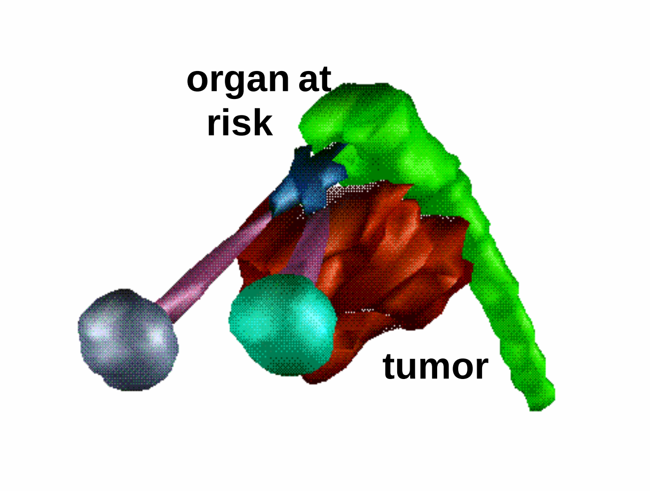
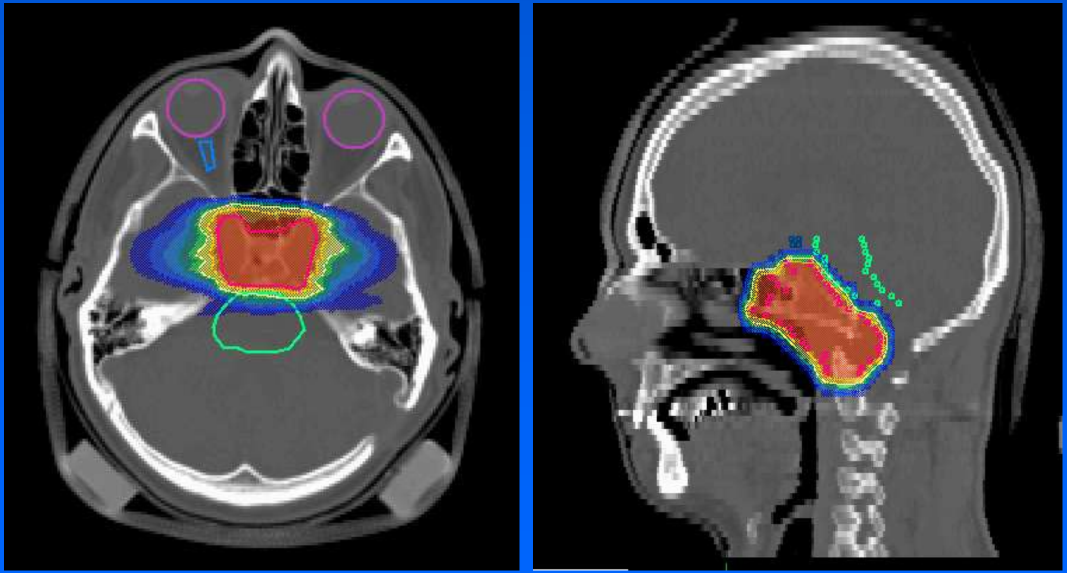
Situation / Indications

- 2/3 patients suffer from a local disease at the time of diagnosis
- In 18% local treatment modalities fail => 280.000 deaths/year in the EC
- Protons and ions have the potential to cure 30.000 patients/year in the EC



Locations: brain, base of the skull, prostate, liver, lung

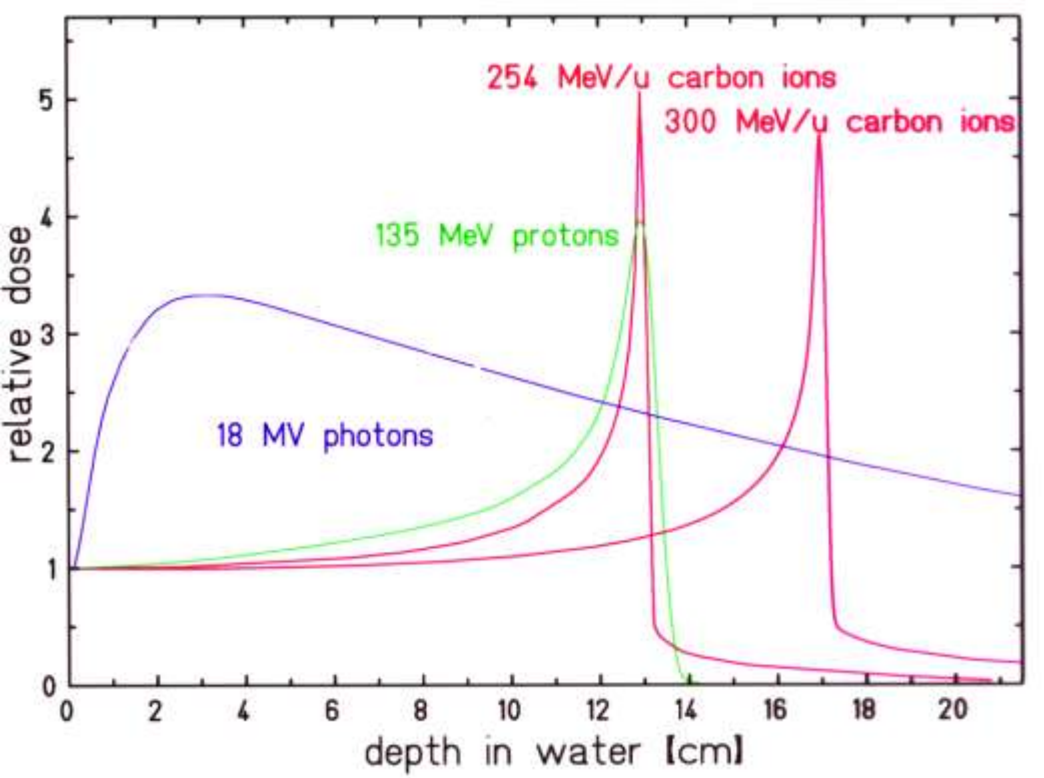
Profile: deep-seated and radioresistant tumor close to organs at risk



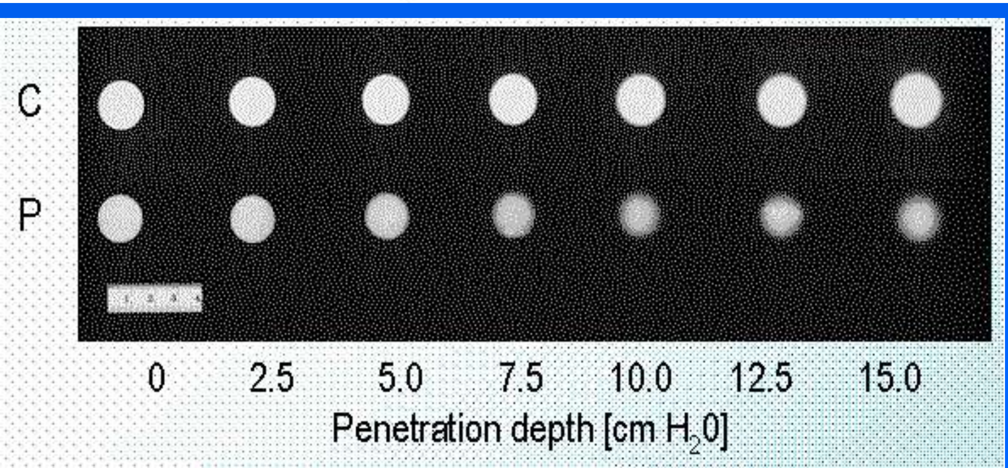
tumor-conformal dose distribution

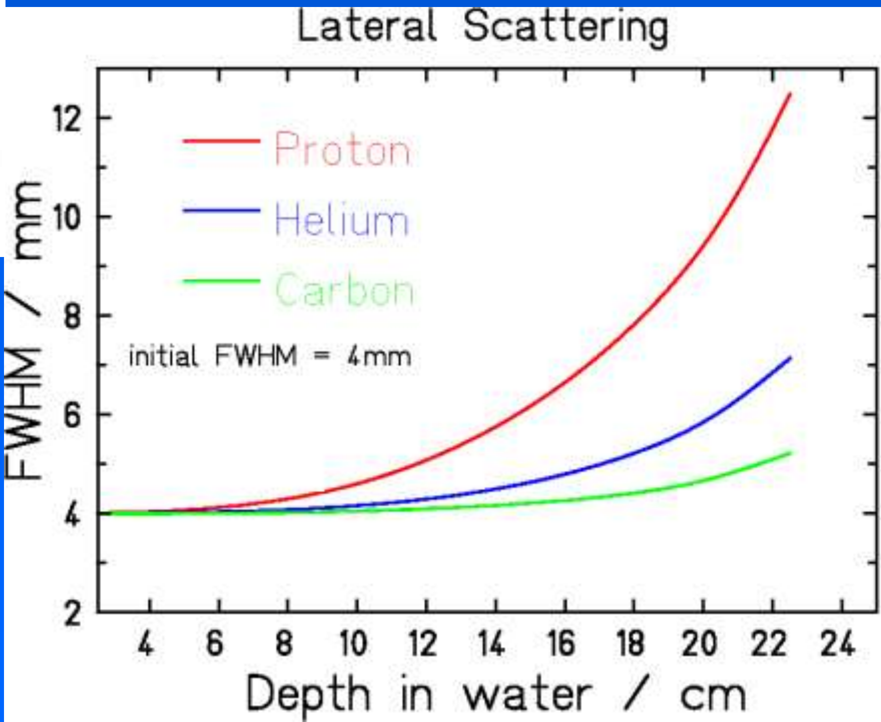
Th. Haberer, Heidelberg Ion Therapy Center

Rationale / Physics

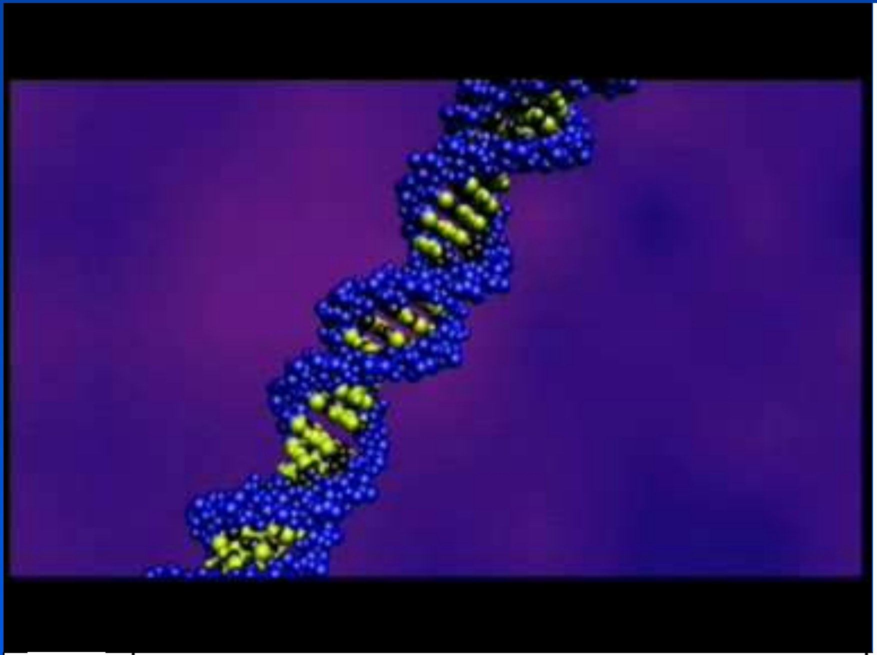


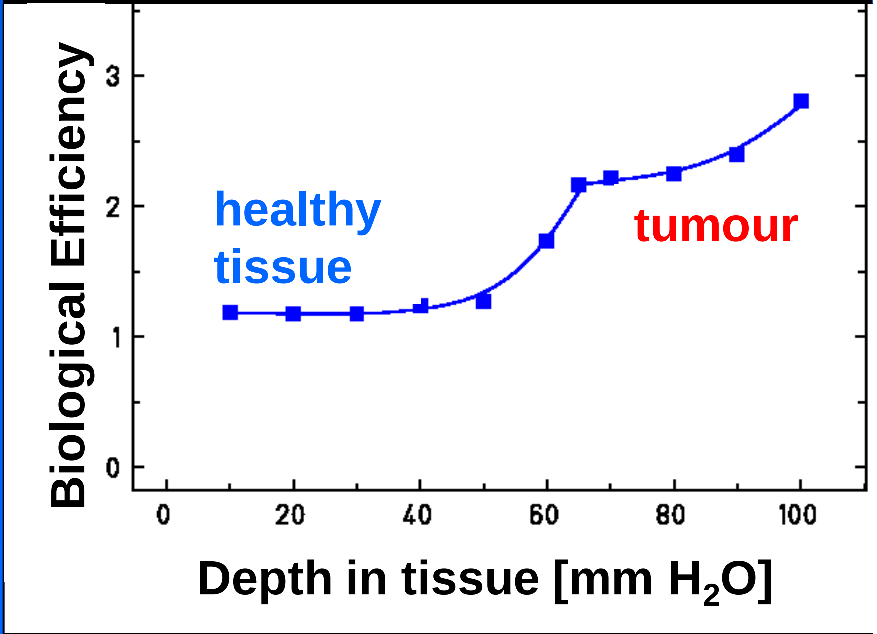
- inverted depth-dose distribution
- mild lateral scattering

