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Hadron Therapy and

The New PArticle Therapy REsearch Center

(PARTREC)

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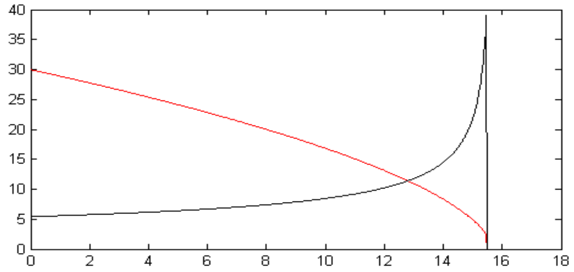
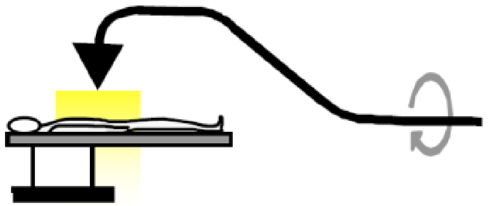
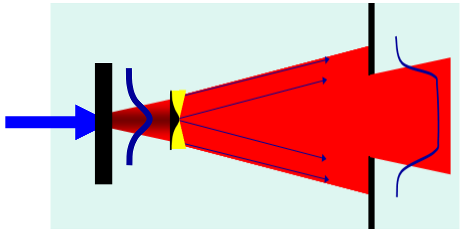
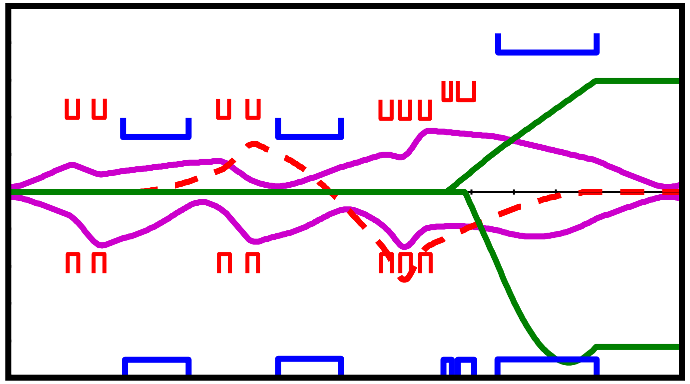
- Beam optics properties
- PARTREC









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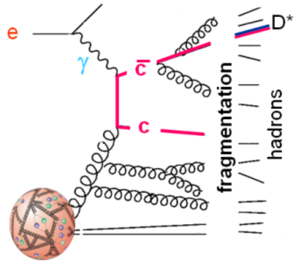
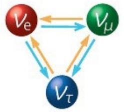
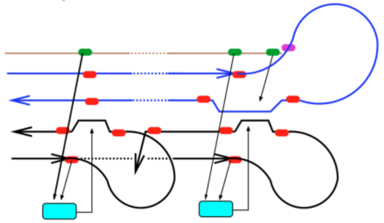
Background Information and Study

- Born in Moscow, moved to Hamburg in 1999
- Interested in particle physics during school time
  - DESY internship on optical fiber linking (2002)
- Study of physics in Hamburg (2005-2008)
- DESY summer school (2008)
  - Determination of parameters of charm production in deep inelastic scattering
- Master’s degree in mathematical physics at Cambridge (2008-2009)
  - Neutrino Oscillation and Neutrinoless Double Beta Decay
- Doctoral Thesis at CERN / Oxford (2009-2013)
  - Thesis topic: CLIC Drive Beam phase stabilisation







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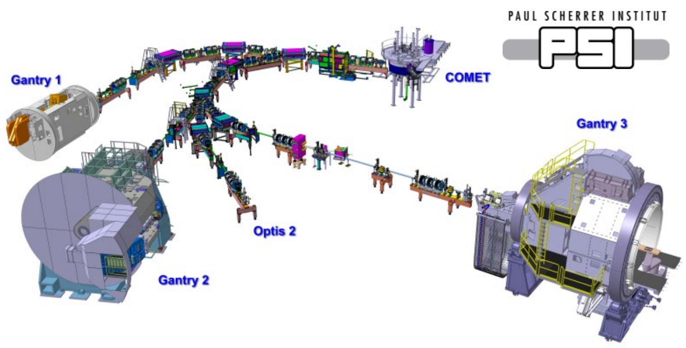
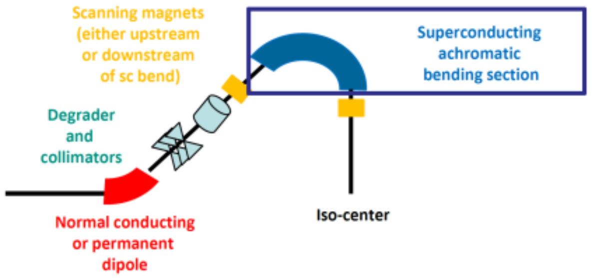
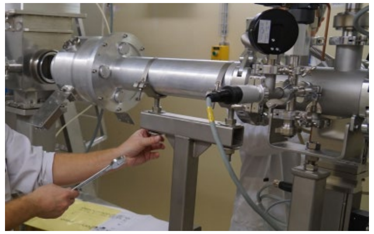
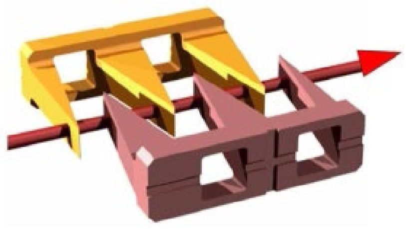
Postdoctoral Fellowship at PSI (2013-2017)

- Operation and maintenance of PROSCAN
  - Switzerland's only proton therapy facility
    - → Very high availability is required
- Leading Gantry 3 beam commissioning
  - First patient treated in 2018
- R&D for proton therapy beamline and gantries
  - Superconducting gantry beam optics design
    - → Prize for best publication of year 2016 by Journal of Medical Physics (ZMedPhys)
  - Testing of non-disruptive beam monitors
    - → Implemented in 2019, worldwide first of the kind
  - Development and testing of B4C degrader

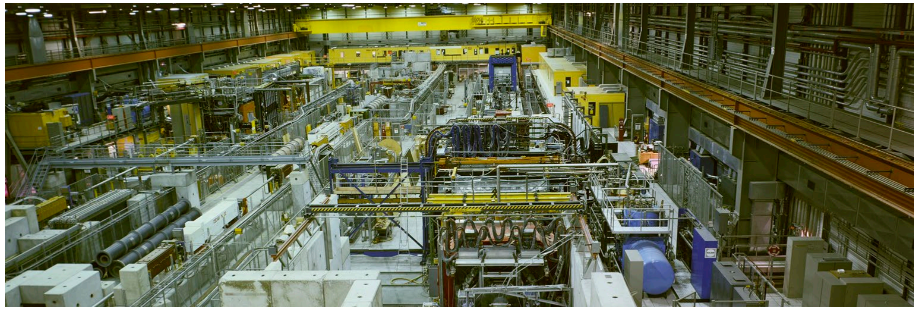




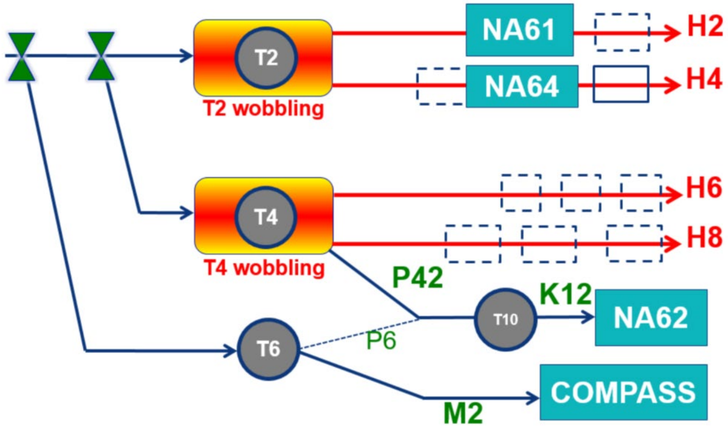


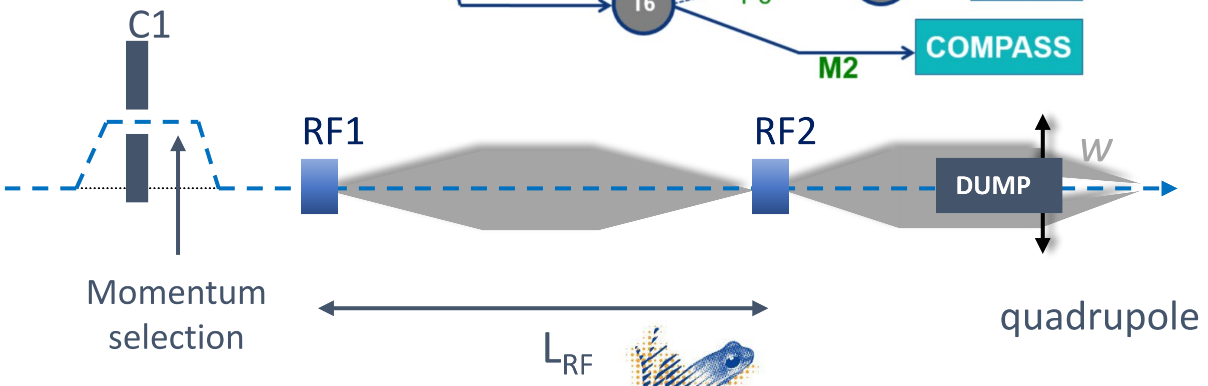


CERN Experimental Areas (2017 - 2022)



- Exploitation of H6, H8 and M2 beamlines in SPS North Area
  - Over 2 km total length
- Liaison with 100s of test beam users per year for
  - Understanding of the experiment requirements
  - Setting up the beams flexibly in regards to particle type, energy, intensity etc.
- Leading RF Separated Beam Study (~60 MCHF project, mostly external funding)
- Developing the beam lines for particle therapy
  - GaToroid gantry for proton and ion therapy
  - FLASH VHEE therapy facility





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UMCG – PARTREC (since 2022)

Professorship at Particle Therapy Research Center (PARTREC) with the task to:

- Develop research programme,
- Lead the advancement of facility capabilities,
- Secure funding,
- Contribute to educational programs.

- Discuss PARTREC at the end of the presentation – stay tuned!

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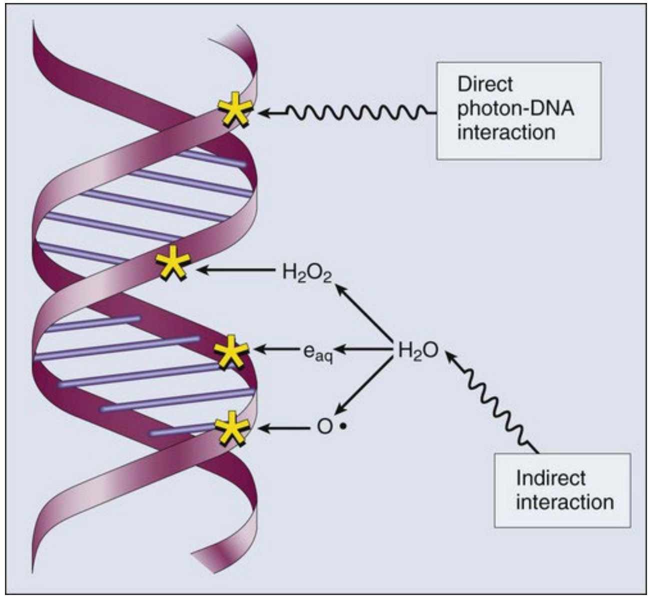
Introduction: Hadron therapy

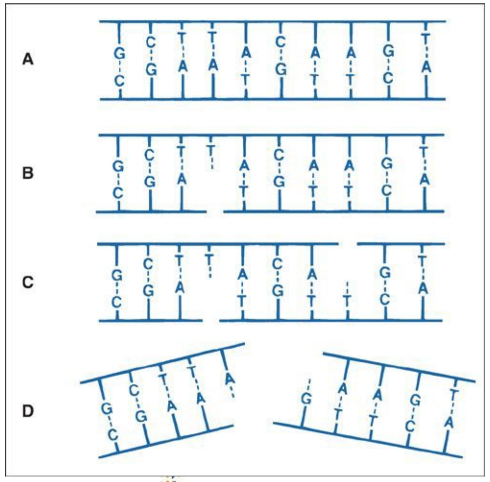
Mechanism of radiobiology



- Direct and indirect interraction
- Single DNA strand breaks are usually reparable
- Double DNA strand breaks are usually irreparable

Dose is measured in gray

$$1\ \text{Gy} = 1\ \frac{\text{J}}{\text{kg}} = 1\ \frac{\text{m}^2}{\text{s}^2}$$



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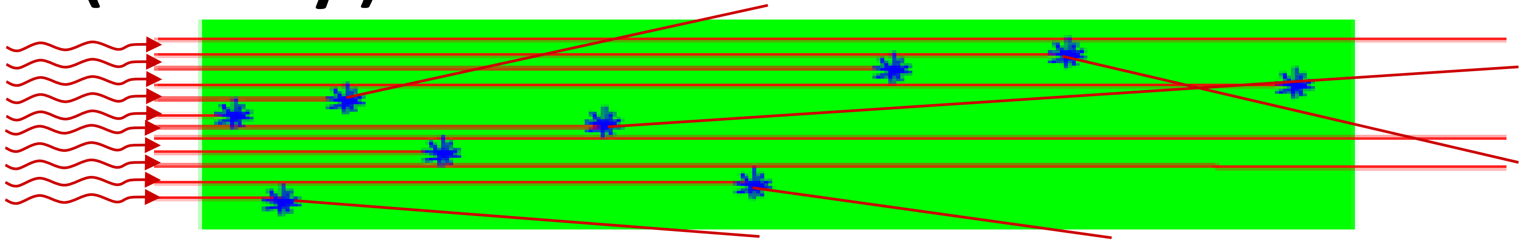
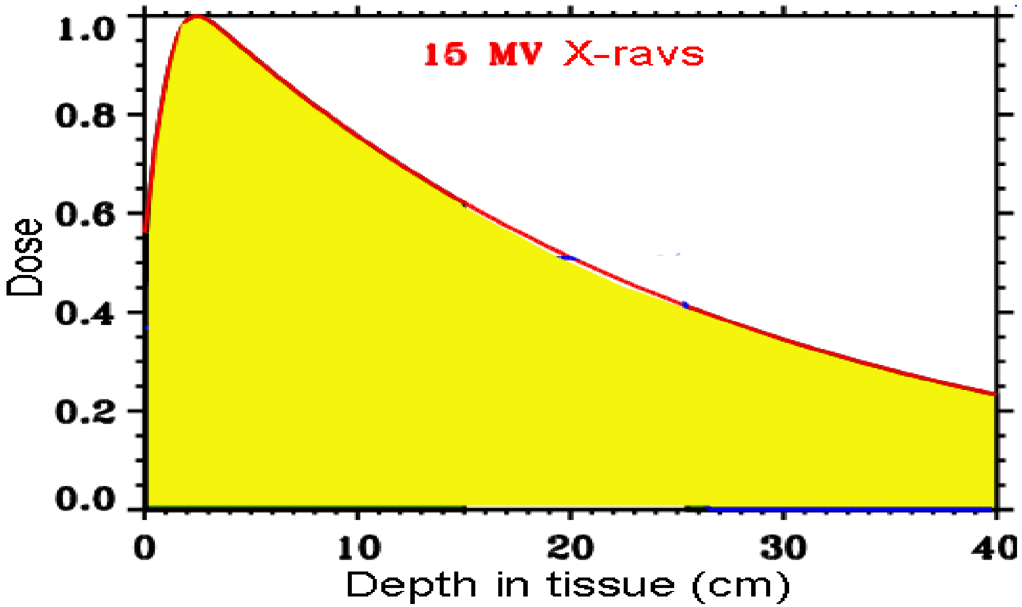
Photon (X-ray) dose



