Status of Hadrontherapy facilities worldwide

EPAC Genoa
24.06.2008

Eros Pedroni

Center for Proton Radiation Therapy
Paul Scherrer Institute
SWITZERLAND

PAUL SCHERRER INSTITUT
PSI

The Gantry 1 of PSI

Author's competence:
Gantry with proton pencil beam scanning
High LET radiation - with pion therapy

Outline of the presentation

1. Motivation of Hadrontherapy
   - Physical selectivity
   - Radiobiology of High LET radiation
2. Scanning beams vs. passive scattering
3. Tour of the world of the hadrontherapy facilities
4. The point of view of PSI: past experience and future plans
5. New accelerator concepts
6. Conclusions

1.
Hadrontherapy: the context

Hadrontherapy

- HT = Radiotherapy (RT)
  using protons and ion beams

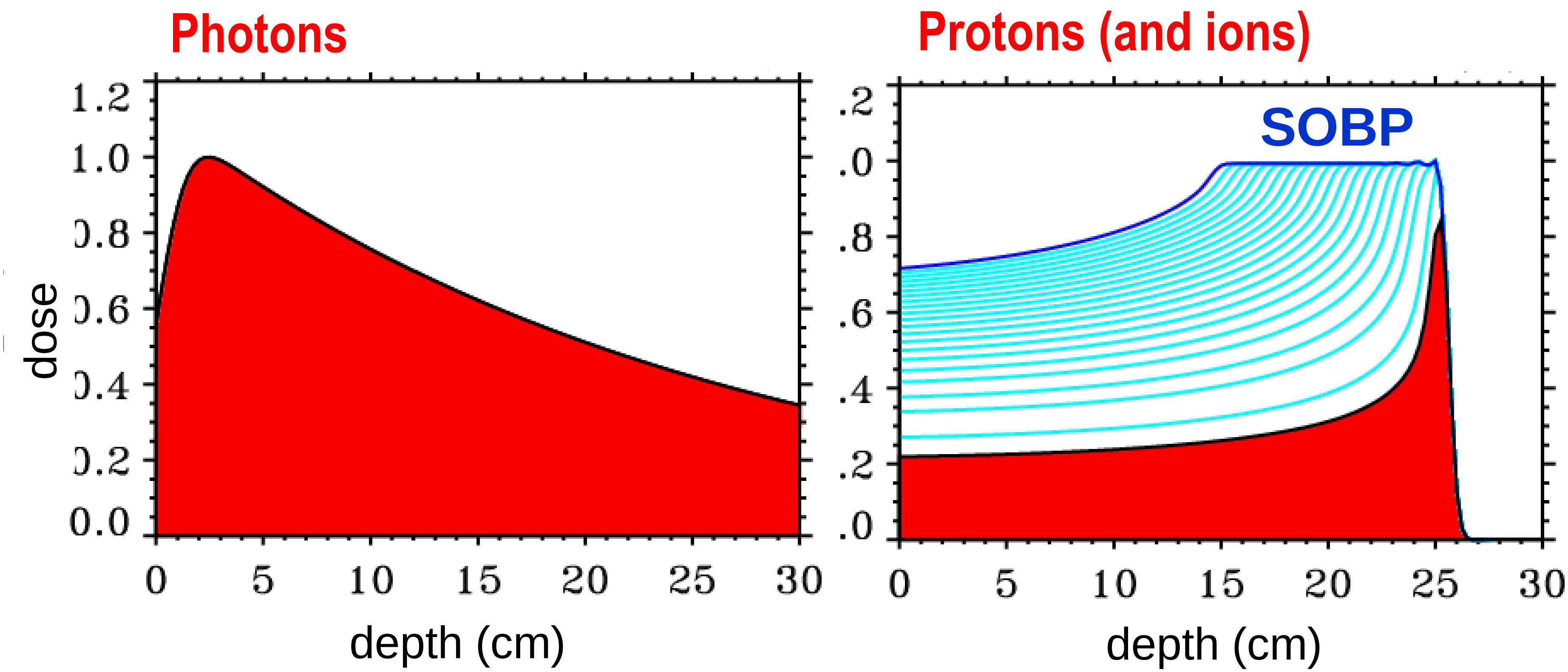
- The term of comparison for hadron-therapy:
  Conventional radiotherapy (RT) with photons
  - Gone through a very strong modernization
    - CT-based computerized treatment planning
    - New dynamic beam delivery techniques
      - Intensity Modulated RT (IMRT)
      - Tomotherapy
    - Recently – Treatment of moving tumors
      - Respiration gated irradiation
      - 4d-CT and 4d-MRI (time resolved images)
    - Image-guided radiotherapy
      (images for positioning adaptation on line)

About half of all people with cancer are treated with radiation therapy, either alone or in combination with other types of cancer treatment
NCI – National Cancer Institute

1A.
Physical selectivity
Protons

Protons: presently, the best low-LET external radiation therapy

The rationale for using protons – the physical selectivity
Finite range - Bragg peak



- No significant radiobiological difference between protons and photons

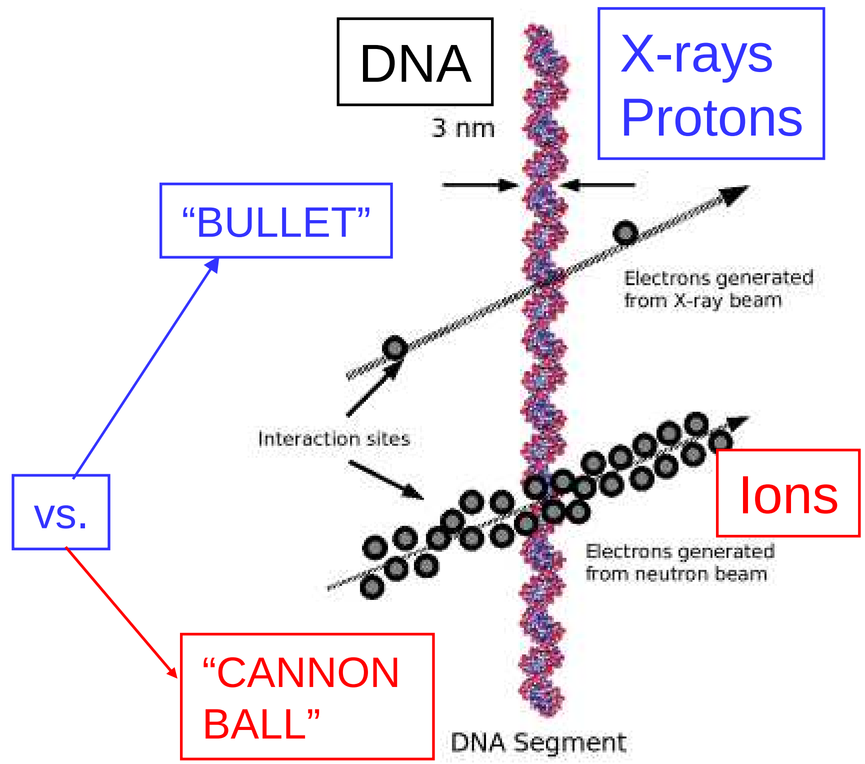
- Main advantage of protons compared to photons – the distribution of the dose
  - Dose burden on the healthy tissues outside of the target volume reduced by a factor 2 to 5

1B.
Radiobiology
of heavier (light) ions
High LET of carbon ions

Carbon ion: presently, the best high-LET external radiation therapy

What is high-LET radiation ?

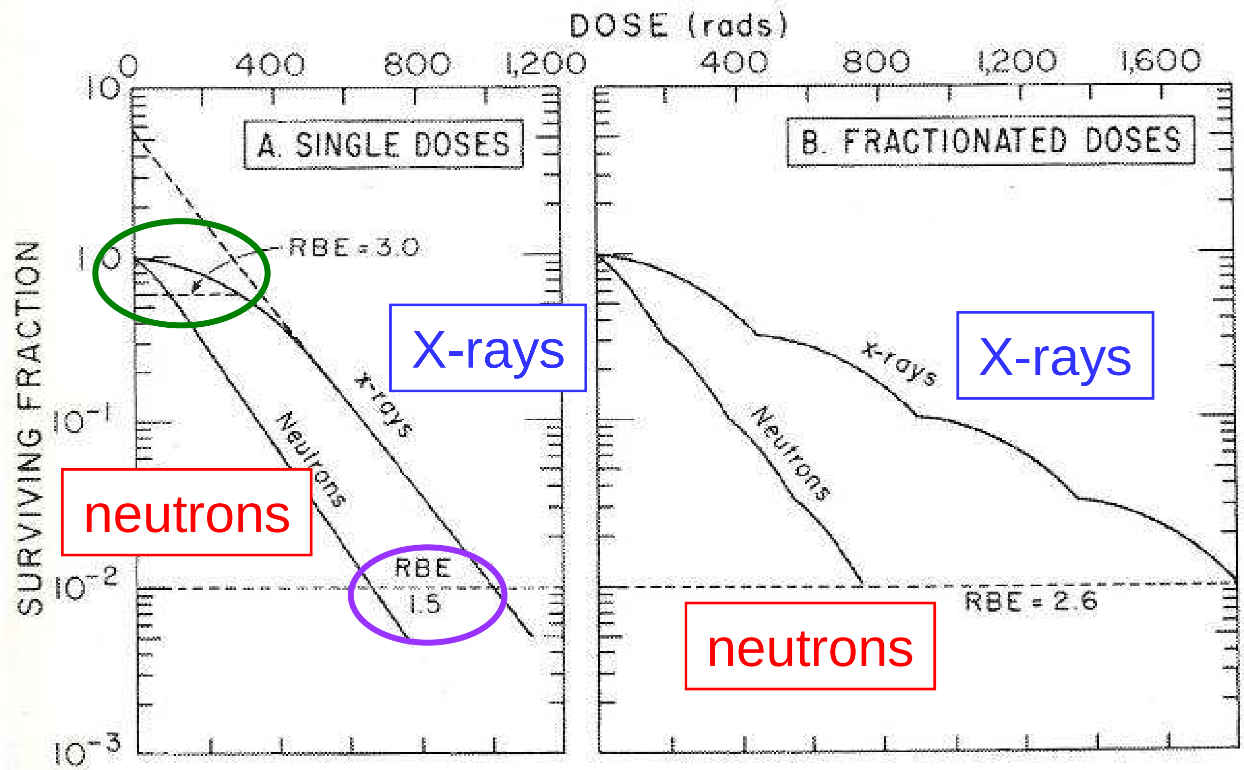
- LET (LET = Linear energy transfer – a way of saying "ionization density")
  - Relevant, the density of the ionization tracks at the size of the DNA structure
  - If LET low at low doses -> single damage to the DNA chain -> Repair
  - If LET high -> multiple damages to the DNA chain -> NO repair



- High LET: means
  - For the tumor cells
    - Increased efficiency of killing
  - For the healthy tissues
    - Increased "collateral damage"
      - Acute effects
      - Late effects
      - Secondary cancer induction
- Value controversial (needs more clinical trials)

(a wikipedia image)

High LET: not new: … past experience with neutrons and pions



(From a lecture of M. Pruschy, University of Zurich)

FRACTIONATION
vs
SINGLE DOSE

Low doses and low LET
Big difference

High LET
No repair
No difference

In the 70s-80s-90s
~~Neutrons~~ vs photons

Now 2008
Carbon vs protons ?

