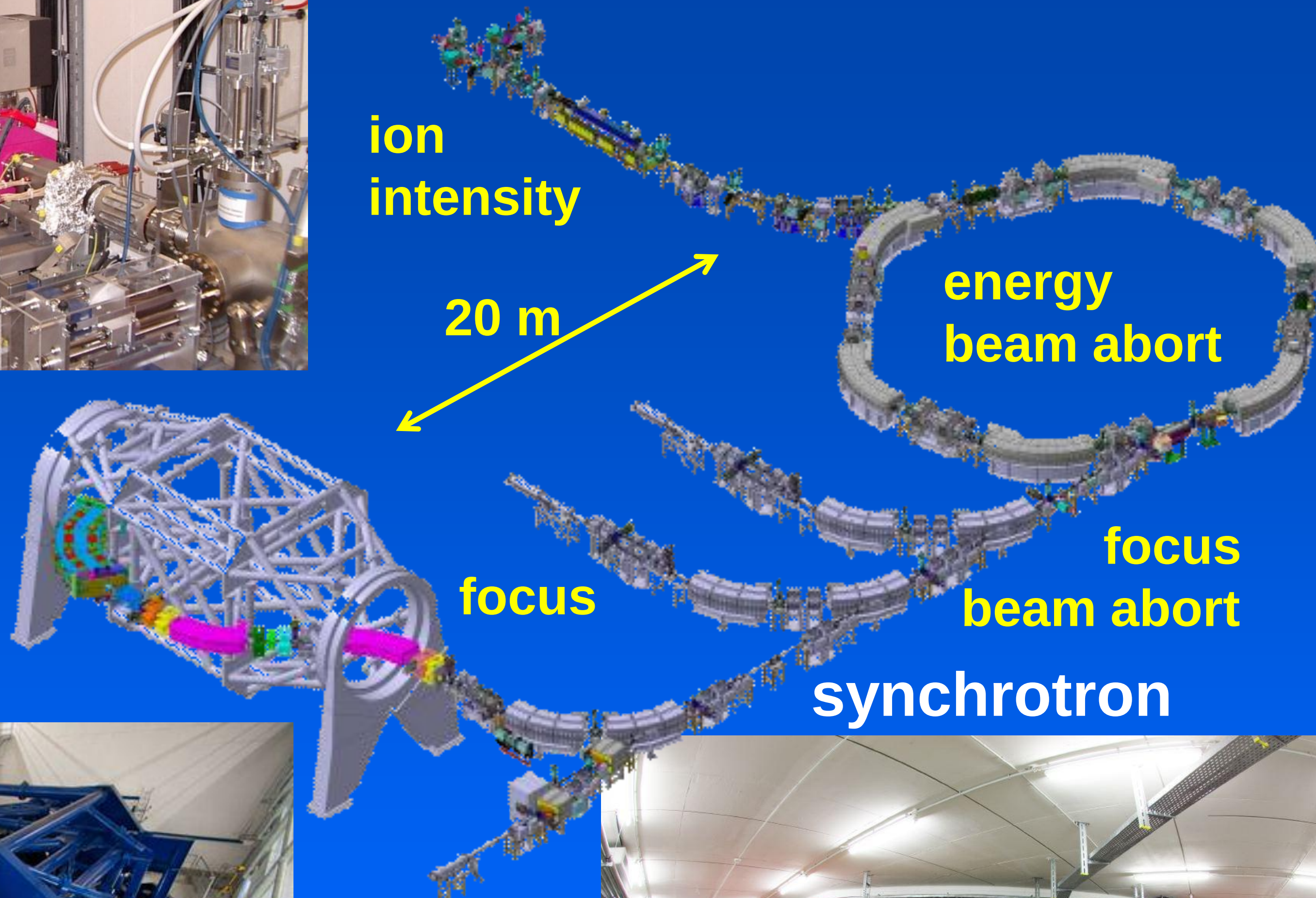
- **University** pays, owns and operates the facility
- **GSI:** feasibility study, facility design, technical proposal, tendering documents, built the accelerator
- **Siemens** supplies all components related to patient environment
- **GSI, DKFZ, Siemens …** are research partners

Heidelberg Ionenstrahl-Therapie Centrum



injector

Gesellschaft für Schwerionenforschung Darmstadt



gantry

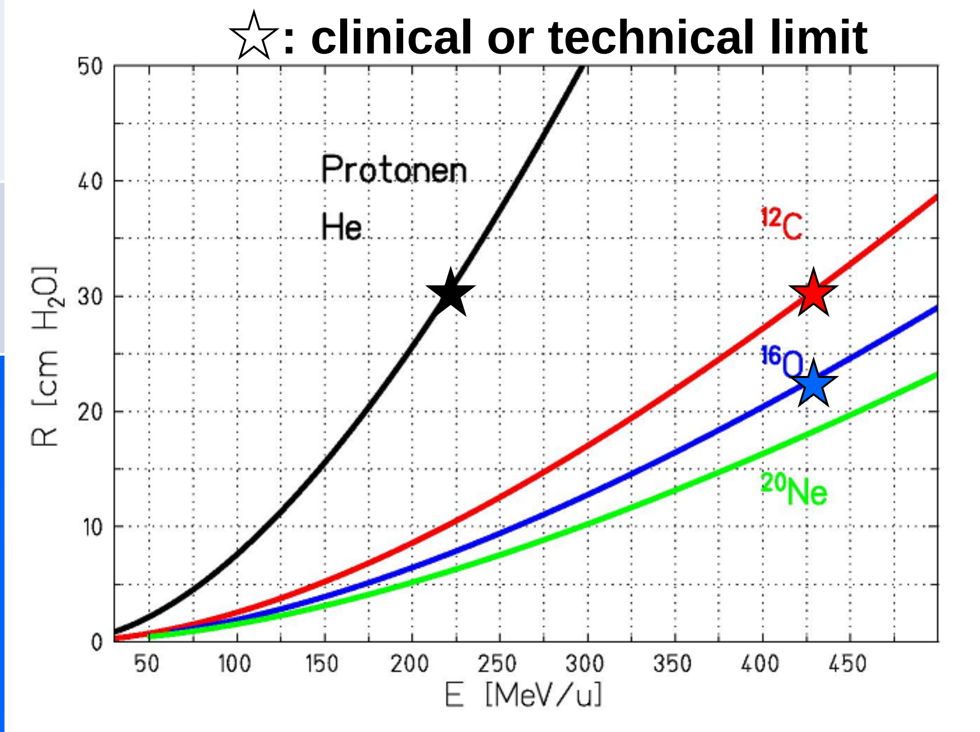
synchrotron

HIT Pencil Beam Library

Parameter	
ions	protons and carbon (**2 ion sources**); planned: helium, oxygen (3 ion sources)
intensity	2×10^6/s to 8×10^7/s for carbon intensity upgrade in progress 8×10^7/s to 4×10^8/s for protons **10 steps**; maximum extraction time 5 s
energy	88-430 MeV/u for carbon 50-221 MeV/u for protons **255 steps**, 1-1.5 mm spacing, 2-30 cm range in water
focus	3.5-13 mm FWHM 11-33 mm FWHM **4 steps**