X-rays **scatter** and are **absorbed** → energy deposition in "dots"



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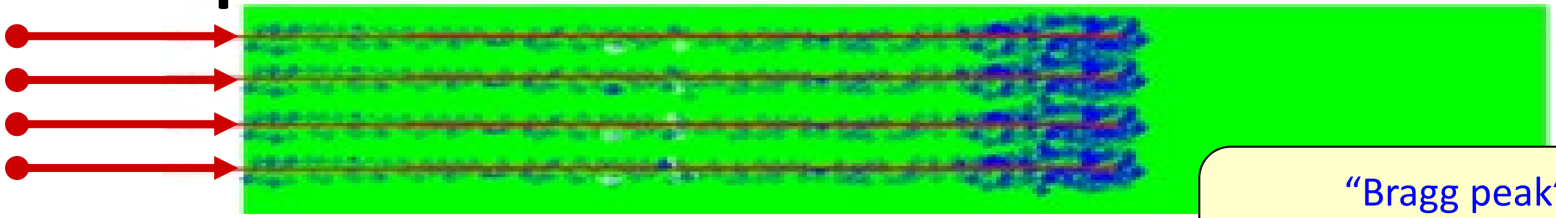
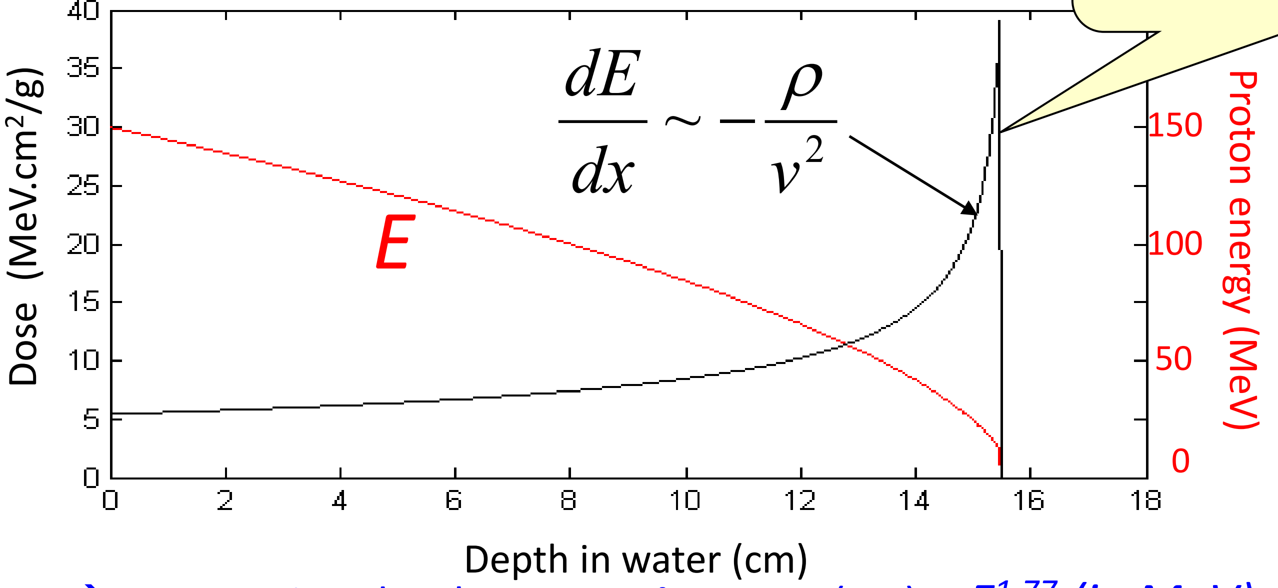
Proton depth-dose curve



Protons **slow down**



"Bragg peak"
(named after
Sir William Henry Bragg)

→ Energy → Penetration depth **Range in water** (cm) ≈ *$E^{1.77}$ (in MeV) / 450*

Range scales with 1/density: $1/\rho$

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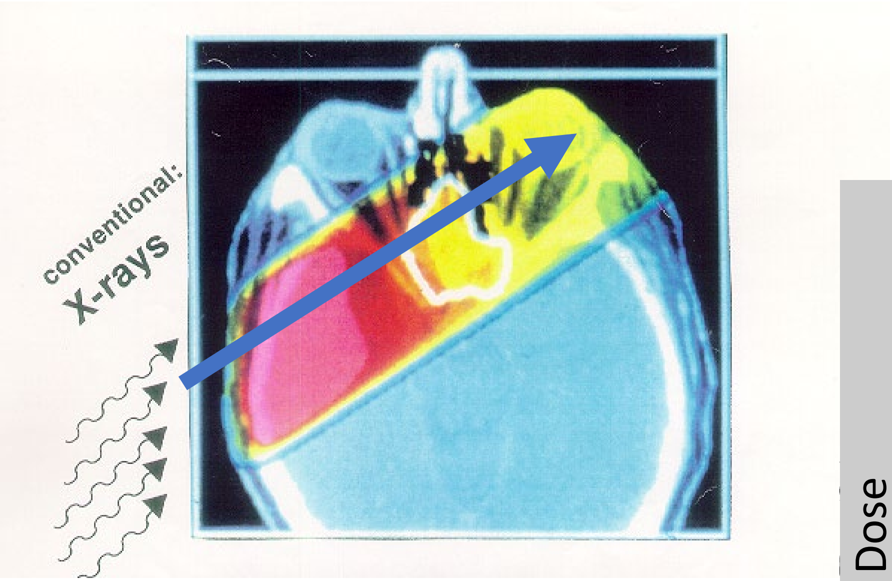
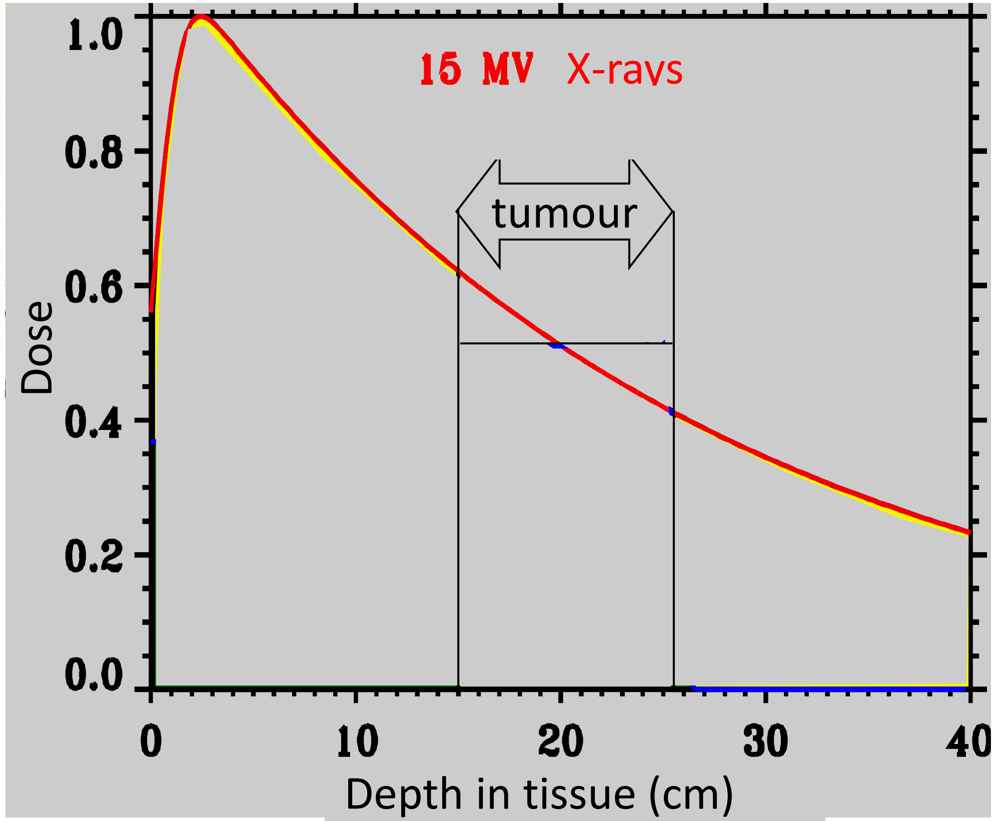
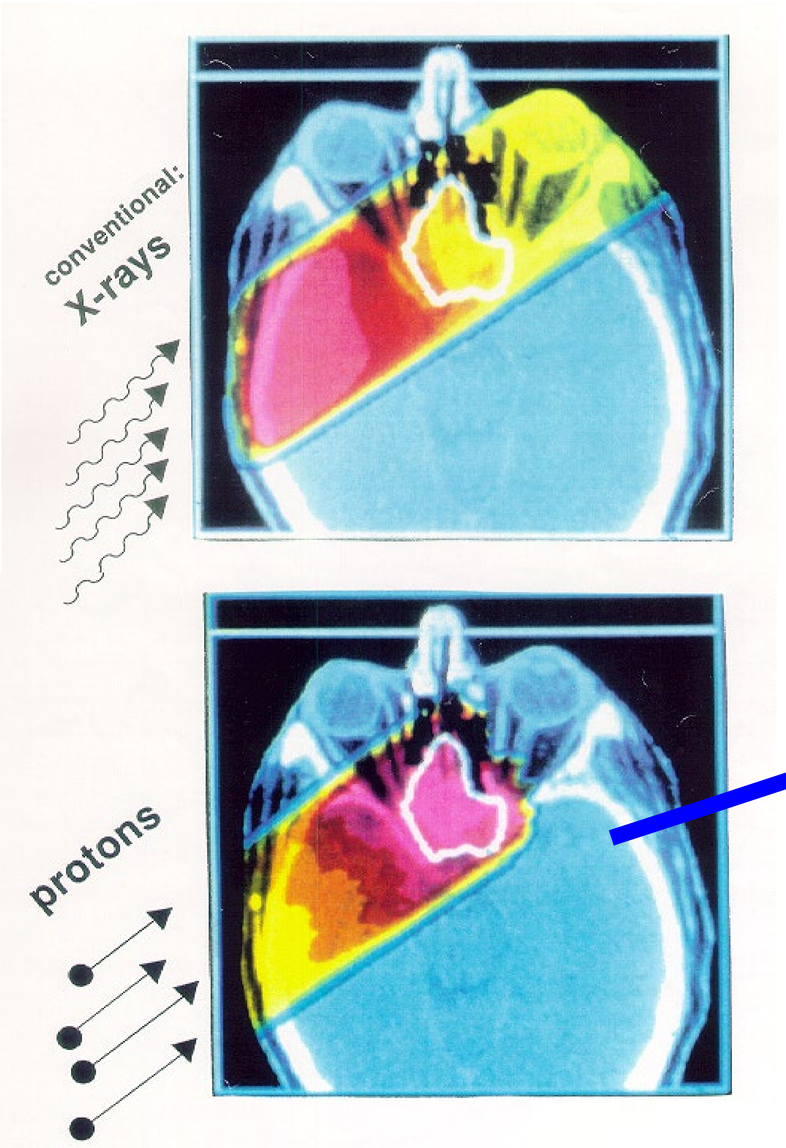
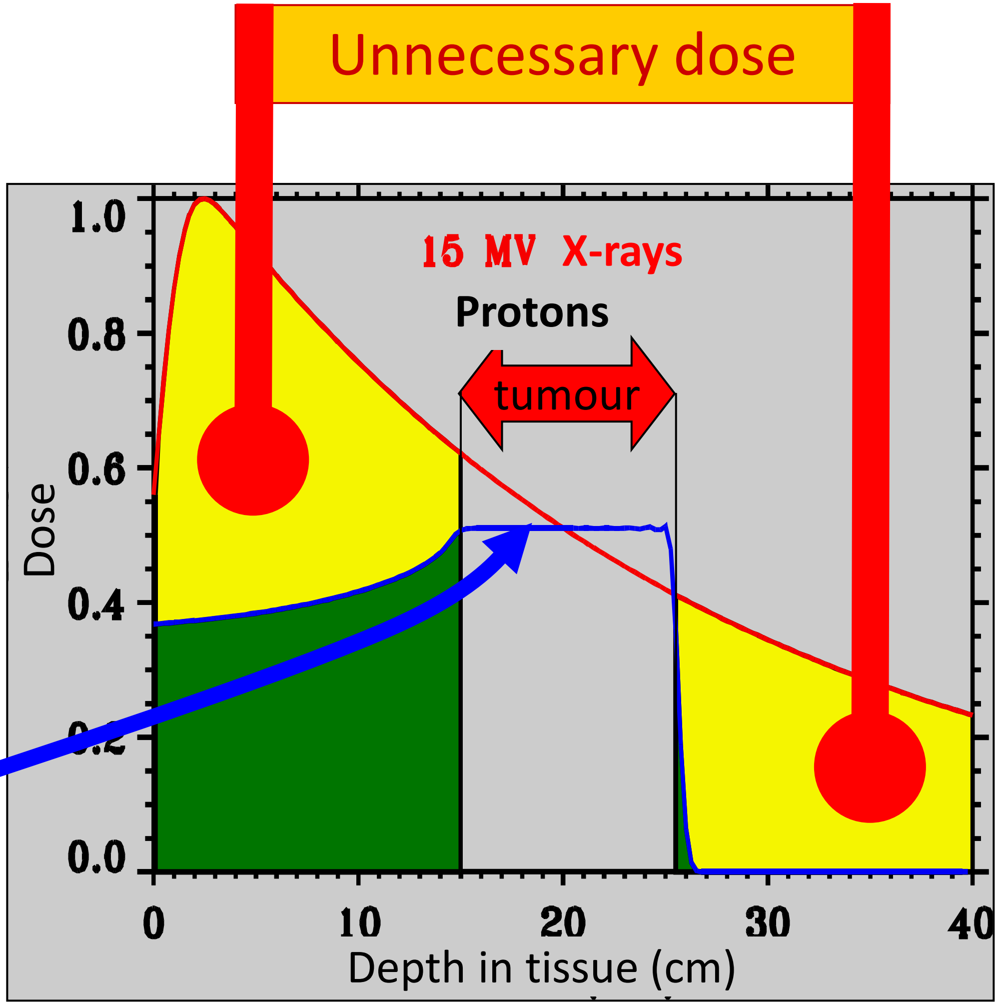
X-rays vs. Protons