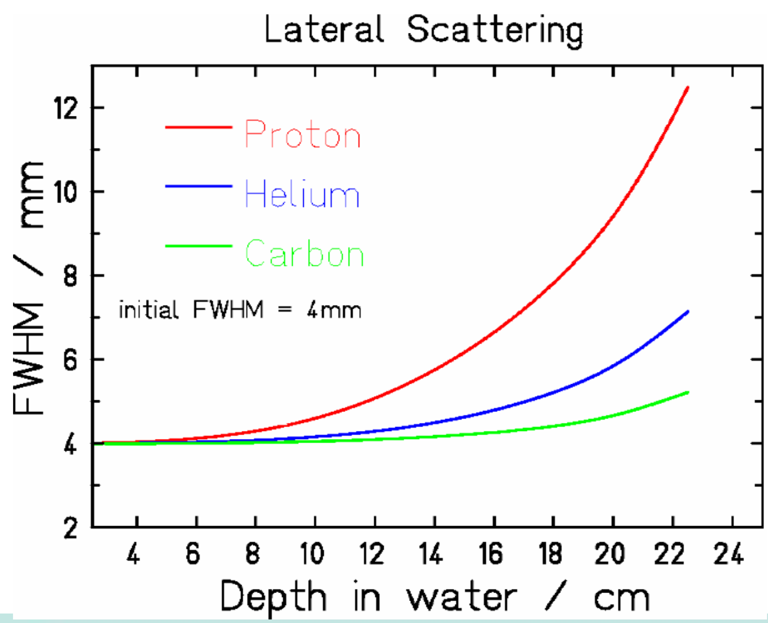
- Neutron therapy:
  - Reported better results from neutron treatments: salivary glands (prostate?-sarcomas?)
  - Experience not convincing enough - now being abandoned
- Pion therapy (Los Alamos, Triumf, PSI):
  - at PSI 500 patients treated with pions – project abandoned in 92

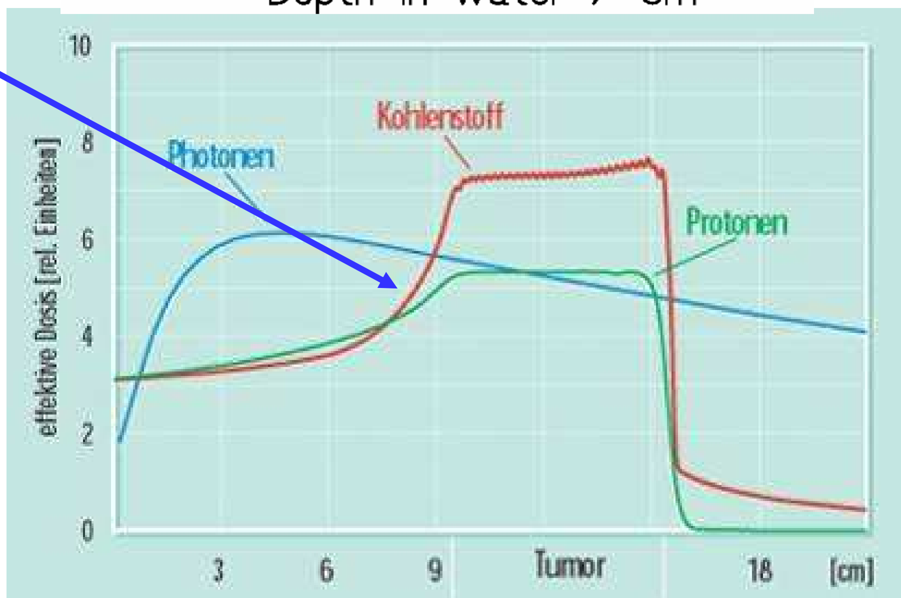
Fractionation

- Radiation Therapy : a balance between
  - Chance of cure -> sterilization of the tumor and
  - Normal tissue tolerance -> damage within the target and on the way of the beam
  - Therapeutic ratio (TR) ⟶ $TR = \frac{\text{surviving healthy cells}}{\text{surviving tumor cells}}$
- Fractionation (rationale + experience)
  - Radio-sensitive tumors - normal tissue tolerance important (large tumors)
    - If TR > 1 at one fraction => $(TR)^n$ >>1 for n fractions
    - The basis of the successes of RT in the hospitals (n~30 sessions) Low LET
    - A contra-indication for High-LET (carbon is not a generic RT alternative)
- Hypo-fractionation
  - Radio-resistant tumors – Tumors deficient of oxygen carbon
    - If TR < 1 –> low fractions -> few high doses (protons <-> carbon getting similar?)
    - Only if tolerance acceptable (small targets – partial organ irradiations)
    - High-LET more tumor-effective than low-LET? MAY BE (to be shown)
- Fractionation (low LET) after initial carbon boost (high LET) carbon

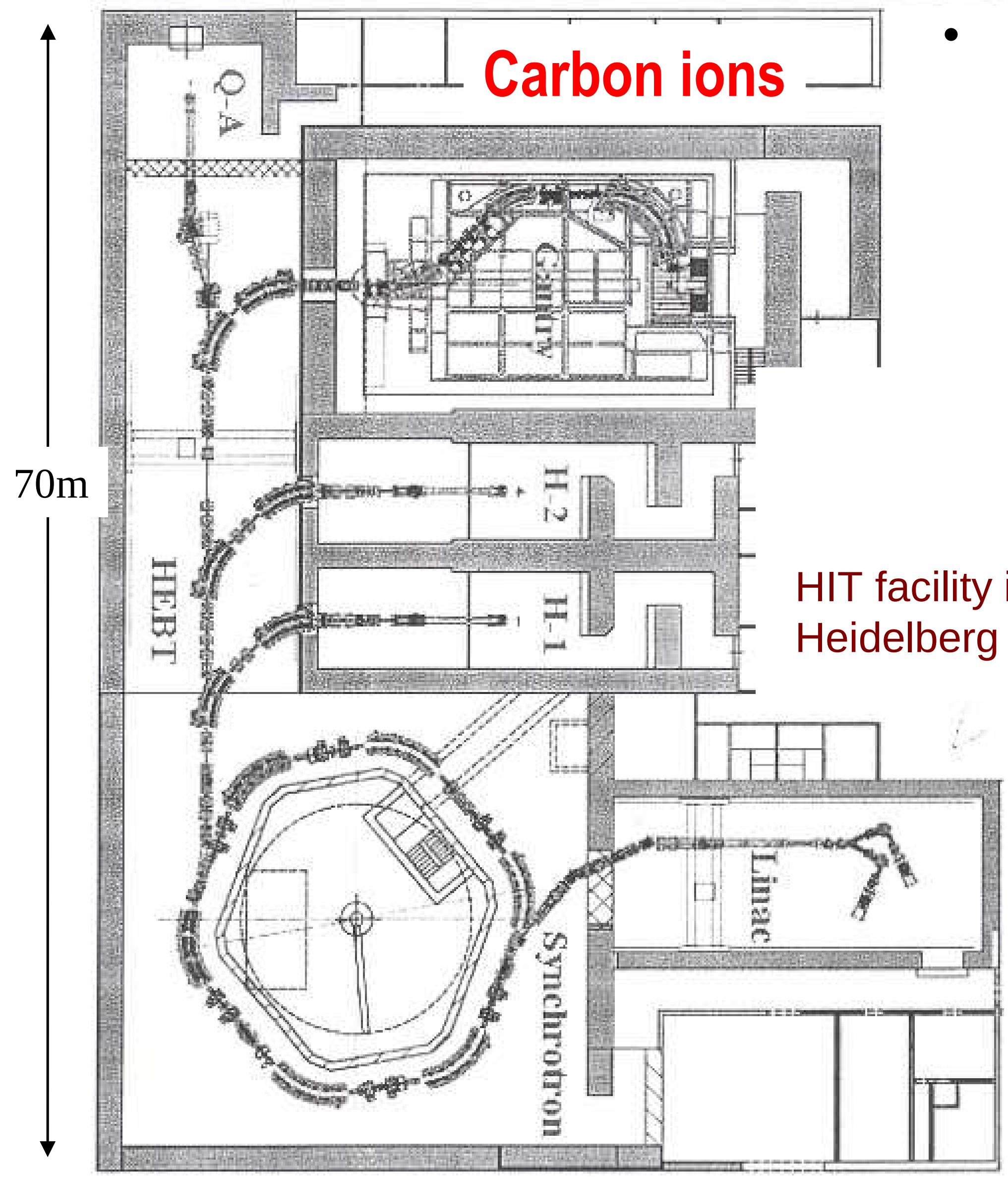
The interest for carbon ions: High LET + very good physical selectivity

- Improved ballistic precision
  - Low multiple Coulomb scattering
    - Improved lateral precision
  - Sharper Bragg peak
    - But loss of primary beam due to fractionation?
  - RBE-Plateau < RBE-SOBP
    - Enhanced dose profile
    - Comparison misleading High LET vs Low LET
      - Fractionation effects
      - Risks of late effects
- Open radiobiological questions …
- Interesting:
  - The use of helium ions
  - a low enough "low-LET radiation" for the highest precision?