protons and carbon: clinically used

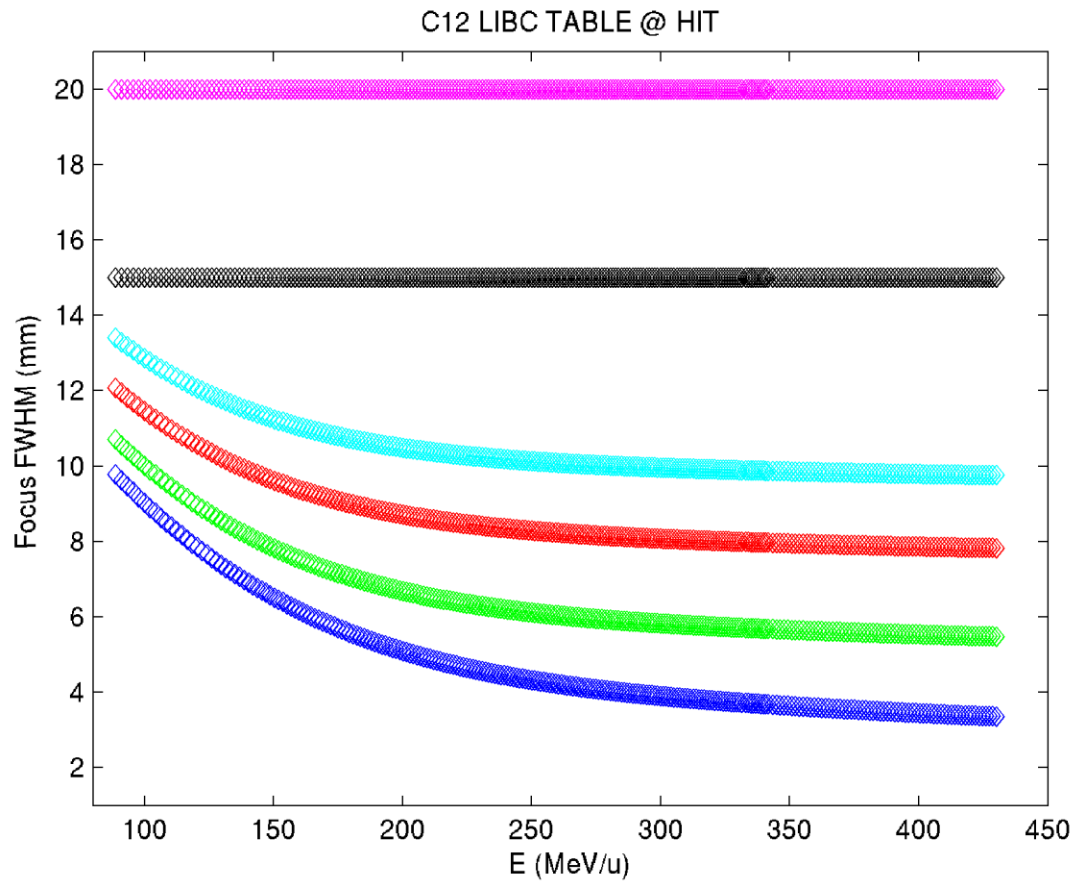
helium and oxygen: under commissioning

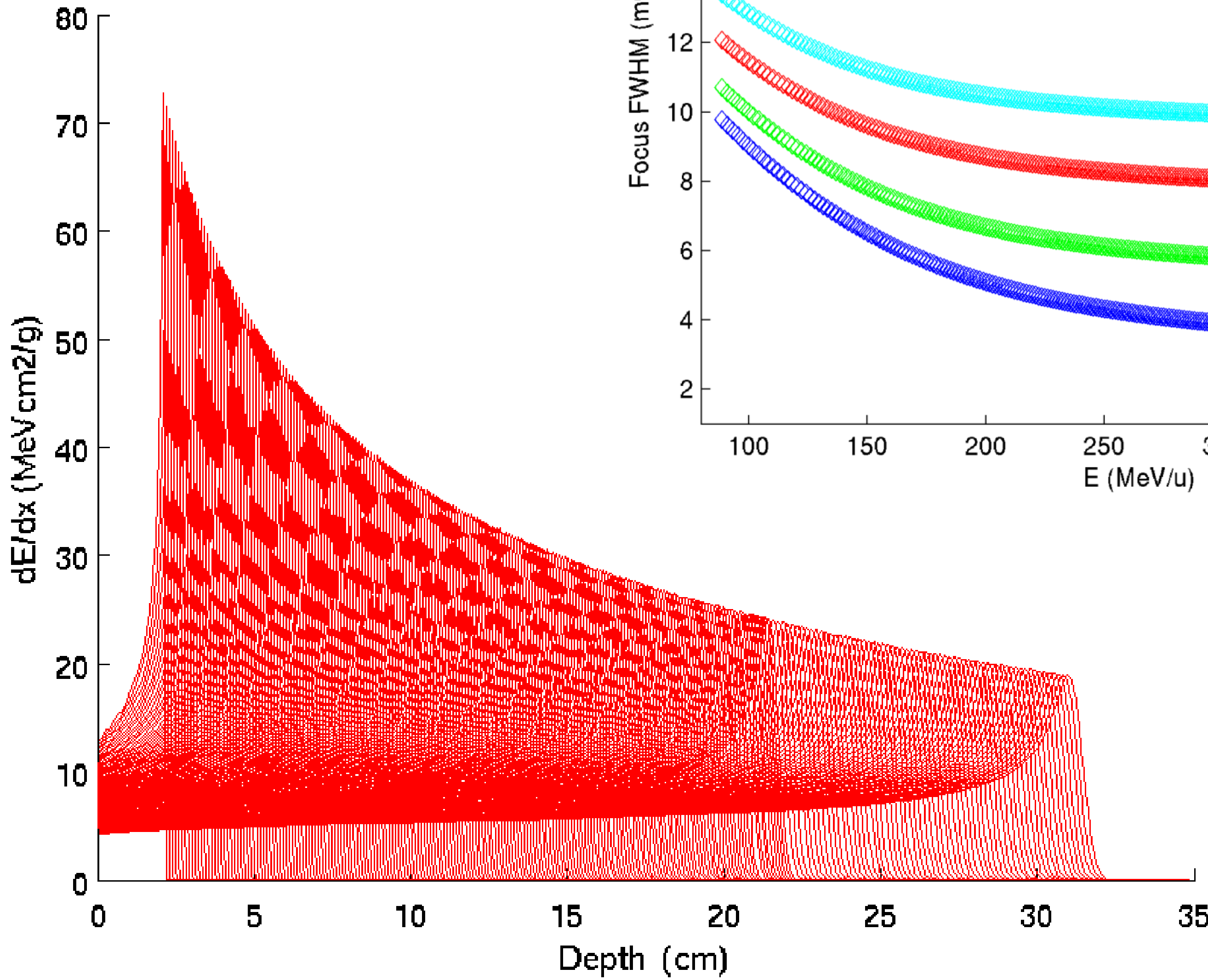


→ a total of 2 x 10 x 255 x 4 = 20400 settings per room!

… the gantry (0.1° steps) adds something …

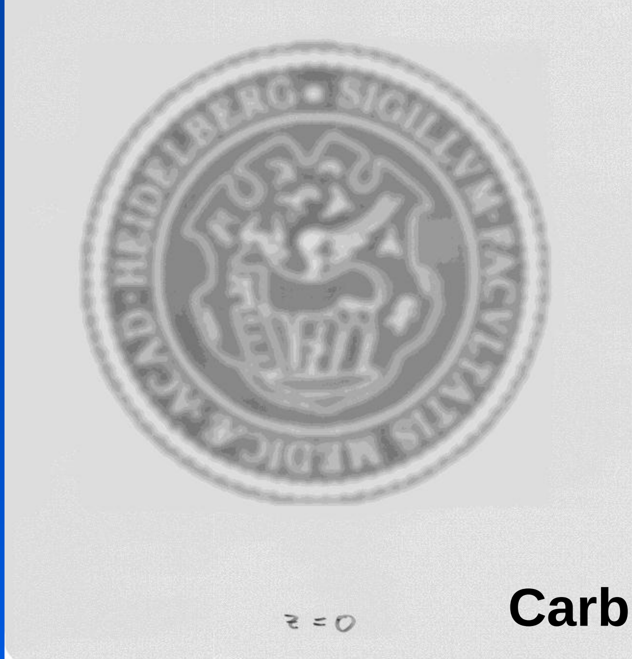
Pencil Beam Libs for Protons and Carbon



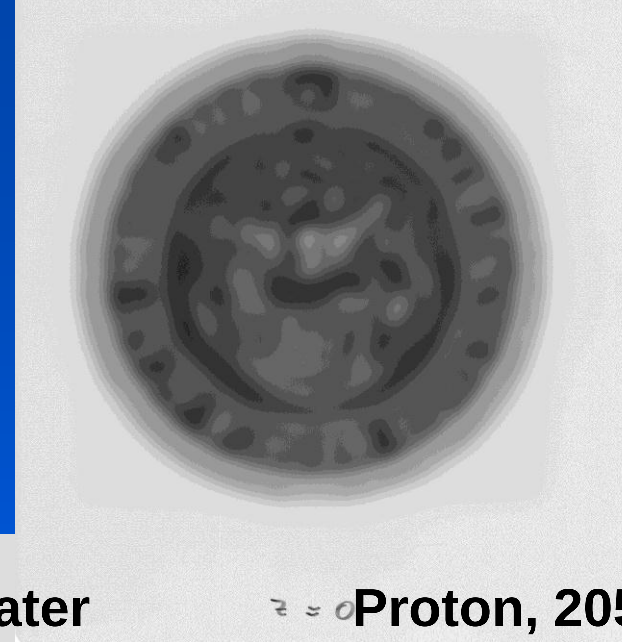


Parodi, Mairani, Naumann, Haberer, Brons, Jäkel, Debus (HIT and FLUKA Collaboration, accepted for publication at PMB)