X-rays vs. Protons

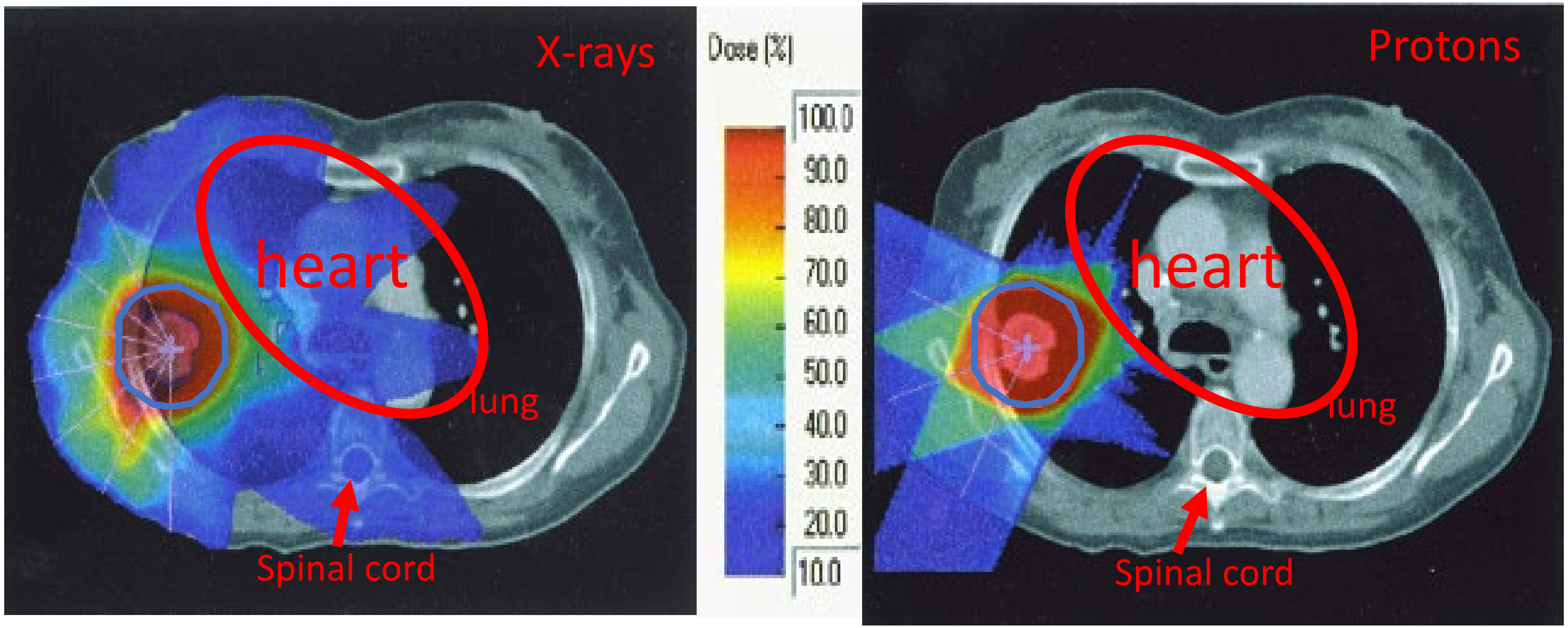




X-rays vs. Protons

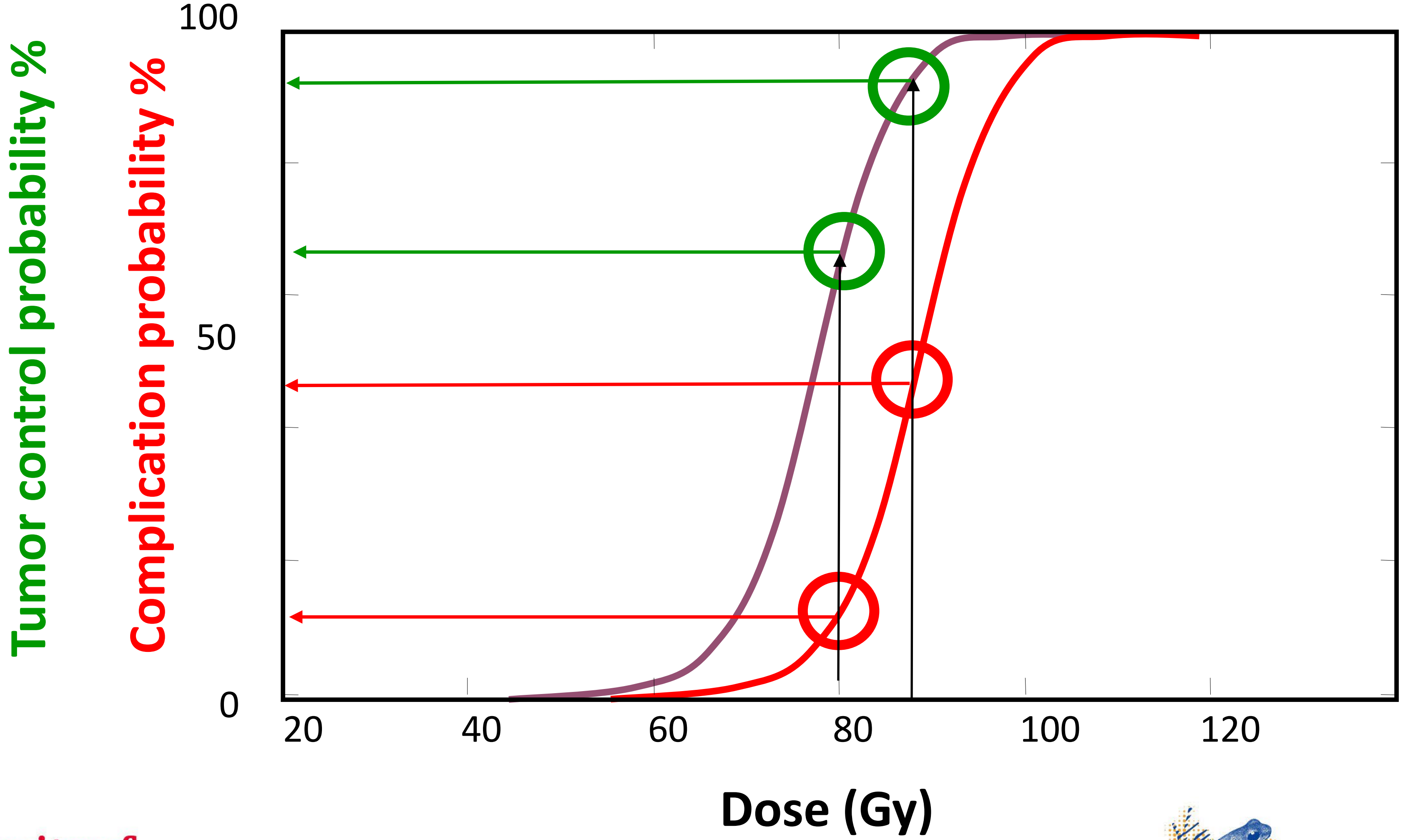
X-ray beams (IMRT)
from 7 directions

Proton beams
from 3 directions



pictures: Medaustron

Therapeutic Window



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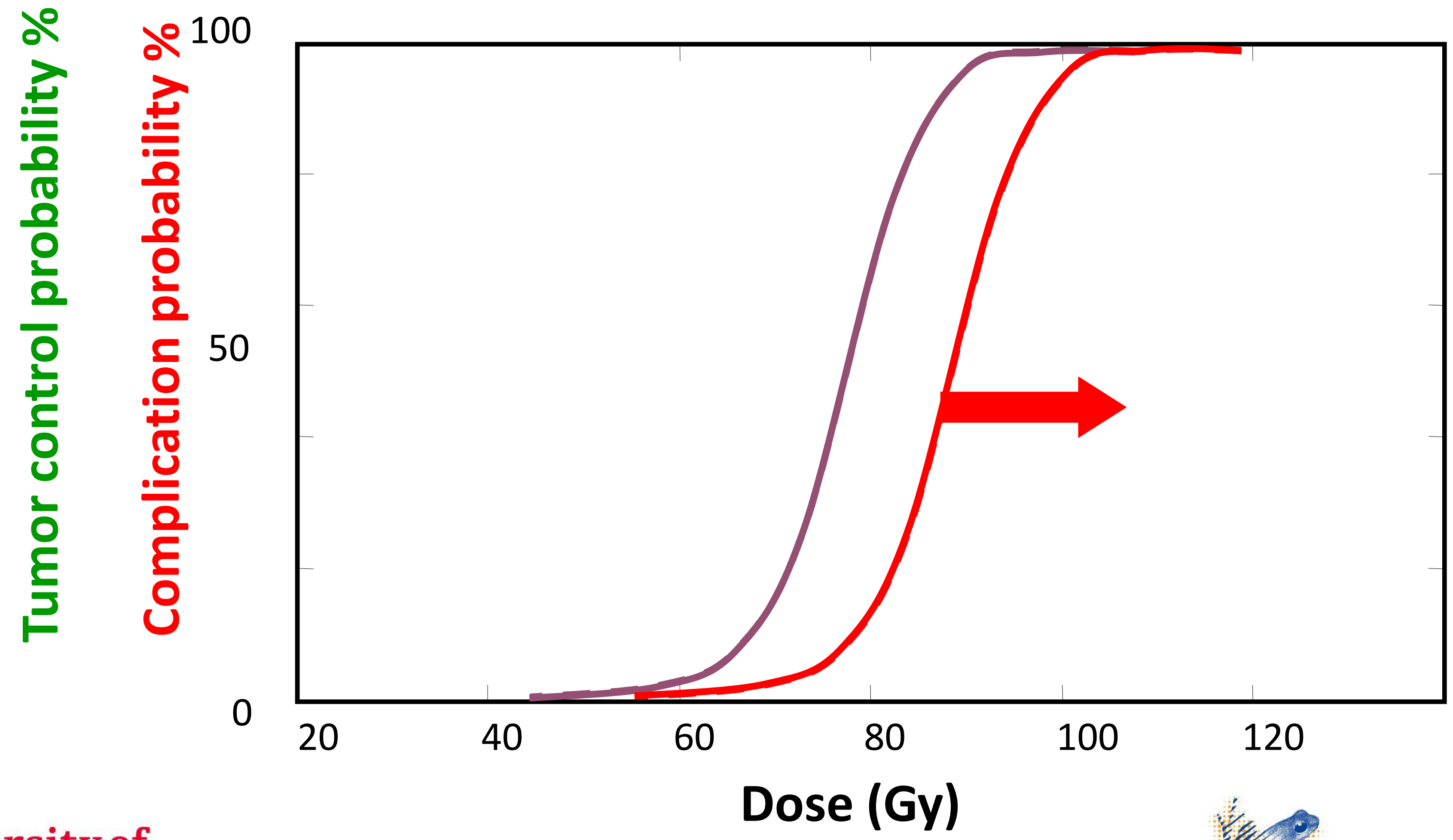
Protons irradiate less normal tissue



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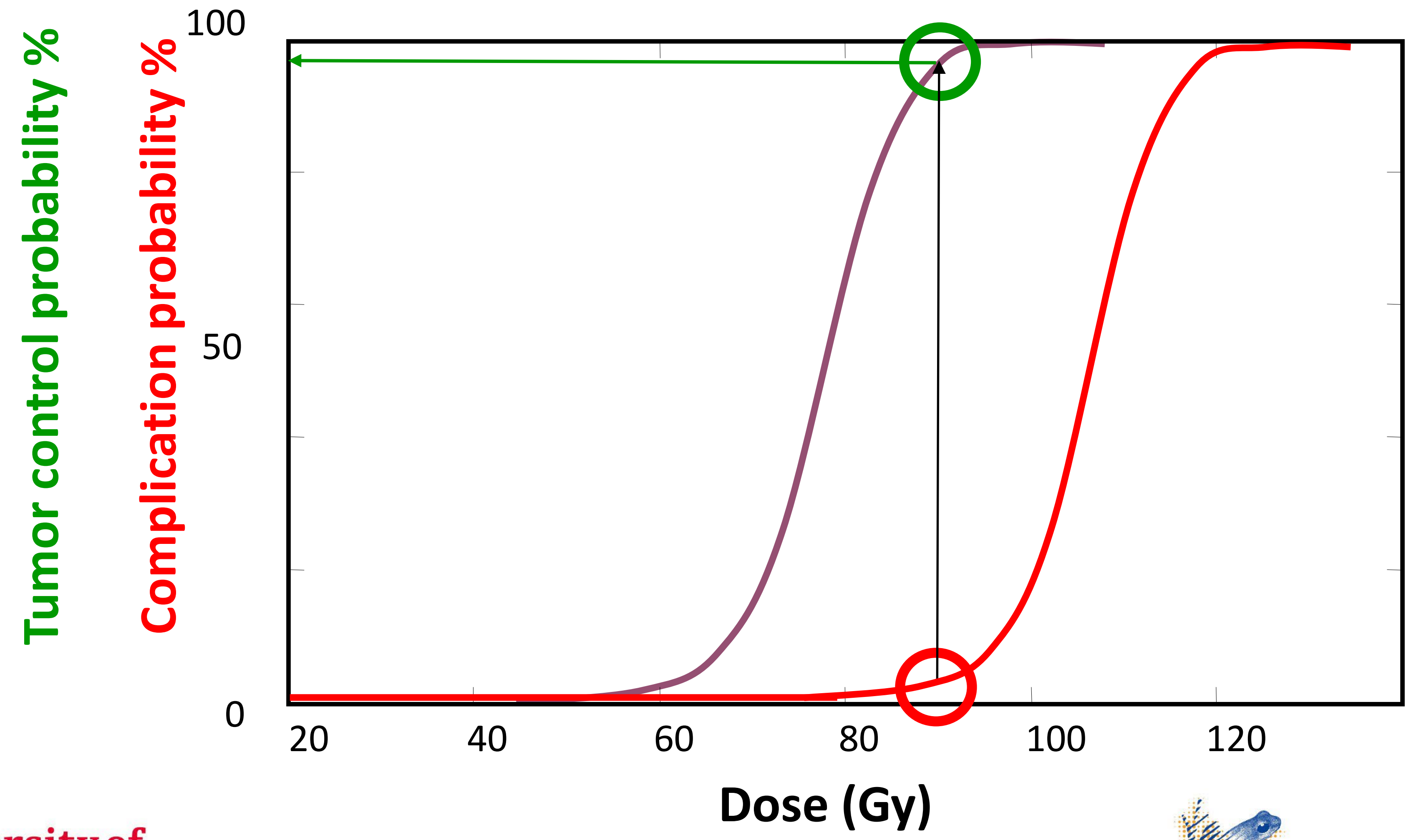
Therapeutic Window



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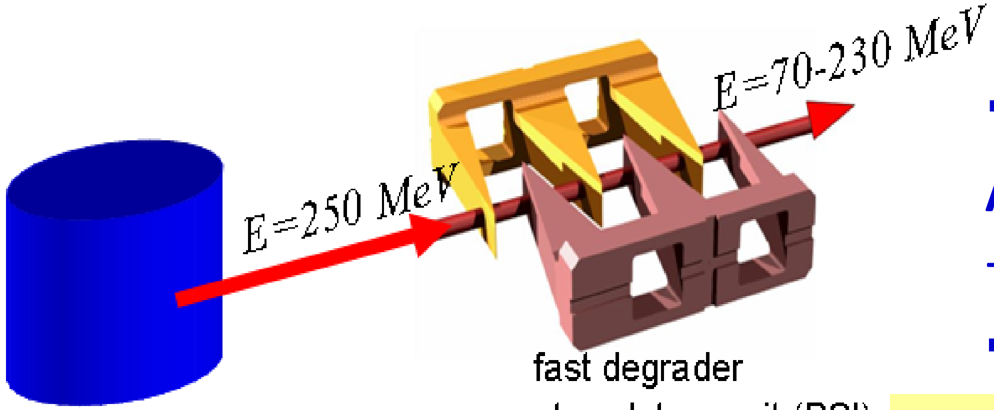
Possible facility and gantry layouts