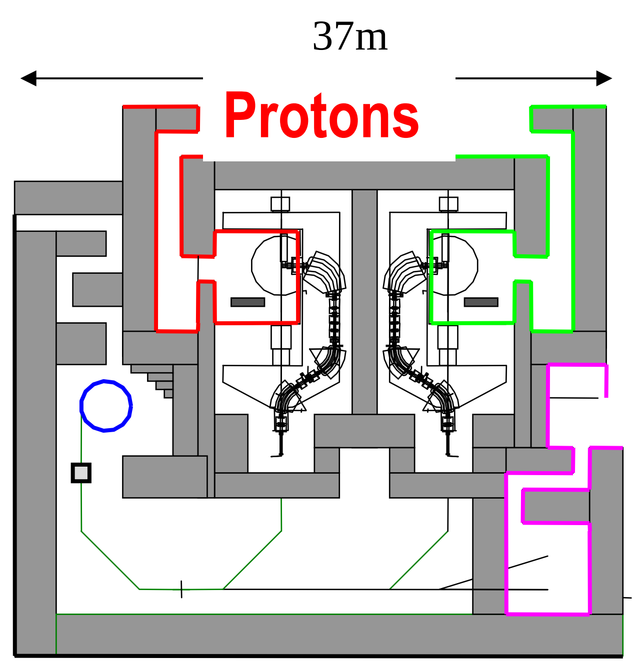
The price of using ions : the increased size of the facility



HIT facility in Heidelberg

- The magnetic rigidity of the beam
  - Carbon ions 3 times higher than protons
    - Size increased by a factor of 2 in all dimensions
    - Costs doubled
  - No gantry or huge gantry

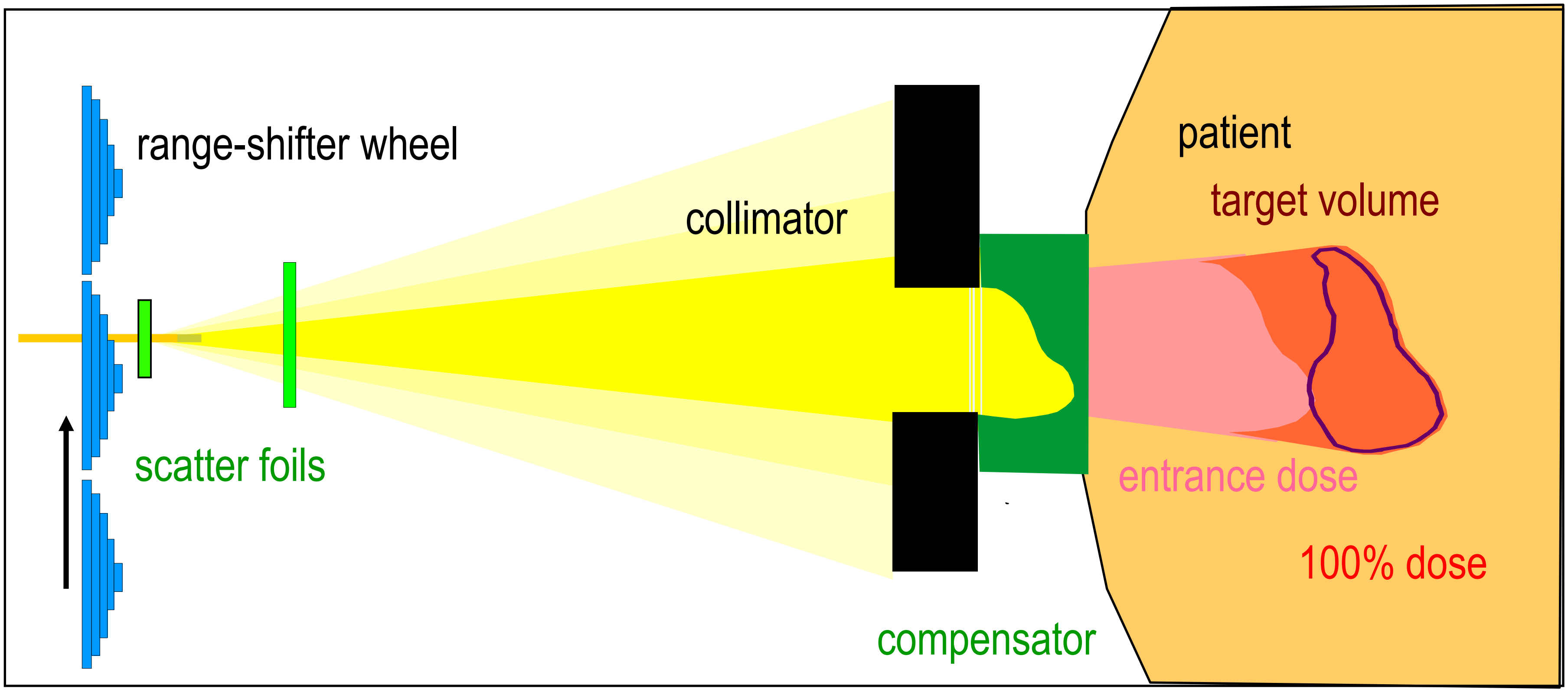
2 Gantries + 1 HR layout



2.
Technical options
Scanning beams vs. passive scattering

Passive scattering

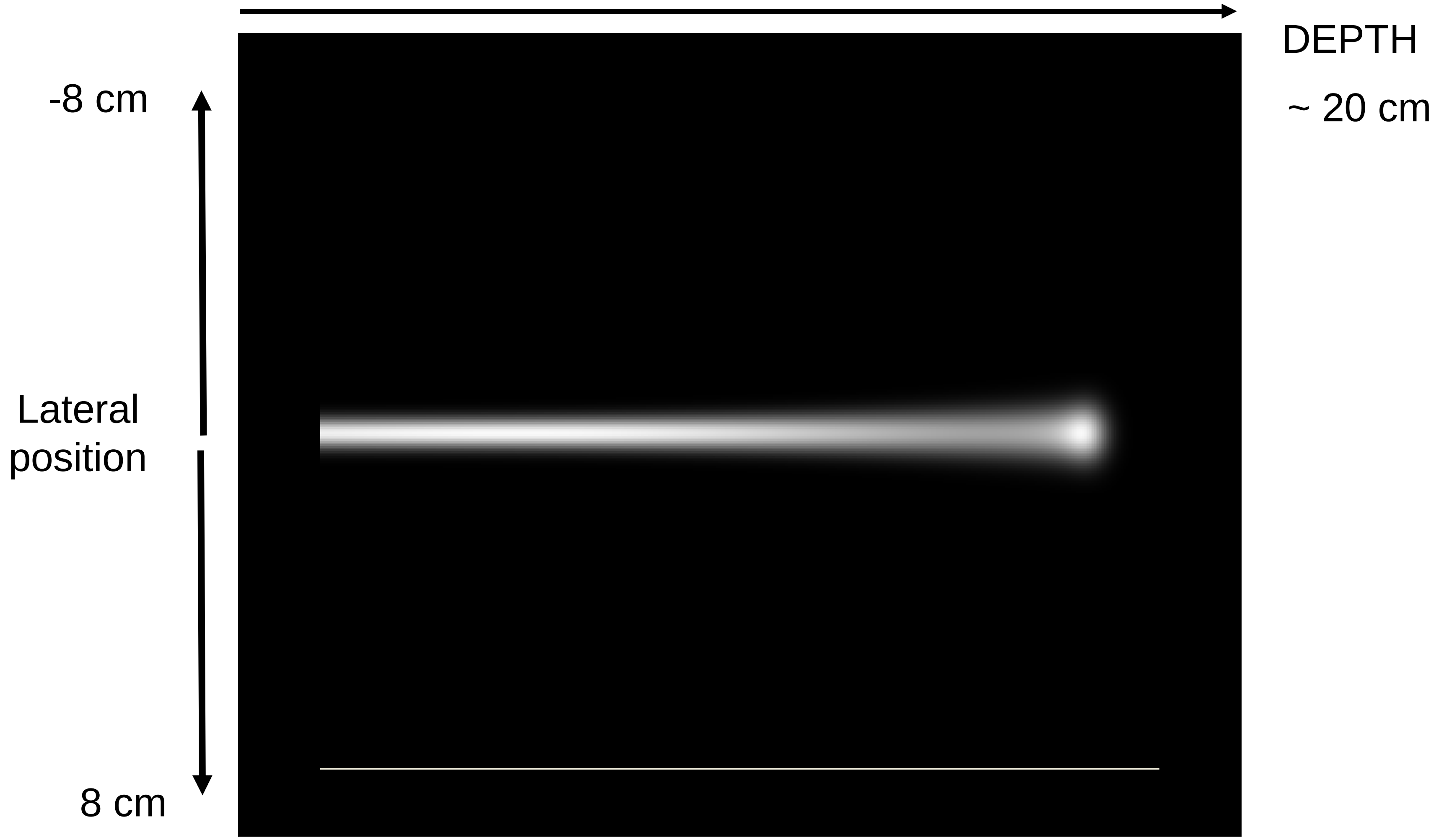
The established traditional method (of the 60s)



- Not truly 3d-conformal (fixed modulation of the range)
- Field specific hardware for each field
- IMRT difficult (not feasible)

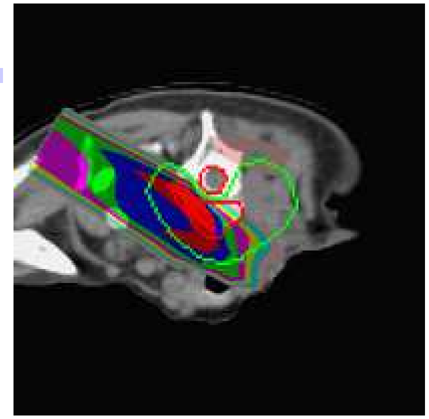
- Less sensitive to organ motion errors than scanning
- Accelerator type unimportant

Pencil beam scanning

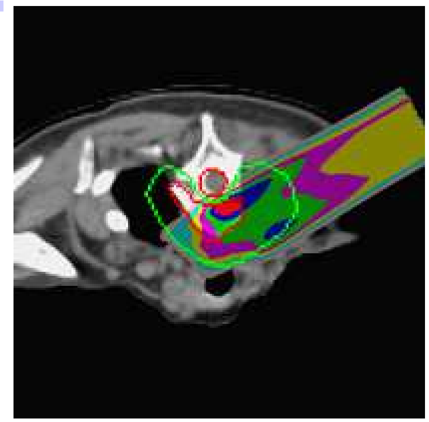


- Fully 3d conformal (fixed range modulation)
- Fully automated (no specific hardware needed)

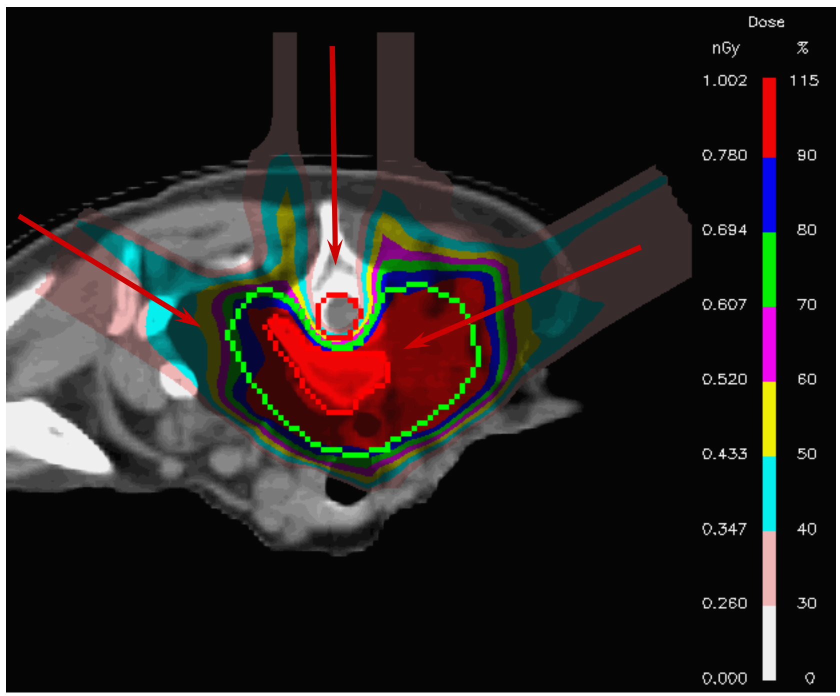
Main advantage of using scanning **IMPT**