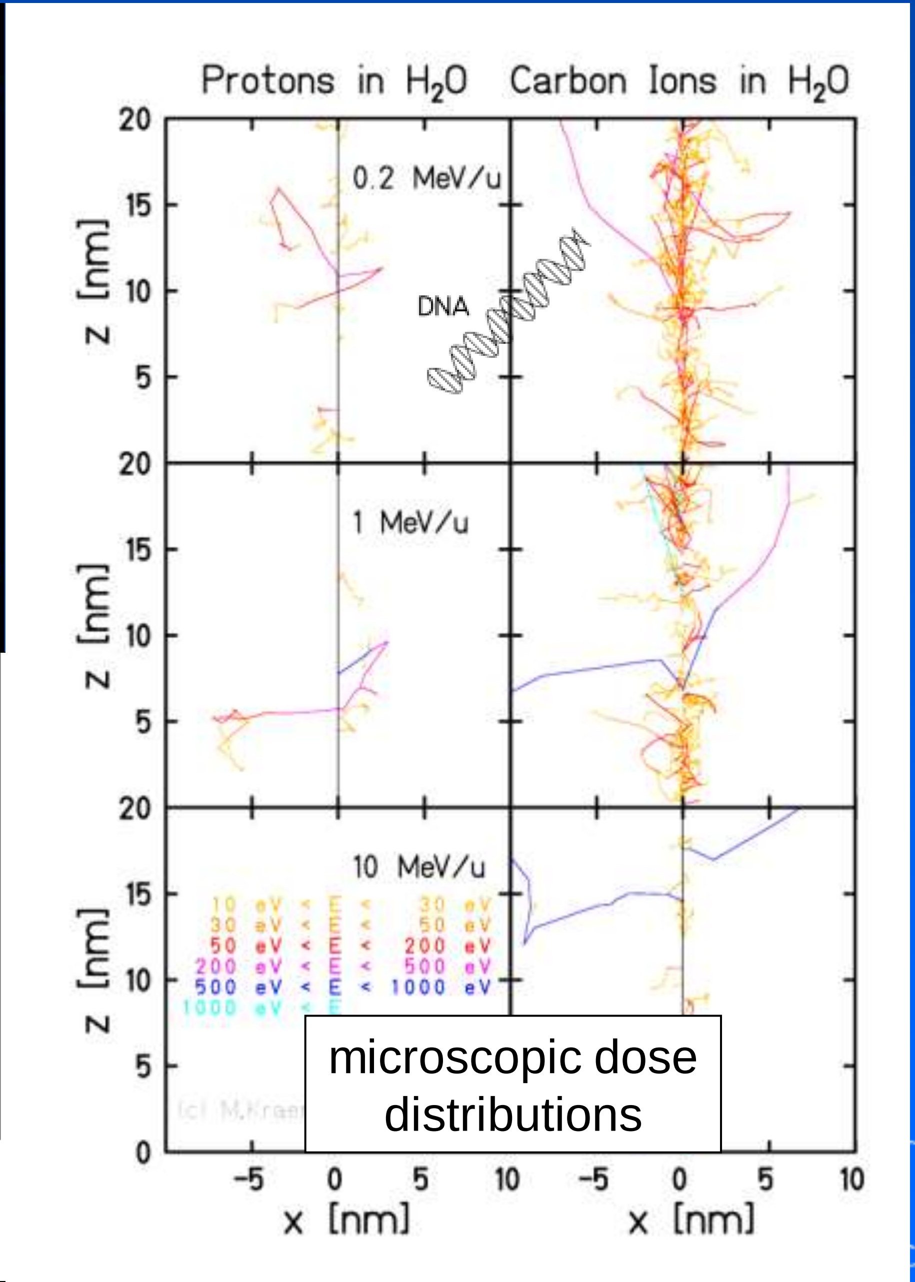




Rationale / Radiobiology

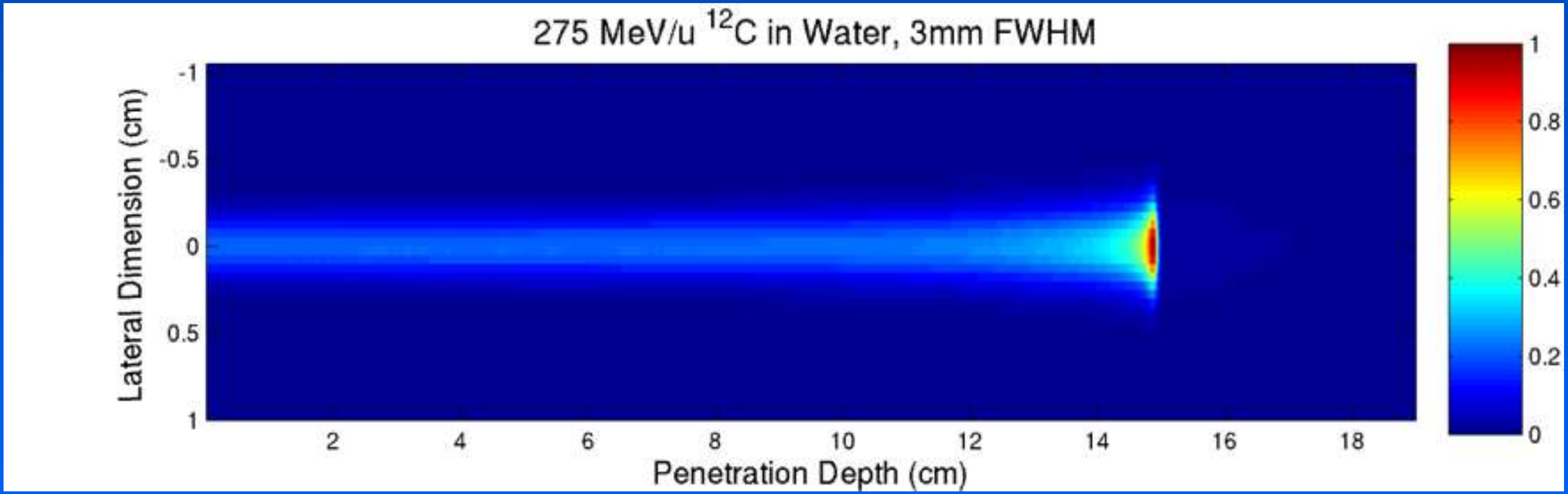






Goal

Light ions will help improving **local control!**



entrance channel:

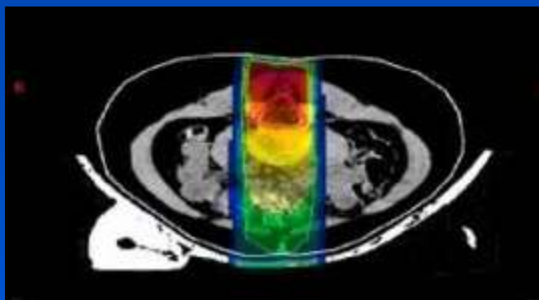
- low physical dose
- low rel. biol. effiency

tumour:

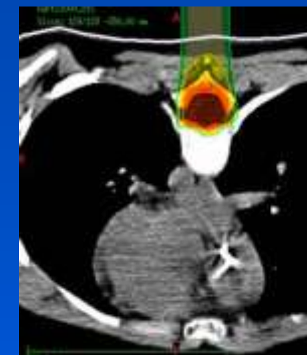
- high physical dose
- high rel. biol. effiency

Medulloblastoma

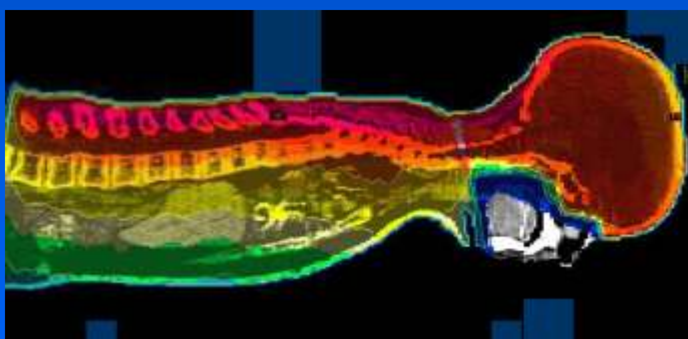
conventional

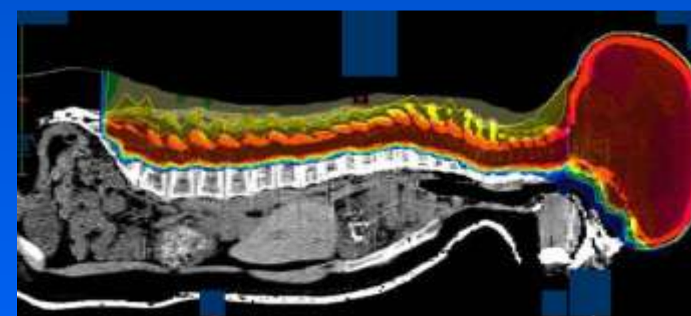


light ions



Target dose 32 Gy/GyE



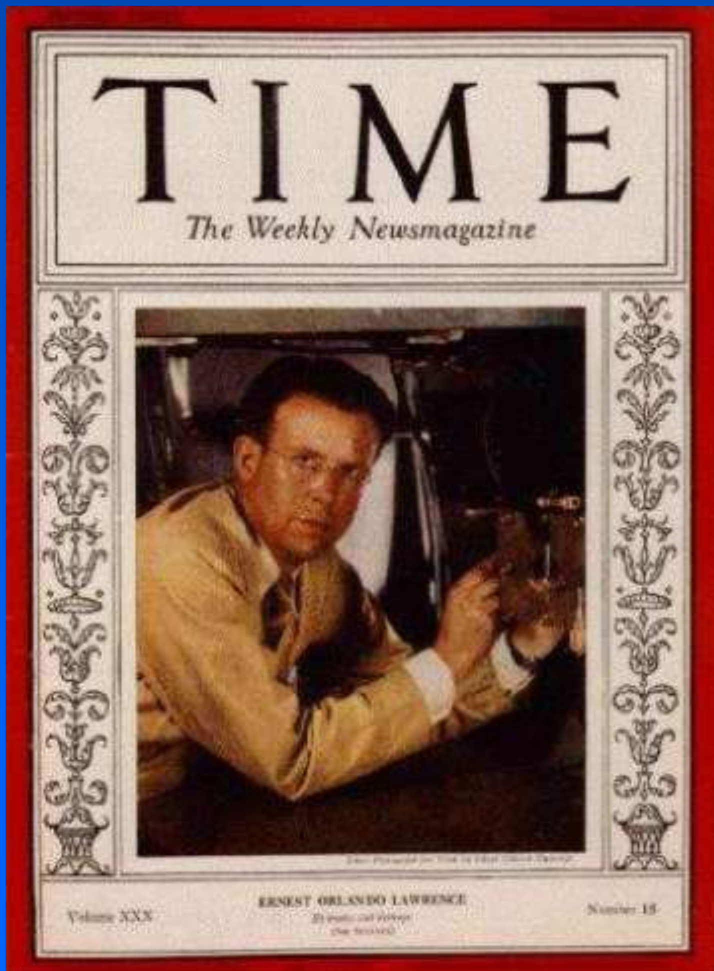


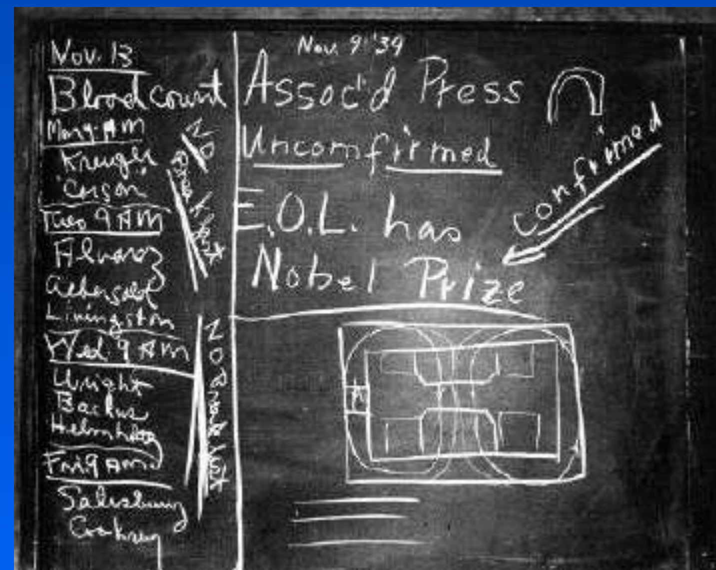
Dose comparison

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

HIT
Heidelberg Ionenstrahl-Therapie Centrum

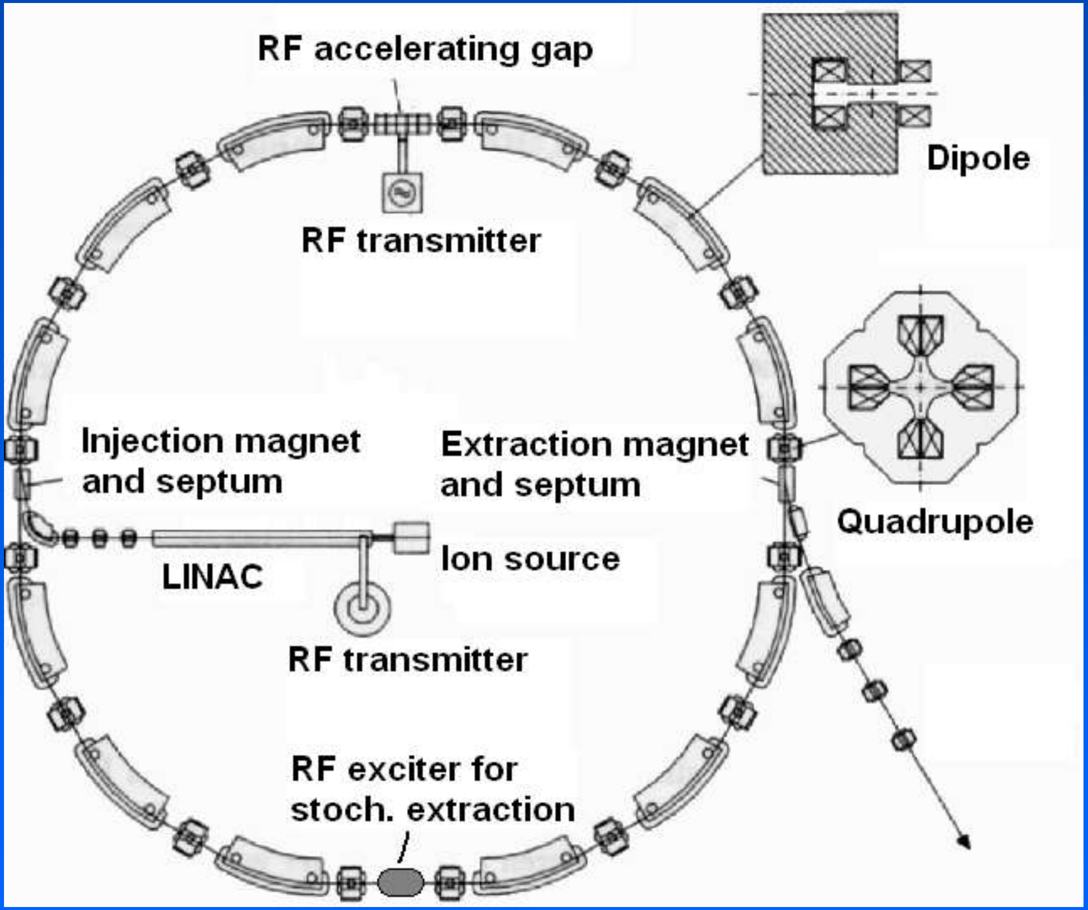
Ernest Orlando Lawrence
Nobel Prize 1939



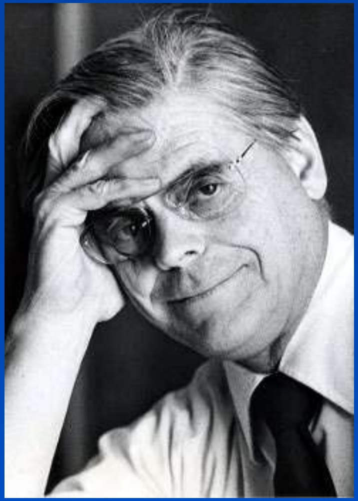


Invention of the cyclotron

Synchrotron
Veksler + McMillan 1945



- Ring accelerator
  V.I. Veksler / E.M. McMillan (1945)
- constant radius, variable magnetic field
- **variable frequency** RF-cavity
- **synchronous** ramping of the magnets and the RF-frequency (beam energy)
- Separate function accelerator