Cyclotron driven facilities

Cyclotron has fixed energy => slow down (degrade) to desired energy

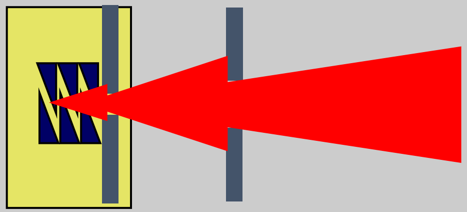


- ➔ Sets range

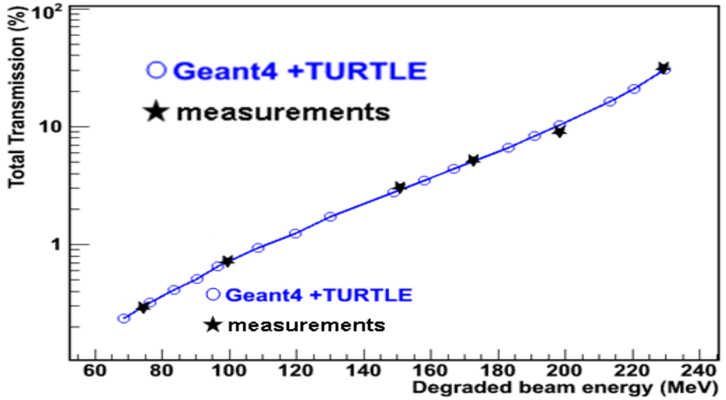
And, if fast enough
+ fast magnets:

- ➔ also energy modulation

: 5 mm ΔRange in 50 ms



Collimators define
transmitted beam size

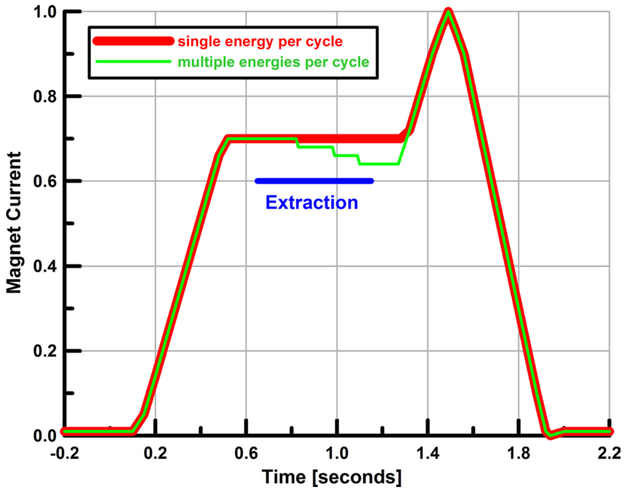


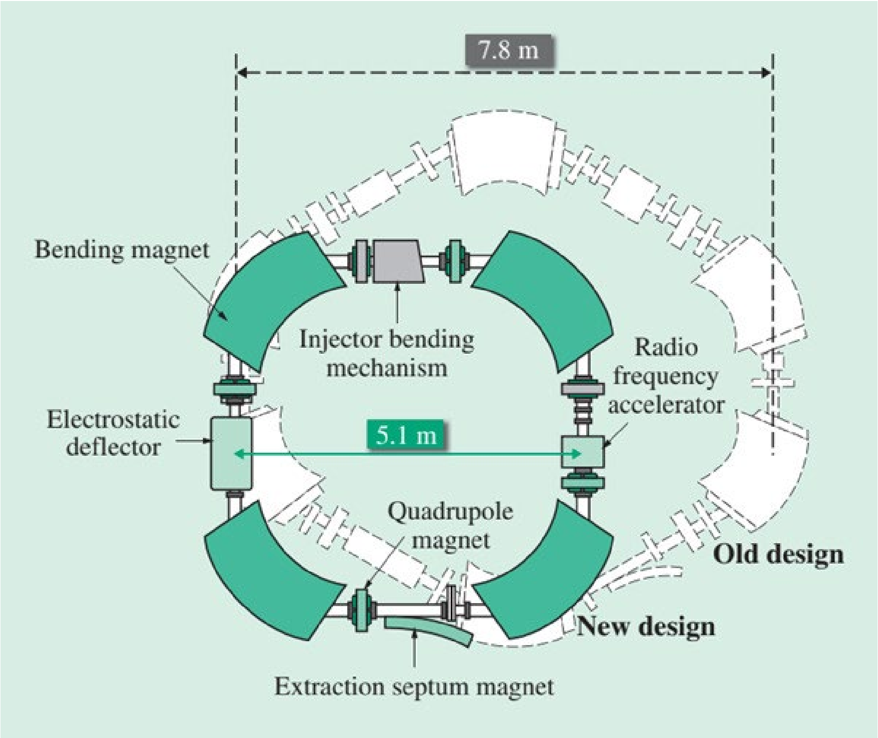
Van Goethem et al., Phys. Med. Biol. 54 (2009)5831

Synchrotrons

- Asymmetric emittance
  - Cause: Extraction in one plane

- Single turn vs multi-turn extraction





Sources: Hitachi, Loma Linda University Medical Center

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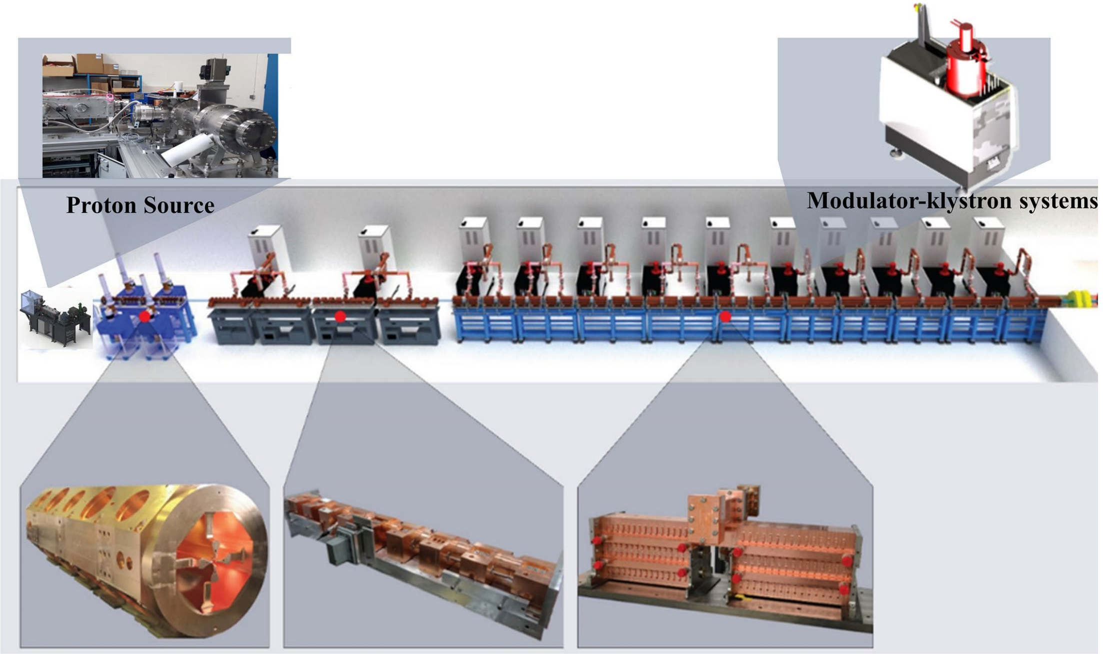
Linacs

- Fast energy switching (milliseconds)
- Very low beam emittance (~1 mm mrad)
- Lower average current than cyclotrons



Radio Frequency Quadrupole (RFQ)

Side Coupled Drift Tube Linac (SCDTL)

Coupled Cavity Linac (CCL)

Source: AVO/ADAM SA

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Small cyclotron on a gantry

H. Blosser, NSCL (~1990):
cyclotron for neutron therapy;
30 MeV protons, mounted on a gantry
Used in Harper Hospital, Detroit

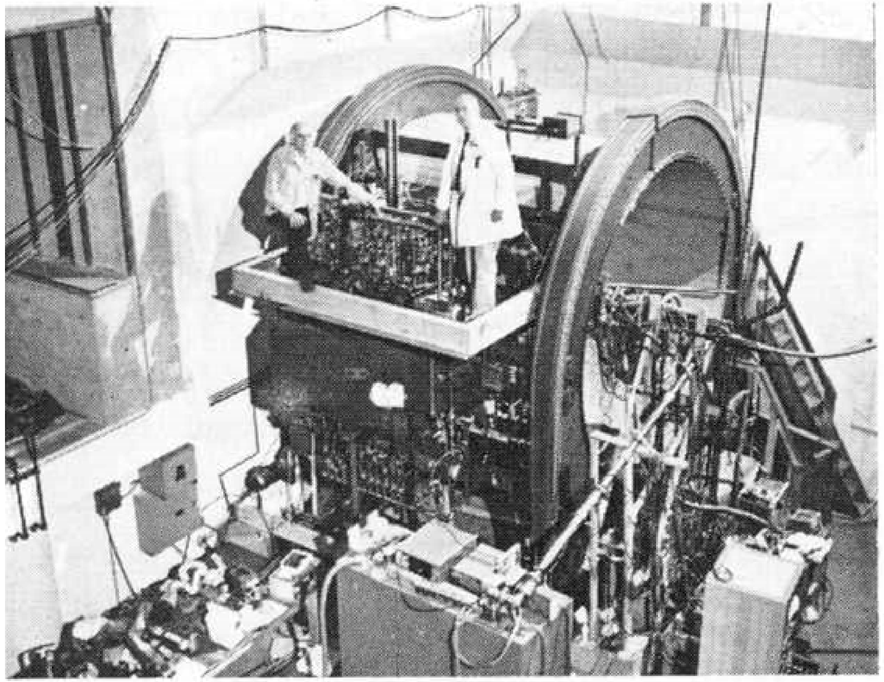
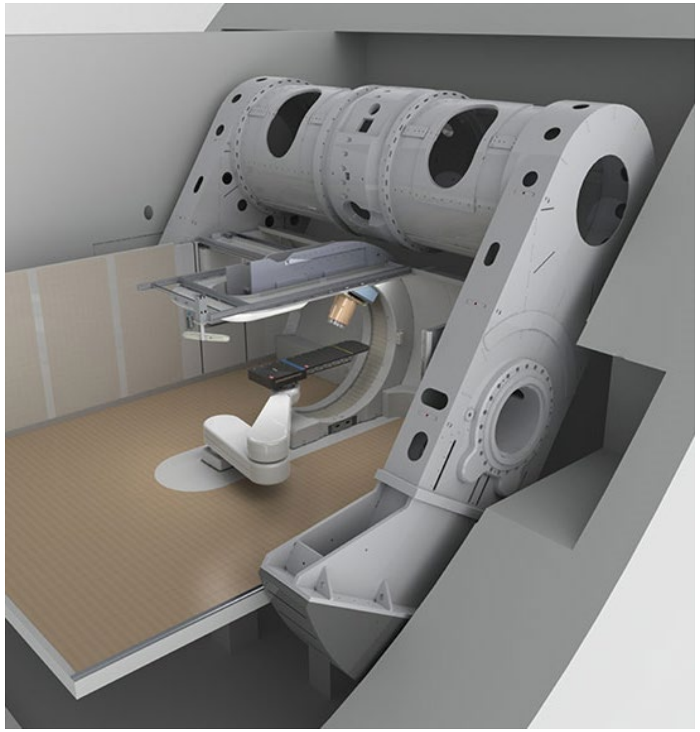


Fig. 2 Photo of the superconducting medical cyclotron on its gantry. Dr. William Powers and

MEVION medical systems

For proton therapy
70-230 MeV
Treating patients since 2013



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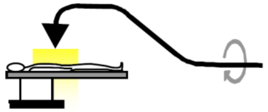
Gantry types and topologies

Patient Isocentric

- Patient is positioned centrally (isocentre) and is not moved, providing direct and uncomplicated access at any time
- Beam delivery system rotates around the patient

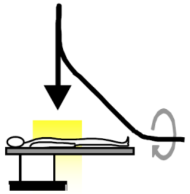
Conventional Gantry

- Very long structure (>12 m)
- Between 180° and 270° bending of which 135° - 180° are mounted eccentrically



Corkscrew-Ganty

- Comparatively short
- 360° bending, of which the last 270° are mounted eccentrically

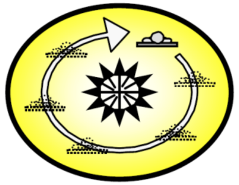


Patient Eccentric

- Patient is moved on a circular path around the central axis of the gantry
- Separate access systems necessary

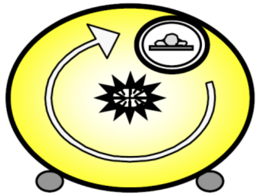
"Riesenrad-Gantry"

- Patient eccentric, ion beam central
- Only one 90° bending magnet, which is mounted on the axis



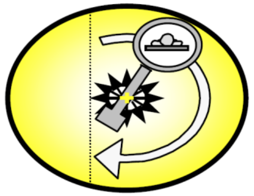
Wheel-Gantry

- Outside bearings
- Extreme stiff and light wheel-structure possible
- Patient enclosure is not structural, allowing for a full 360° rotation



Cabin-Gantry

- Supported on a central axis
- Patient enclosure is structural ("cabin"), allowing only for ~180° rotation
- Compact size possible (only half a wheel)



Patient & beam eccentric

- Patient and magnets rotate around the central axis
- Smallest possible diameter of gantry

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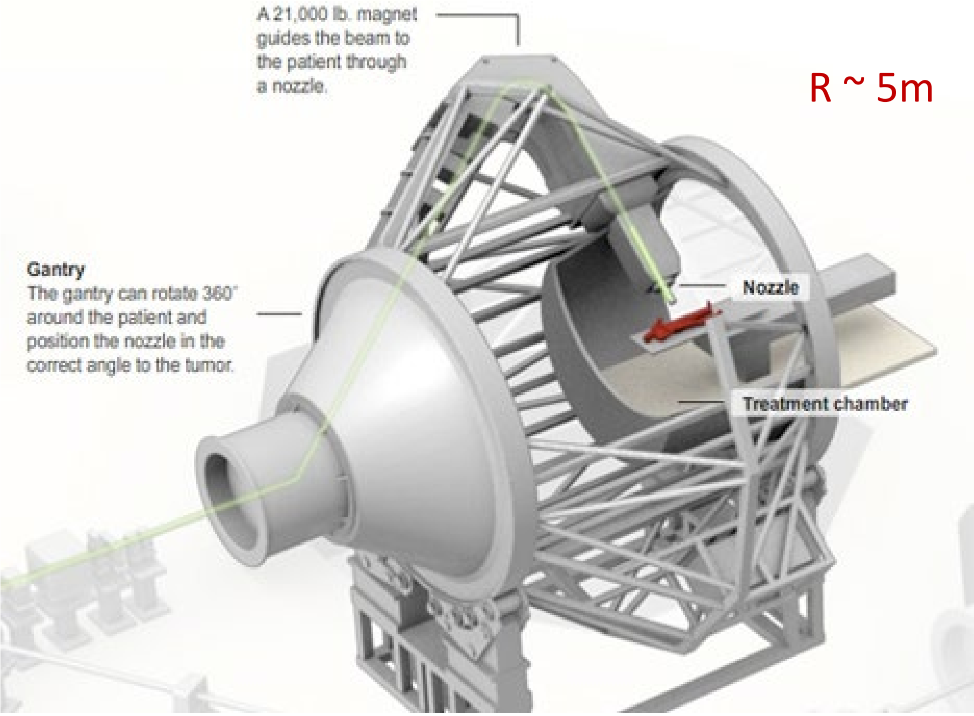
Conical gantry - Commercial standard layout