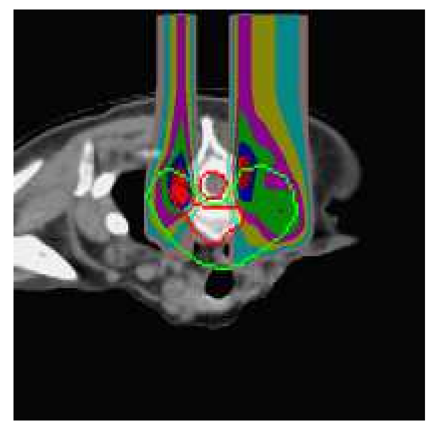


- Flexibility to shape the dose within the target
  - Intensity modulated therapy IMPT (40% of the PSI treatments)
    - Attract large interest due to competition with photon IMRT
  - Biological targeting (non-uniform dose distribution)



- Disadvantage
  - Sensitivity to organ motion
- Need to develop
  - Faster scanning
  - Repainting
  - Gating
  - Tracking
- Accelerator type could play a role





3.
Tour of the world of hadrontherapy facilities

Overview of hadron facilities in the world

- Facilities in the USA:

	start of treatments	method	particle	accelerator	company
Loma Linda (California)	1990	ps	p	synchrotron	Optivus
Boston (Massachusetts)	2001	ps	p	cyclotron	IBA
Bloomington (Indiana)	2004	ps	p	cyclotron	IBA
Houston (Texas)	2006	ps+as	p	synchrotron	Hitachi
Jacksonville (Florida)	2006	ps	p	cyclotron	IBA

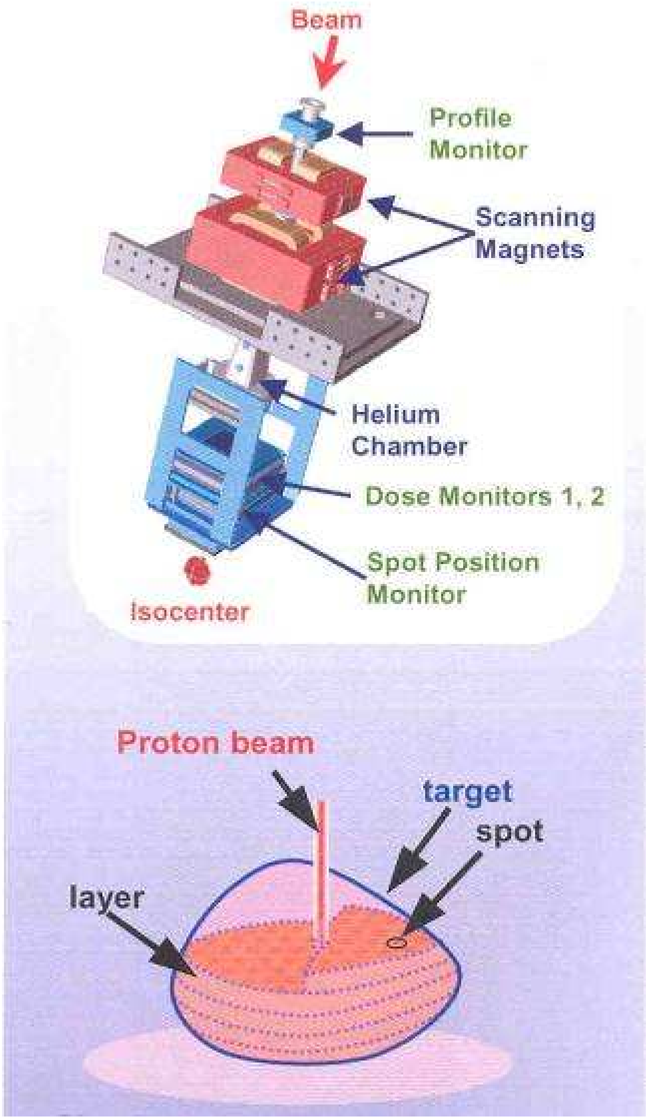
ps = passive scattering as = active scanning

- Boston (previously Harvard cyclotron) has provided most of the clinical evidence (for PT)
- Loma Linda is the first hospital-based proton facility in the world (11'414 patients)
    - Shown that proton therapy can be provided on a commercial basis
    - Amortization completed – University earning money from proton therapy

- In the USA we have only proton facilities
- All facilities use proton gantries and scattering
- Scanning is being developed as an addition to scattering (for competing with IMRT)
- No ion therapy since the shutting down of the Berkeley facility

Important achievement …

- At the new proton therapy facility in Houston
- One of the 3 gantries equipped with scanning
  - First patient treated
    with proton pencil beam scanning
    on 19-May-2008
    at the M. D. Anderson Hospital (Texas)



- Scanning is not anymore a specialty of physics laboratories
- HITACHI is the first company providing pencil beam scanning as an industrial product

- **Japan**

• Chiba	1994	synchrotron	ps	c	Companies consortium
• Kashiwa	1998	cyclotron	ps	p	Sumitomo (IBA)
• Tsukuba	2001	synchrotron	ps	p	Itachi
• Hyogo	2001	synchrotron	ps	p + c	Mitsubishi
• Wakasa	2002	synchrotron	ps	p	Misubishi
• Shizuoka	2003	synchrotron	ps	p	Mitsubishi

- **Rest of Asia**

– Zibo (China)	2004	cyclotron	ps	p	IBA
– Seoul (Corea)		cyclotron	ps	p	IBA

- Chiba – the only dedicated facility using only carbon ions
  - The place producing the most important clinical results with carbon (3’819 patients)
    - With scattering
- Hyogo – the only running facility with combined carbon and proton therapy
    - Reported patient treatments
      - Proton = 1656 Carbon = 271 (15%)

- **Europe (facilities under construction)**
  - Munich (Germany) p Accel Varian
  - Essen (Germany) p IBA
  - Heidelberg (Germany) c+ p GSI
  - Pavia (Italy) c+p INFN CERN
  - Marburg (Germany) c+p Siemens
- **Europe (coming next)**
  - Proton: Orsay - Trento - Uppsala p
  - Carbon: Vienna – Lyon – Kiel c + p

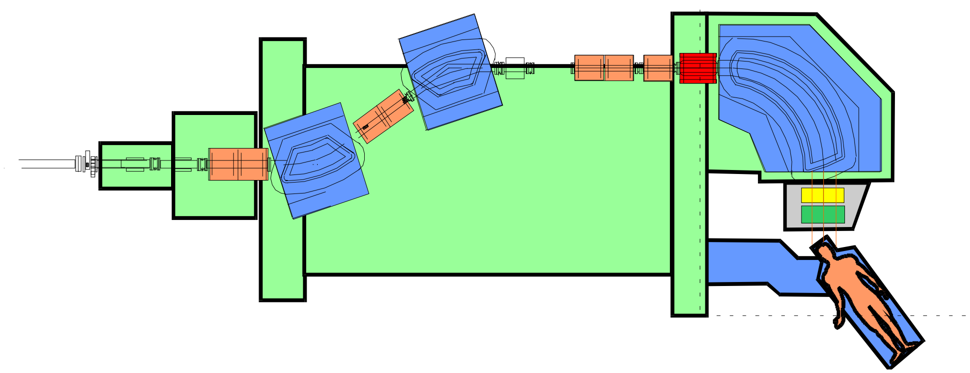
- All new European facilities will be based solely on active scanning
  - Despite the fact that the organ motion problem with scanning is still unsolved
    - Strong need to find new solutions to this problem
  - Protons facilities are all with gantry
  - Carbon facilities are only with horizontal beam lines (except HIT at Heidelberg)

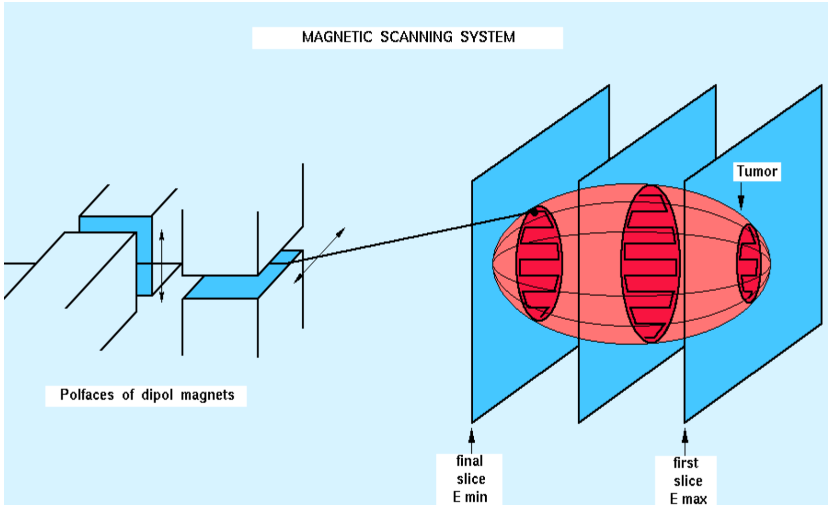
The two centers pioneering pencil beam scanning in the last decade

- The gantry 1 of PSI (~350 patients treated since 1996)*
  - Protons delivered with a cyclotron and a degrader
  - The first scanning gantry in the world
  - Discrete spot scanning (magnetic scanning – range shifter – patient table motion)

