PAUL SCHERRER INSTITUT

PSI

Martin Grossmann :: Center for Proton Therapy :: Paul Scherrer Institute

Protontherapy


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Island
Schweden
Norwegen
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Estland
Lettland
Litauen
Moskau
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Nordsee
Dänemark
Irland
Niederlande
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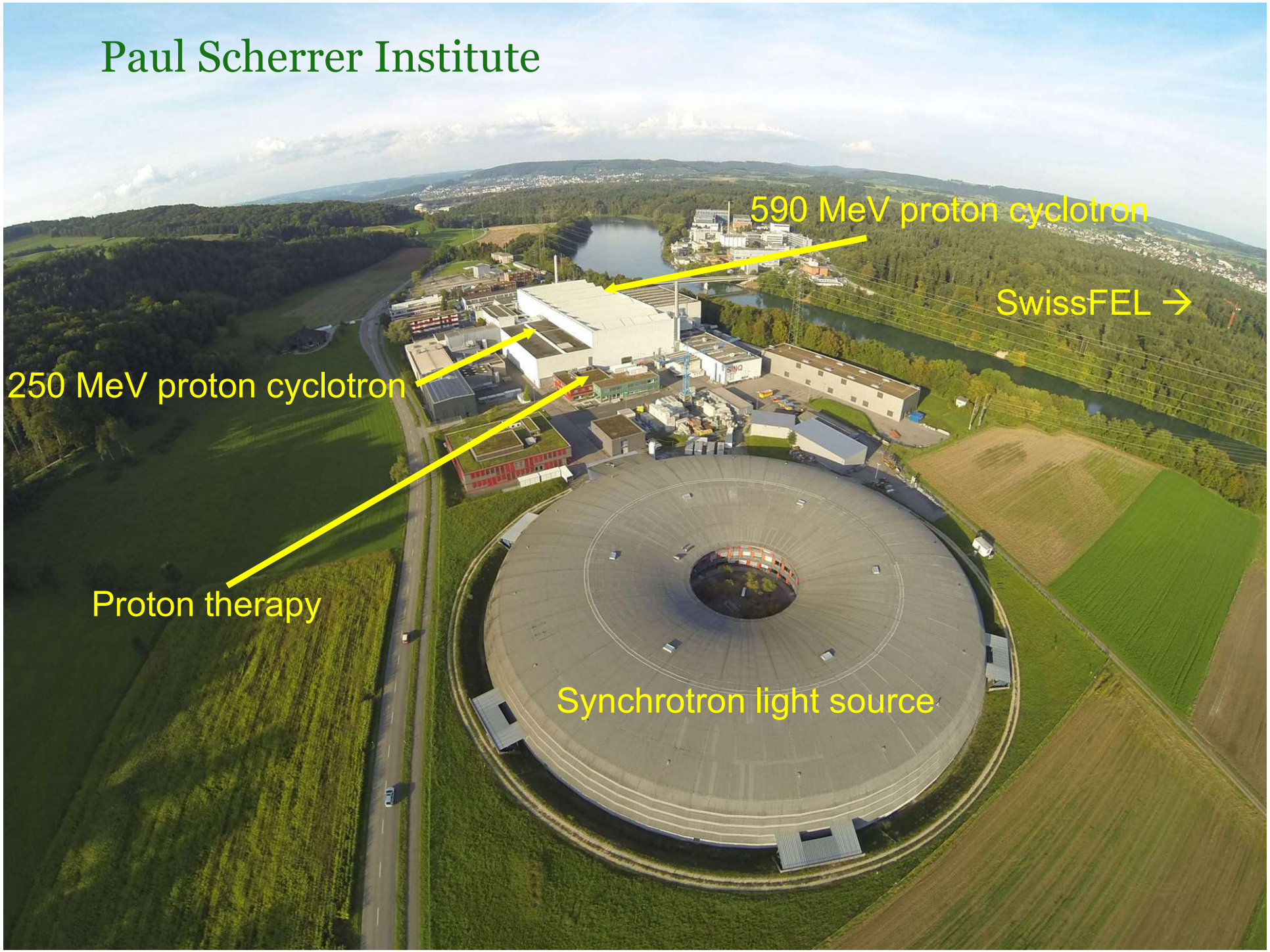
Weißrussland
Berlin
Deutschland
Prag
Tschechien
Wien
Slowakei
Ukraine
Österreich
Moldawien
Ungarn
Frankreich
Rumänien
Kroatien
Serbien
Schwarzes Meer
Italien
Rom
Barcelona
Bulgarien
Georgien
Kaspisches Meer
Usbek
Portugal
Madrid
Spanien
Tyrrhenisches Meer
Istanbul
Griechenland
Türkei
Aserbaidschan
Turkmenistan
Syrien
Libanon
Irak
Afgh
Tunesien
Mittelmeer
Iran
Marokko
Jordanien
Google


Paul Scherrer Institute
590 MeV proton cyclotron
SwissFEL →
250 MeV proton cyclotron
Proton therapy
Synchrotron light source

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Radiotherapy with Protons

Why Protons?