R ~ 5m

IBA
Sumitomo
Hitachi
Mitsubishi
Varian

Munich

- 135°bending magnet
  - Shorter length - but larger radius
  - Cylindrical treatment cell
- Initially only for passive scattering
- Lately also for scanning

First commercial scanning-gantry of Varian in Munich

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Dose delivery techniques

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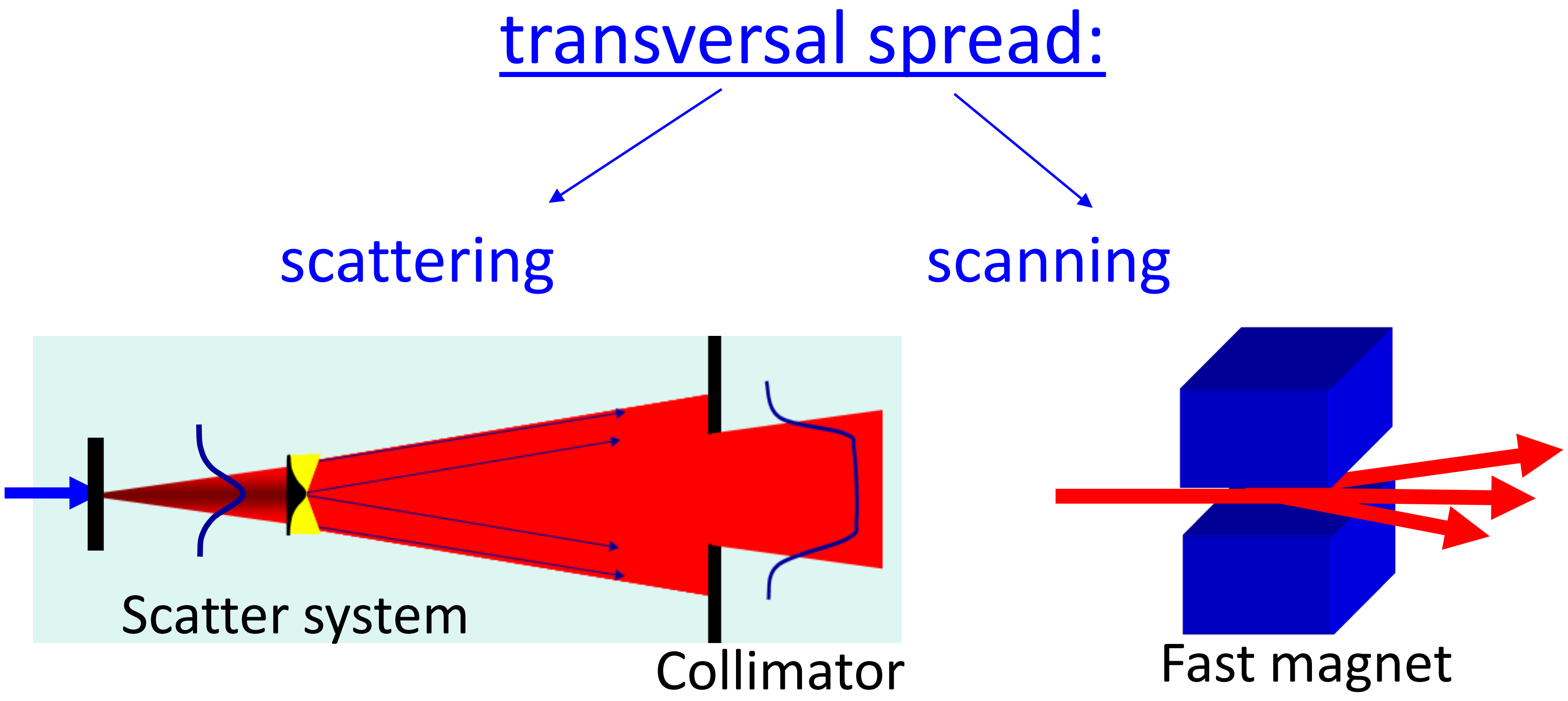
Dose delivery techniques: Width



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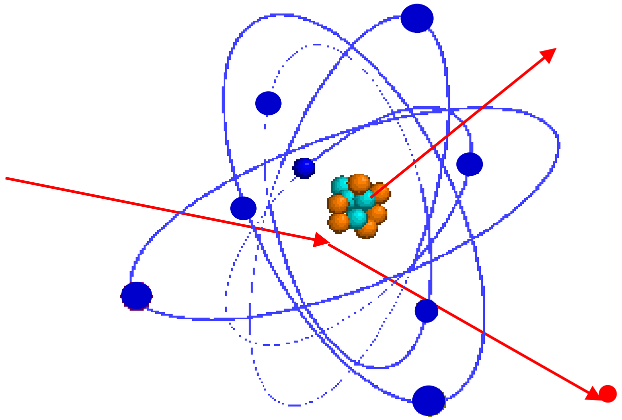
Scattering

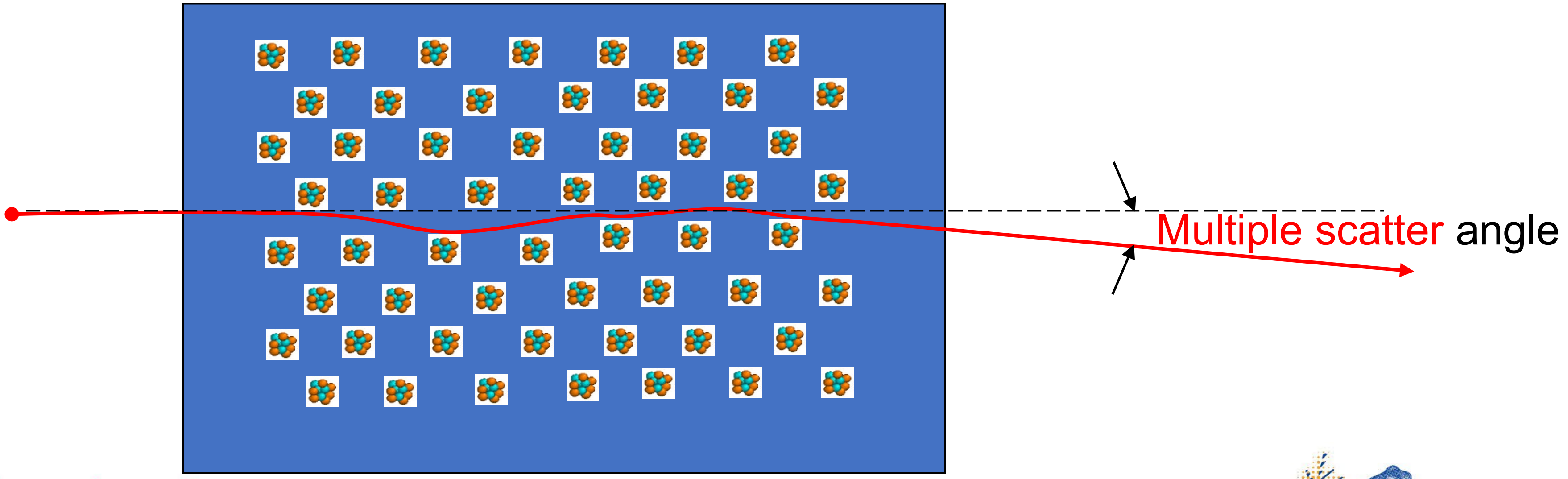
Nuclear Coulomb scattering



Nucleus is several times heavier as a proton

→ Almost no energy loss („elastic“)

→ Much larger deflection than from electrons



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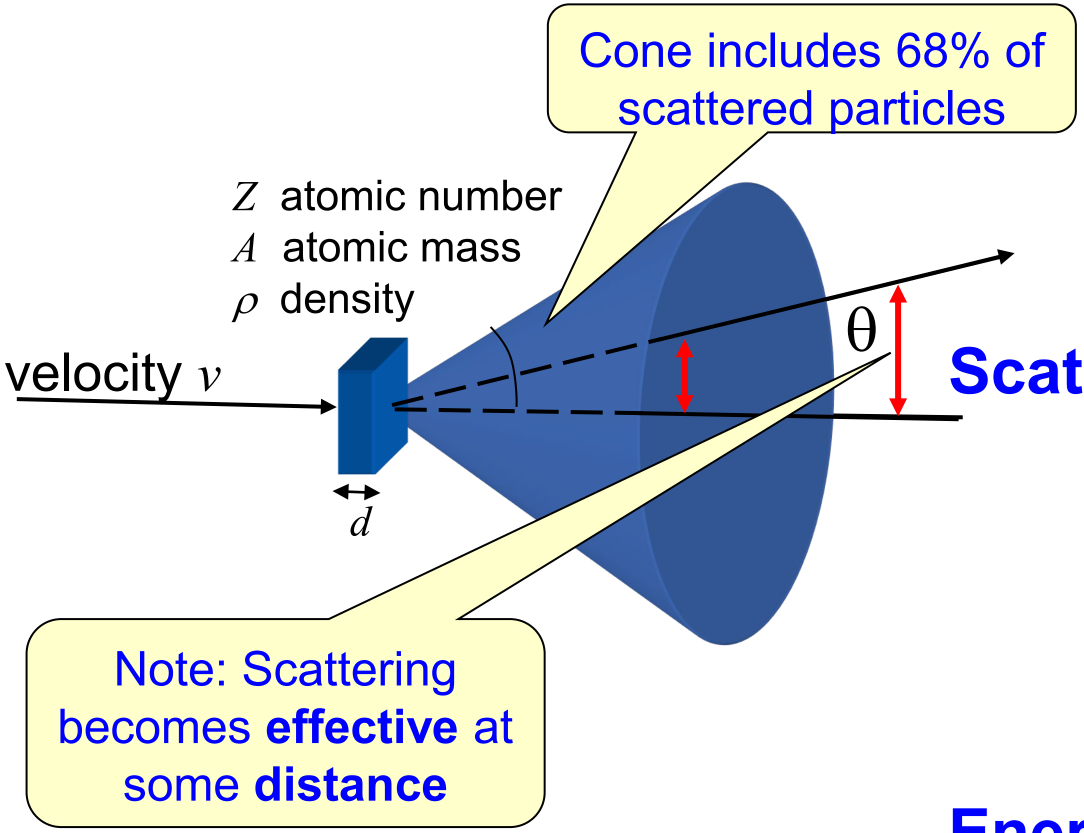
Scattering



$$\theta \sim \frac{\sqrt{d}}{v^2}\frac{Z}{\sqrt{A}}$$

Scattering: from **nuclei.**

$$\Delta E \sim d\frac{\rho}{v^2}\frac{Z}{A}$$

Energy loss: slow down by **electrons.**

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Scattering

	Energy loss	Scattering
(Z ; A)	$\frac{dE}{dx} \sim \frac{Z}{A}$	$\theta \sim \frac{Z}{\sqrt{A}}$
Water (8 ; 16)	0.5	2
Tungsten (74 ;184):	0.4	5.4

=> More scatter at heavy materials

250 MeV p:		1 cm H_2O	1 mm W
Energy loss:	ΔE =	4 MeV	4 MeV
Scattering angle:	θ =	5 mrad	16 mrad

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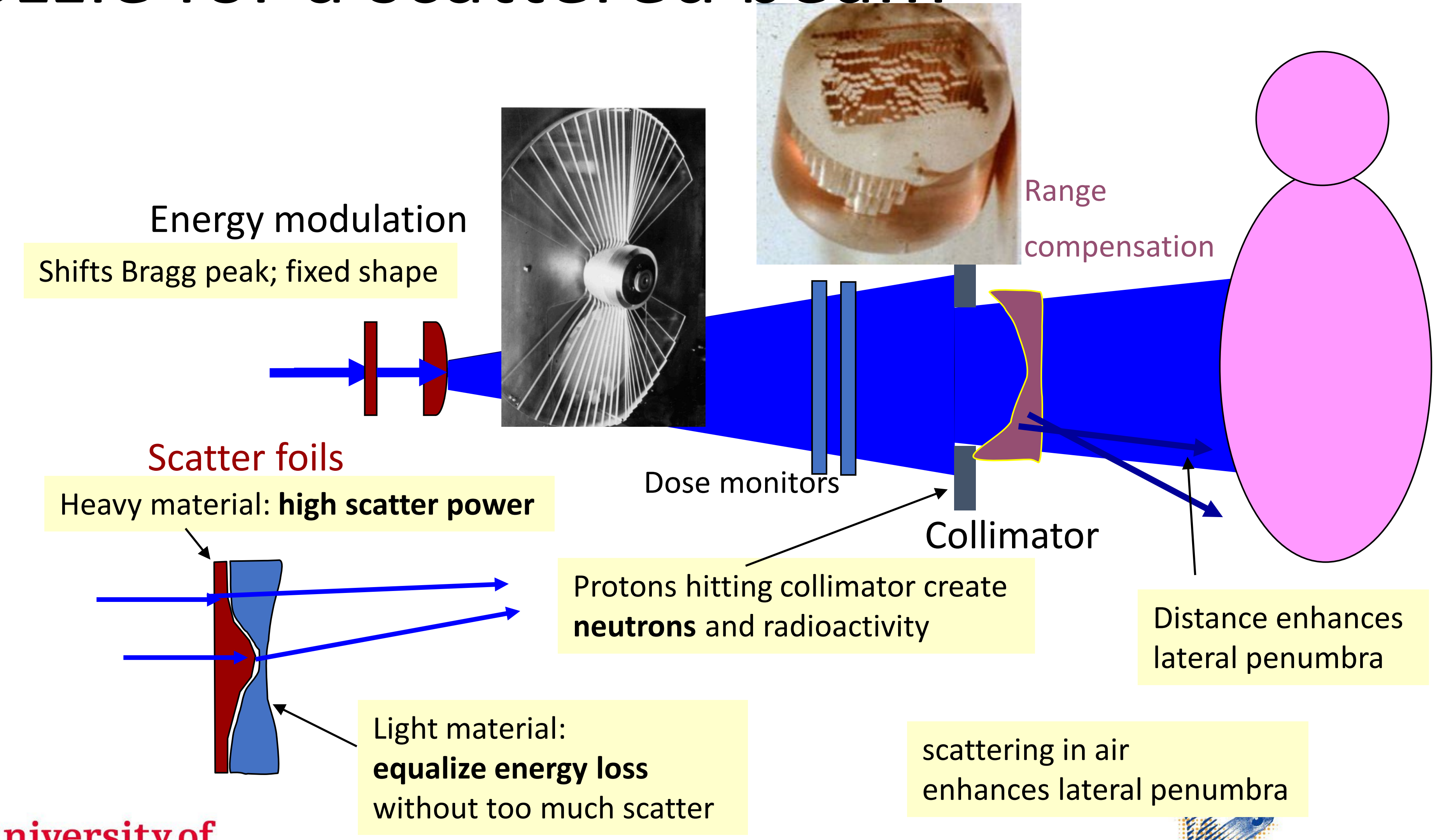
Nozzle for a scattered beam