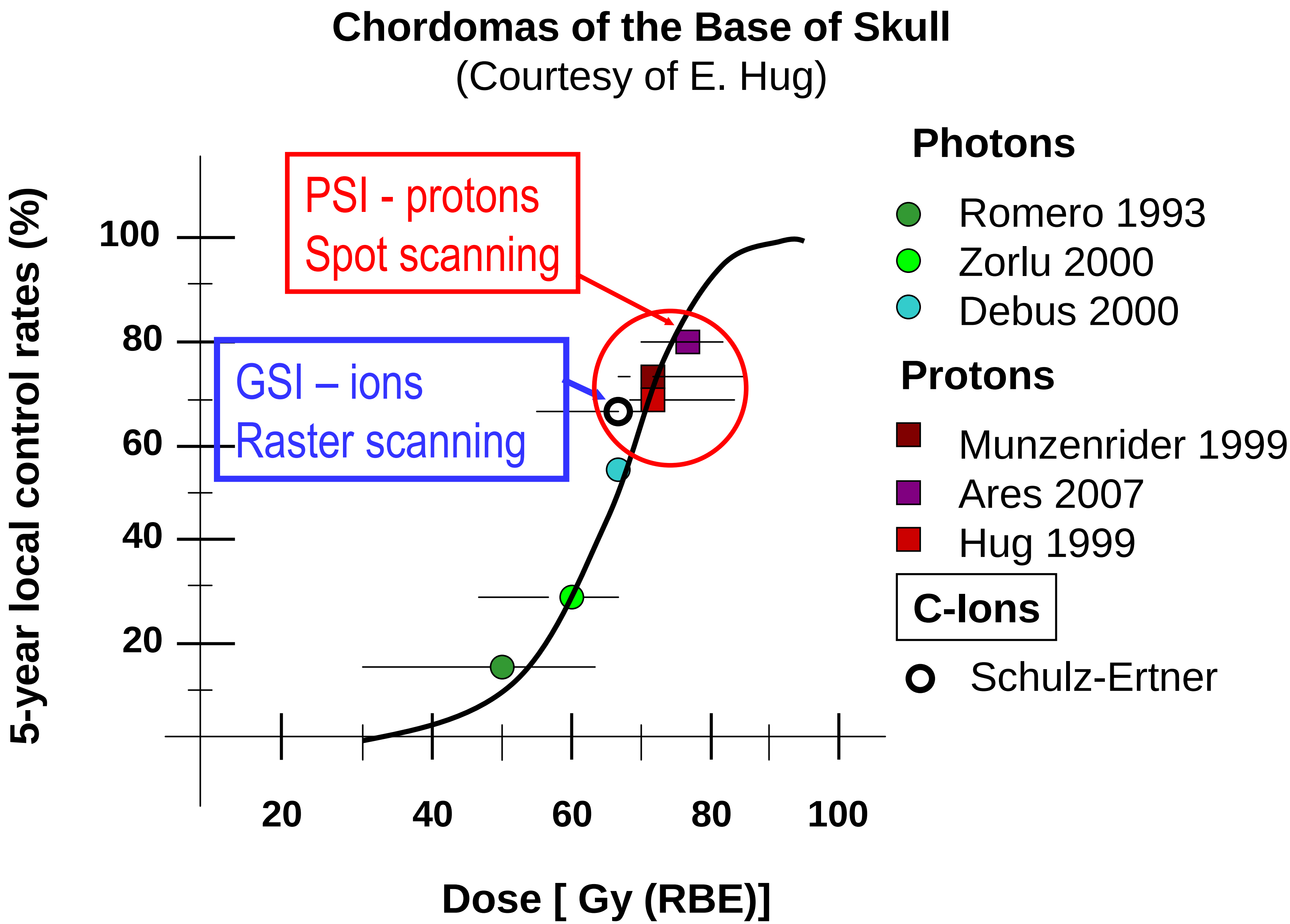
* + 4'875 proton eye treatments

- Horizontal beam line at GSI (~400 patients – since 1997)
  - Carbon ions - synchrotron with slow extraction
  - 2D magnetic scanning – dose painting in energy layers (fixed energy per pulse)
  - Raster scanning technique (Beam ON from spot to spot)
- Same indications





Comparison of the 5-year survival data of PSI and GSI

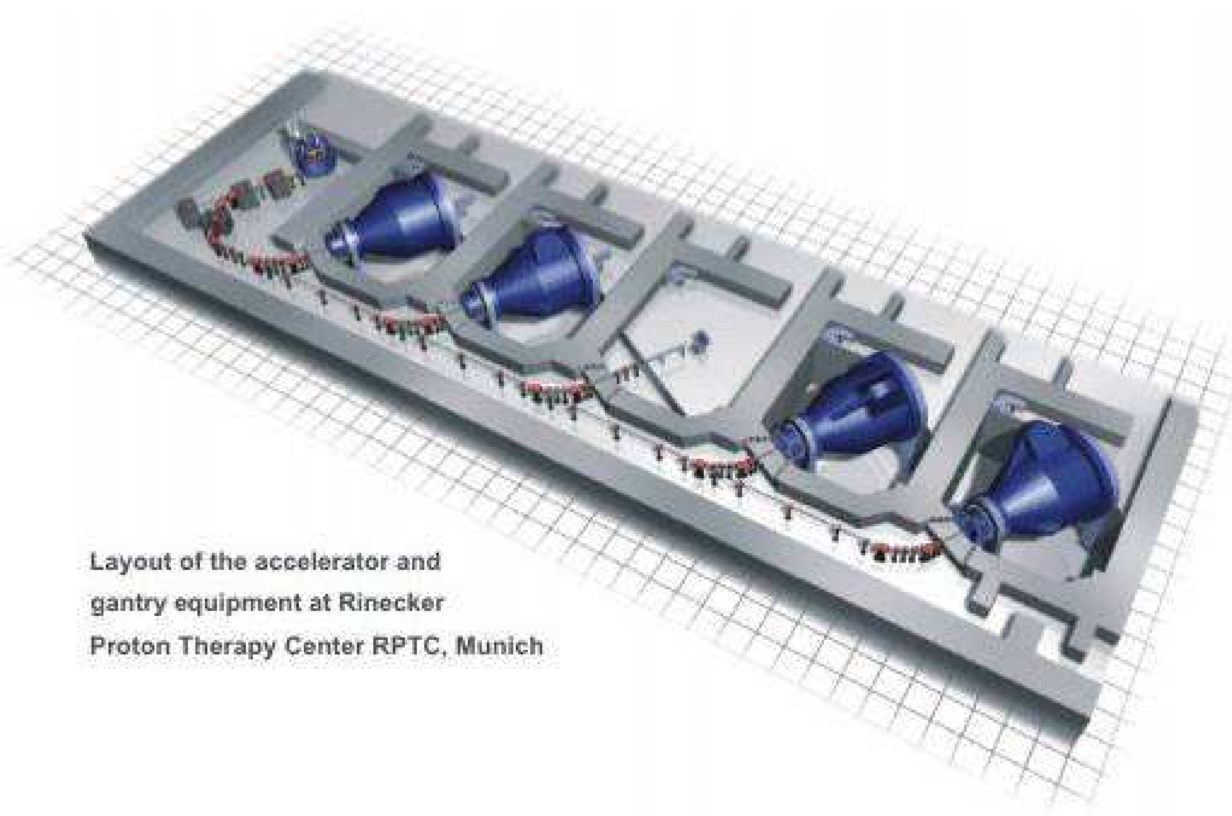


ACCEL VARIAN

- The RPTC in Munich
  - The first industrial proton facility based solely on scanning (operation planned for beginning 2009)
  - Same accelerator as used at PSI

Control and safety systems
Certification

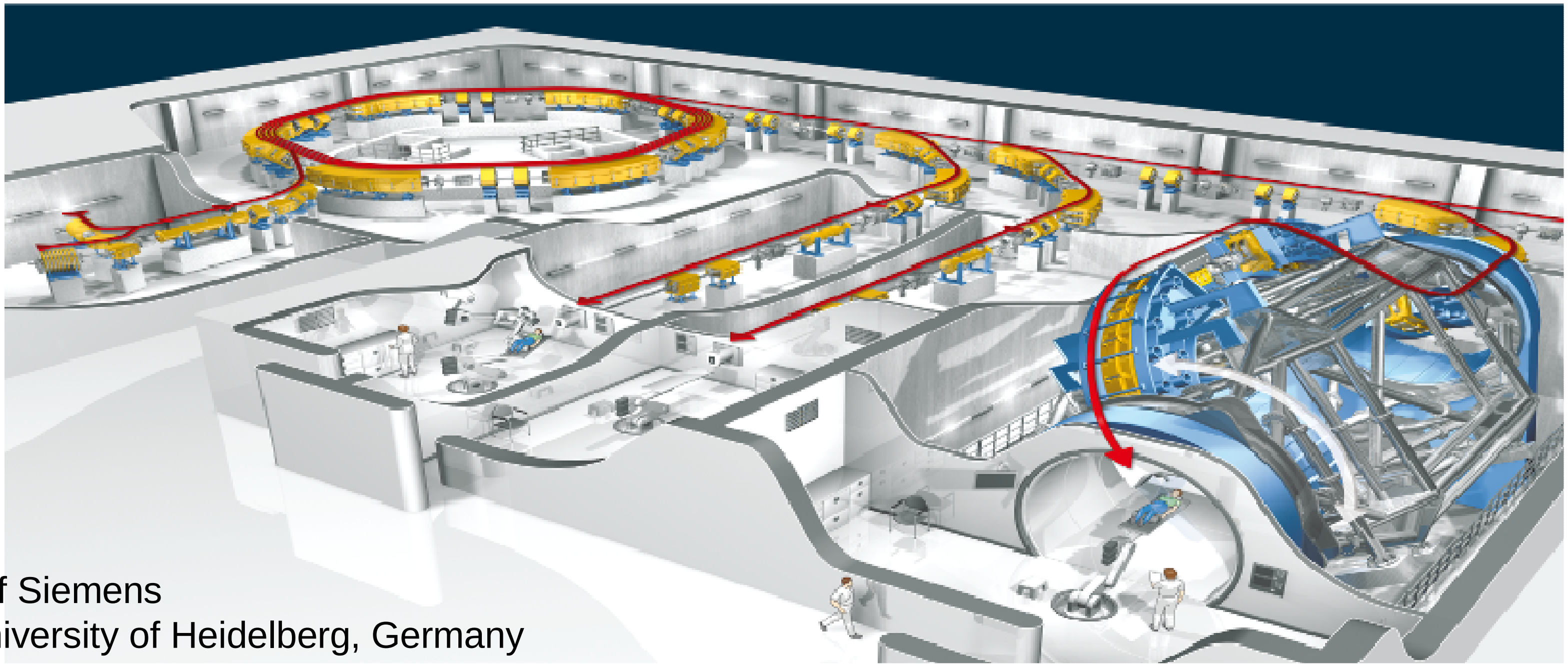
The issues causing delays of
commissioning
commercial systems



Layout of the accelerator and gantry equipment at Rinecker Proton Therapy Center RPTC, Munich

The University of Heidelberg Project
Heidelberg Ion Therapy Center (HIT)

- The first and only gantry for carbon ions therapy in the world
  - 600 tons
- Facility design by GSI
  - Commercial partnership with Siemens