Proton therapy

Mass: ~200 tons

Diameter: ~8 m

Conventional therapy (LINAC)

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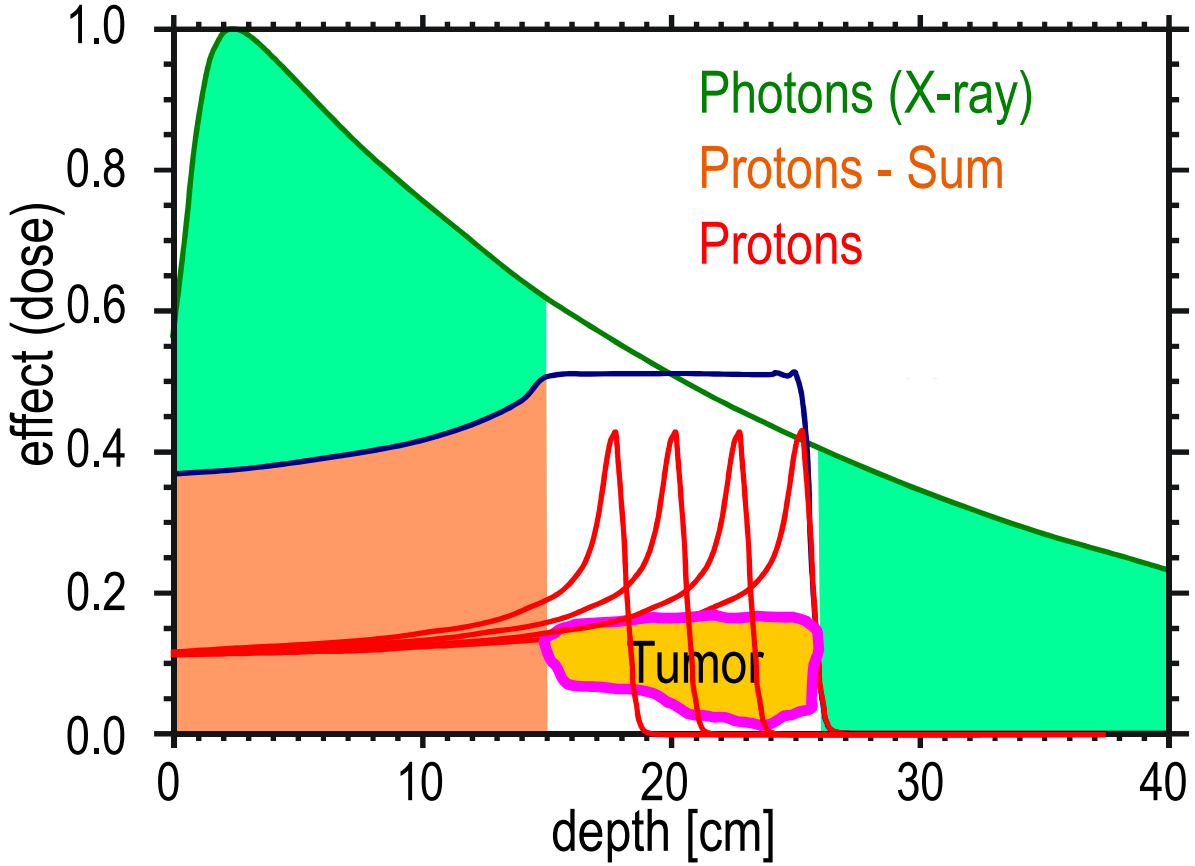
Why Protons?