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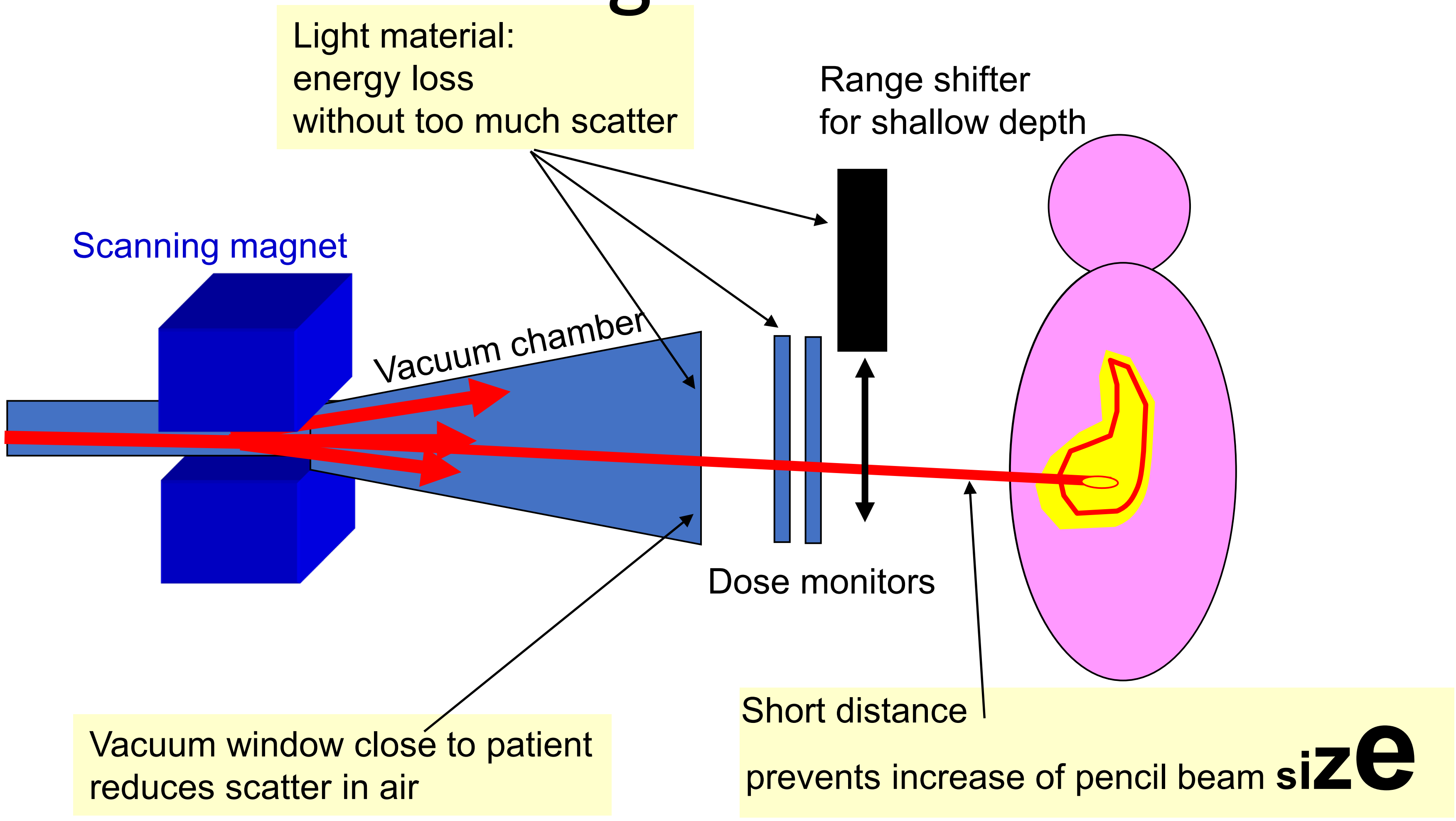
Nozzle for a scanning beam



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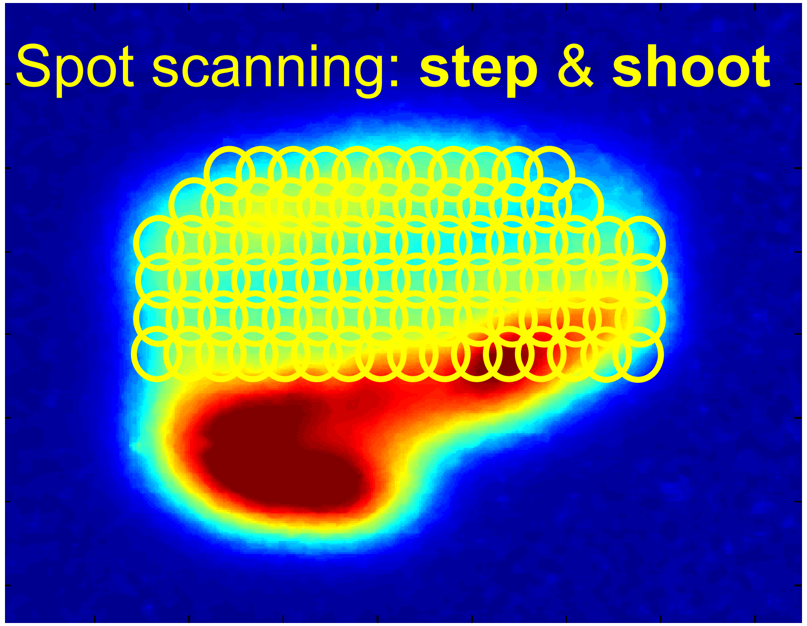
Spot scanning



Beam size 7 mm FWHM
5 mm steps

10'000 spots/liter (21 x 21 x 21)
Dose painted only once

~1 Gy / liter / minute

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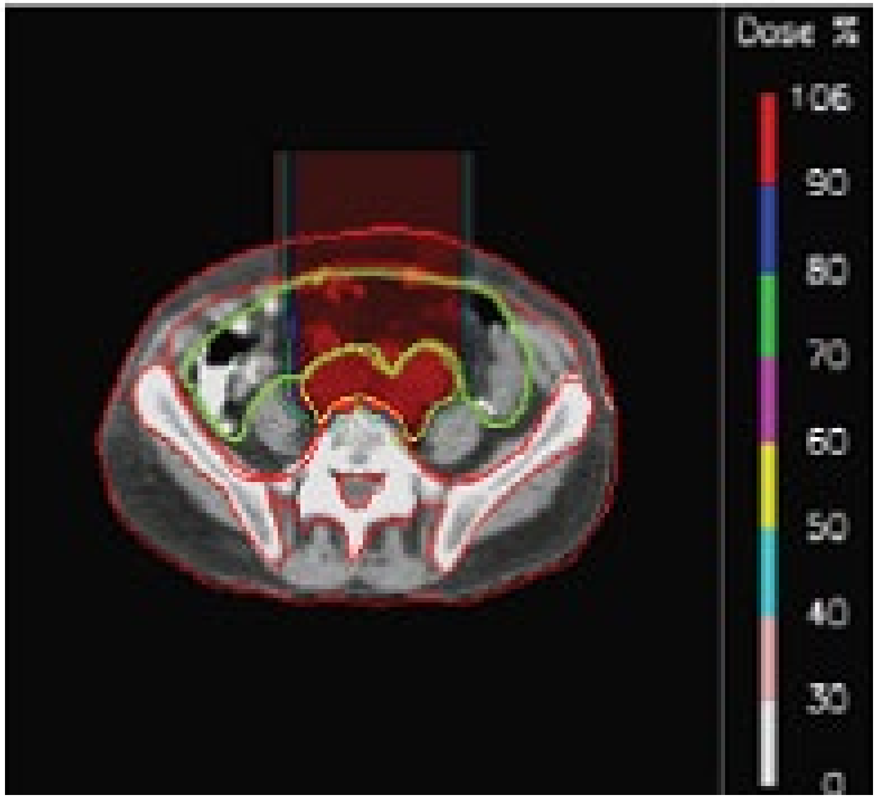
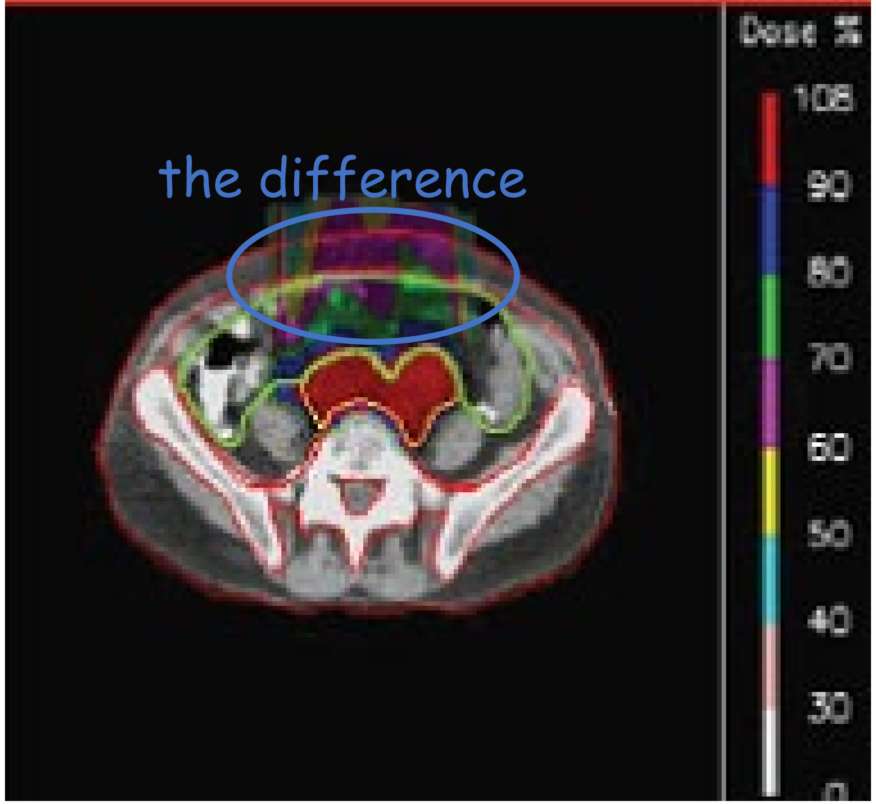
Scatter – IMPT

Scattered beam



Scanned beam with IMPT



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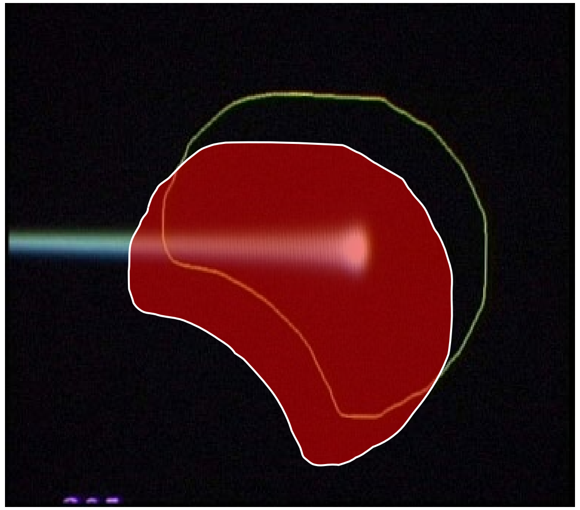
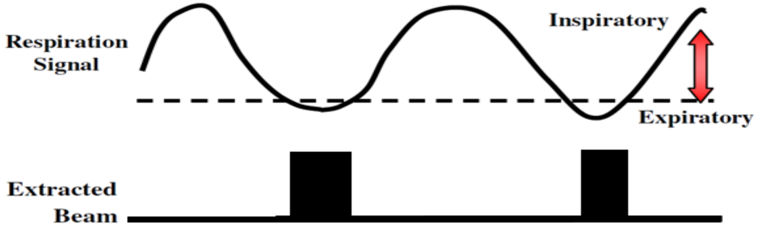
Organ / tumor motion

Organ motion



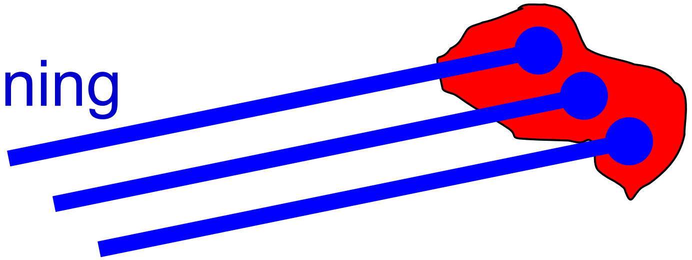
Possible solutions:

- Gating

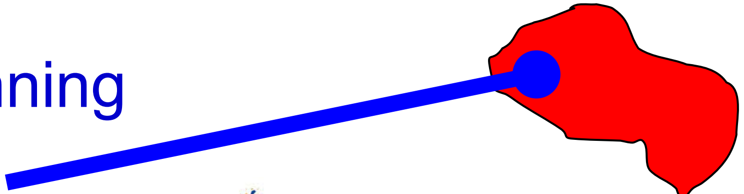


- Adaptive scanning

  (tumor tracking)