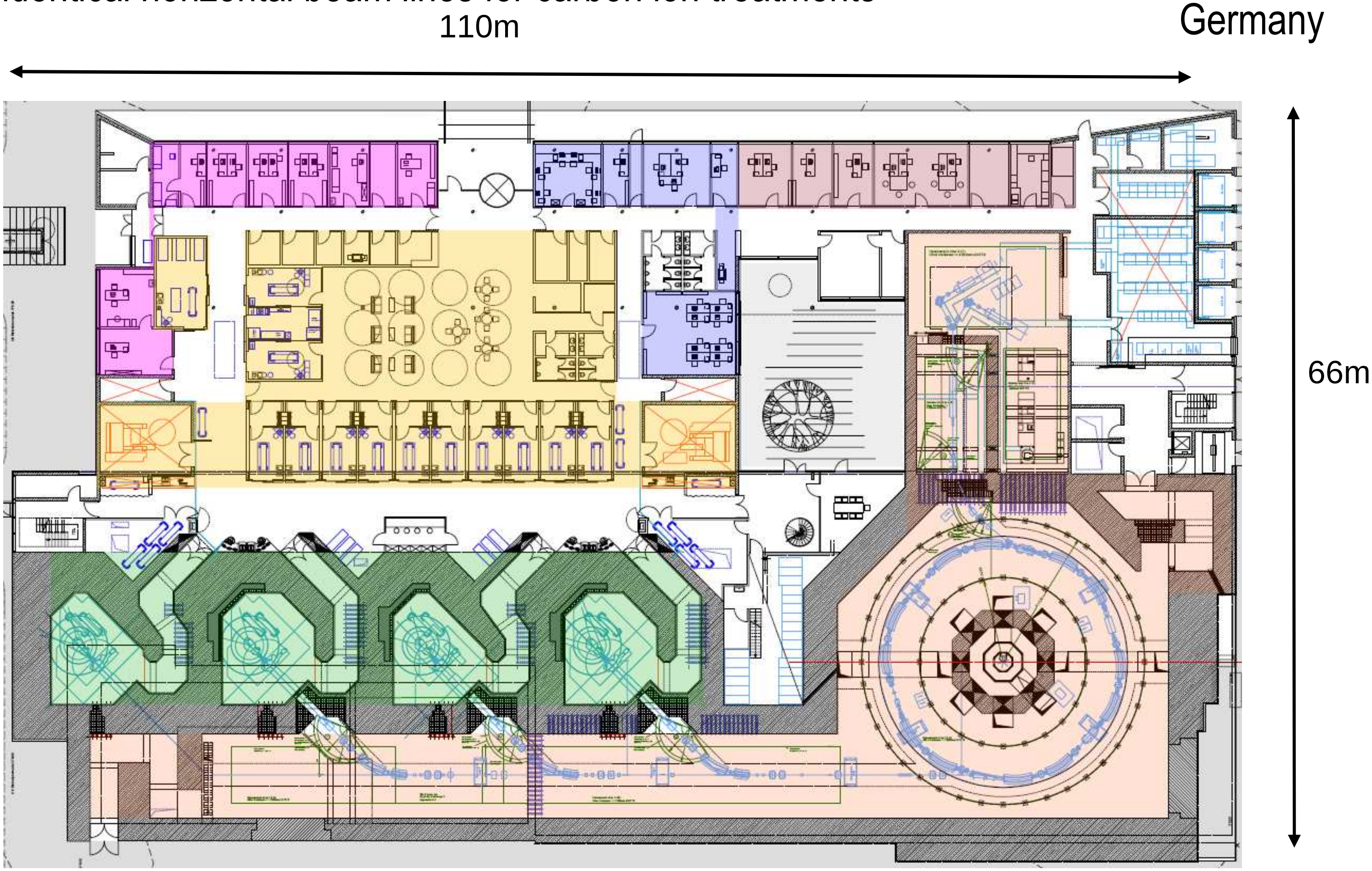


Courtesy of Siemens
And the University of Heidelberg, Germany

Rhön Klinikum AG - University of Marburg /Giessen

Courtesy of Siemens and Rhön-Klinikum AG, Germany

The first commercial system for carbon therapy in Europe
4 identical horizontal beam lines for carbon ion treatments

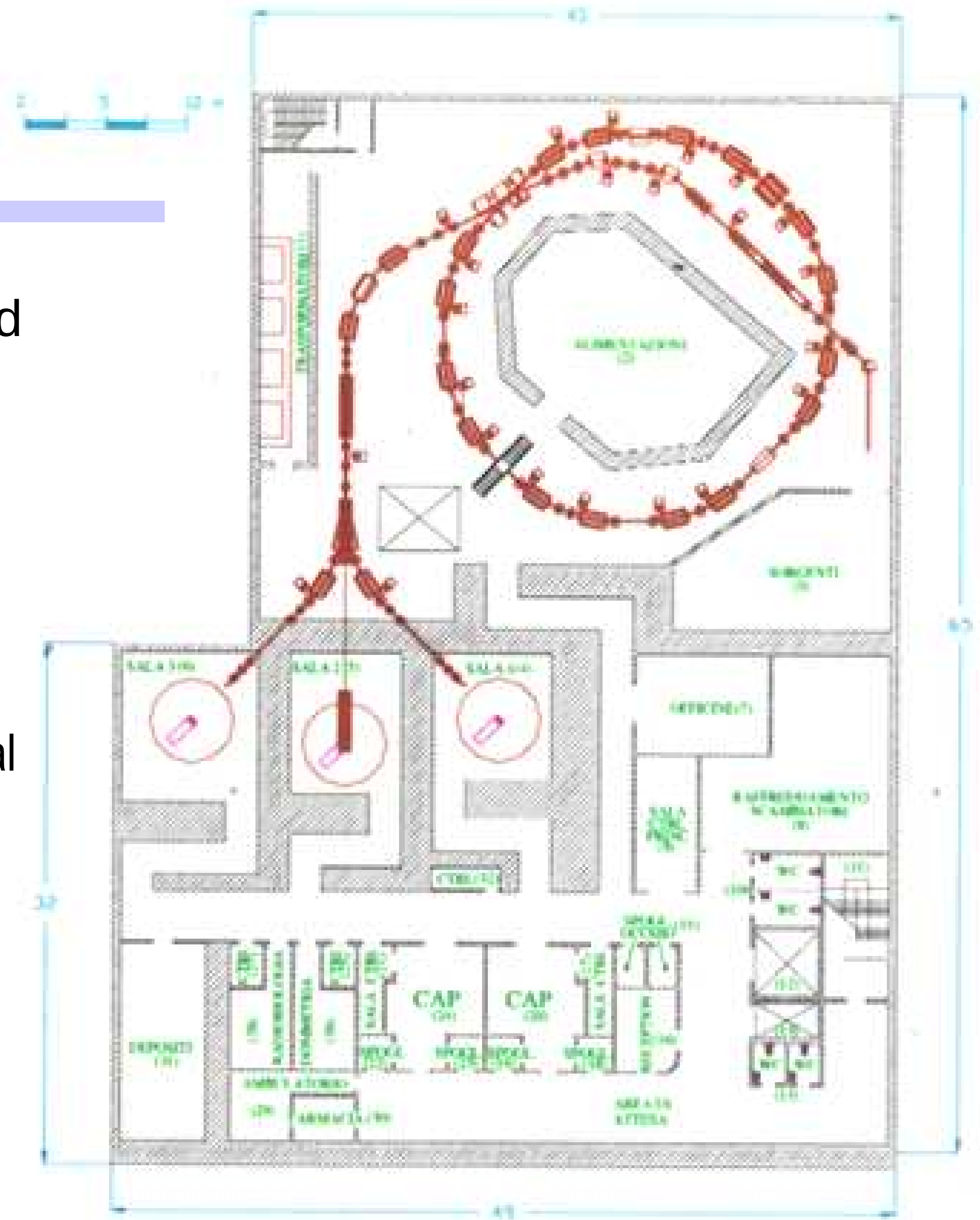


CNAO
Centro Nazionale di Adroterapia Oncologica, Pavia, Italy

- Combined system for protons and carbon

  Initiated by Ugo Amaldi at CERN (TERA project)
  - Synchrotron
  - 3 areas with fixed beams
  - One area with horizontal and vertical beam line

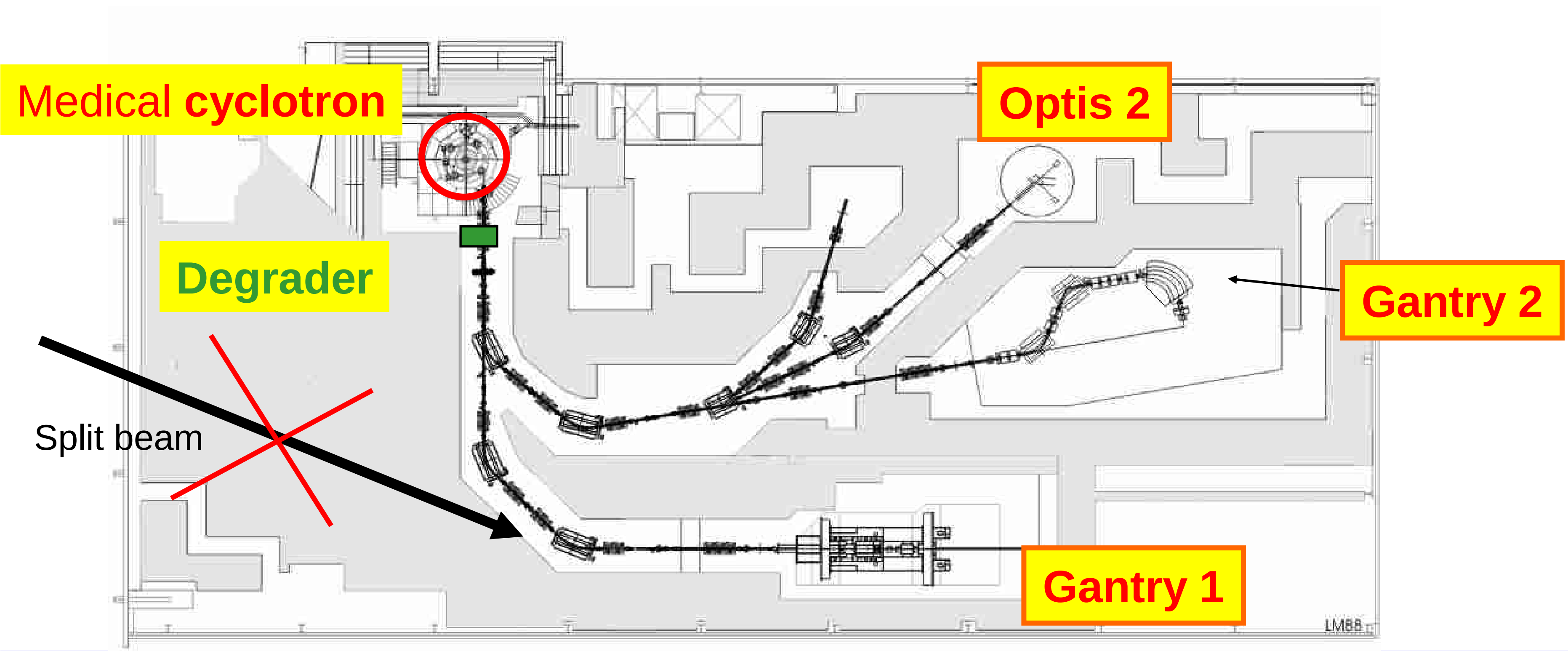
- Open possibility to expand the facility with proton gantries later
  - Eventually a good idea …