Dose burden - photons

Dose burden - protons

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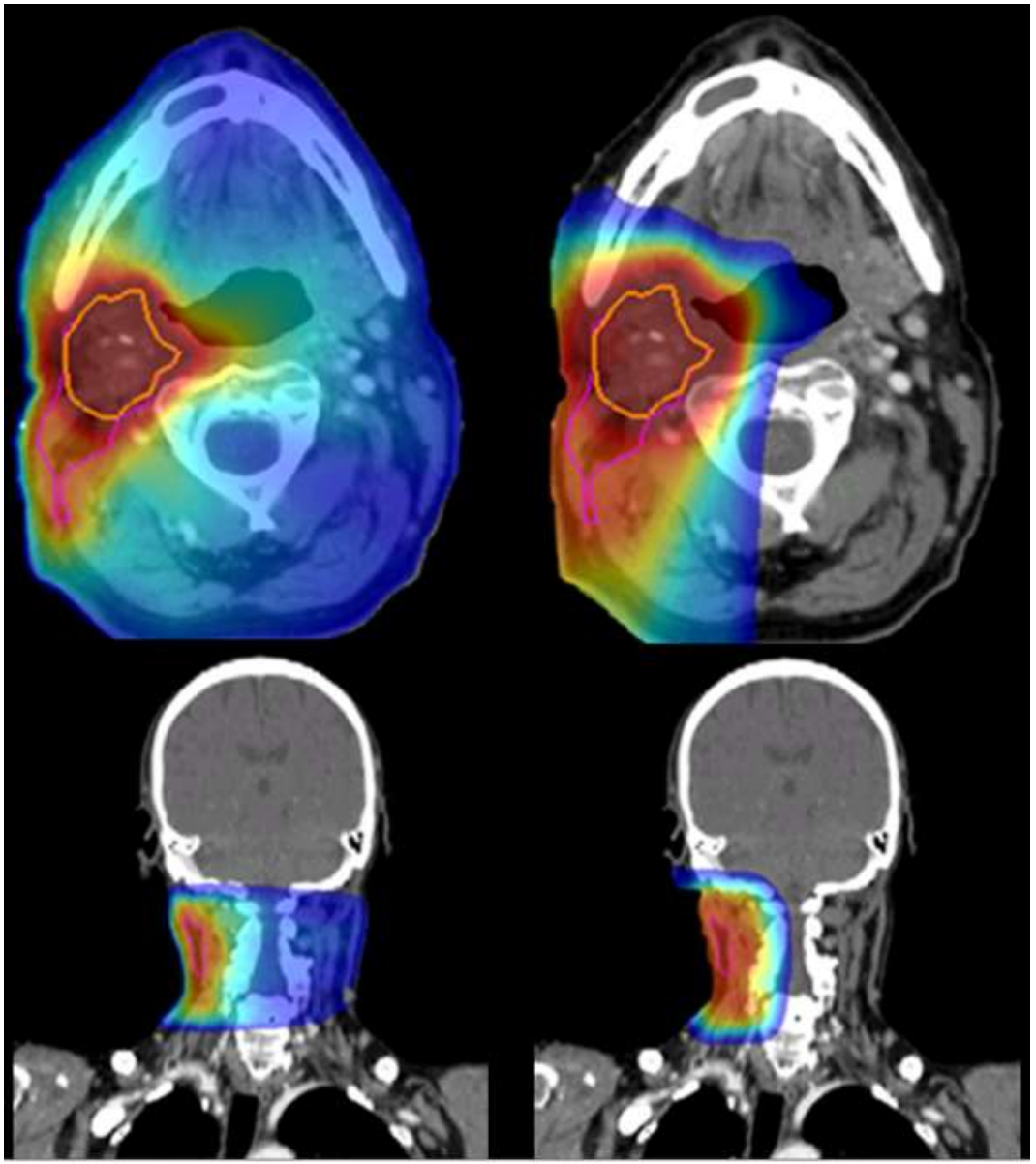
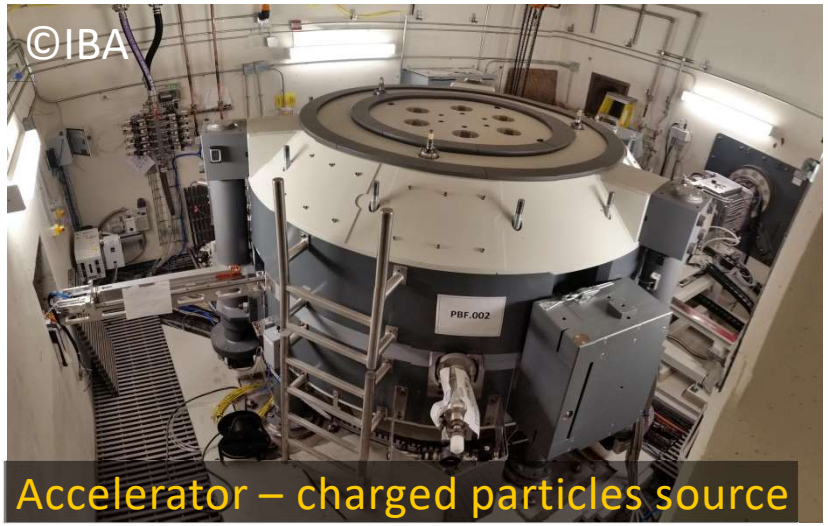
Why Protons?