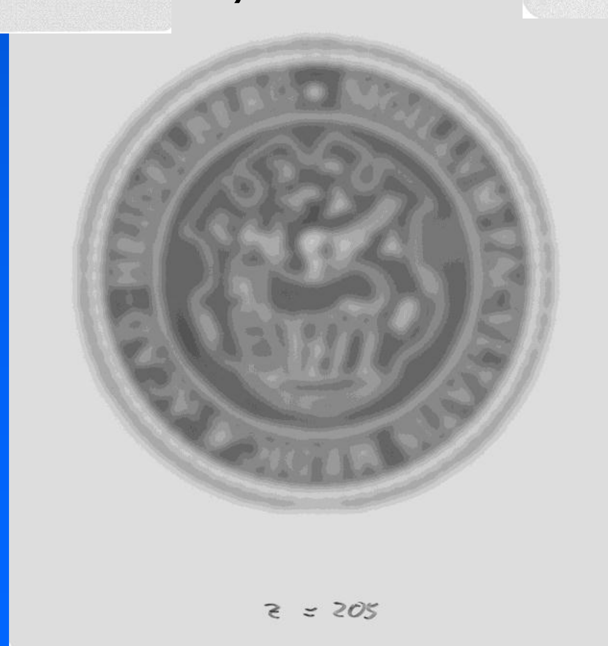
Carbon, isocentre



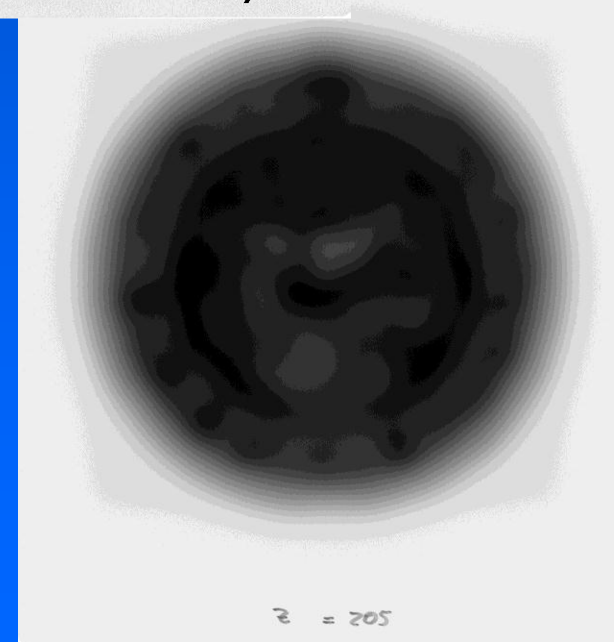
Proton, isocentre



Carbon, 205mm water



Proton, 205mm water



Medical Equipment

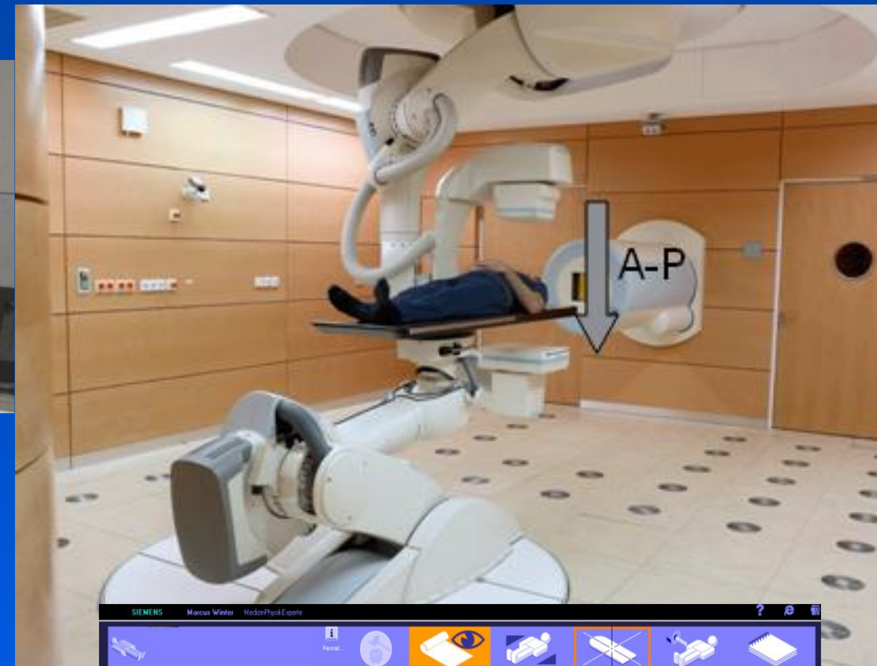
Identical patient positioning systems
- fixed beam
- gantry

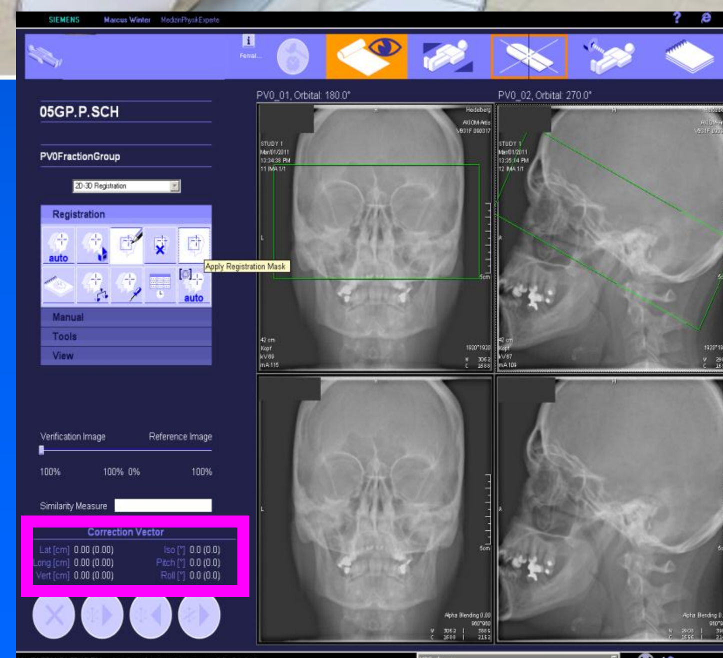
Workflow optimization
- automated QA procedures
- automated patient hand over from shuttle

Inroom position verification
- 2D
- 3D Cone beam CT

Open for future applications and workflows

IGRT / 2D – 3D Matching





- 2D orthogonal X-ray projections
- Calculation of a DRR (Digital X-Ray Reconstruction) based on the planning-CT
- Matching of X-ray and DRR
- Calculation of a correction vector in 6 dimensions:
  3 translations (lat/vert/long)
  3 rotations (iso/pitch/roll)

Workflow

Heidelberg Ionenstrahl-Therapie Centrum

HIT / Approval + CE-Label …

Baden-Württemberg
REGIERUNGSPRÄSIDIUM KARLSRUHE
ABTEILUNG 5 - UMWELT

Regierungspräsidium Karlsruhe · 76247 Karlsruhe

Universitätsklinikum Heidelberg
- Kaufmännische Direktorin -
Im Neuenheimer Feld 672
69120 Heidelberg

Heidelberg 31.10.2009
Name Christiane Griesbach
Durchwahl 06221 1375-221
Aktenzeichen 54.4b1-467/Uniklinik HD, Rad. Klinik (INF 450), 5. HIT
(Bitte bei Antwort angeben)

Kassenzeichen: 8911240005569 Bitte bei Zahlung angeben!	
Betrag:	3306,00 EUR

Durchführung der Strahlenschutzverordnung (StrlSchV)
Genehmigung zum Betrieb einer Anlage zur Erzeugung ionisierender Strahlen gemäß § 11 Abs. 2 StrlSchV
Ihr Antrag vom 01.09.2009 und Ihre Schreiben vom 15. und 30.10.2009

Anlagen
1 Sachverständigenverzeichnis
1 Messstellenverzeichnis
1 Überweisungsträger

Genehmigung Nr. A/12/099/09

4. Verwendungszwecke:
- Bestrahlung von Menschen in Ausübung der Heilkunde im Horizontal-bestrahlungsplatz H1
- Bestrahlung von Messaufbauten mit Phantomen und Strahlungsdetektoren im Rahmen der Grundlagenforschung
- Bestrahlung von Materialien zur Veränderung von Materialeigenschaften im Rahmen von Forschungsprojekten
- Bestrahlung belebter Objekte (biologische Zellen / Zellkulturen, Gewebe / Gewebebestandteile, Pflanzen und Versuchstiere)
- Qualitätssicherung und Dosimetrie
- Wartungsbetrieb

UniversitätsKlinikum Heidelberg

HIT
Heidelberger Ionenstrahl-Therapie

Erklärung zu Produkten für besondere Zwecke gemäß Anhang VIII der Richtlinie 93/42/EWG vom 14. Juni 1993 über Medizinprodukte

© Universitätsklinikum Heidelberg, Im Neuenheimer Feld 672, 69120 Heidelberg

Hersteller: Universitätsklinikum Heidelberg, Im Neuenheimer Feld 672, 69120 Heidelberg

Medizinprodukt: **Heidelberger Ionenstrahl-Therapie (HIT) Anlage Bestrahlungsplatz H1**

Klassifizierung: **Klasse IIb** gemäß Anhang IX der Richtlinie 93/42/EWG

Konformitätsbewertungsverfahren: **Anhang VIII 2.1**

Die o.g. Eigenherstellung entspricht den unter Berücksichtigung ihrer Zweckbestimmung auf sie anwendbaren, in Anhang I der Richtlinie 93/42/EWG genannten grundlegenden Anforderungen. Eine Auflistung der nicht bzw. nicht vollständig eingehaltenen grundlegenden Anforderungen ist in Anlage I zu dieser Erklärung enthalten.

Heidelberg, den 14.11.2009

Dipl.-Volkswirtin Irmtraut Gürkan
(Kaufmännische Direktorin des Universitätsklinikums Heidelberg)

Der Unterzeichner erklärt, dass er verantwortlich zeichnet für die Ausstellung dieser Herstellererklärung, die ihre Gültigkeit bei einer wesentlichen Änderung an dem o.g. Medizinprodukt verliert.