The Proton Proposal 1946

Radiological Use of Fast Protons

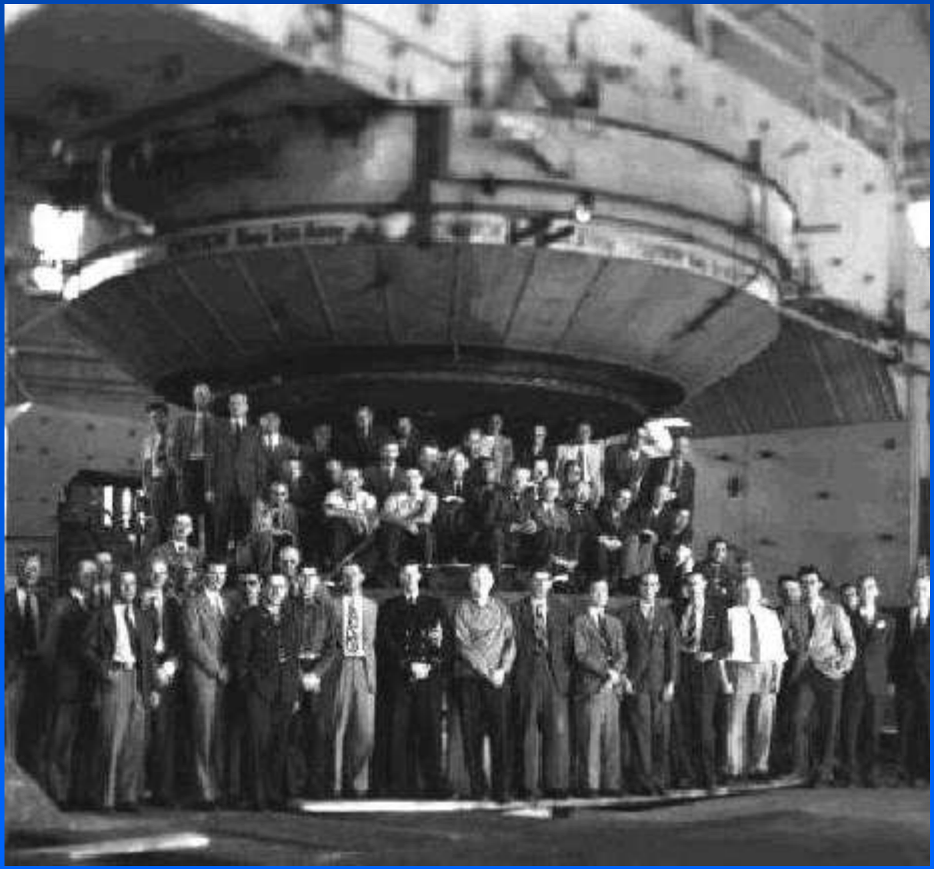
ROBERT R WILSON

Research Laboratory of Physics, Harvard University Cambridge, Massachusetts
Accepted for publication in July 1946

…The range of a 125 MeV proton in tissue is 12 cm, while that of a 200 MeV proton is 27 cm. It is clear that such protons can penetrate to any part of the body. The proton proceeds through the tissue in very nearly a straight line…

…It is well known that the biological damage depends not only on the number of ions produced in a cell, but also upon the density of ionization. Thus the biological effects near the end of the range will be considerably enhanced due to greater specific ionization, the degree of enhancement depending critically upon the type of cell irradiated…

184 inch Cyclotron @ LBL 1947 / 1986



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Bevalac @ LBL 1950 / 1993

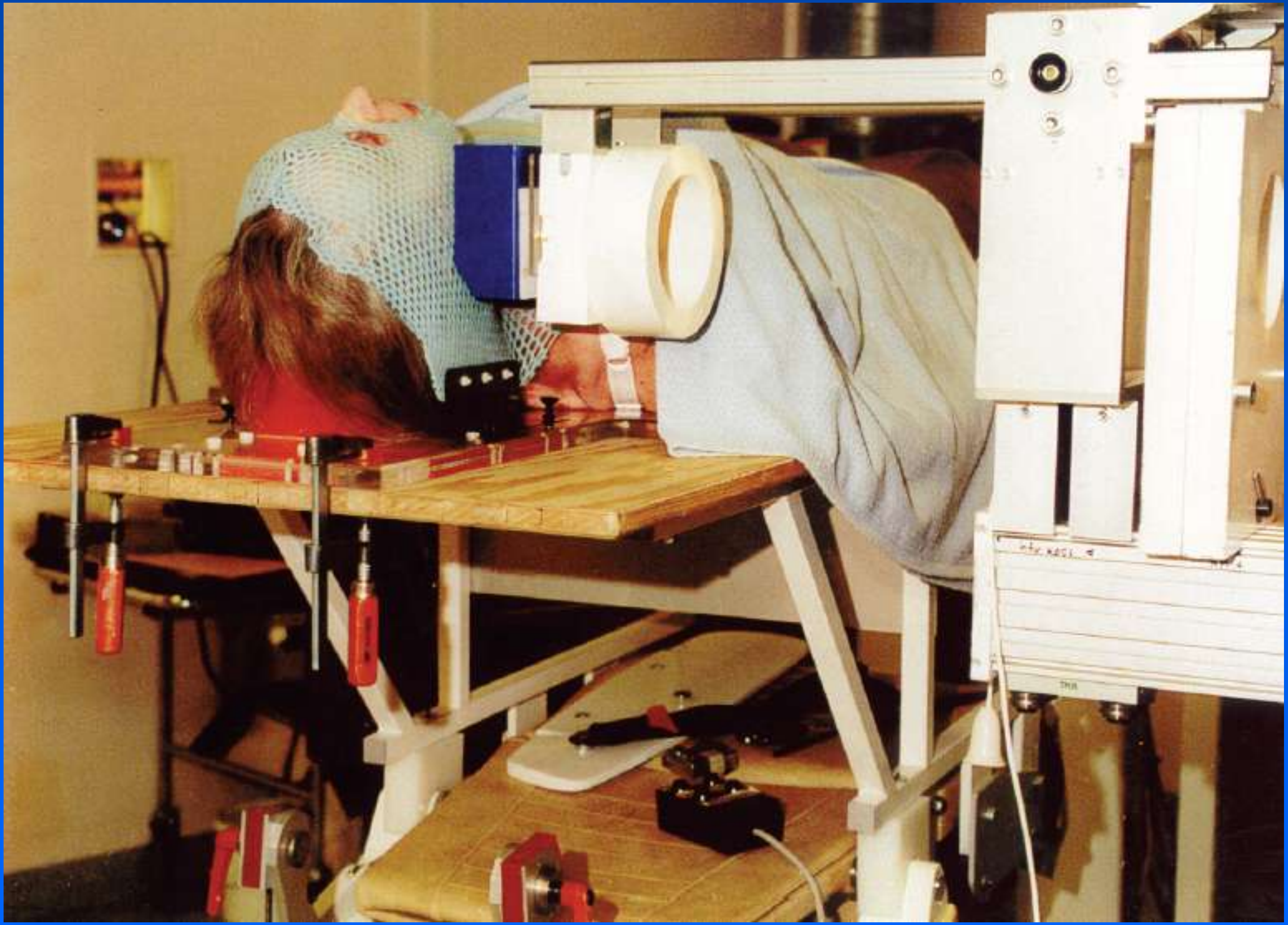
Courtesy Jay Flanz, MGH, Boston

Historical Milestones

1930's	Experimental neutron therapy
1946	R.R. Wilson proposes proton & ion therapy
1950's	Proton & helium therapy, LBL (184" cyclotron)
1975	Begin carbon therapy in Bevalac synchrotron including wobbling & scanning
1984	Proton therapy begins at PSI
1990	Neutrons on gantry mounted SC cyclo, Harper-Grace
1990	Protons with 1st hospital based synchrotron, LLUMC
1993	Precision raster scanning with carbon, GSI
1994	Carbon therapy begins at HIMAC, Chiba
1996	Spot scanning, PSI
1997	Protons with 1st hospital based cyclotron, MGH

Courtesy Steve Peggs, BNL

Patient Treatment in Labs



Courtesy E. Blomquist, Svedborg Lab, Uppsala

Standard Approach

- Facilities being built at existing research accelerators
- Fixed energy machines with moderate flexibility (if at all)
- Dose delivery not exactly tumor-conform


Th. Haberer
LBL-33403
UC-406
Preprint

Lawrence Berkeley Laboratory
UNIVERSITY OF CALIFORNIA

Accelerator & Fusion
Research Division

Submitted to Review of Scientific Instruments

Instrumentation for Treatment of Cancer Using Proton and Light-Ion Beams

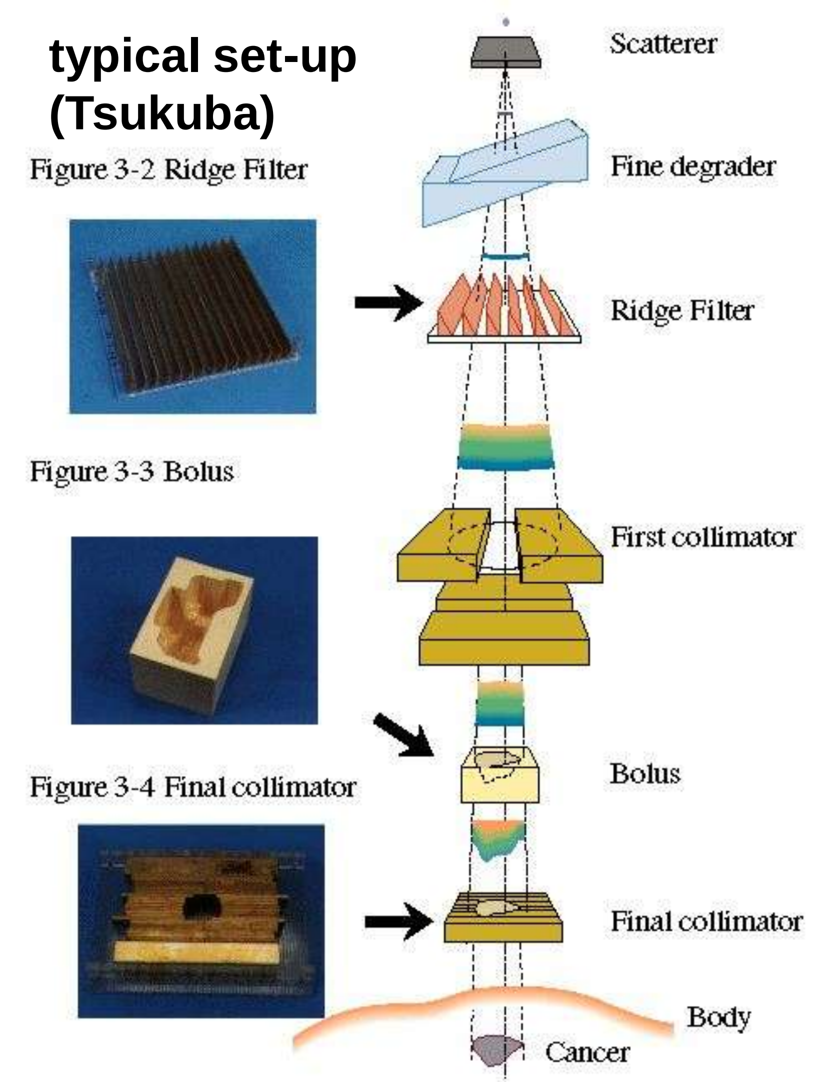
W.T. Chu, B.A. Ludewigt, and T.R. Renner

February 1993

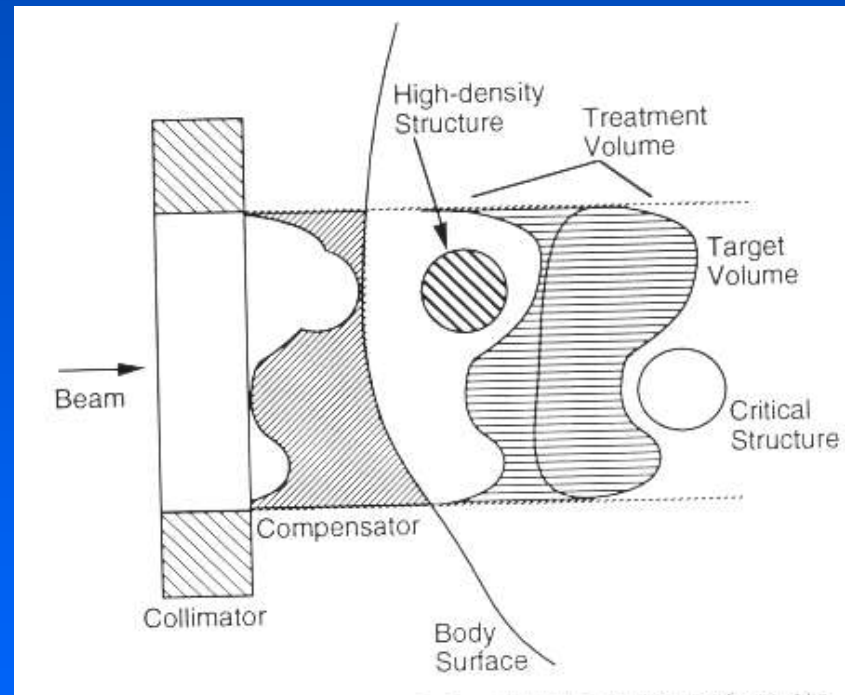
Prepared for the U.S. Department of Energy under Contract Number DE-AC03-76SF00098

Standard / System + Dose Distr.

typical set-up (Tsukuba)



Distal edge shaping using a bolus pulls dose back into healthy tissue

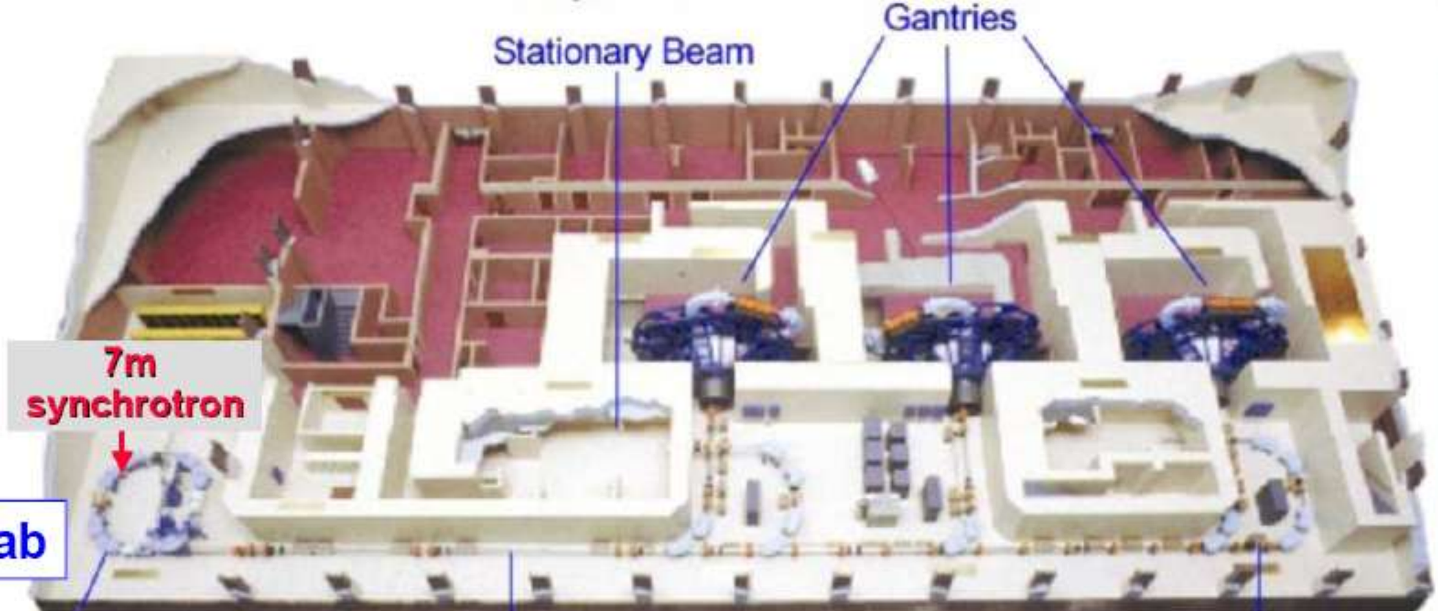


Patient Treatment in Labs

Patient Statistics (for the facilities out of operation):