Photons

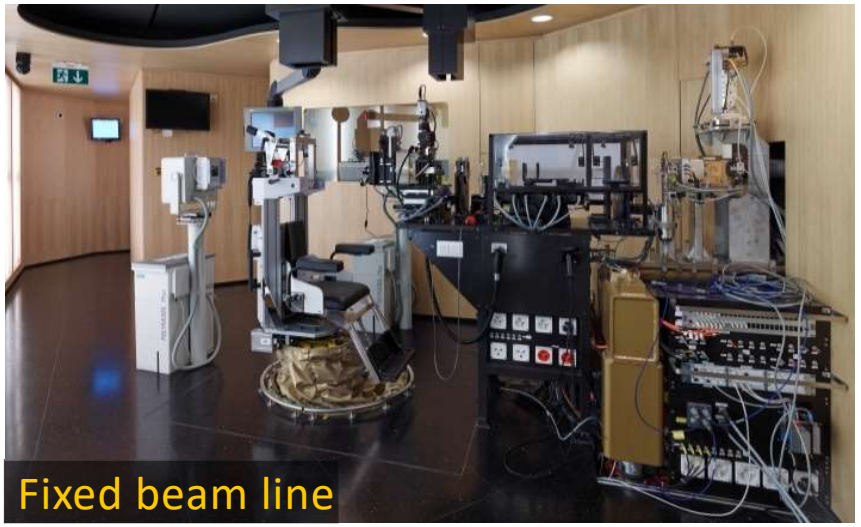


Protons

Main parts of a particle treatment facility



Accelerator – charged particles source

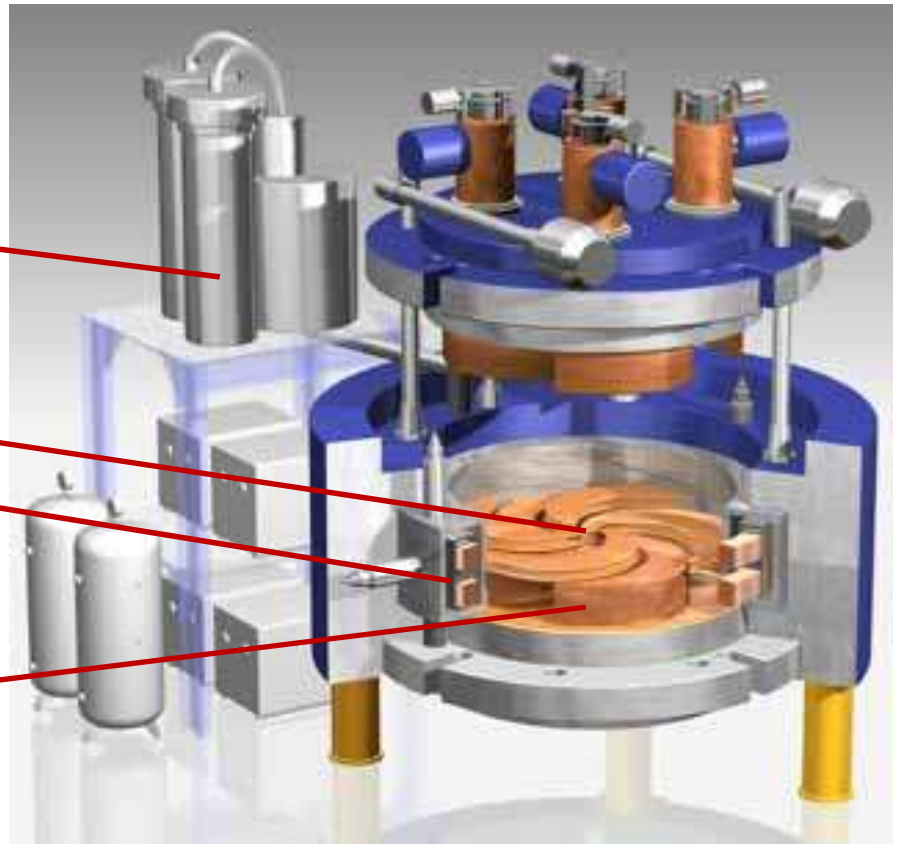

Fixed beam line


Beam transfer lines to treatment areas


Gantry – rotating beam line

Superconducting Cyclotron COMET (Accel/Varian)