Autor: A.Höss/H.Risch	Erstellung: 26.10.2009	Revisions-Nr. V01-000	Seite 1 von 1
Titel: HIT-Herstellererklärung		Pfad/Dateiname: HIT-Herstellererklärung V01-000.doc	

SIEMENS

EC DECLARATION OF CONFORMITY

according to Annex II.3 of Council Directive 93/42/EEC of June 14, 1993

Manufacturer	Siemens AG Wittelsbacherplatz 2 DE-80333 Muenchen Germany
Facility	Siemens AG, Medical Solutions Business Unit Particle Therapy System Hofmannstrasse 26, DE-91052 Erlangen, Germany
Medical device	IONTRIS Treatment room H2
Product identification	10013850
Classification	Class IIb (according to Annex IX to Council Directive 93/42/EEC)

We declare the compliance of the above medical device with the requirements of the Council Directive 93/42/EEC of June 14, 1993.
The conformity of the full quality assurance system is certified by:
TÜV SÜD Product Service GmbH
Ridlerstrasse 65
80339 Muenchen
Germany

The identification number of the notified body for implementation of the procedure set out in Annex II to the above Directive is 0123.
This declaration of conformity is issued under the sole responsibility of Siemens AG.
This declaration supersedes any declaration issued previously for the same treatment room.

Place and date: Erlangen, September 14, 2010

Name: Holger Schmidt (Head of Business Unit); Jürgen Buckow (Head of Quality Management)

Signature

For conditions of guarantee and liability please refer to our General Conditions of Sale.

Document number 10013802-VA1X QCE ION 04 — Page 1 of 1

EC DECLARATION OF CONFORMITY

Approval radiation protection law

Medical device directive „In-house-product declaration“

CE-label by Siemens Health Care

November 2009

HIT Heidelberg Ionenstrahl-Therapie Centrum

Patient Treatment @ HIT

- center directly connected with the existing department of radiation oncology
- specialized clinics for primary contact and for follow-up
- outpatient treatment or inpatient on 3 wards
- individual positioning devices: head masks etc., patient shuttle
- target volume definition on CT, MRI, PET-CT
- ICRU-criteria: GTV, CTV, PTV...
- Siemens Dosimetrist/Oncologist for target volume definition
- Siemens PT Planning, Siemens, Erlangen, Germany for treatment planning
- patient positioning prior to each treatment with orthogonal X-rays focussing on bony landmarks (3d/2d-matching)
- gating available, anaesthesia

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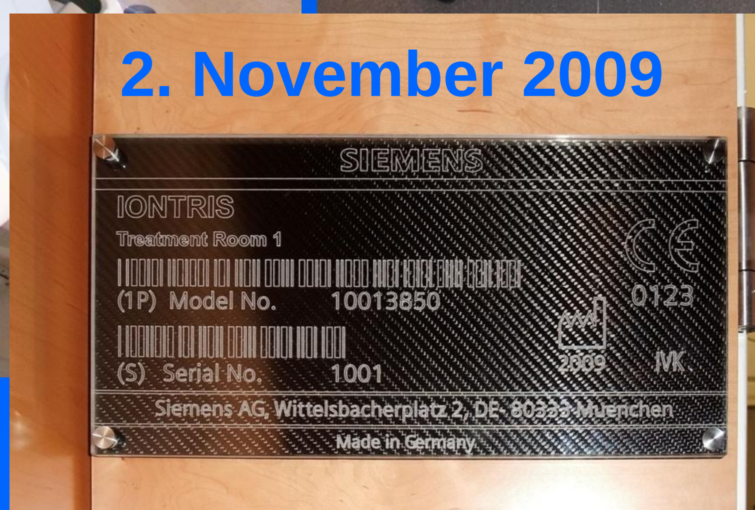
1st Patient @ HIT-H1



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New Version (VA11) @ HIT-H2

- Improved Matching
- Rangeshifter
- MPA-software (QA and R+D)
- TPS verification more efficient
- Stability improved
- Gating
- Shuttlesystem

pediatrics
(anaesthesia, protons)
prostate
liver (Gating)

28. September 2010

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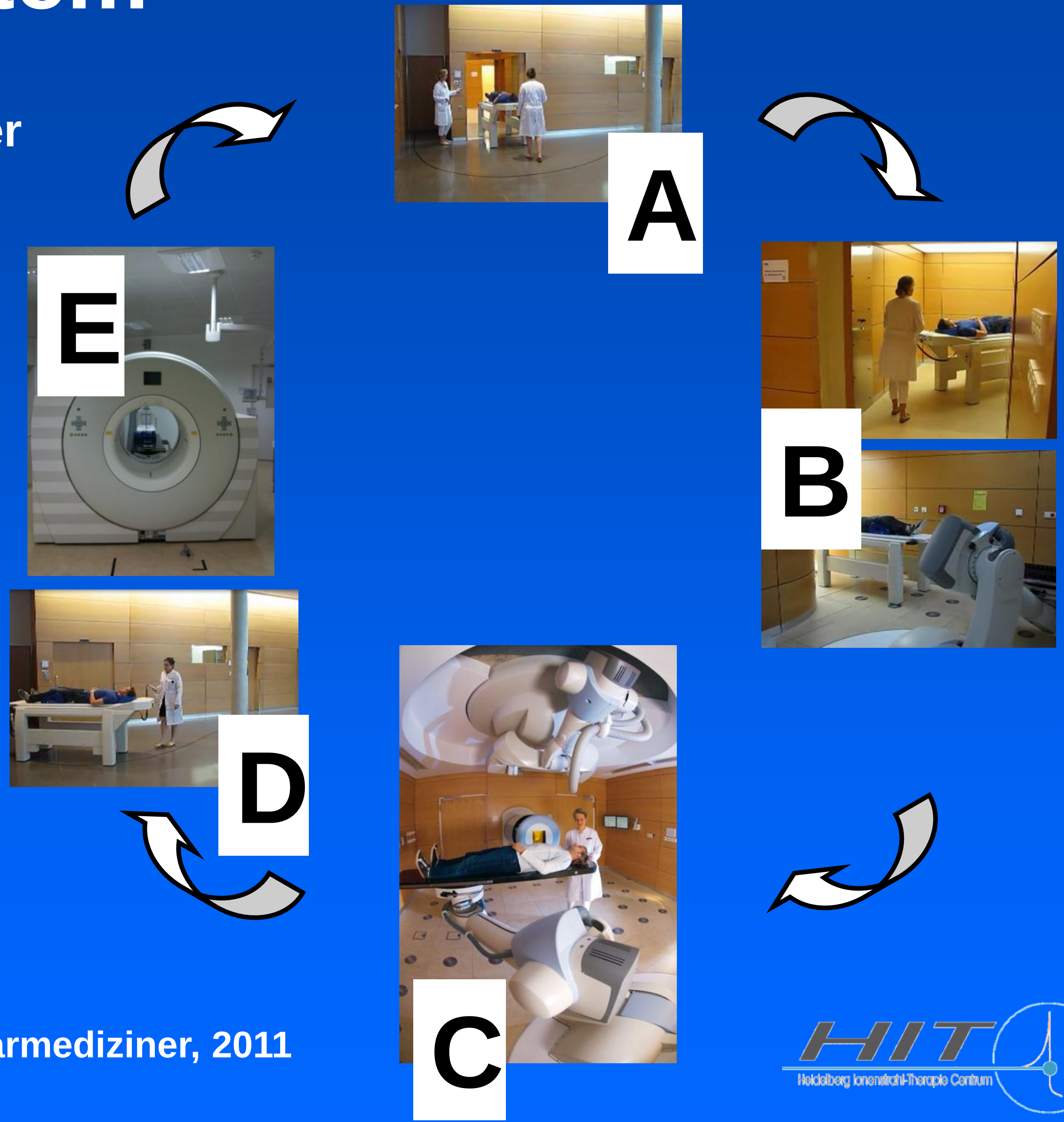
Shuttlesystem

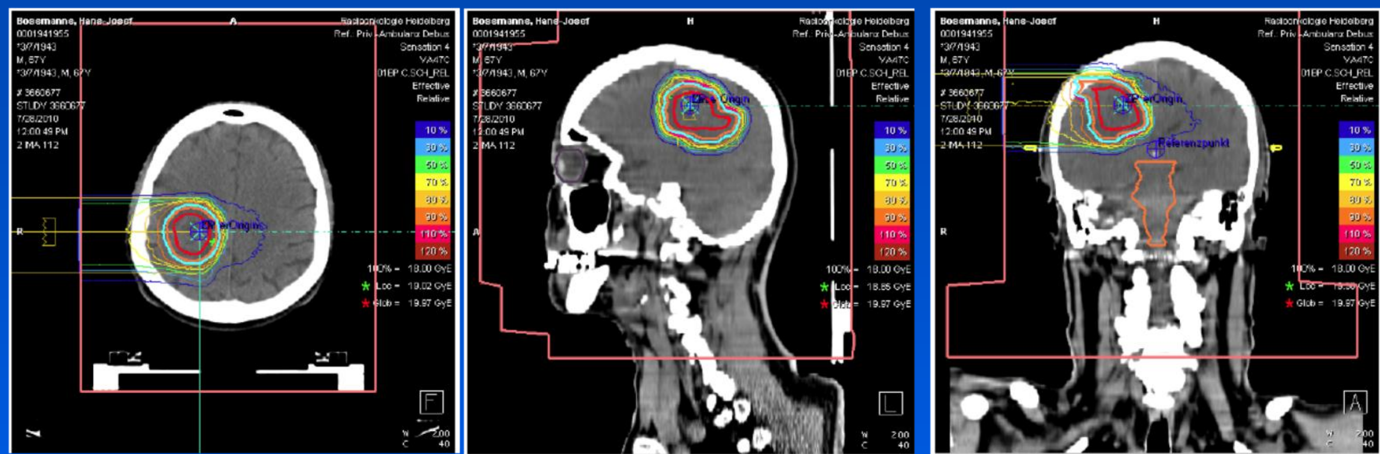
- oncolog dignity carrier
- connection between PET-CT and treatment rooms