WHERE		WHAT	FIRST PATIENT	LAST PATIENT	PATIENT TOTAL	
Belgium	Louvain-la-Neuve	p	1991	1993	21	ocular tumors only
Canada	Vancouver (TRIUMF)	π^-	1979	1994	367	
Germany	Darmstadt (GSI)	ion	1997	2009	440	
Japan	Tsukuba (PMRC, 1)	p	1983	2000	700	
Japan	Chiba	p	1979	2002	145	ocular tumors only
Russia	Dubna (1)	p	1967	1996	124	
Sweden	Uppsala (1)	p	1957	1976	73	
Switzerland	Villigen PSI (SIN-Piotron)	π^-	1980	1993	503	
CA., USA	Berkeley 184	p	1954	1957	30	
CA., USA	Berkeley	He	1957	1992	2054	
CA., USA	Berkeley	ion	1975	1992	433	
IN., USA	Bloomington (MPRI, 1)	p	1993	1999	34	ocular tumors only
MA., USA	Harvard	p	1961	2002	9116	
NM., USA	Los Alamos	π^-	1974	1982	230	
					14270	**Total**
				thereof	2054	He
					1100	pions
					873	ions
					10243	protons

PTCOG homepage http://ptcog.web.psi.ch/Archive/Patientenzahlen-updateMar2010.pdf



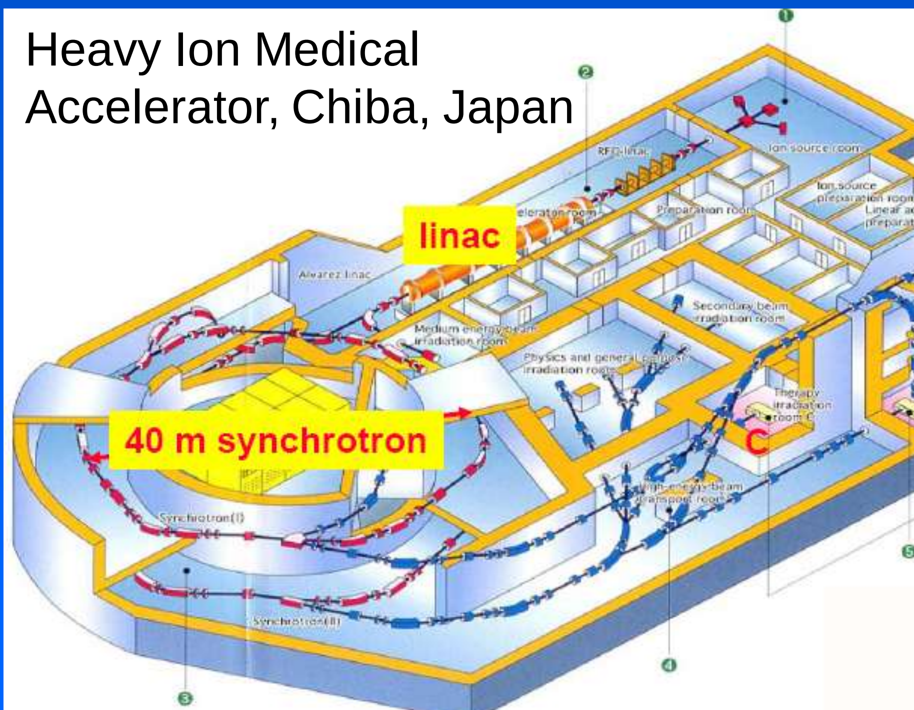
Loma Linda University Medical Center, Proton synchrotron, Loma Linda, CA, US designed at Fermilab

In 1994 the first dedicated clinic-based facilities, LLMUC (protons) and HIMAC (carbon), started

Nowadays more than 50 proton treatment protocols are approved and reimbursed in the US

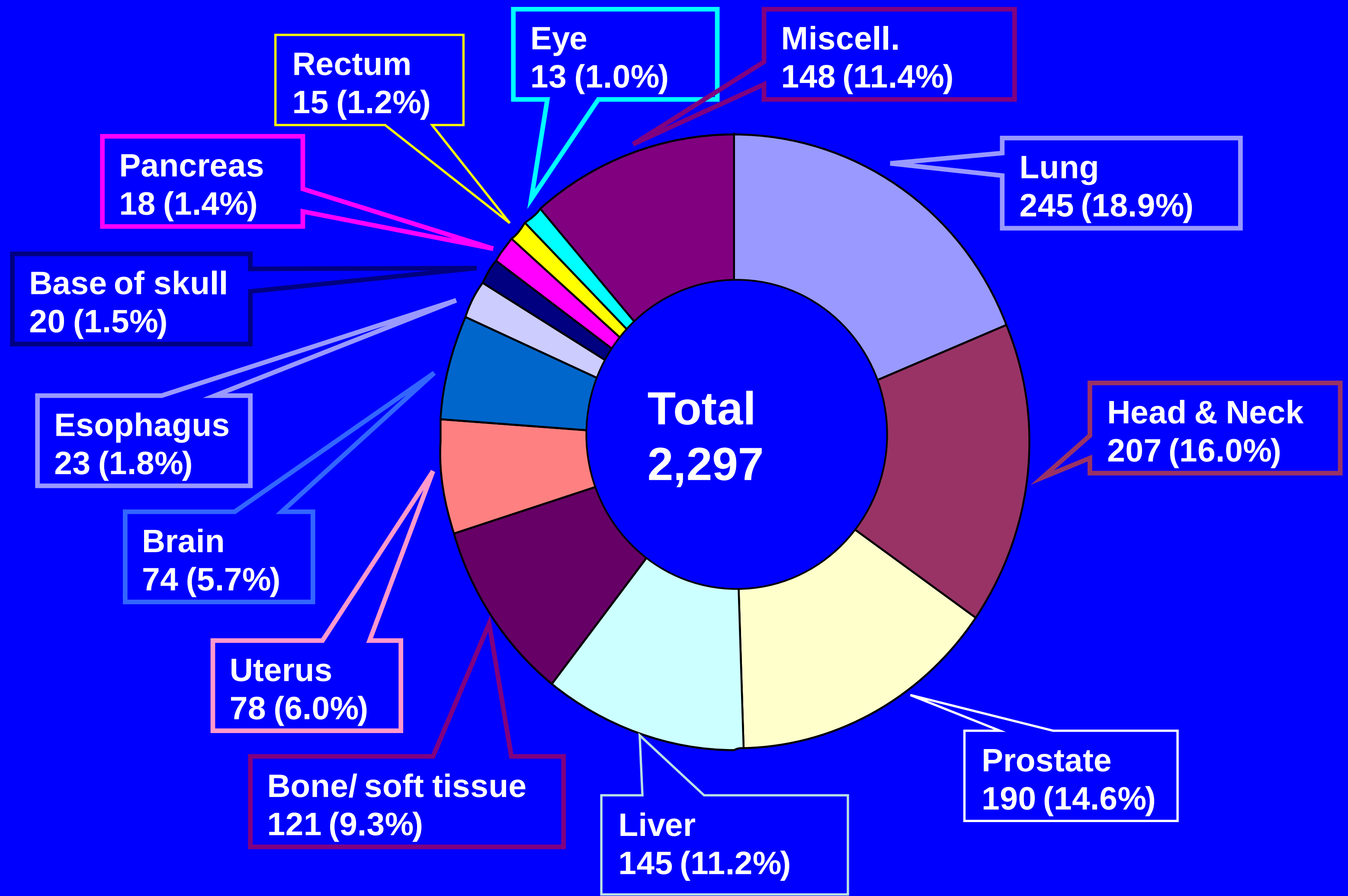
LLUMC treats up to 180 patients per day

Heavy Ion Medical Accelerator, Chiba, Japan



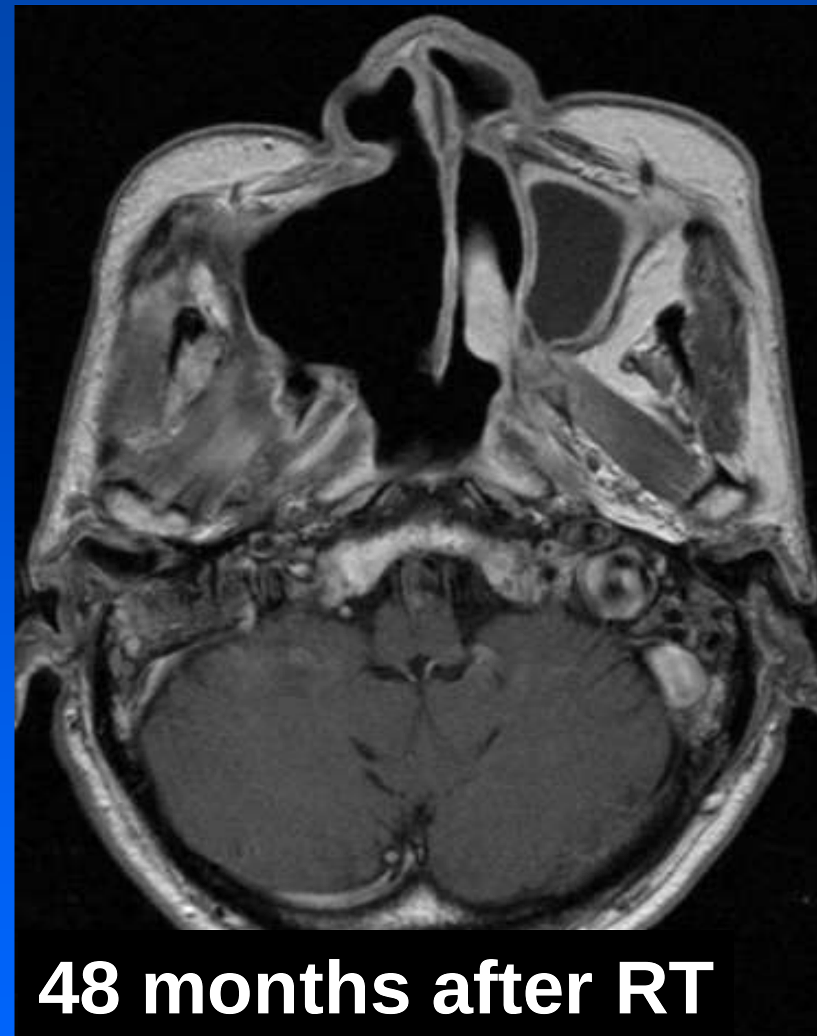
Carbon Ion Therapy at NIRS / HIMAC

(June 1994-August 2004)