- 90 tons, 300 kW
- Closed He system
  4 cryostats @ 4K
- Protons source
- Superconducting coils 2.4 – 3.8 T
- 4 RF cavities 72 MHz @ 80 kV



Superconducting Cyclotron COMET (Accel/Varian)

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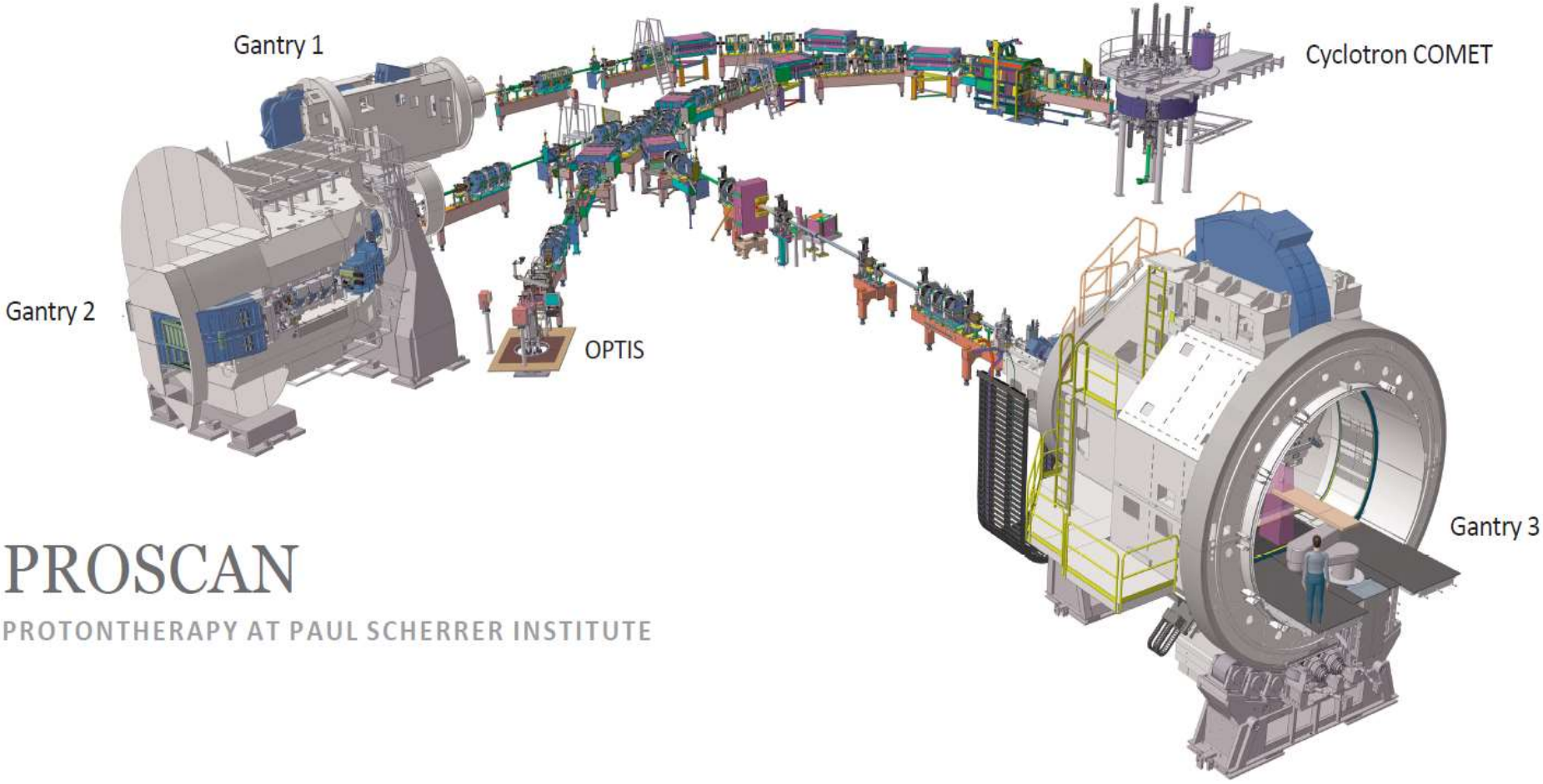
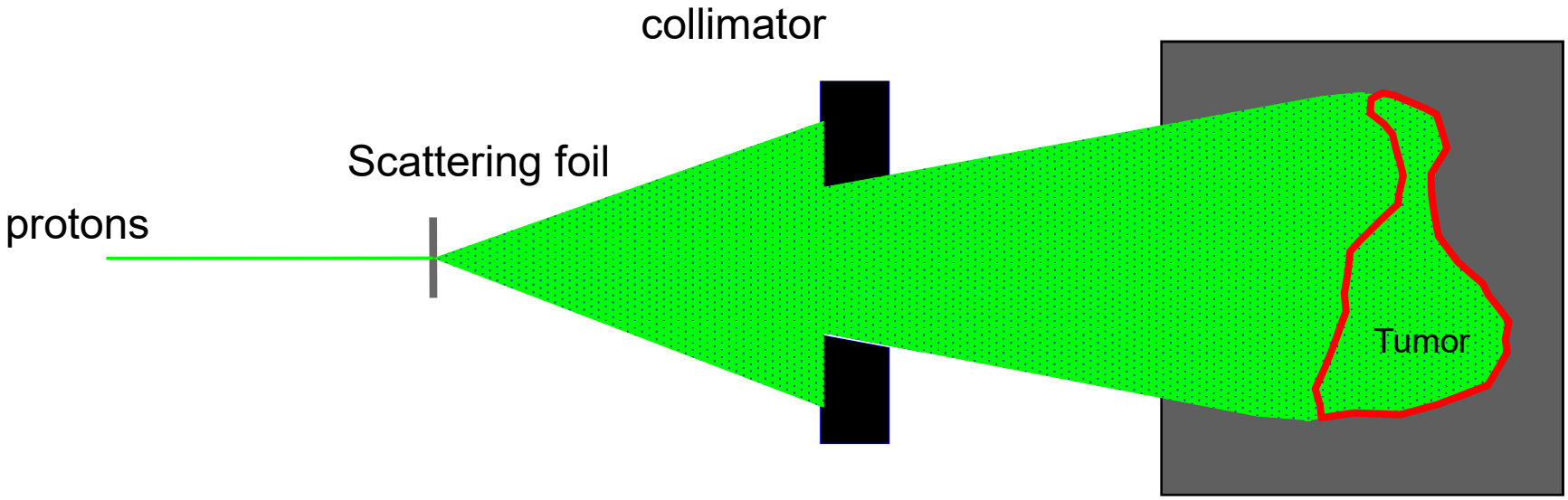