5.
The strategy of PSI
past experience and concepts for the future

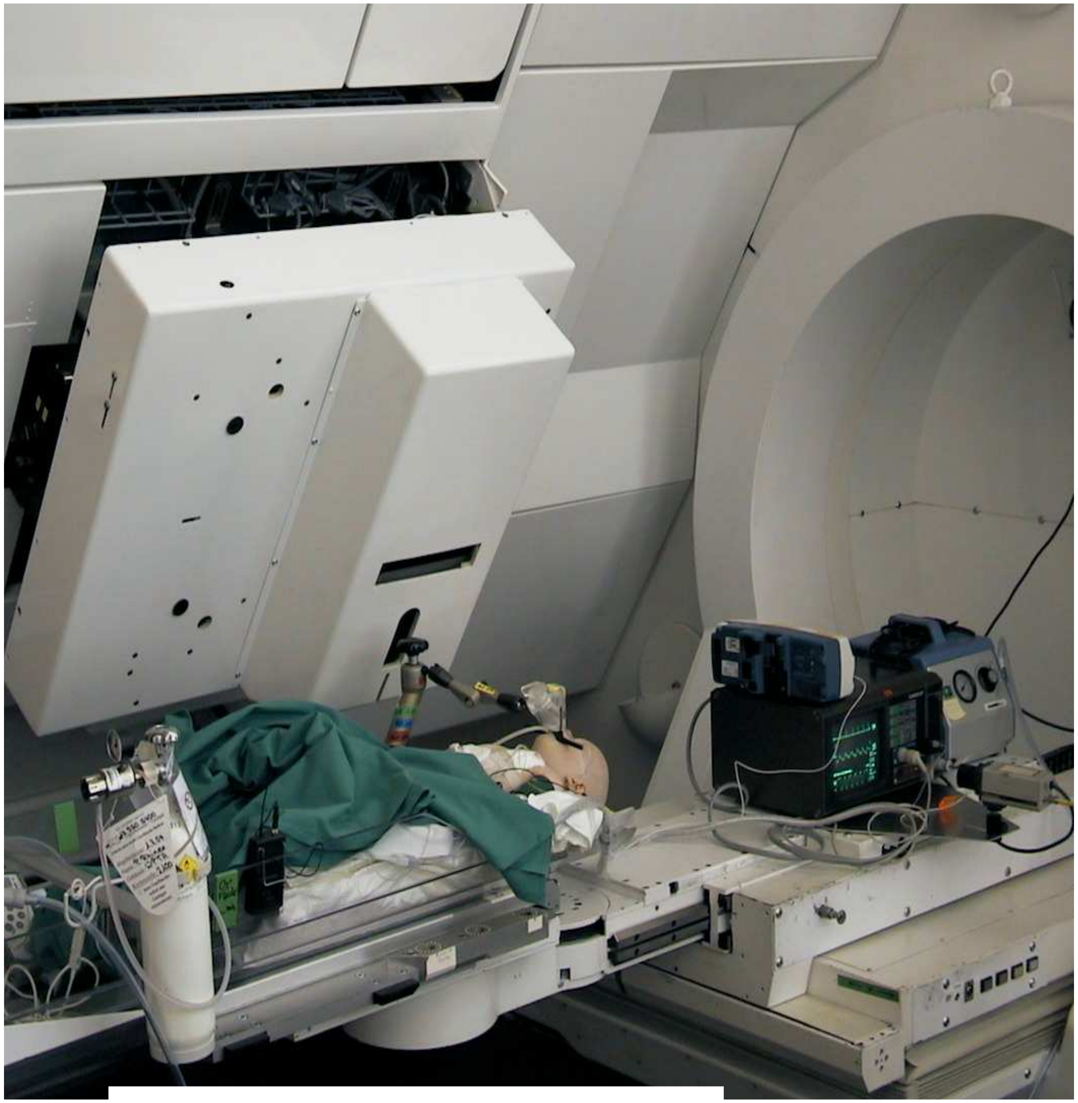
The ongoing expansion of the PSI proton therapy project

- A new dedicated accelerator (superconducting cyclotron COMET)
- Treatments with Gantry 1 restarted in April 2007
- A new Gantry 2 (for the further advancement of our scanning technology)
- Optis 2 (transfer of the eye treatments from Injector 1 to COMET)



Continuation of the successful treatments with Gantry 1

- 15 patients/day (8:00-16:00)
- Clinically proven indications
  - Base of skull and spinal chord and low pelvis
  - Only non moving tumors (due to scanning)
    - Excellent results
- Of great interest
  - Pediatric tumors (1/3 patients)
  - Below 5 years with anesthesia
- Gantry 1 is fully booked
  - Not possible anymore to explore new indications
  - Example of a child treatment under anesthesia at PSI



Courtesy of B. Timmermann PSI

The new Gantry 2 of PSI: the next generation system for developing the treatments of moving targets with pencil beam scanning

- First beam through the new PSI Gantry 2 on May 9 2008

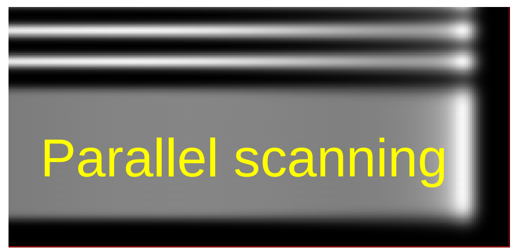
- New development goals
  - Much faster scanning …

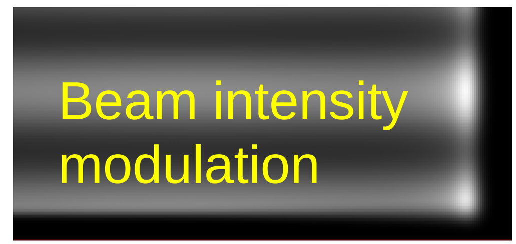
The cyclotron used as an active component for the beam delivery

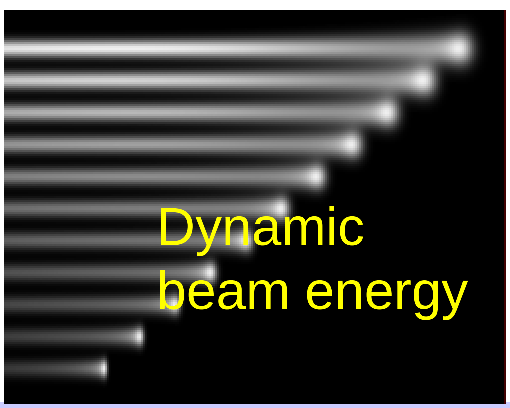
- 250 MeV superconducting cyclotron (COMET)
  - Delivered by ACCEL Varian in 2005
- DC beam
  - Very stable beam at the ion source
- Dynamic control of the beam intensity
  - Deflector plate at the first turn of the spiral
    - Control at a few 100 μs time scale
- Fast dynamic energy changes
  - With degrader and beam line
  - 150 ms for a 5 mm step of proton range
    - *90 ms shown in the beam line to Gantry 2*
  - Much faster than with a synchrotron

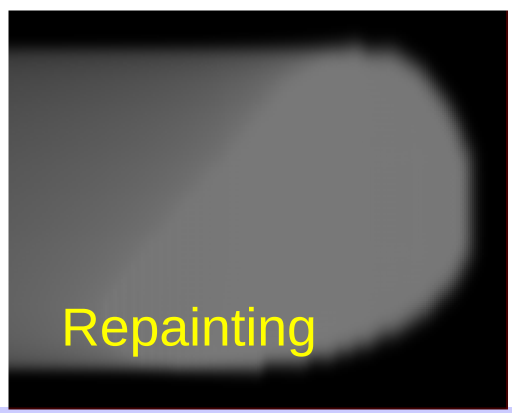
Cyclotron solution with advanced scanning: …. a new state-of-the art soon?

- Double parallel magnetic scanning
  - Continuous scan - speed of 1 cm/ms (equivalent to 2 kHz pulses on a 5 mm grid)
- Dose control through
  - Dynamic modulation of the beam intensity (1mm = time scale of 100 μs)
- Fast energy variations (for volumetric repainting)
  - With degrader and beam line 150 ms per energy step (90° gantry magnet - the limit)
- Repainting capability
  - Factor 10 compared to Gantry 1





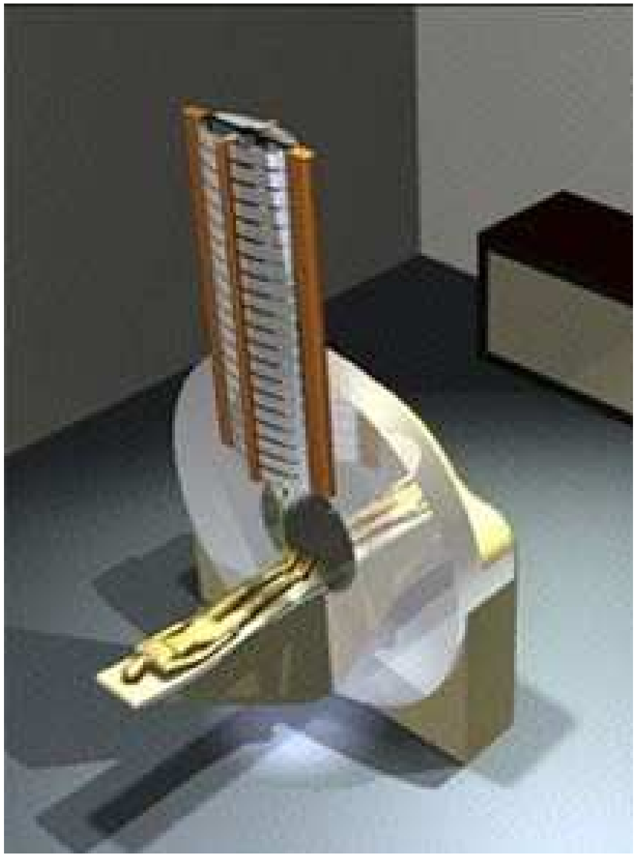




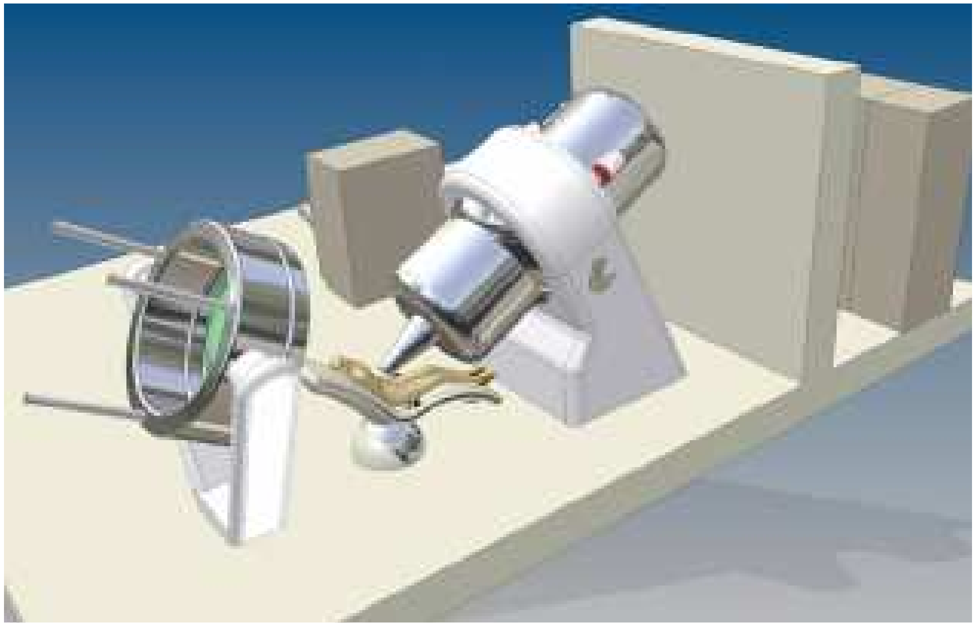
6.
New accelerator concepts

The “dream” solution

- Why not proton therapy like photon therapy?
  - From Photon-Tomotherapy to Proton-Tomotherapy ?
    - Distal tracking? Rotational therapy with protons?
  - (T.R. Mackie)