- Fast rescanning



Beam optics properties

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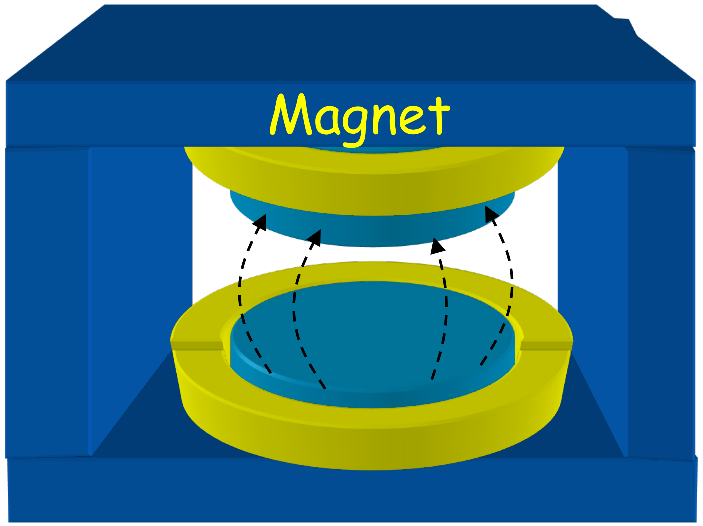
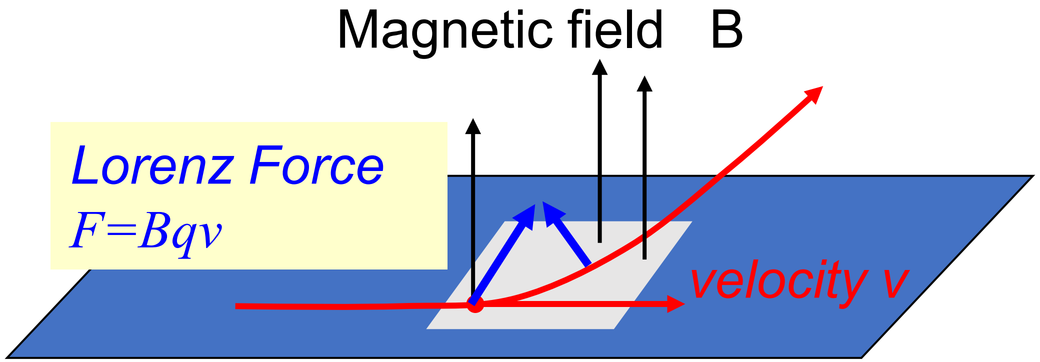
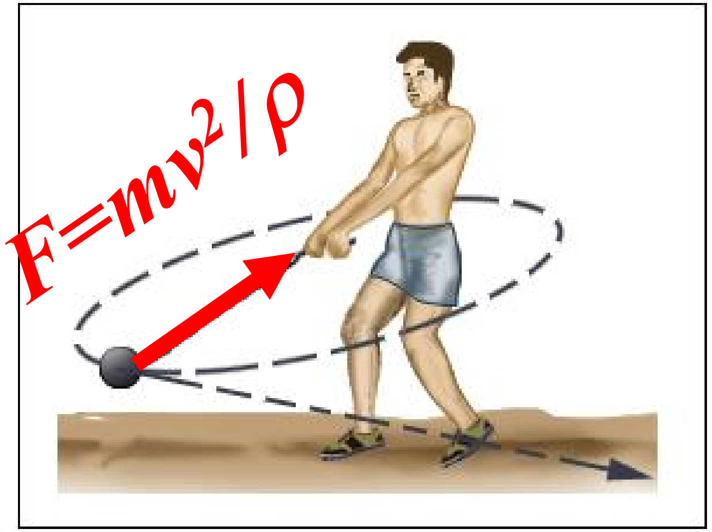
Magnetic fields







Lorenz force = “centripetal force” mv^2/ρ

⇒ track = circular orbit with radius ρ

energy E and charge q

determine magnetic rigidity $B\rho$:

magnet strength B to bend with radius ρ

$B\rho$ [in Tm] = p/e = 3.3356 p [in GeV]

250 MeV p: $B\rho$ = 2.4 Tm

450 MeV/nucl C^{6+}: $B\rho$ = 6.8 Tm

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Optimal gantry beam line design

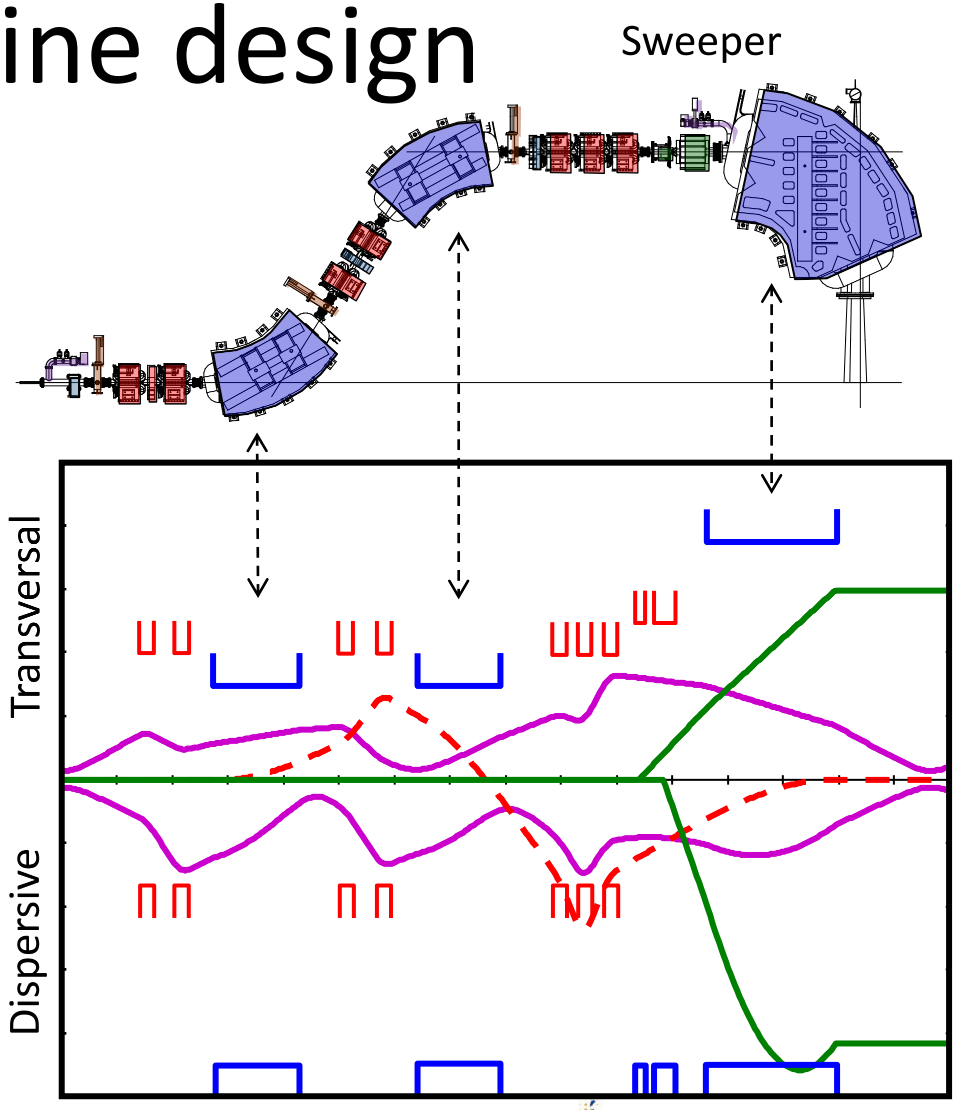
Coupling point

- Rotational symmetrical phase space
- Fixed collimator

Beam optics

- Imaging from coupling point to iso-center ($R_{12} = R_{34} = 0$)
- Achromatic beam optics ($R_{16} = R_{36} = 0$)
- Point-to-parallel setting from scanning magnets to iso-center ($R_{22} = R_{44} = 0$)

Purple: Beam envelopes trough Gantry 2
Green: Action of the sweepers
Red: Dispersion trajectory for a 1% momentum band



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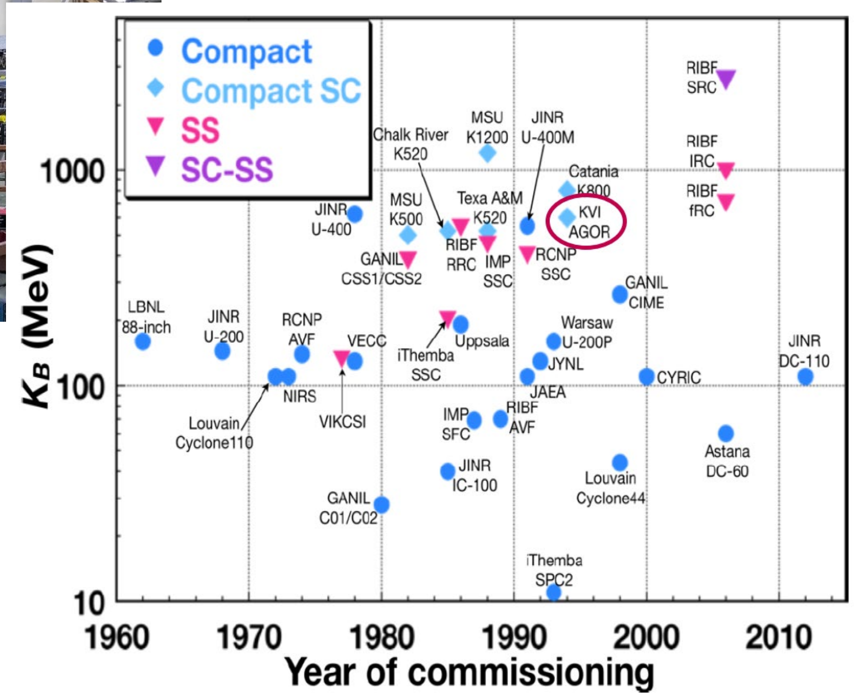
Our Facility

- Formerly known as KVI-CART
- We operate a superconducting cyclotron for experimental research
- From 1996 – 2013 beams mainly used for research in nuclear physics (light ions) and on fundamental symmetries (heavy ions)
- Emphasis has shifted towards detector development and radiation hardness testing (since 2005, mainly commercial with some funded experimental research) and biomedical research (since 2014)
- Reorganization:
  - KVI's accelerator facility, staff and medical physics group was integrated into UMCG and became PARTREC



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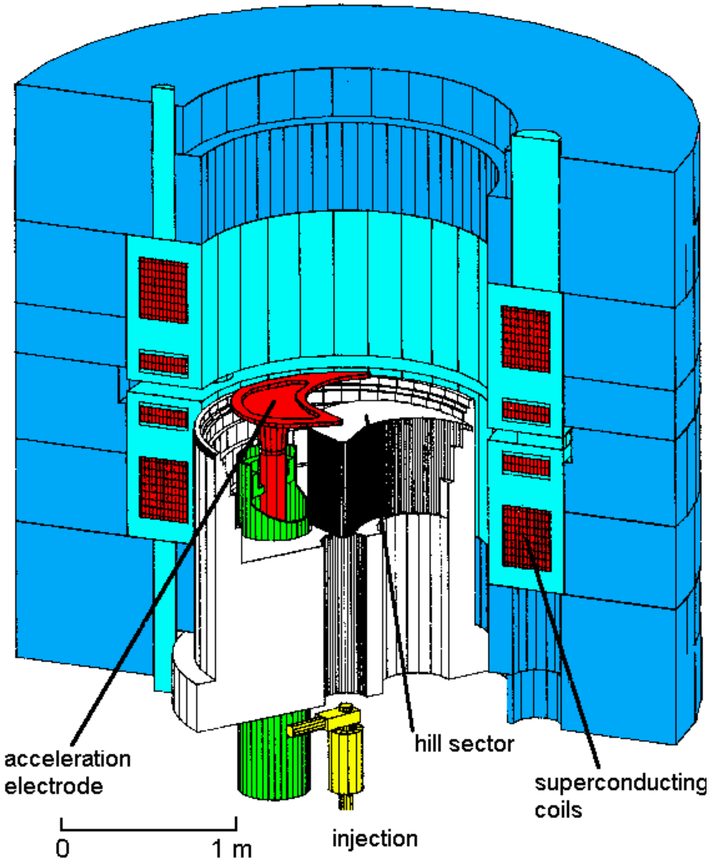
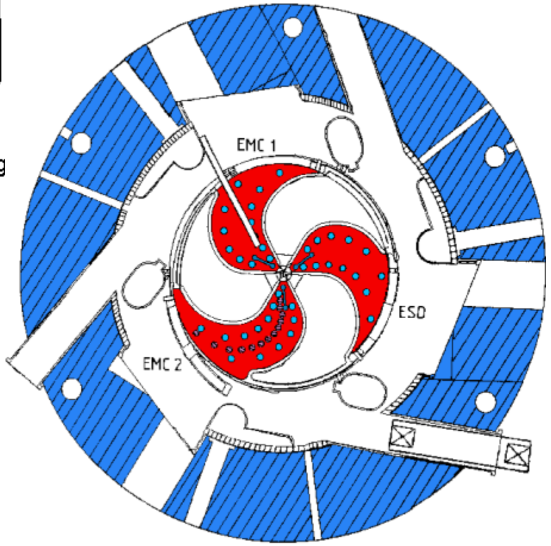
AGOR Cyclotron

- Superconducting AGOR cyclotron is a multi-particle, variable energy AVF-cyclotron
- French-Dutch collaboration built 1987 – 1994
- Operational since 1996
- Magnetic field (1.7 to 4.1 T) produced by
  - Two pairs of superconducting main coils
  - fifteen trim coils
  - three iron hill sectors for focussing
- 3 halfwave RF cavities, 24 - 62 MHz; h = 2, 3 or 4
- Three external ion sources (two ECR sources for heavy ions, multi-cusp source for light ions) are axially injected
- Extraction
  - 300 - 500 turns depending on harmonic mode
  - extraction radius 870 - 890 mm depending on E/A
  - turn separation at extraction 2 - 3 mm ~ beamwidth





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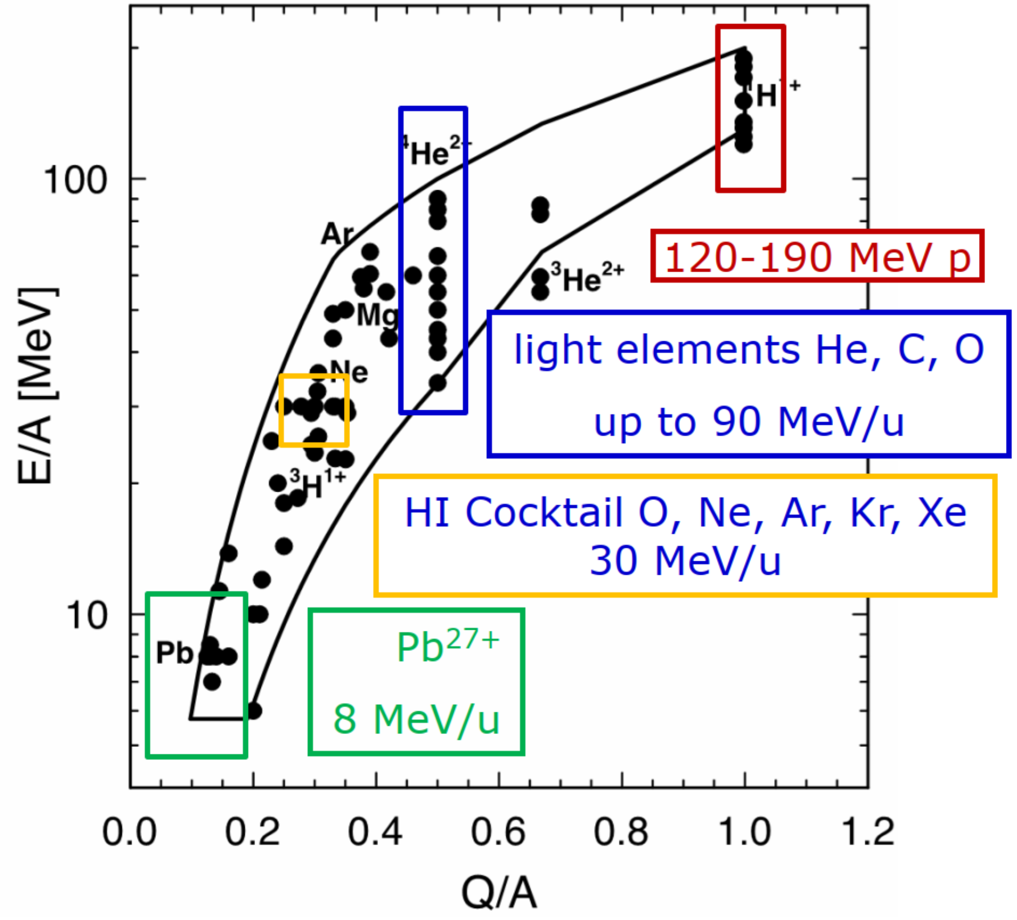
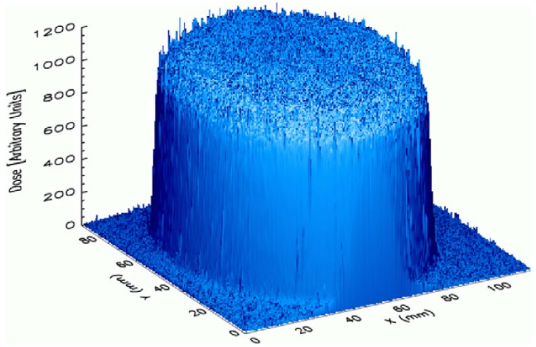
Beam Parameters