PROSCAN

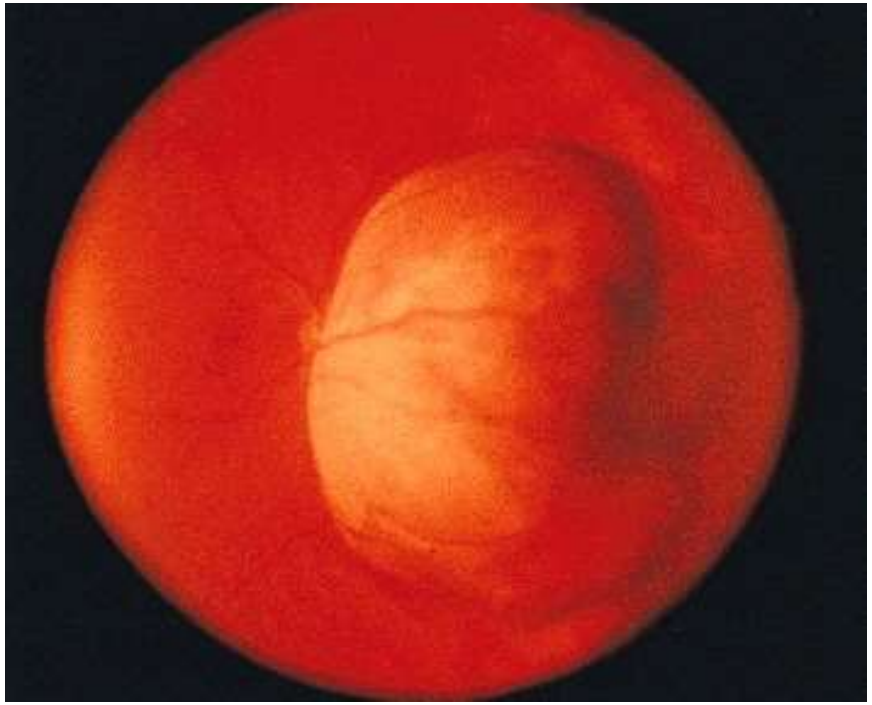
PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

Irradiation technique - classical



PSI's OPTIS program

- Treating Eye Melanoma
- Collaboration with eye clinic in Lausanne
  (Hôpital Ophtalmique Jules Gonin,
  Prof. L. Zografos)