Combs SE et al., Der Nuklearmediziner, 2011

PET For Dose Verification
offline after 2 min

Planned dose (on planning CT)



Measured PET/CT

Parodi et al 2010


FlexScan S1901
Isozentrum (nah)
Isozentrum (weit)
Strahlaustritt
Imager
In-Room Display
Signalleuchten
Zugang
Roentgenraum
Lasertracker

Clinical Trials @ HIT

1 **Not yet recruiting** [Treatment of Malignant Sinonasal Tumours With Intensity-modulated Radiotherapy (IMRT) and Carbon Ion Boost (C12)]
Conditions: Sinonasal Malignancies:; Adenocarcinoma and Squamous Cell Carcinoma of the Paranasal Sinuses
Intervention: Radiation: carbon ion boost

2 **Recruiting** [TPF Followed by Cetuximab and IMRT Plus Carbon Ion Boost for Locally Advanced Head and Neck Tumors]
Condition: Locally Advanced Squamous Cell Carcinoma of the Head and Neck (SCCHN): Oro-, Hypopharyngeal and Laryngeal Cancer
Intervention: Radiation: carbon ion boost

3 **Recruiting** [Trial of Proton Versus Carbon Ion Radiation Therapy in Patients With Low and Inter-mediate Grade Chondrosarcoma of the Skull Base]
Condition: Chondrosarcoma
Interventions: Radiation: carbon ion therapy; Radiation: proton therapy

4 **Recruiting** [Trial of Proton Versus Carbon Ion Radiation Therapy in Patients With Chordoma of the Skull Base]
Conditions: Chordoma; Tumor; Treatment
Interventions: Radiation: Carbon ion; Radiation: Protons

5 **Recruiting** [CO(Mbined Therapy of Malignant) S(Alivary Gland tu)M(Ours With)I(MRT and) c(Arbon Ions): COSMIC]
Conditions: Malignancy; Salivary Glands; Tumor
Intervention: Radiation: carbon ion boost

6 **Not yet recruiting** [Carbon Ion Radiotherapy for Atypical Meningiomas]
Condition: Meningioma
Intervention: Radiation: Carbon Ion Radiotherapy

7 **Not yet recruiting** [Carbon Ion Radiotherapy for Recurrent Gliomas]
Condition: Glioma
Interventions: Radiation: Carbon Ion Radiotherapy; Radiation: Fractionated Stereotactic Radiotherapy (FSRT)

8 **Recruiting** [Carbon Ion Radiotherapy for Primary Glioblastoma]
Condition: Primary Glioblastoma
Interventions: Radiation: Carbon Ion Radiotherapy; Radiation: Proton Radiotherapy

9 **Not yet recruiting** [Adenoid Cystic Carcinoma, Erbitux, and Particle Therapy]
Condition: Adenoid Cystic Carcinoma
Intervention: Drug: cetuximab weekly

10 **Not yet recruiting** [Carbon Ion Radiotherapy for Hepatocellular Carcinoma]
Condition: Hepatocellular Carcinoma
Intervention: Radiation: Carbon Ion Radiotherapy

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

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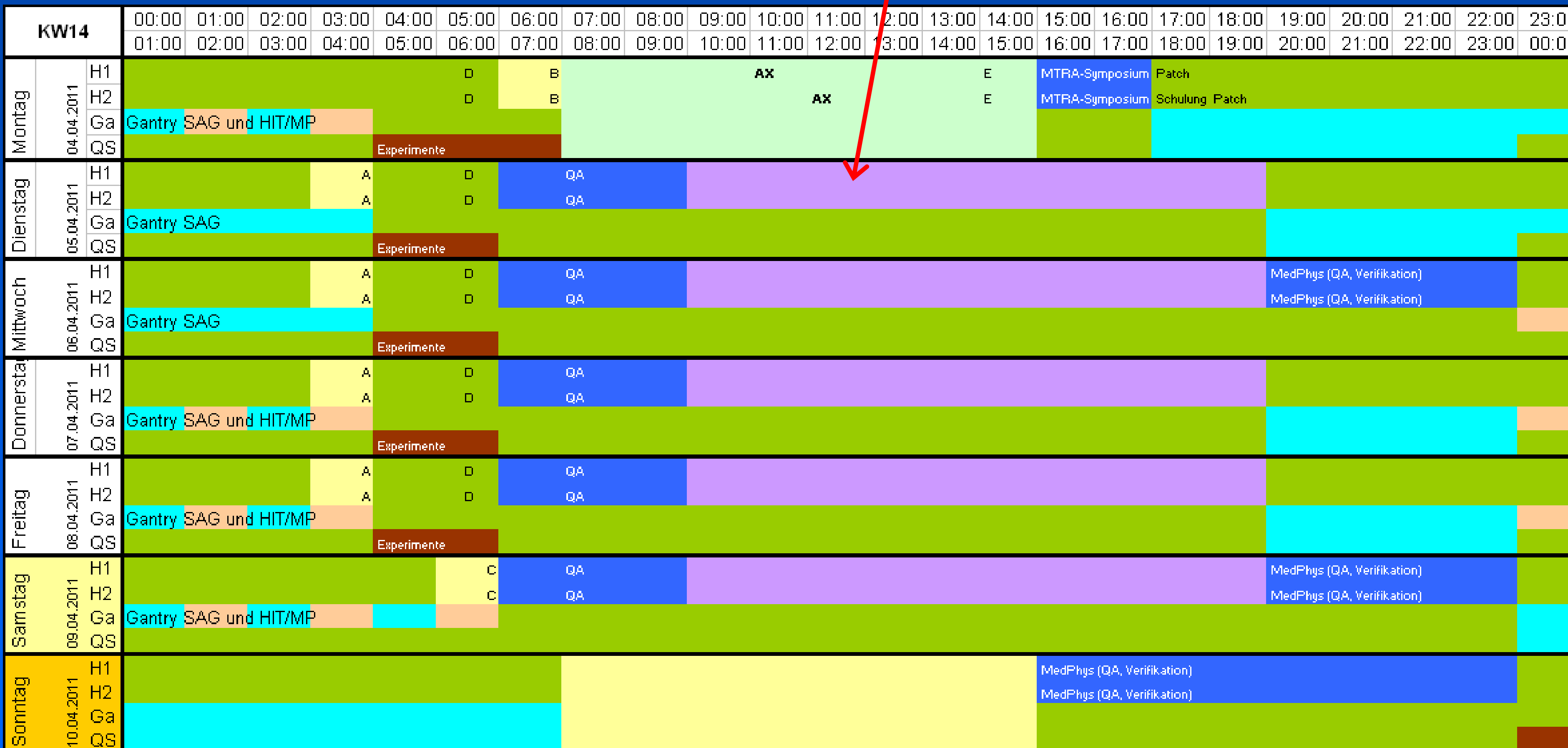
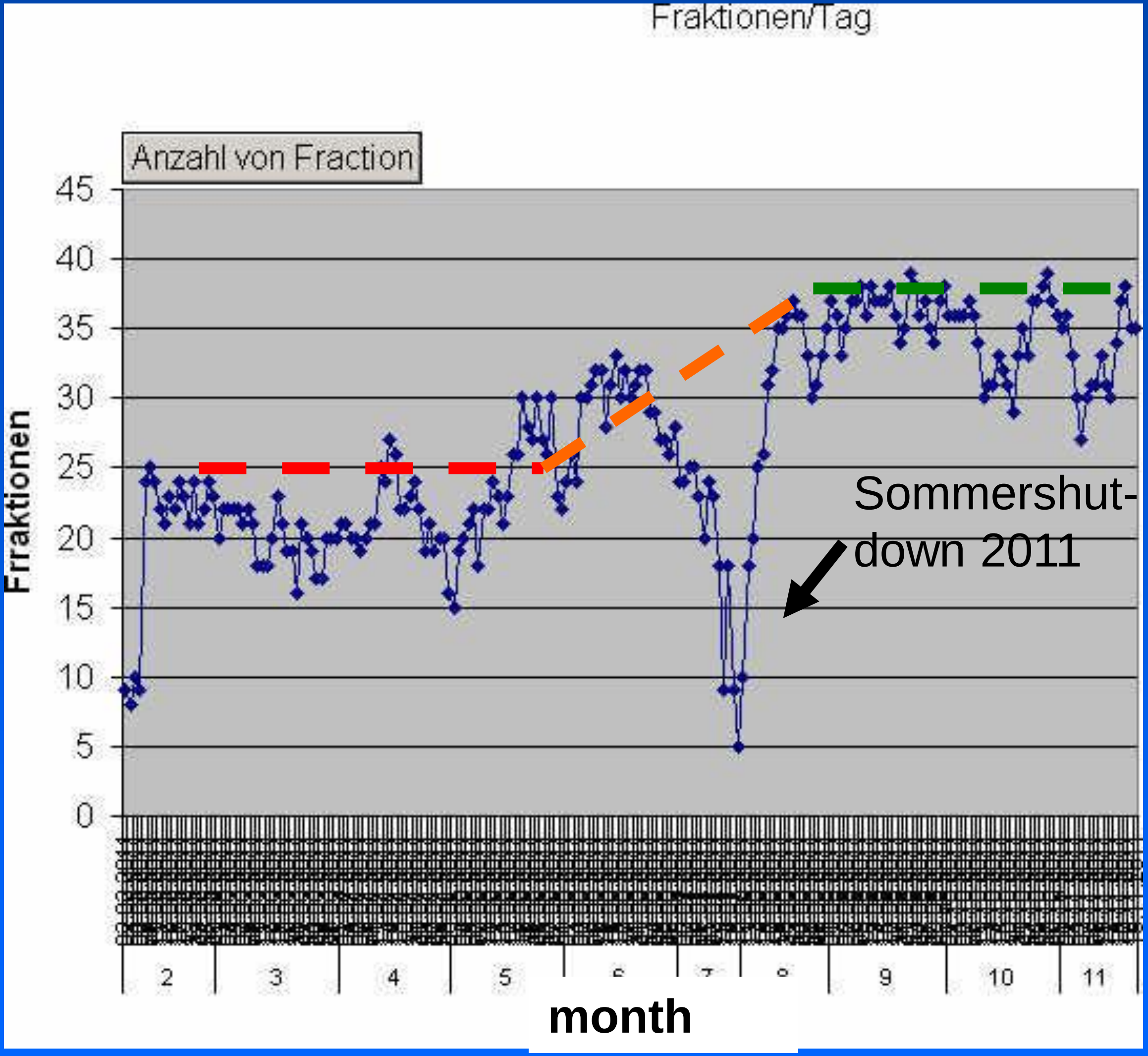
Weekly Beam Time Schedule