AGOR can deliver beams of all elements up to Xe

	Protons	Ions
Kinetic energy (MeV/amu)	≤ 190	≤ 90 for C and O ≤ 30 for all up to Xe
Attainable flux (particles per s)	> 10^{13}	≤ 10^{13} for Ne ≤ 10^{11} for heavier ions
Field size (cm²)	≤ 10 x 10 (scanned beam) ≤ 8 x 8 (scattered beam)	≤ 7 x 7 for light ions (scanned beam) ≤ 3 x 3 for heavy ions (scanned beam)
Field homogeneity	± 2 % (scattered beam) ± 1 % (scanned beam)	± 2 % (scattered beam) ± 1 % (scanned beam)





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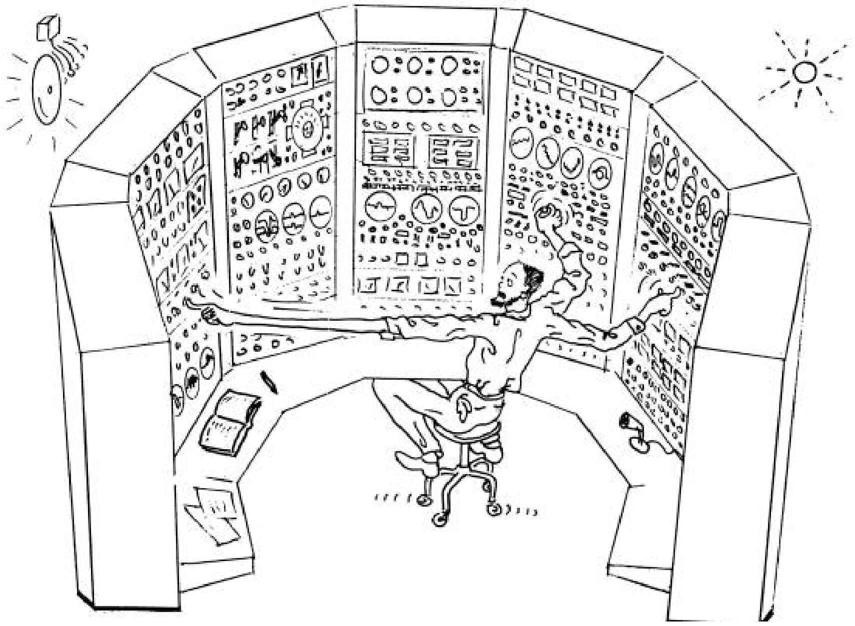
Our Team

- Faculty (4)
- Post-docs (2)
- PhD-students (5)
- Technical staff (24)
  - Operators to operate and maintain the accelerator (5)
  - Cryogenics, cooling, compressed air and vacuum (2)
  - Design/Mechanical: mechanical repairs, design and construct mechanical components that have become obsolete and contribute to scientific and infrastructure projects (5)
  - Electronics: maintenance of the magnet power supplies, RF-amplifiers, low level RF-electronics, PLC-systems and interfaces of all these systems to the central control system of the accelerator (5)
  - IT Support needed for operation, maintenance and upgrading of the accelerator control system as well as the irradiation control system (3)
  - Experimental and project support provided to internal/external scientists as well as companies, ECR sources (4)



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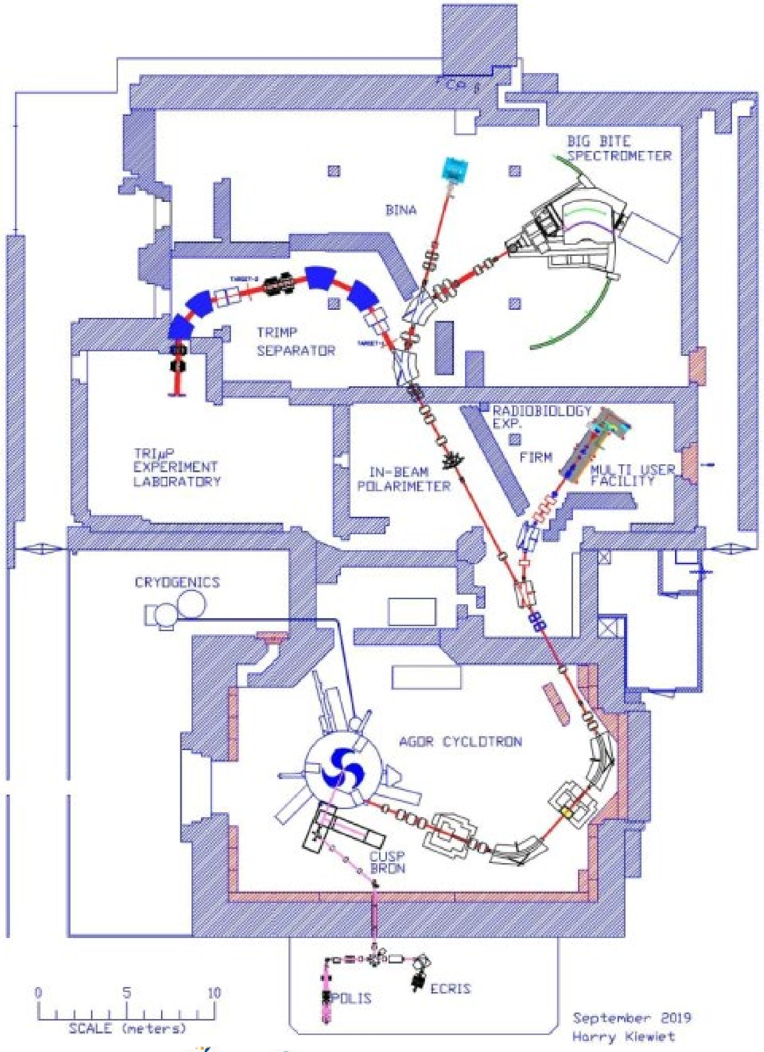
PARTEC Operation

- We strive to provide a reliable and reproducible ion beam to satisfy the needs of the user
- We also provide support
- Operational 120 hours/week, 26 weeks/year
- Beam requests: irradiations.partrec@umcg.nl
- With shift from fundamental physics to radiation biology and physics and technology of particle therapy the number of individual experiments increased while their duration has decreased
- Over the past few years proton beams provided for over 80% of beam time

KVI facility layout before PARTREC upgrades



Our Users and Funding

- Recognized by ESA as Ground-Based Facility (CORA-IBER,
- Investigating biological effects of space radiation)
- Supported by EU as Large-Scale Facility (IAs RADNEXT, INSPIRE)
- Commercial Funding:
  - Mainly proton in-air irradiations
  - Expanding heavy ions
  - Mostly non-domestic aerospace
- Local and national funding (RUG, UMCG, KWF, NWO)
- Examples
  - Radio-sensitization of cells/spheroids with nanoparticles
  - Determination of the lateral dose response functions of detectors in proton beams
  - Prediction, prevention and treatment of radiotherapy-induced complications
  - Proton SOBP irradiation of cell cultures and organoids
  - A test measurement to study recombination effects at high dose rate
  - Evaluation of proton and carbon-ion RBE for cell killing in radio resistant and hypoxic patient derived Glioblastoma stem cells
  - The interaction of chemotherapy with high and low LET radiation in pancreatic cancer cell lines
  - Measurement of the production cross section of the short-lived b+ emitters of interest in proton therapy
  - Neuronal responses to particle irradiation and potential interaction with stress hormones

esa
European Space Agency

University Medical Center Groningen

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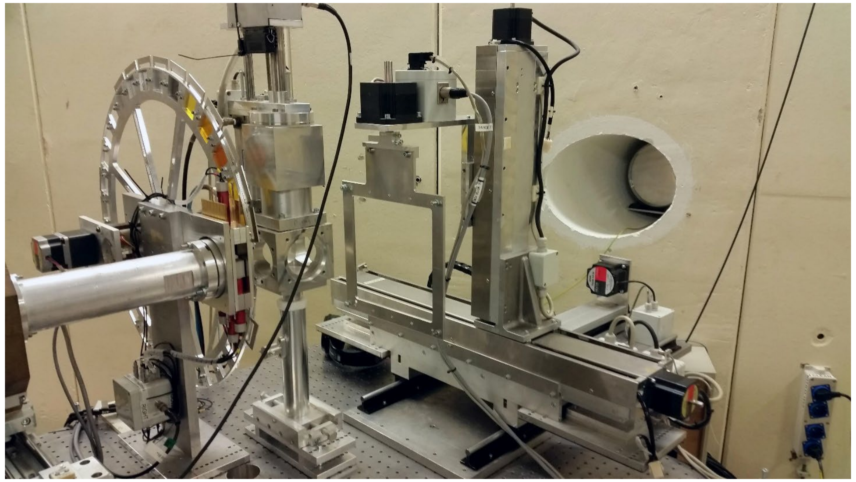
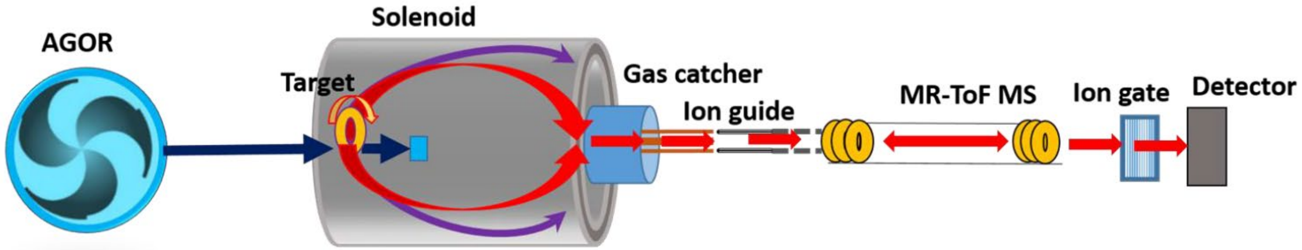
Heavy Ion Beams



- Research areas
  - Radiobiology (RuG, UMCG, PSI)
  - Detector tests & development (ESA)
  - Experiment development (ESA)
  - Radiation hardness (ESA, companies)
- AGOR can deliver beams of all elements up to Pb
- New experimental research on the production of neutron-rich heavy nuclei using multi-nucleon transfer reactions between heavy nuclei (e.g. ^{136}Xe on ^{208}Pb) has recently been started
- ECR ion source development, improvement of transmission from source to extraction
- A new experimental station consisting of a 3 T superconducting solenoid fragment separator and MR-ToF mass spectrometer is developed with RUG and will be installed



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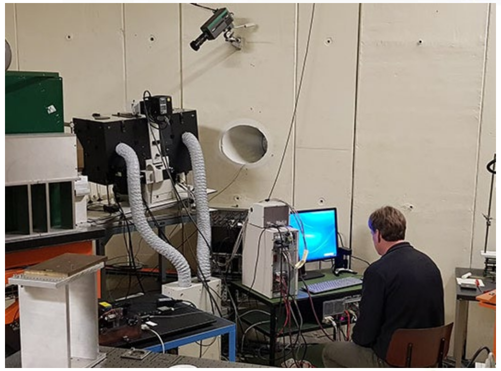
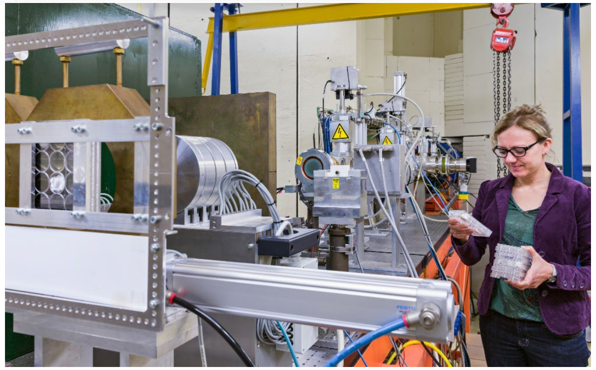
One Stop Shop for Radiobiology

- Experiment development
- Ethics authorisation process
- Animal procurement logistics
- On site animal accommodation with IVCs
  - capacity 200 rats and mice
  - no long term stay
  - two additional accommodations planned
- Irradiation + follow-up
- Twin Beam capability
  - Precisely replicating the beam parameters of commercial particle therapy facilities
- Laboratory for animal handling prior and post irradiation
  - GronSAI imaging center: optical, molecular, CT, MRI
- Data management facilities





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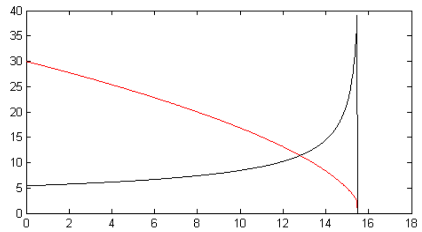
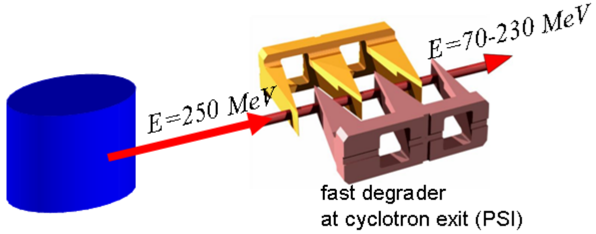
Summary

- Proton therapy makes use of the Bragg peak

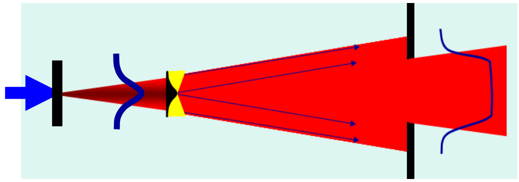


- In most facilities the beam is accelerated in a cyclotron

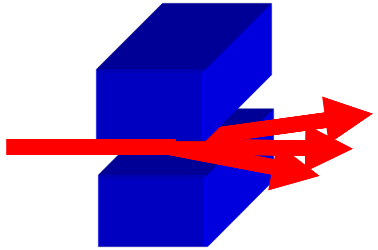
  and the energy is reduced by a degrader



- The target can be
  - irradiated by a scattered beam or



  - scanned by a pensil beam with sweeper magnets



- PARTREC
  - Is an open access facility
  - Provides proton and ion beams for pre-clinical research
  - Is particularly strong in clinical translation thanks to integration in UMCG

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Thank you for your attention!
Questions?

Acknowledgements:

Research at PARTREC is supported by the Dutch Cancer Foundation KWF, the Dutch Organization for Scientific Research NWO, the European Union, the European Space Agency ESA, Ion Beam Applications S.A., the University Medical Center Groningen and the University of Groningen.

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