Results

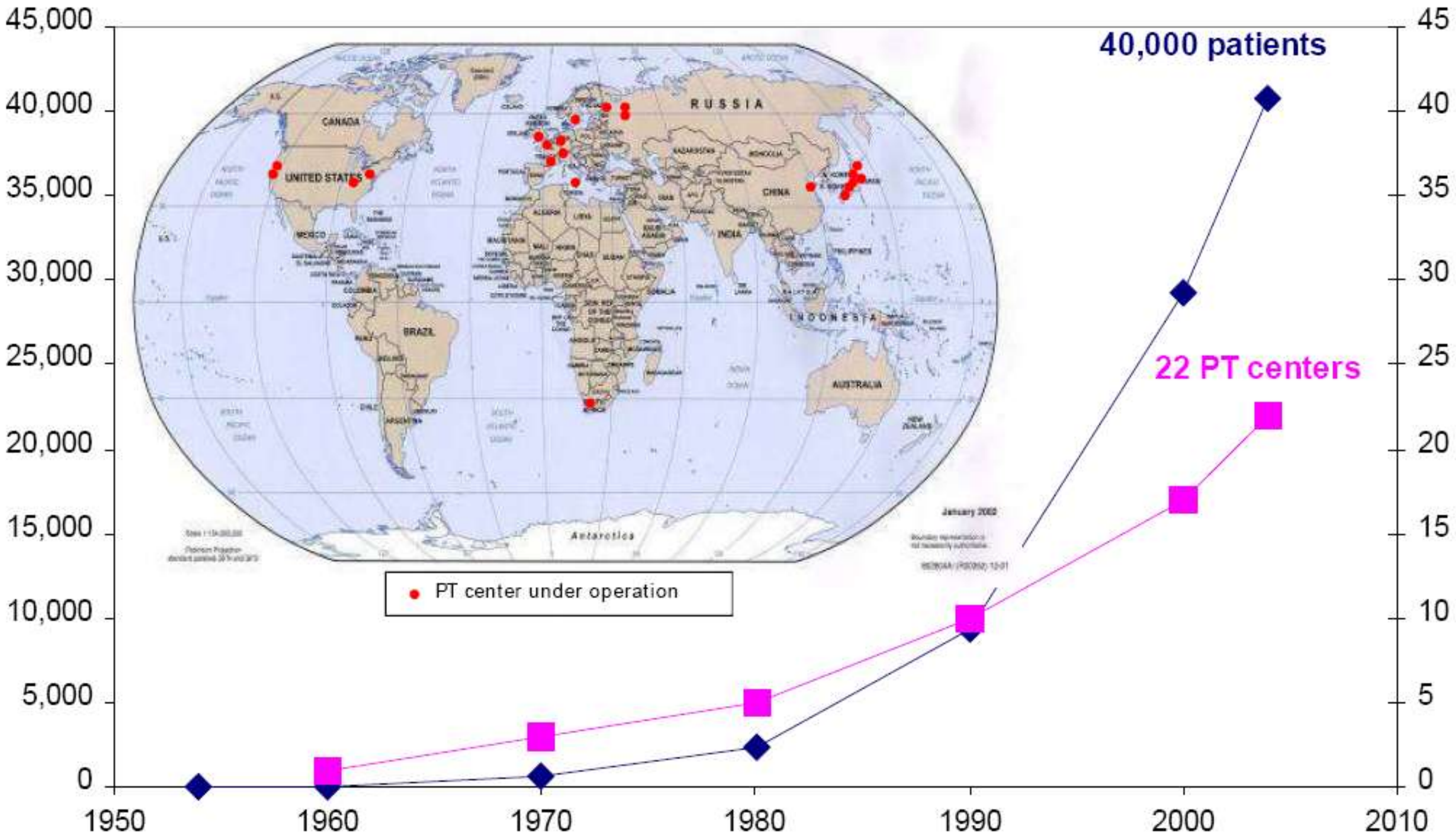
Before RT



48 months after RT

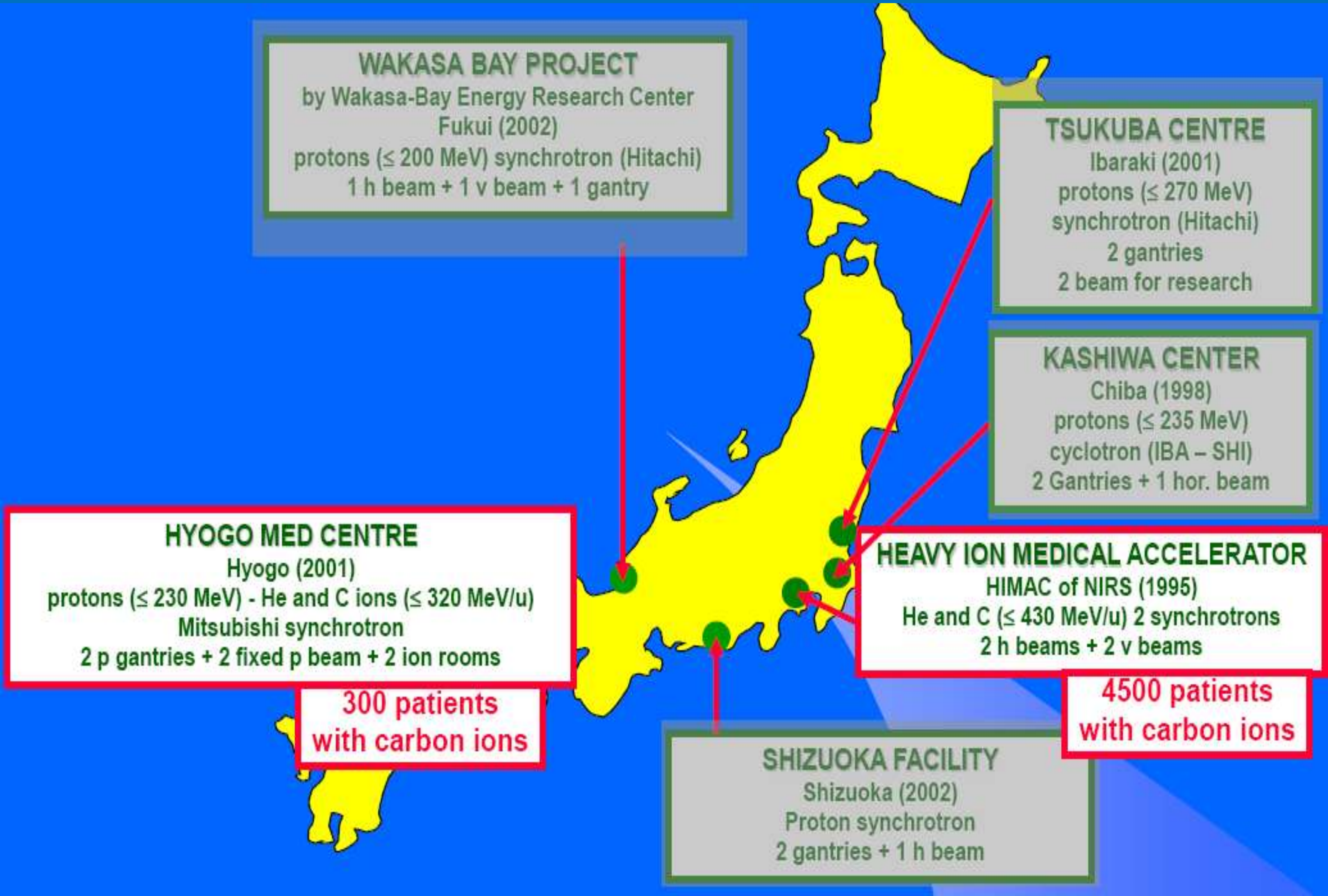
Malignant melanoma 57.6GyE/16fx (NIRS)

Particle Therapy Centres Worldwide



Courtesy J. Sisterson, MGH

Japan will have 10 facilities soon



Patient Treatment < 2010

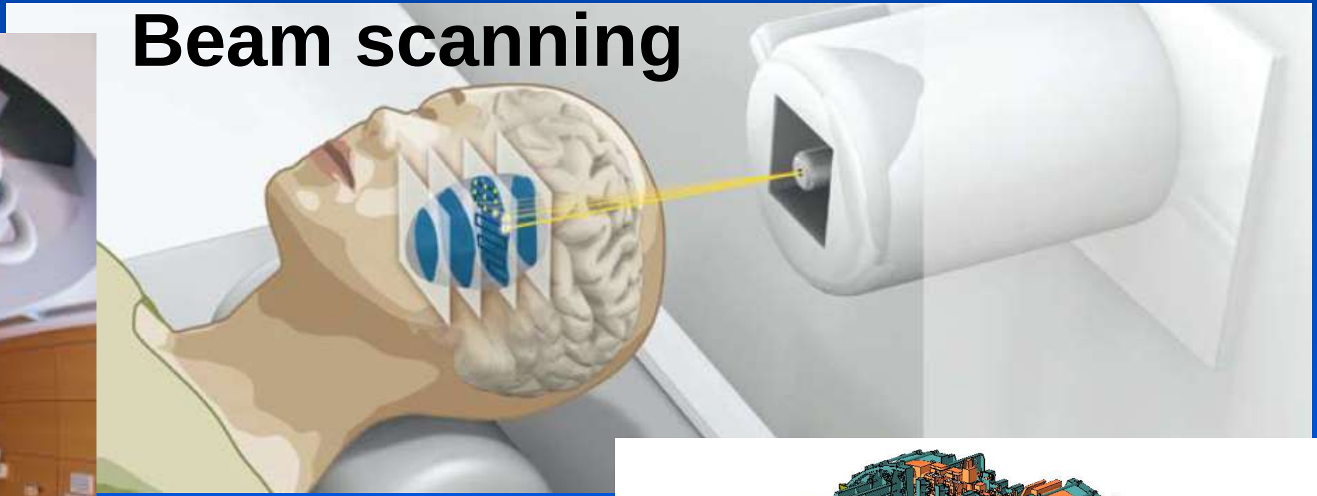
Patient Statistics (for the facilities in operation end of 2009):

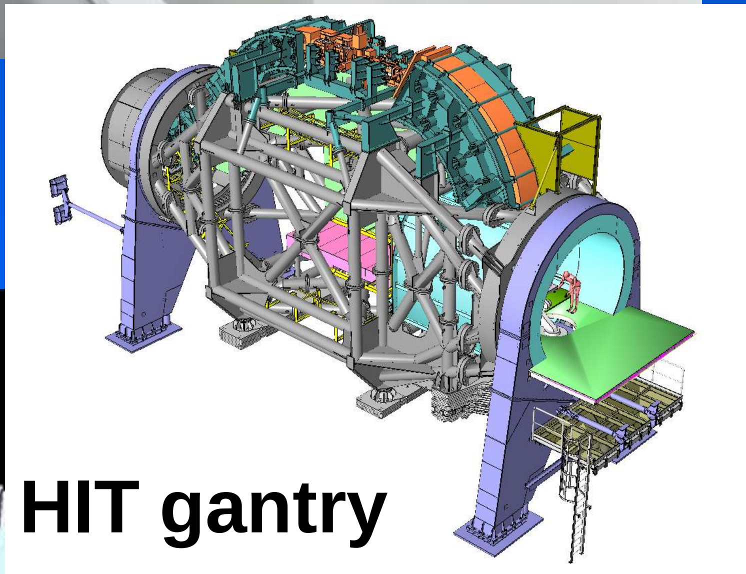
WHERE		WHAT	FIRST PATIENT	PATIENT TOTAL	DATE OF TOTAL
Canada	Vancouver (TRIUMF)	p	1995	145	Dec-09
China	Wanjie (WPTC)	p	2004	977	Dec-09
England	Clatterbridge	p	1989	1923	Dec-09
France	Nice (CAL)	p	1991	3935	Dec-09
France	Orsay (CPO)	p	1991	4811	Dec-09
Germany	Berlin (HMI)	p	1998	1437	Dec-09
Germany	Munich (RPTC)	p	2009	78	Dec-09
Italy	Catania (INFN-LNS)	p	2002	174	Mar-09
Japan	Chiba (HIMAC)	C ion	1994	4504	Feb-09
Japan	Kashiwa (NCC)	p	1998	680	Dec-09
Japan	Hyogo (HIBMC)	p	2001	2382	Nov-09
Japan	Hyogo (HIBMC)	C ion	2002	638	Nov-09
Japan	Tsukuba (PMRC, 2)	p	2001	1586	Dec-09
Japan	WERC	p	2002	56	Dec-08
Japan	Shizuoka	p	2003	852	Dec-09
Korea	Ilsan, Korea	p	2007	519	Dec-09
Russia	Moscow (ITEP)	p	1969	4162	Jul-09
Russia	St. Petersburg	p	1975	1353	Dec-09
Russia	Dubna (JINR, 2)	p	1999	595	Dec-09
South Africa	iThemba LABS	p	1993	511	Dec-09
Sweden	Uppsala (2)	p	1989	929	Dec-08
Switzerland	Villigen PSI (72 MeV-Optis)	p	1984	5300	Dec-09
Switzerland	Villigen PSI (230 MeV)	p	1996	542	Dec-09
CA., USA	UCSF - CNL	p	1994	1200	Dec-09
CA., USA	Loma Linda (LLUMC)	p	1990	14000	Oct-09
IN., USA	Bloomington (MPRI, 2)	p	2004	890	Dec-09
MA., USA	Boston (NPTC)	p	2001	4270	Oct-09
TX, USA	Houston	p	2006	1700	Dec-09
FL, USA	Jacksonville	p	2006	1847	Dec-09
OK, USA	Oklahoma City (ProCurePTC)	p	2009	21	Dec-09
				62017	**Total**
			thereof	7151	C-ions
				56854	protons

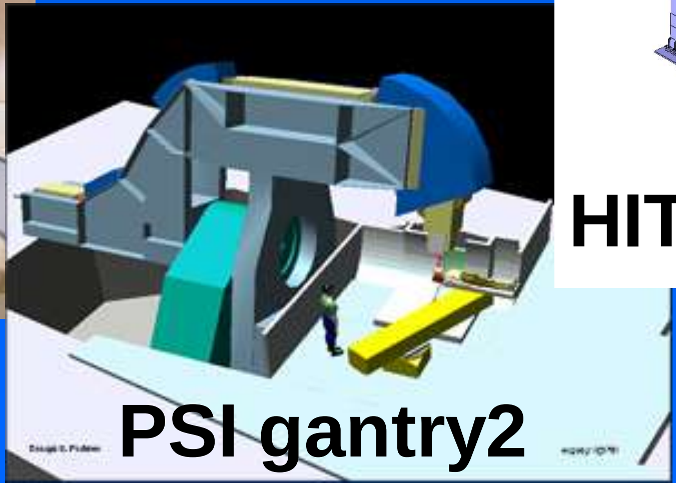
Total for all facilities (in operation and out of operation):	2054	He
	1100	pions
	7151	C-ions
	873	other ions
	67097	protons
	78275	**Grand Total**

PTCOG homepage: http://ptcog.web.psi.ch/

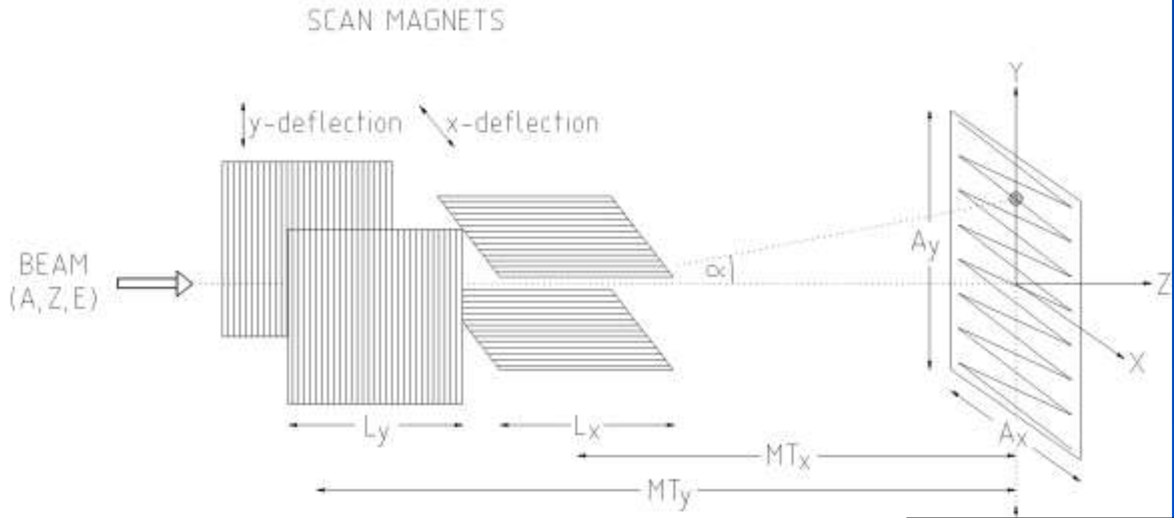
Advanced Approach







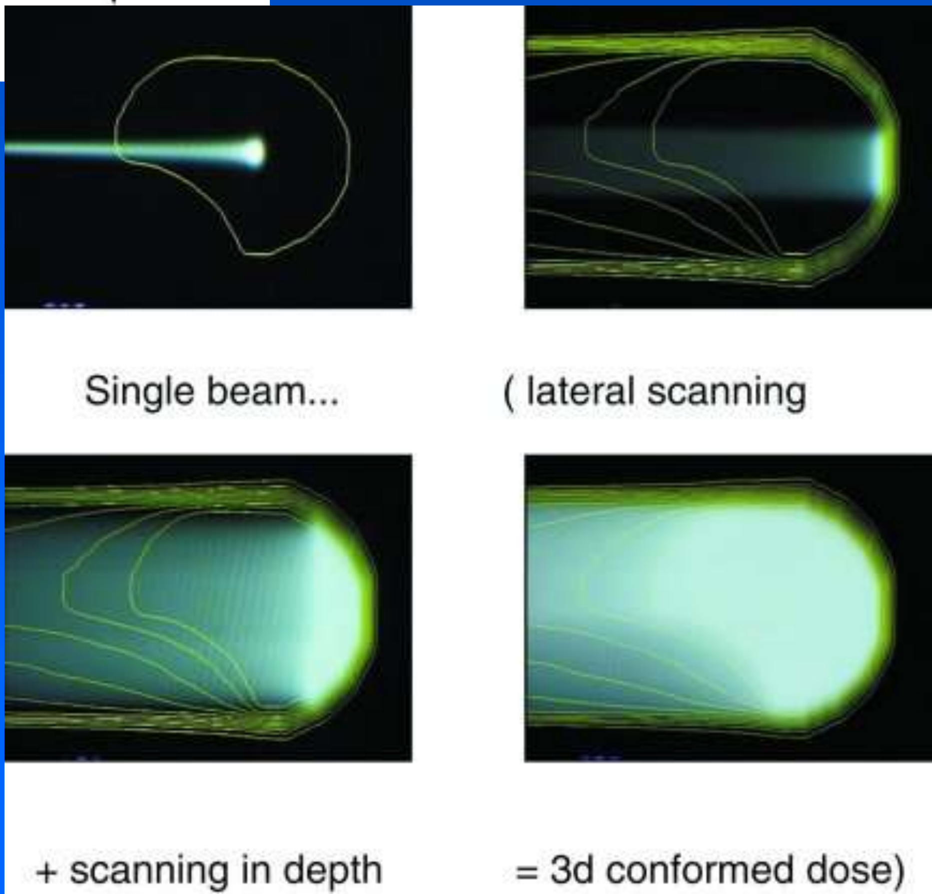
Beam Scanning



Haberer et al., NIM A , 1993

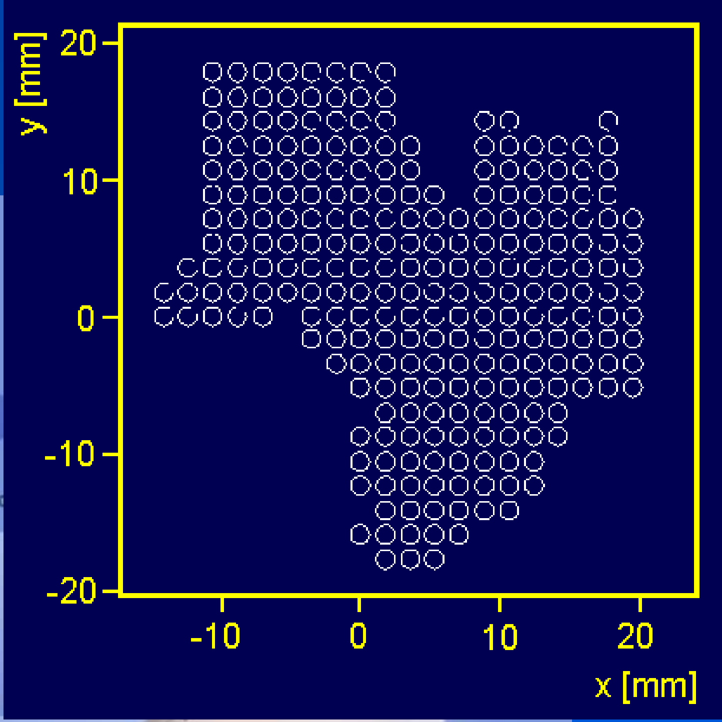
Protons (Pedroni et al., PSI):
spot scanning gantry
1D magnetic pencil beam scanning
plus
passive range stacking (digital range shifter)