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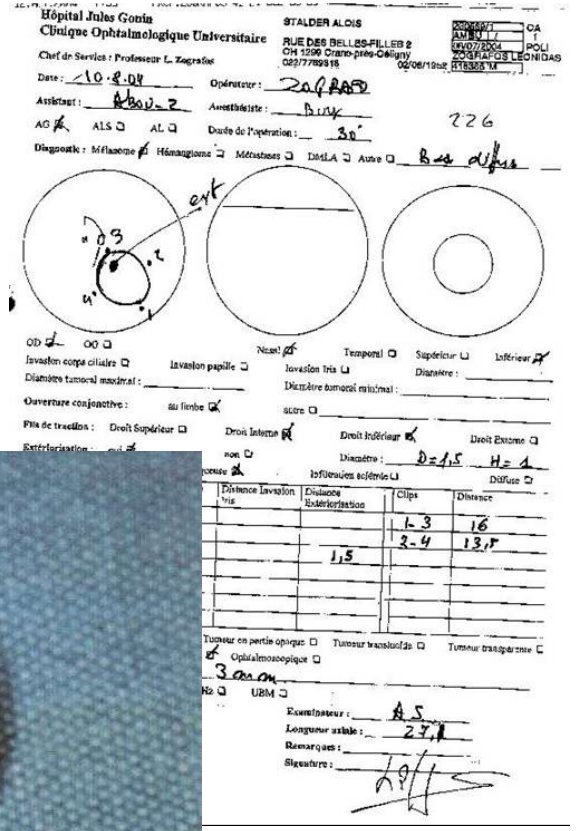
PSI's OPTIS program



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PSI's OPTIS program

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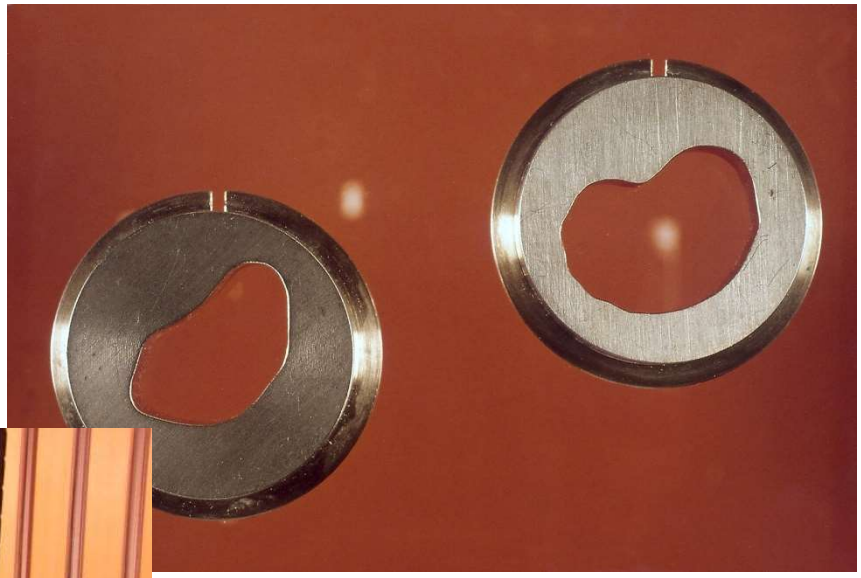
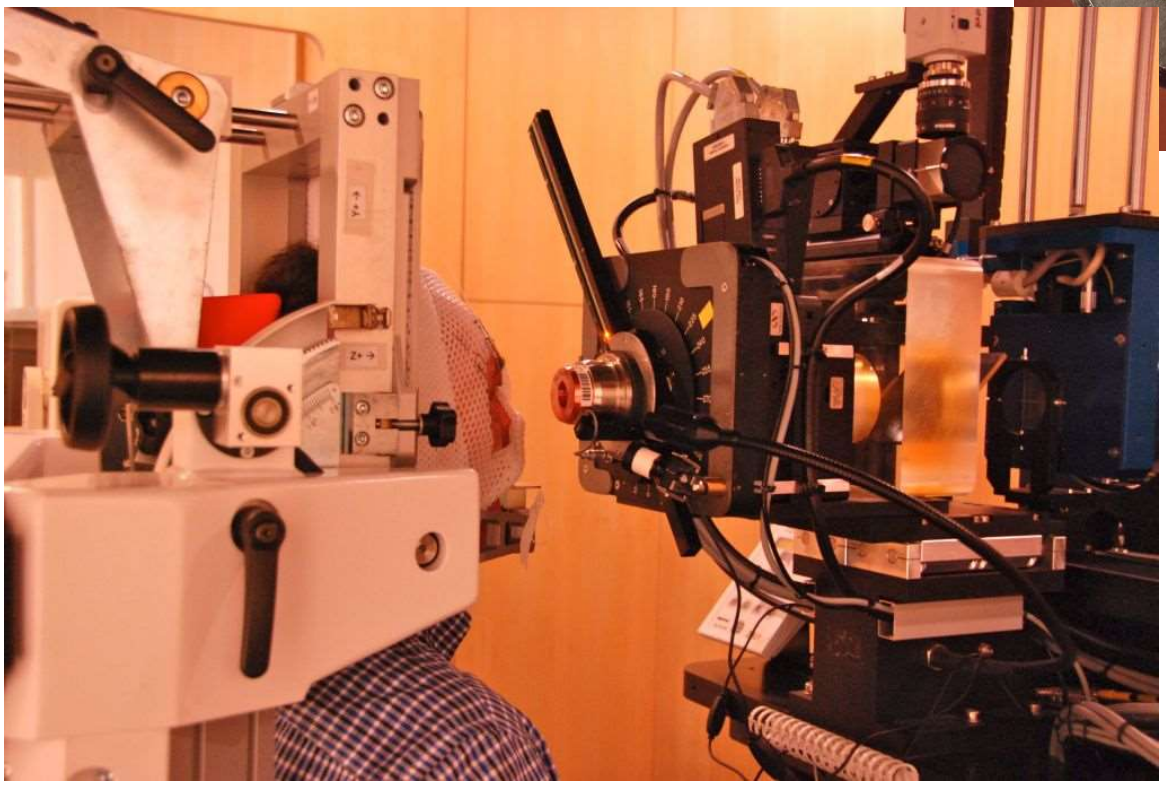
OPTIS