Patient treatment 5-6 days a week



- **06:00 – 08:00:** Daily QA
- **08:00 – 19:00:** Patient treatment
- **19:00 – 06:00:** Treatment plan verification, Gantry dev., experiments, accelerator QA

Patient Throughput 2011



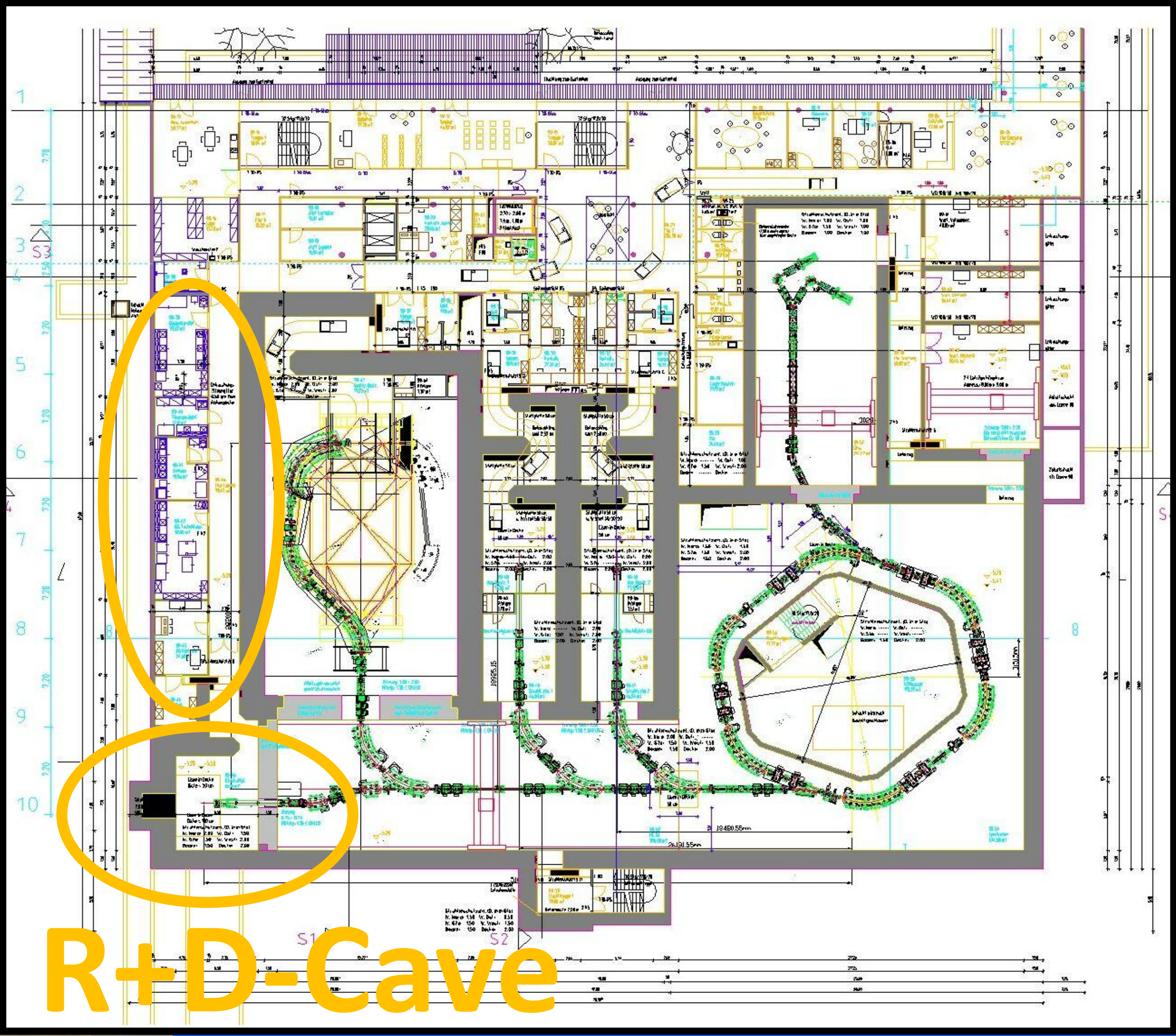
R+D-Infrastructure @ HIT

Dosimetry / PET – Lab

Animals

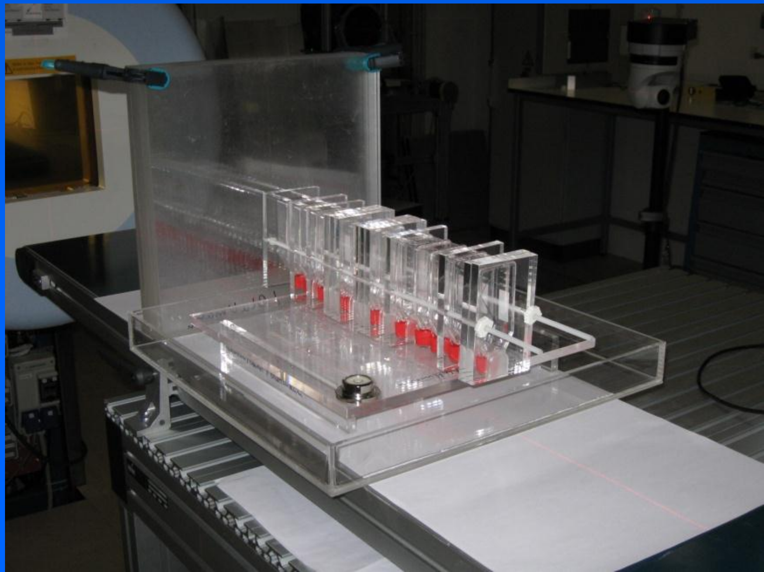
Radiobiological Lab (S2)