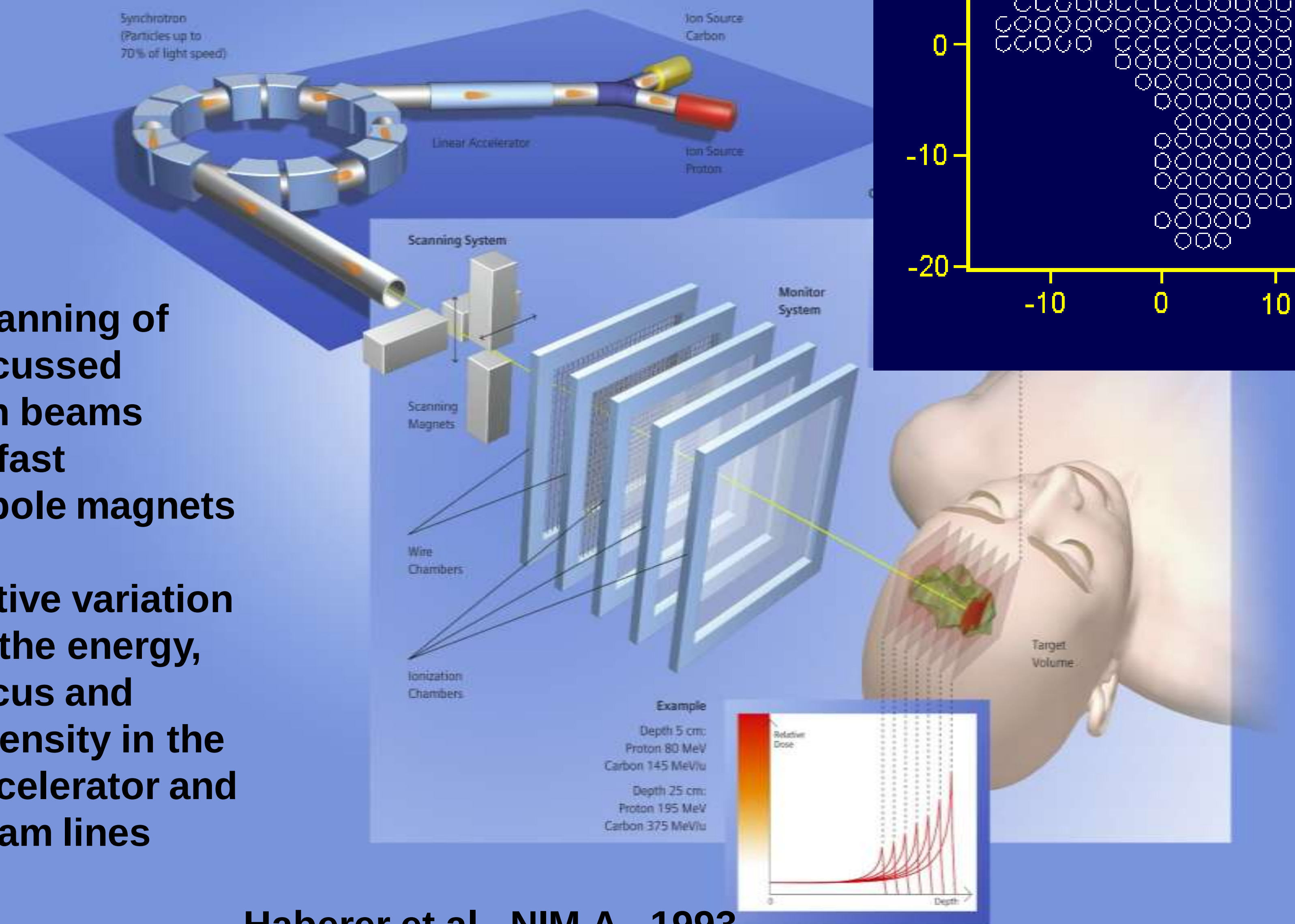
Ions (Haberer et al., GSI):
raster scanning, 3D active,
2D magnetic pencil beam scanning
plus
active range stacking (spot size, intensity) in the accelerator



Th. Haberer, Heidelberg Iontherapy Center

Rasterscan Method



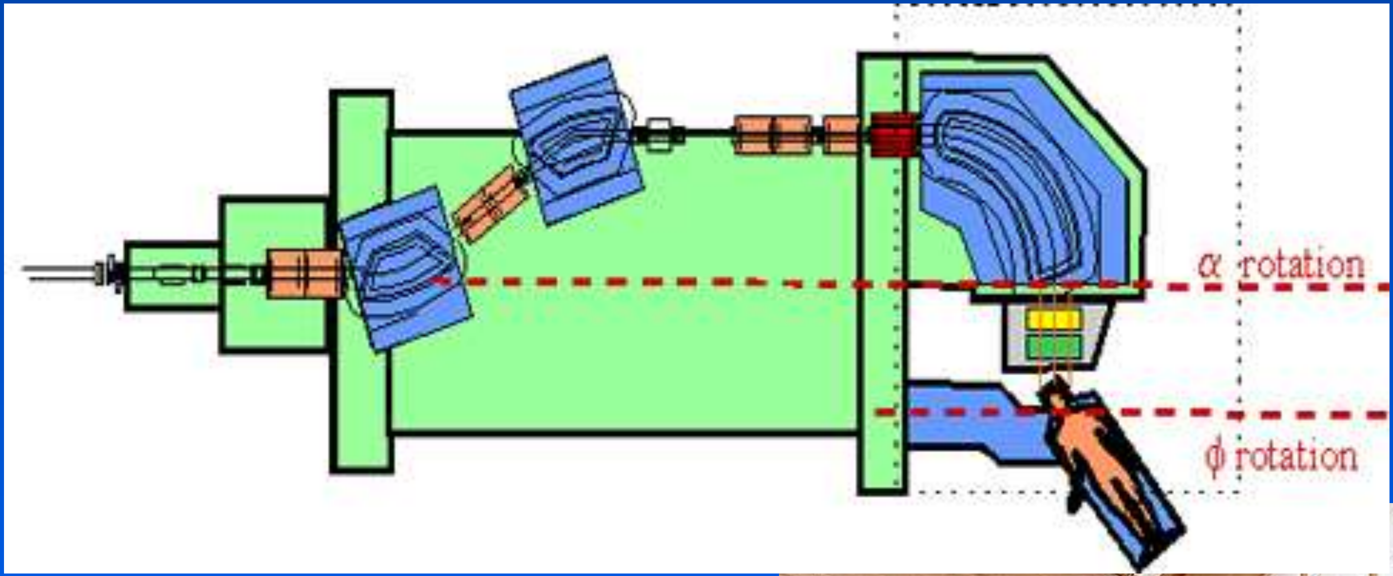


scanning of focussed ion beams in fast dipole magnets

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

Haberer et al., NIM A , 1993

Proton Therapy @ PSI



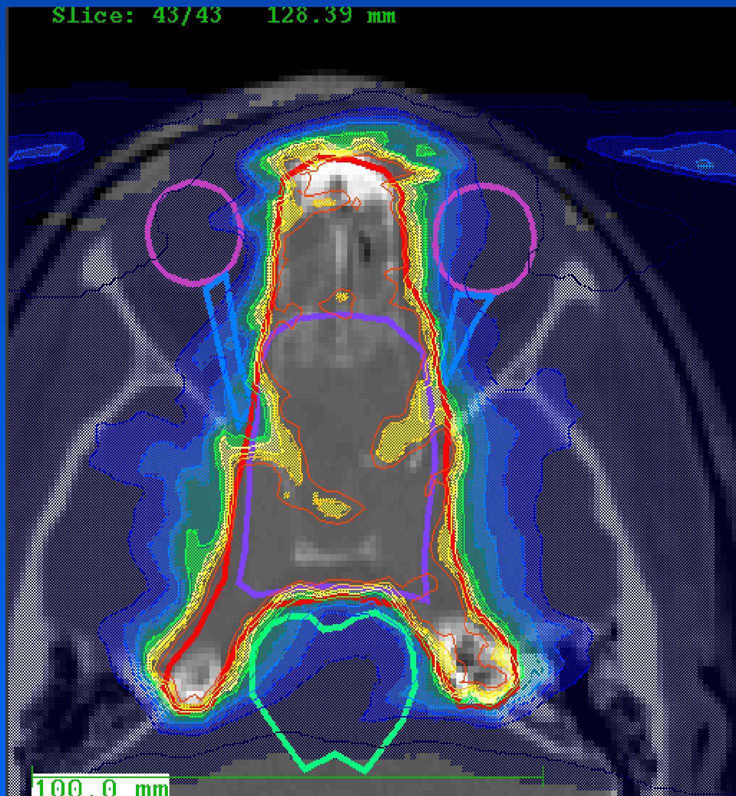
- **Proton cyclotron**
- **1d beam scanning at an excentric gantry**
- **Upcoming: PROSCAN**
  2d beam scanning
  iso-centric gantry

Carbon Ion Therapy @ GSI

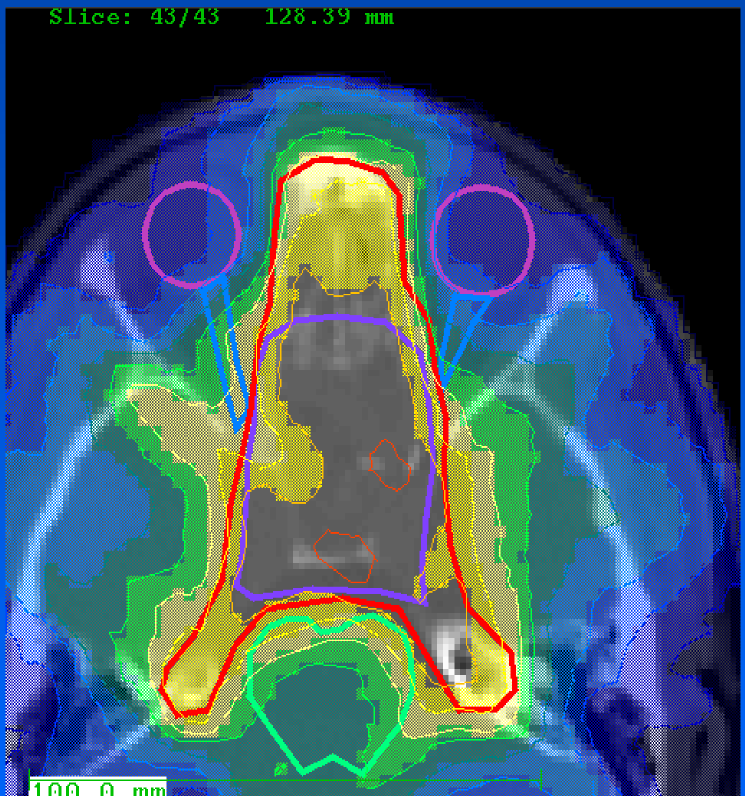
Fig. 4-4a The GSI Accelerator Facility

Scanned Carbon vs. Intensity Modulated Photons

scanned carbon 3 fields



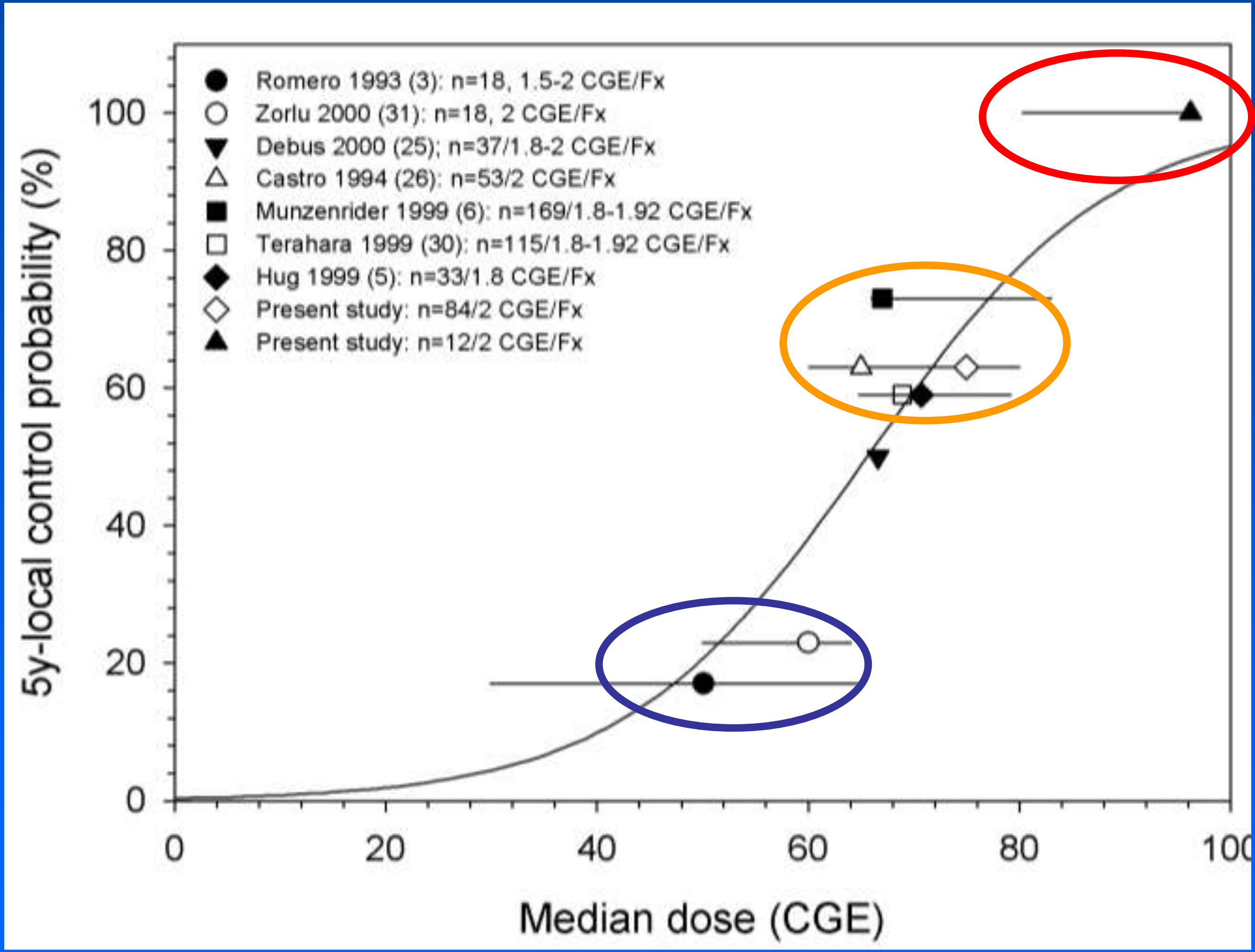
IMRT 9 fields



reduced integral dose
steeper dose gradients
less fields
increased biological effectiveness