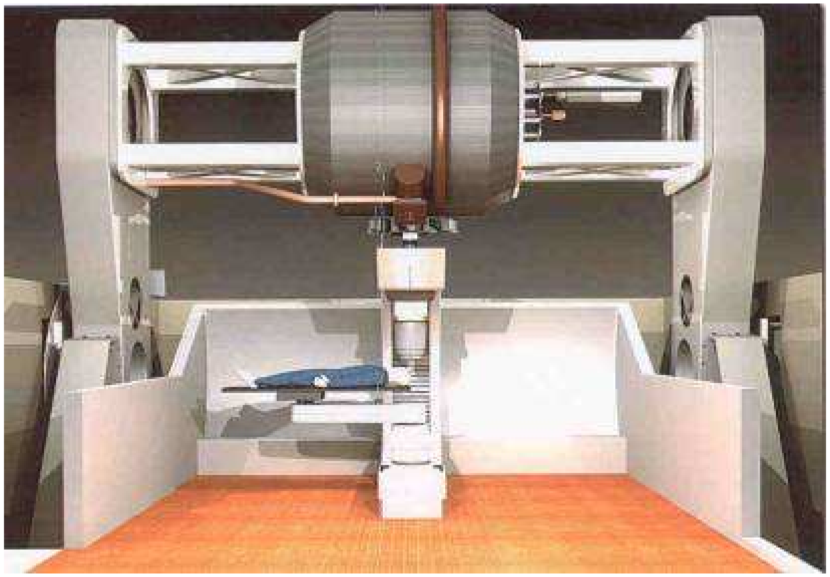
High gradient (100 MeV/m) Linac (dielectric wall)



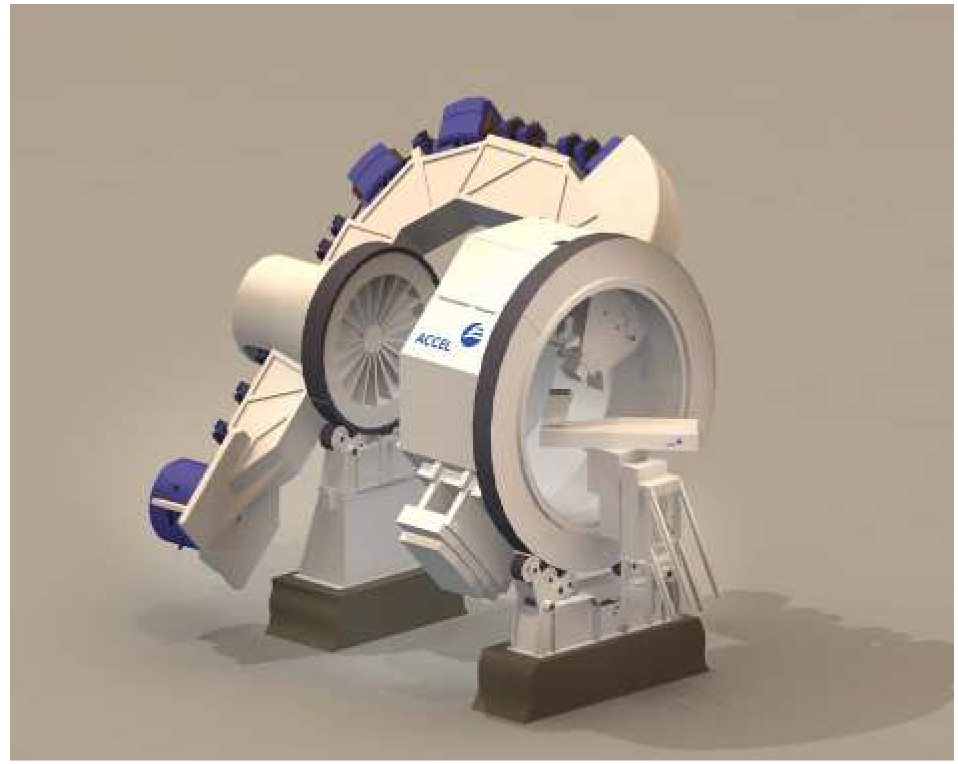
Caporaso et al, Nucl Instr Meth B 261 (2007) 777

…going for further simplifications?

- Very compact synchro-cyclotron
  - Single room solutions for small size hospitals



- Still/River company (USA)
  - Passive scattering
    - Neutron background?
  - How many compromises?
- Half a dozen of system already sold beforehand?



- ACCEL Varian
  - Compact synchrocyclotron on gantry
  - With degrader and beam analysis

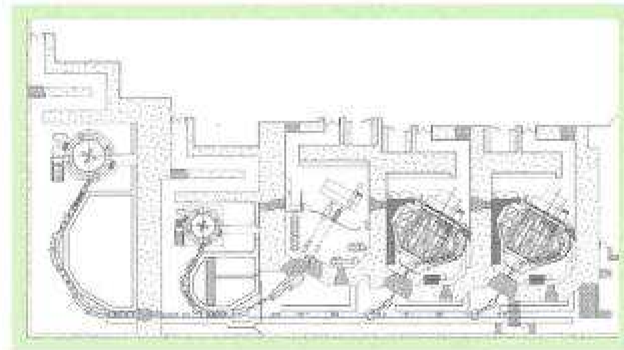
Accelerators related-to-therapy new developments

- New interesting concepts
  - Cyclinac: isotope production cyclotron coupled to a boosting Linac (Ugo Amaldi)
  - Fixed Field Alternating Gradient (static beam line)
    - FFAG Gantry (energy changes as fast as in lateral direction – ideal for tracking?)
  - Laser driven acceleration (how to control energy and dose simultaneously?)
  - Plasma wake field acceleration
- Common to the mentioned solutions: the idea to provide
  - Variable energy with the accelerator (to avoid the use of a degrader – a big issue?)
- Challenges for the (rapid) pulsed beam solutions
    - To compete with a continuous fast scanning with a cyclotron (for repainting – for mitigation of organ motion errors) one needs
    - Repetition rate of ~ 1 KHz?
    - Control of the dose pulse by pulse: pulse dose precision of < 1%?
- The difficulty
  - Reduce size and costs and improve beam delivery performance

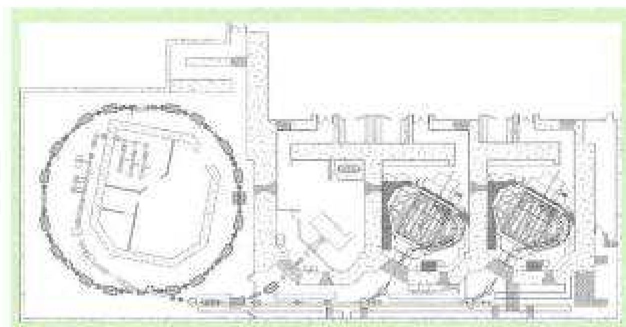
And for the ions?

- The missing points …
- Superconducting gantry for ion therapy
  - Same dimensions as a proton gantry
- Superconducting cyclotron for ion therapy
  - Advantages for fast scanning and intensity modulation of the beam
    - Prototype being build in CAEN France by IBA
- Two cyclotrons layout (protons + ions later)
  - Stepwise realization
  - Acquire experience with protons first (simpler) approach carbon ions (more complex – the research part – boost therapy) later
- New exciting initiatives of Ives Jongen
  - IBA entering the field of ion therapy

Two steps approach*



Synchrotron approach*



From an IBA flier

7.
Conclusions

The general trend in hadrontherapy today in the world

- The field is just now "booming"
- Equipment available on commercial basis
  - Big industry entering the field (the most established radiotherapy providers)
- Pencil beam scanning is accepted as a need
  - For competing with IMRT
- Proton therapy
  - Well established indications (and more to discover)
    - Eye treatments, base of skull, spinal chord, low pelvis
    - Pediatric tumors (should not be treated with high LET)
    - Developments towards treatments of moving targets
    - And Hypo-fractionation
  - Decision based only on the quality of the dose distribution (comparison protons-photons)
  - Costs reimbursed by the health insurances
  - Estimate: 10-15% of all radiation therapy patients should profit from protons
  - Worldwide experience: 45'577 patients treated with protons (end 2007)

The general trend in hadrontherapy today in the world

- Carbon ion therapy (only)
  - Still a research issue (radiobiology expertise – molecular radiobiology potential)
  - Treatment reimbursement?
  - Total number of treated ion patients: 4’450
  - Estimated fraction of patients profiting from ions: 1/5 of the (protons + ions) cases
    - But: Ion therapy has more potential for surprises than protons (radiobiology)
  - Recent good results with hypo-fractionated lung treatments in Chiba
    - Exciting results (but the comparison with hypo-fractionated protons is missing)
  - Clinical evidence of superiority of carbon ions over protons? – task for the new centers
- Ion facilities delivering also proton therapy (mixed facility)
  - Not fair, if this is only for cross-financing carbon therapy
  - Yes, if proton therapy is properly done
    - Proton gantries - Nozzle optimized for proton therapy (for a small pencil beam)
    - The most attractive treatment with such a facility? (not feasible with protons alone)
      - Initial carbon ion boost (1 room) followed by fractionated protons (gantry rooms)
      - Back to the original idea? … Proton facilities with a carbon ions option?

For sure
A new field with new interesting job opportunities
for young accelerator physicists and engineers

Thank you

This is an overview talk. I apologize if I could have offended some copyright issues by using scanned images and pictures from the web. The intention was to give credit to the mentioned authors and institutions.