Physics / Technology Lab

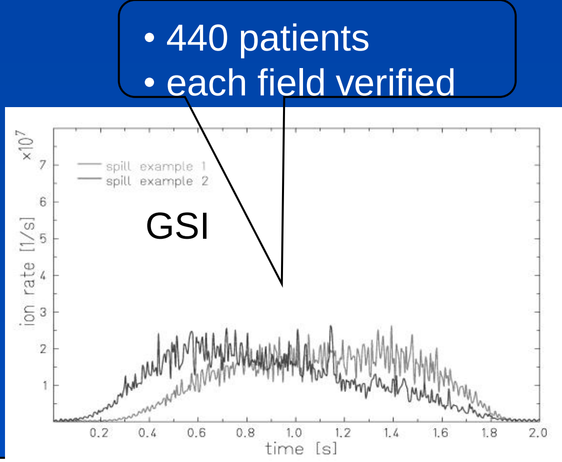


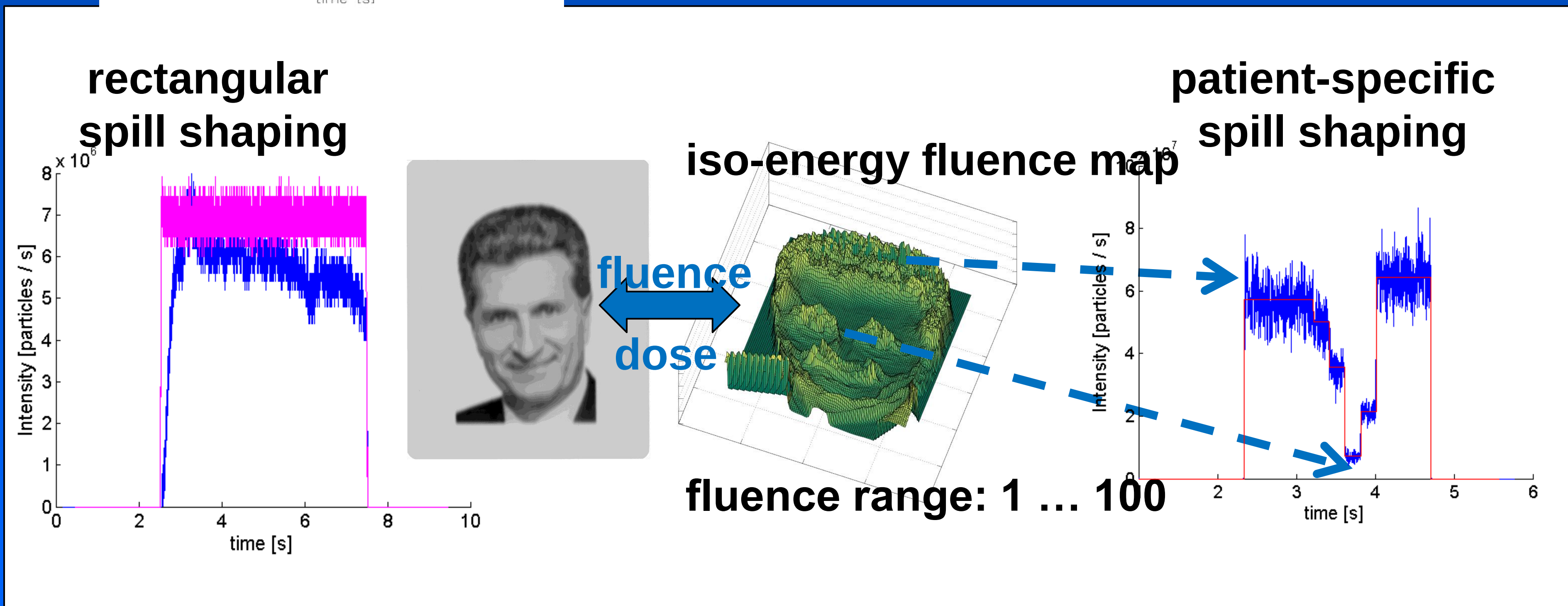
R+D @ HIT

- Radiobiology
- Treatment of moving organs (collaboration with C. Bert /GSI)
- Particle-tomography
- Beam characterization (Helium …), precise scattering measurements for TPS-improvements
- Linac testbench (Helium source, intensity upgrade)
- Scanning ion gantry
- Magnetic field feedback for synchrotron and HEBT
- In-cycle energy variation
- Dynamic spill shaping
- …



Synchrotron Spill Structure Optimization





Dynamic intensity control boosts the beam scanning dose delivery!

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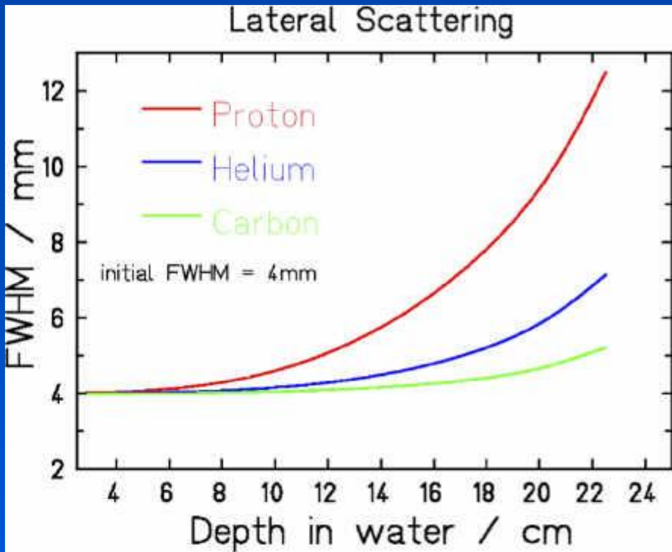
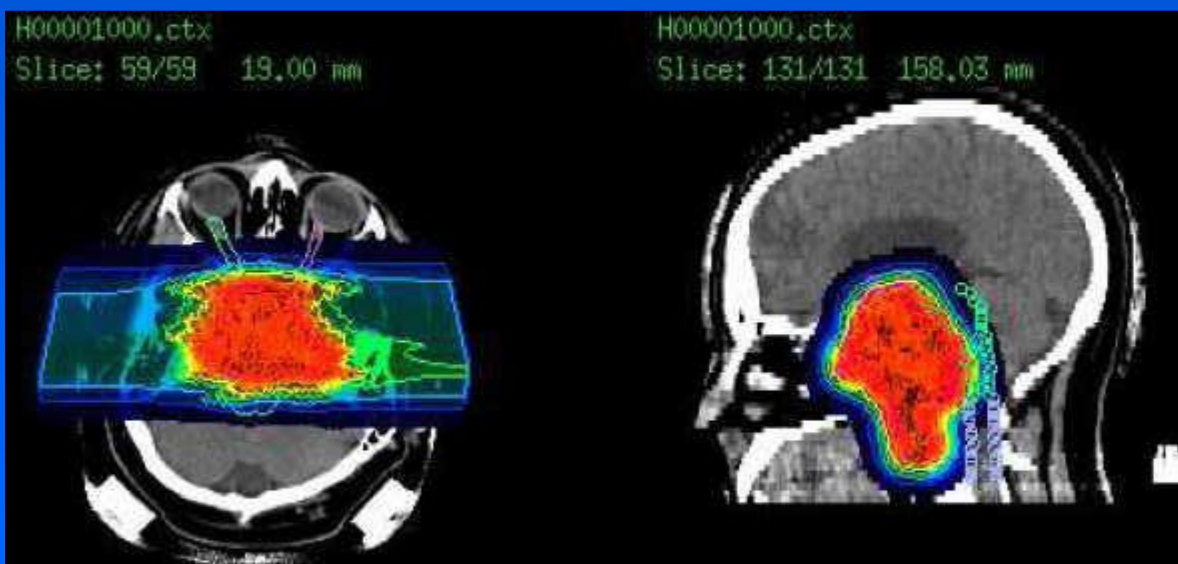
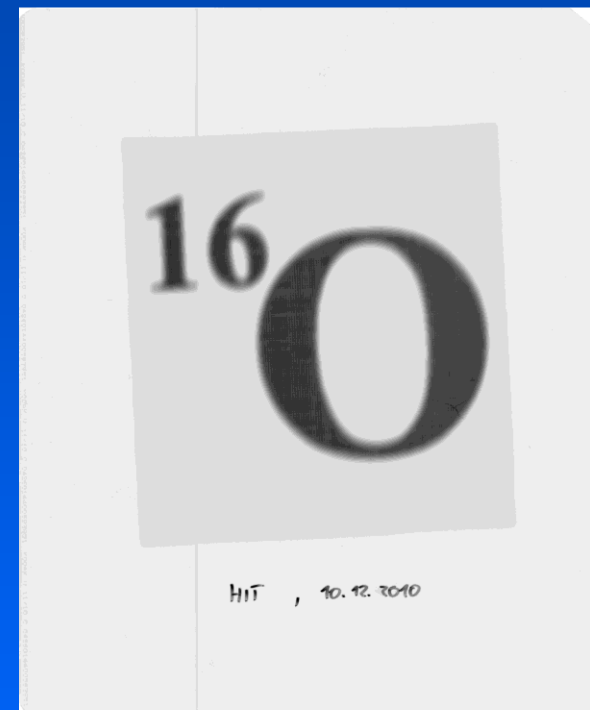
Other Ions: Helium and Oxygen



Penumbra comparison (90% => 10%):

Protons:	**17,4 mm**
Helium3:	**14,4 mm**
Helium4:	**10,9 mm**
Carbon:	**7,4 mm**





Rasterscan @ HIT-R+D-Cave

Th. Haberer

Scanning Ion Gantry / Requirements

Clinical:

- Iso-centric set-up and a fixed floor
- Identical field size in all beamlines of 20 cm x 20 cm
- Integration of fluoroscopy systems in two planes (IGRT, organ movement)

Technical / financial:

- 2D-parallel scanning mode via edge focussing (large SAD ~ 50m)
- Full 360° rotation (clinical workflow, minor investment saving)
- Normal conducting elements (field quality ~10^{-4} in 90-degree bending magnet, price, 330 days 24/7 op.)
- Barrell-type (less bending than cork-screw)
- Scanning upstream to the last bending (radius vs. weight)
- Truss-based structure