courtesy O. Jäkel, HIT

GSI: clinical trial I: skull base chordomas / chondro-sarcomas



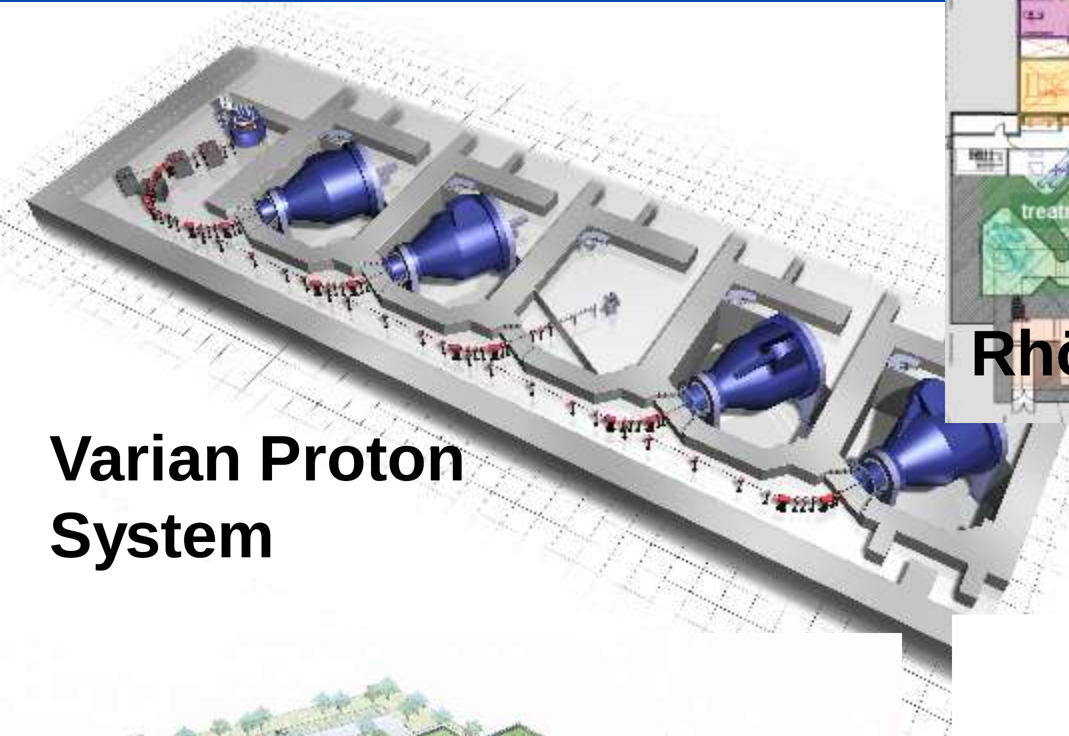
C-12 RT

particle RT

conv. Photon RT

[Schulz-Ertner et al., IJROBP 2006]

Hospitals

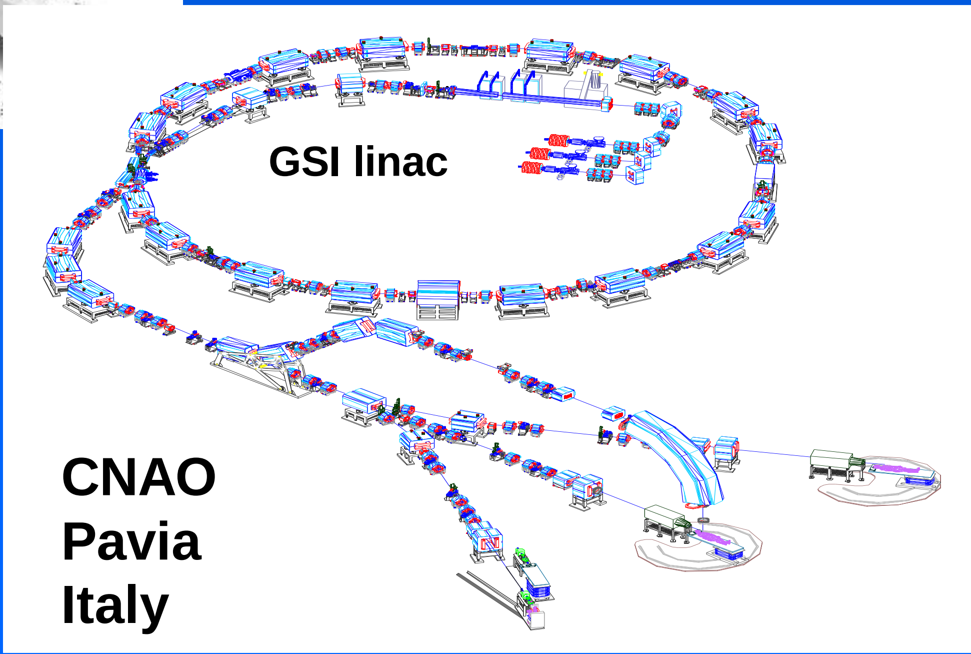


Varian Proton System

Rhön-Klinikum Marburg

IBA, VARIAN, SIEMENS, HITACHI, MITSUBISHI

Gunma Carbon Therapy



CNAO
Pavia
Italy

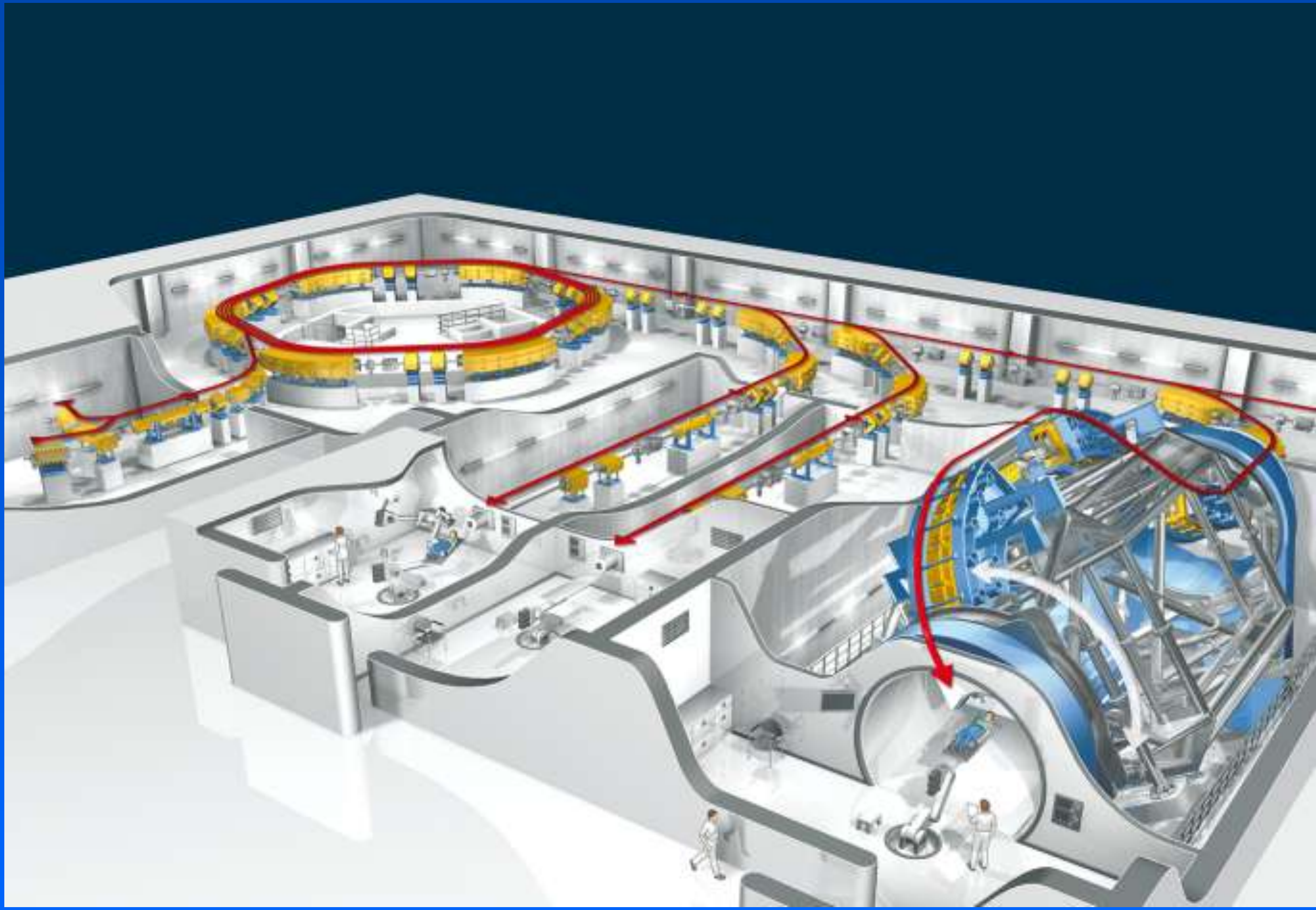
Economic requirements

- change of particle type < 60 s (dead time)
- change of treatment room < 30 s (dead time)
- number of treatment rooms ← utilization of accelerator
- 300 days per year, 16 hours per day
- ~1-2 min per treatment field (~1l, ~1-2 Gy)
  (target fraction duration: 15 min incl. 4 min beam)

- initial cost
- operational & maintenance cost

Heidelberg Ion Therapy Center

- compact design
- full clinical integration
- rasterscanning only
- low-LET modality: Protons (later He)
- high-LET modality: Carbon (Oxygen)
- ion selection within minutes
- world-wide first scanning ion gantry
- > 1000 patients/year > 15.000 fractions/year



Indications @ HIT (1)

Tumors in children, in particular retinoblastomas, medulloblastomas, gliomas, lymphomas, sarcomas, neuroblastomas, and germ cell tumors. For children it is important to avoid long-term side effects of therapy. Ion beams make it possible to protect the healthy tissue, so growth and development disorders and the development of secondary tumors can be avoided.

Liver cell carcinomas

Bronchial carcinomas, stages IIIa and IIIb, which cannot be treated curatively with photons within the tolerance of the surrounding organs (lungs, spinal cord) (mean lung dose > 19 Gy with a target volume dose of 70 Gy or FEV1 < 1.5 l/sec.)

Lung carcinomas in stage I and II with medical contraindication against surgery and with a curative approach.

Pancreas carcinomas, locally advanced, TxNxM0 with neo(-adjuvant) proton therapy and if inoperable.

Large soft tissue sarcomas of the extremities after limb-sparing operation, for which there is an increased risk of side effects with photon radiation therapy.

Indications @ HIT (2)

Chordomas and chondrosarcomas of the skull base.

Paraspinal sarcomas and carcinomas in curative therapy concepts and inoperable osteo- and chondrosarcomas of the axial skeleton.

Advanced head-neck tumors without distant metastases; may have been already treated with radiation.

Arterio-venous malformations of the brain, > 15 ccm.

Gliomas in adults, grade II/III.

Prostate carcinomas, localized.

Meningiomas of the base of the skull (>15 ccm) and atypical and postoperative remnants and sinus cavernosus.

Gynecologic malignomas, locally advanced, which have already been treated with radiation or are not suitable for a brachytherapy boost.

Indications @ HIT (3)

Esophagus carcinomas (technically and prognostically incurable, resectable T3-4 and T1-2, medically inoperable).

Stomach carcinomas, locally advanced, post-operative after R1/2 resection.

Recurrent rectal carcinomas, non-resectable, regardless of previous radiation treatment.

Some Facts

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

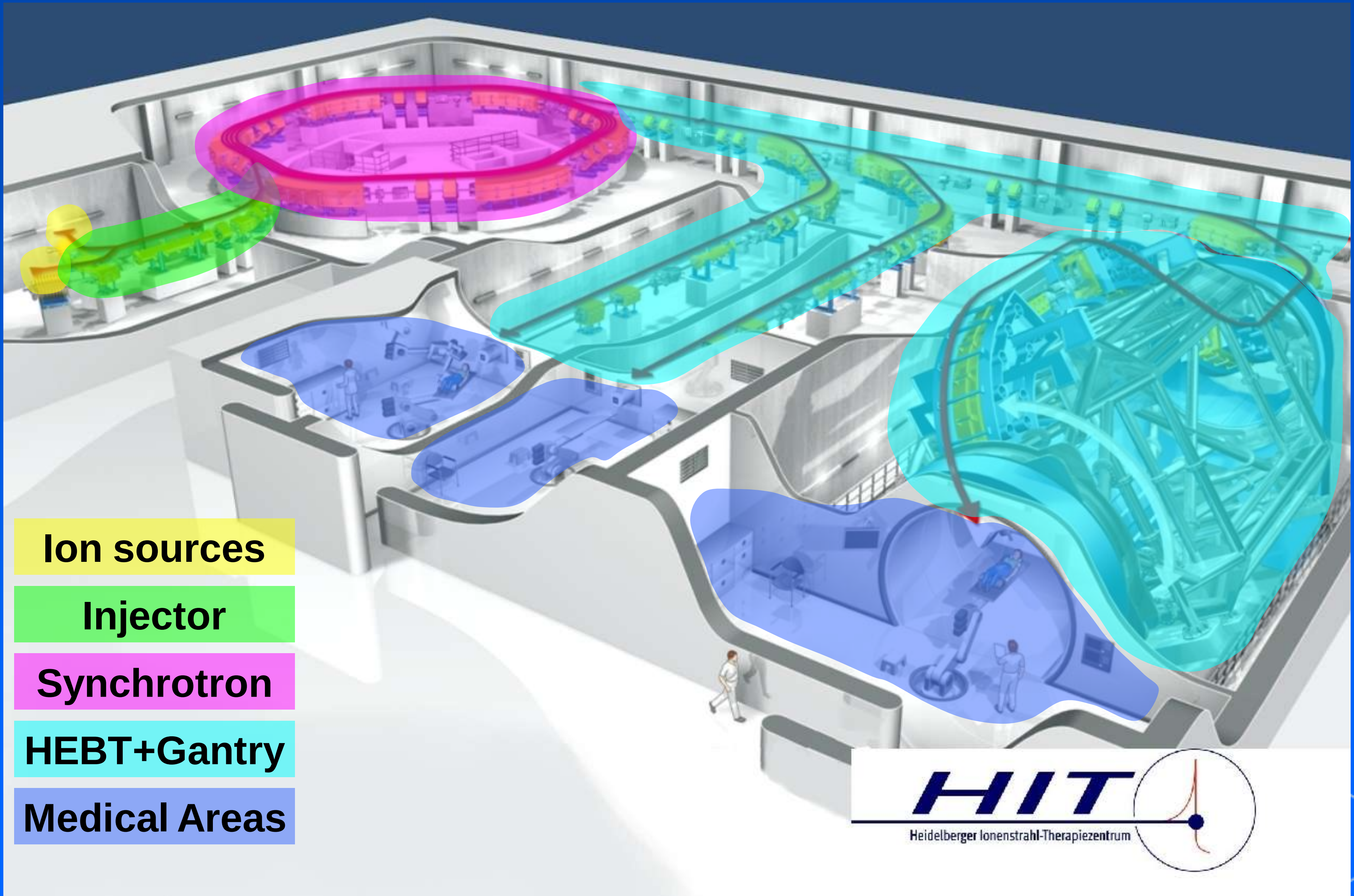
Start of construction: November 2003
Completion of building and acc.: June 2006
First patient planned: late in 2009