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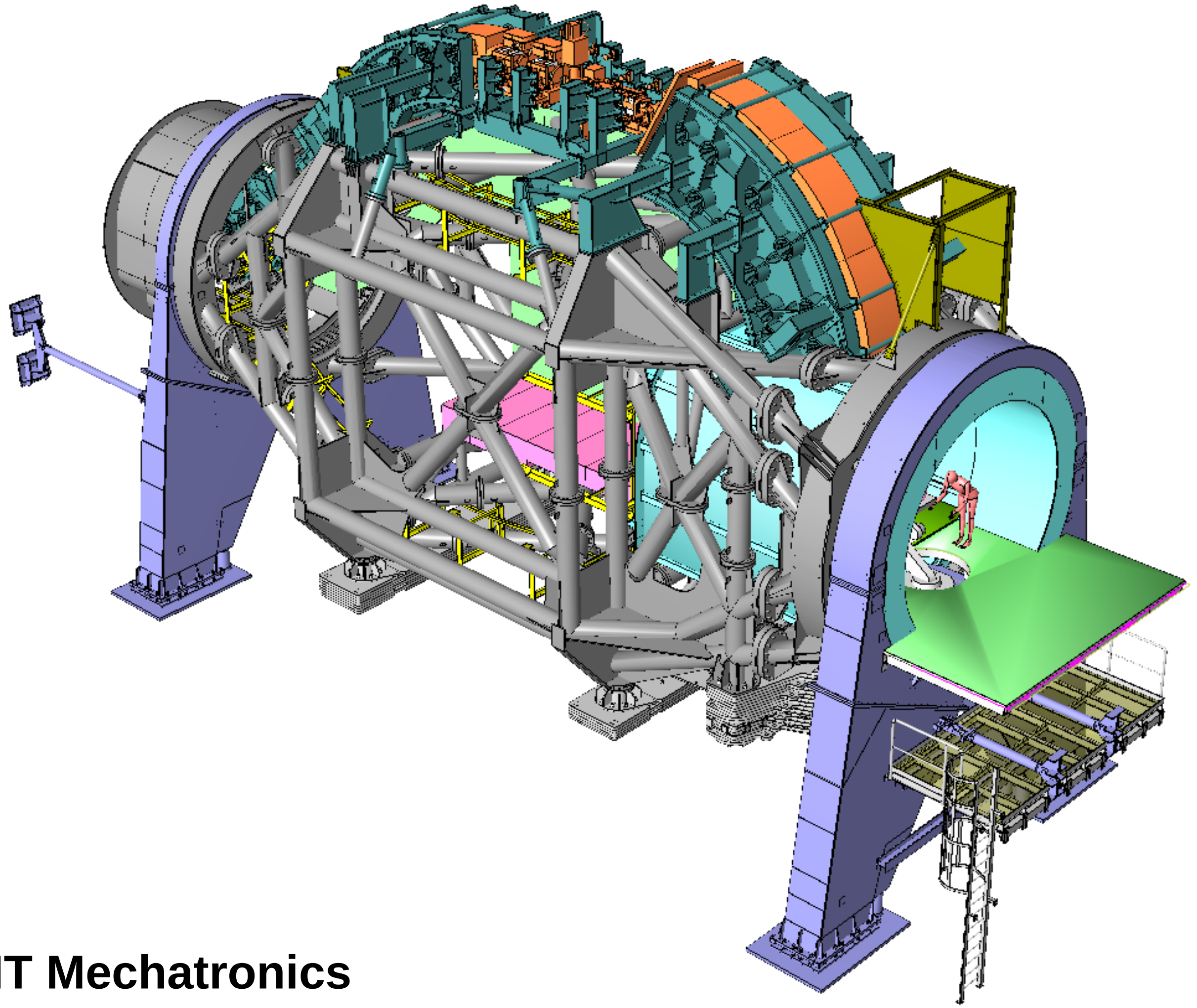
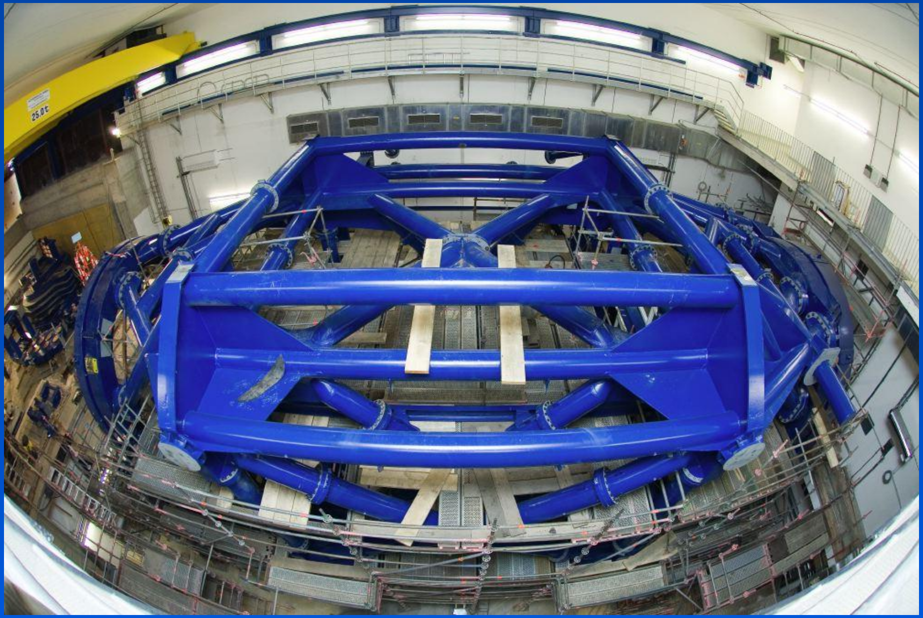
Design for HIT

- isocentric barrel-type
- world-wide first ion gantry
- 2D beam scanning upstream to final bending, almost parallel due to edge focussing
- ± 180^o rotation 3^o / second
- 13m diameter 25m length 600 to rotating (145 to magnets)



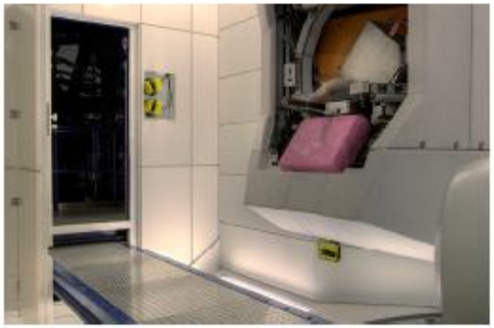
MT Mechatronics

Mounting



Patient Environment / Nozzle

Patient Gantry Room November 2007



Tilt floor, pending on Gantry position

Nozzle

Bumber mats

Patienttable, Roboter

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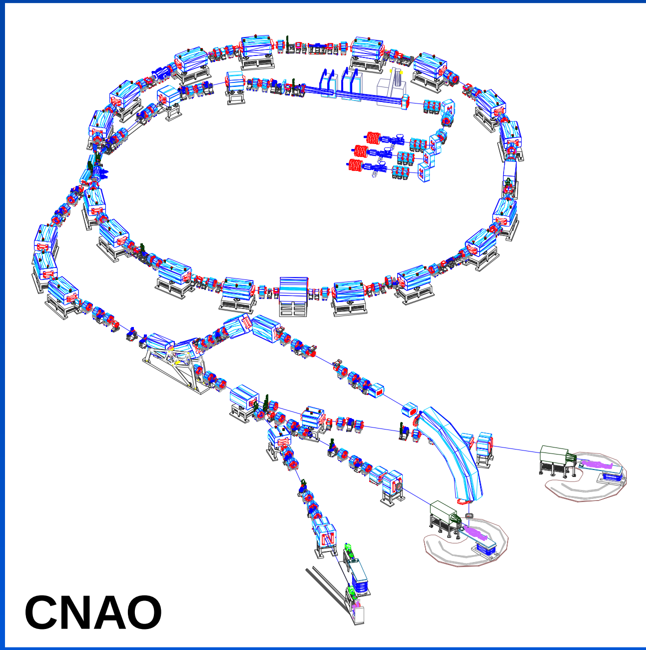
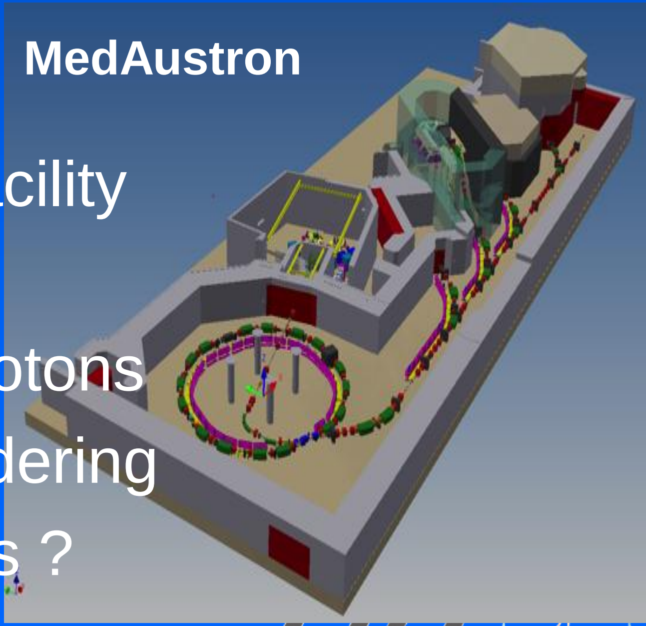
The HIT Gantry Rotates

European Projects

- Uppsala: protons, IBA
- Prague: protons, IBA
- Dresden: protons, IBA, R+D-oriented
- Krakow: protons, IBA, fixed-beam, R+D
- Essen: protons, IBA
- Trento: protons, IBA
- Halle, Berlin, …
- Marburg: carbon/protons, Siemens test facility
- CNAO, Pavia, carbon/protons
- MedAustron, Wiener Neustadt, carbon/protons
- Lyon/ETOILE: carbon/protons, active tendering
- Caen/ARCHADE: carbon (protons), status ?





Thank you!

Rasterscan@HIT/Gantry Carbon

Rasterscan@HIT/H1 Carbon 430 MeV/u

www.hit-heidelberg.com

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