Project Partners:

- **University** pays, owns and operates the facility
- **GSI** built the accelerator
- **Siemens** supplies all components related to patient environment
- **GSI, DKFZ, Siemens …** are research partners

Heidelberg Ionenstrahl-Therapie Centrum

HIT Accelerator System



Functions

Ion: source, LEBT
Intensity: LEBT
Energy: Synchrotron, HEBT
Focus: HEBT
Beam Abort: Synchrotron, HEBT

Medical Equipment

Identical patient positioning systems
- fixed beam
- gantry

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

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

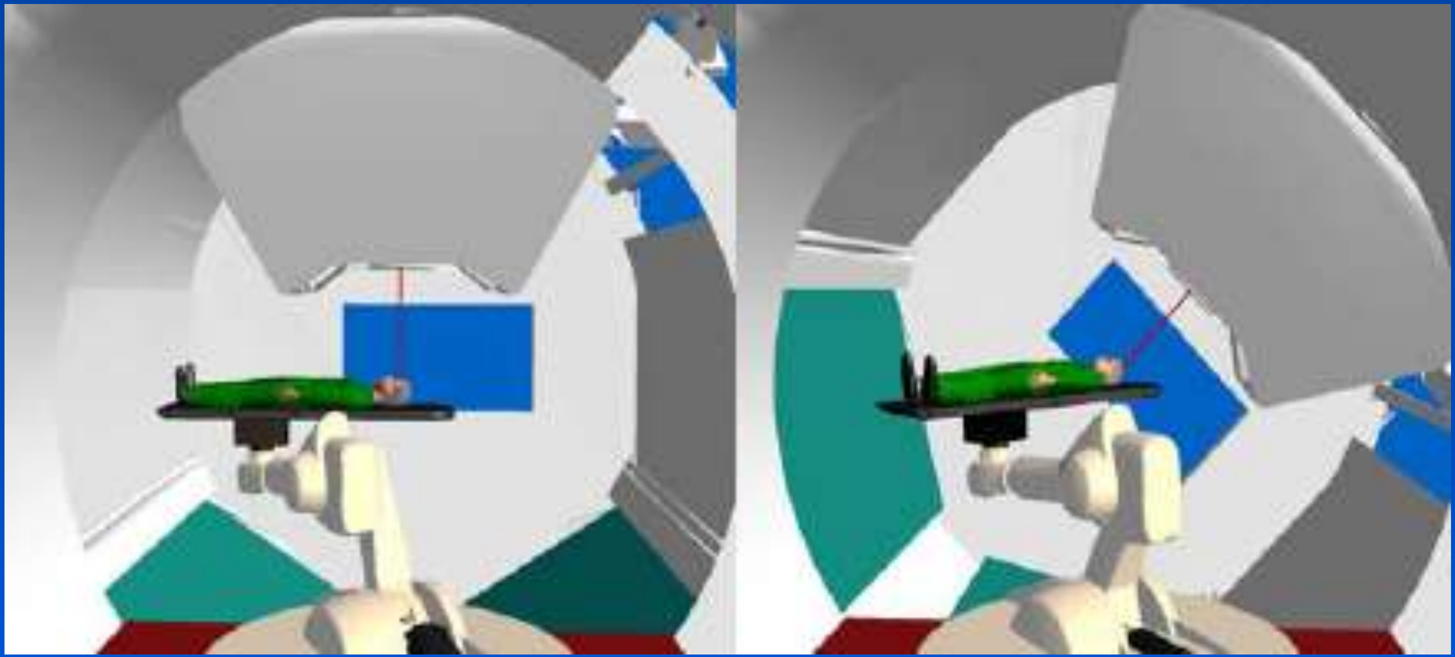
Open for future applications and workflows

1st Patient @ HIT

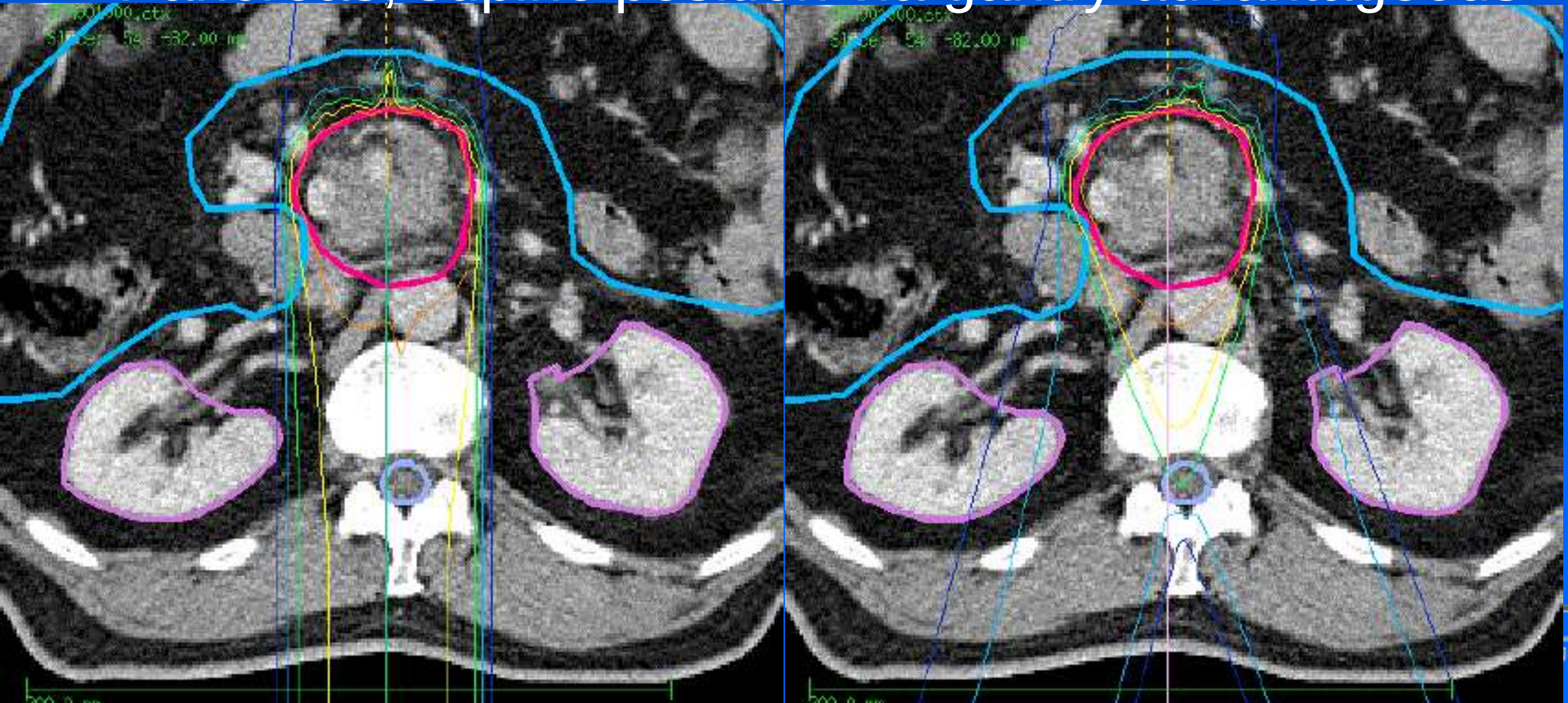
November 15th, 2010,
horizontally-fixed beamline #1
rasterscanned carbon ions

Motivation Gantry

Advantage of a rotating beamline



Pancreas, supine position via gantry advantageous



Scanning Ion Gantry

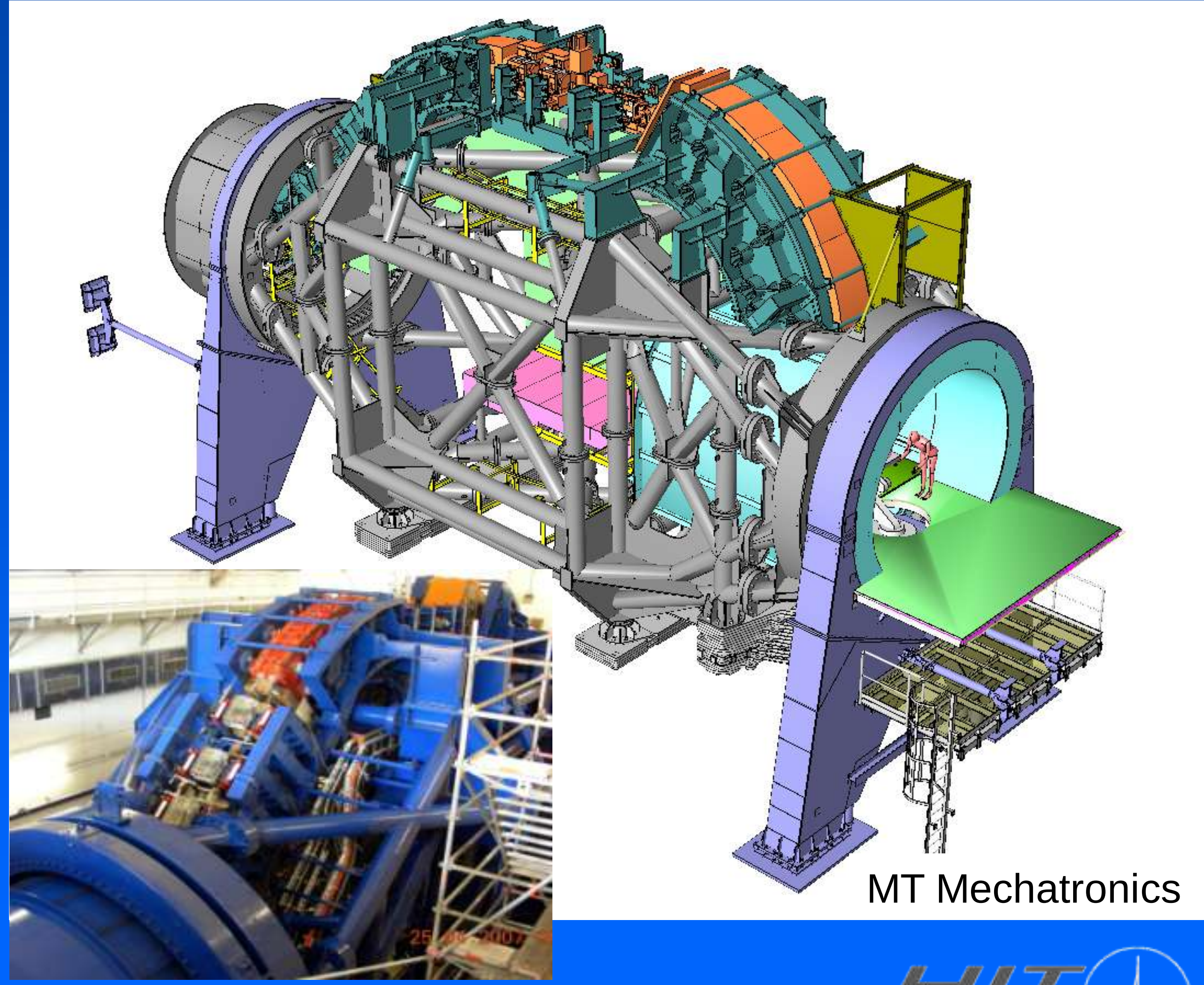
- optimum dose application

- world-wide first ion gantry

- world-wide first integration of beam scanning

- 13m diameter
  25m length
  600to overall weight
  0,5mm max. deformation

- prototype segment tested at GSI



MT Mechatronics

Gantry / Medtech

Patient Gantry Room November 2007

Tilt floor, pending on Gantry position

Nozzle

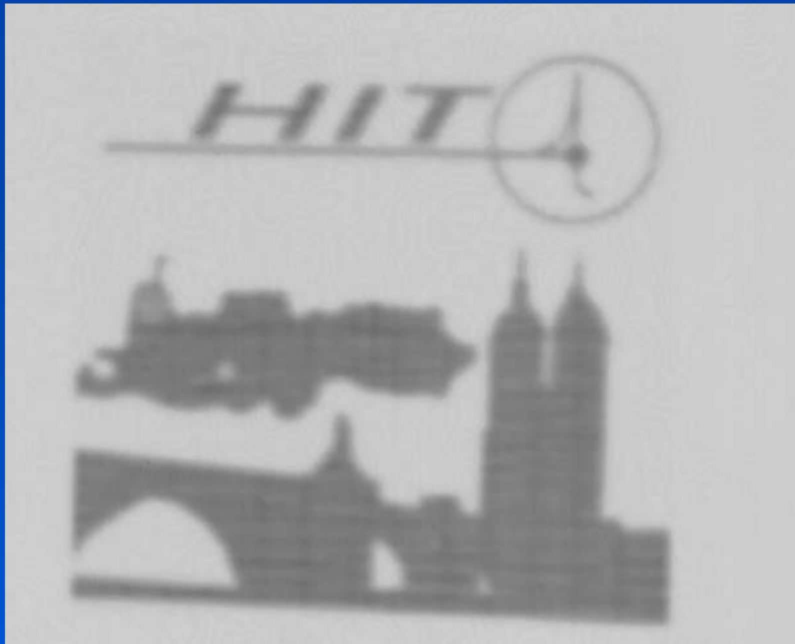
Bumber mats

Patienttable, Roboter

Outlook

- Particle therapy will cover the full spectrum of radiotherapeutical indications
- Per 10 million inhabitants one particle therapy facility may be required.
- Upcoming: CNAO/Pavia, Rhön-Klinikum/Marburg, Kiel,MedAustron/Wiener Neustadt , Chicago, Essen, Prague, Lyon, Bejing….

- New technology is in the lab aiming at compact and low investment facilites
- > 10 years R+D !?
- Single room facilites would boost the modality
- „tabletop“ lasers
- Dielectric wall accelerators
- Superconducting and gantry-mounted systems



(Intensity modulated raster scan, ^{12}C at 430 Mev/u, October 15th 2007)

Rasterscan@HIT/H1 Carbon 430 MeV/u

Thank you!

Questions?

www.hit-heidelberg.com