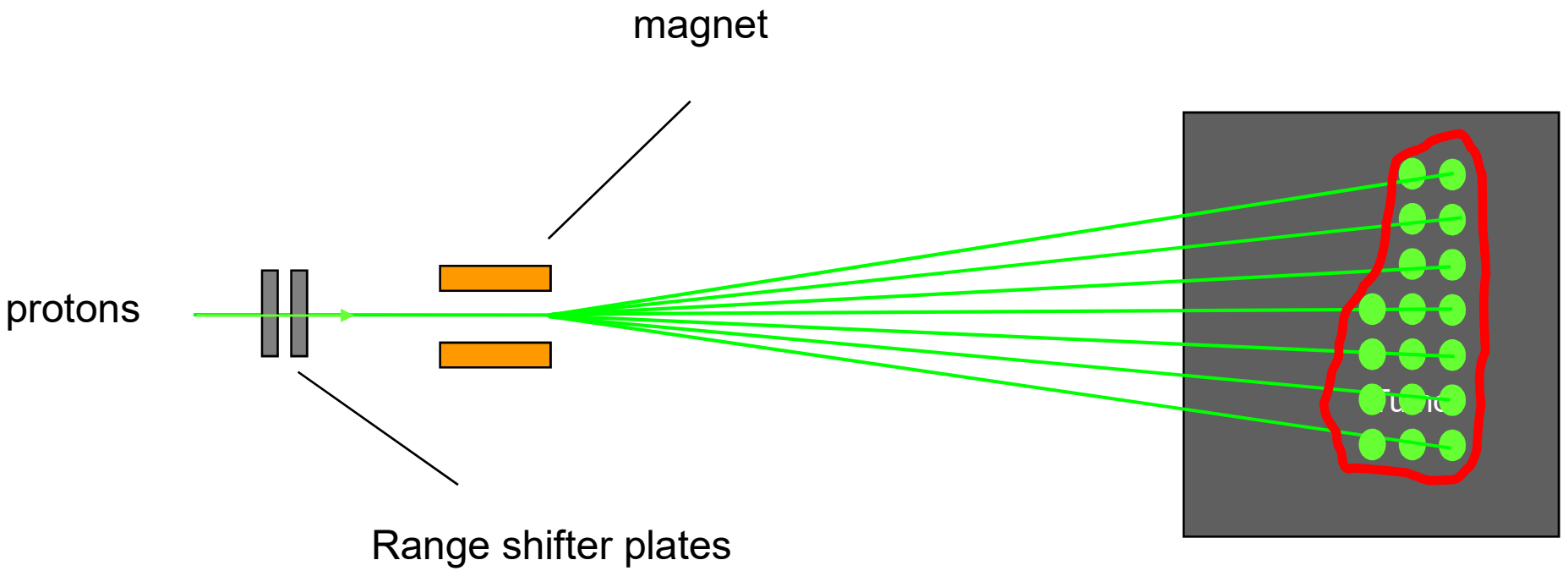


OPTIS – a success story

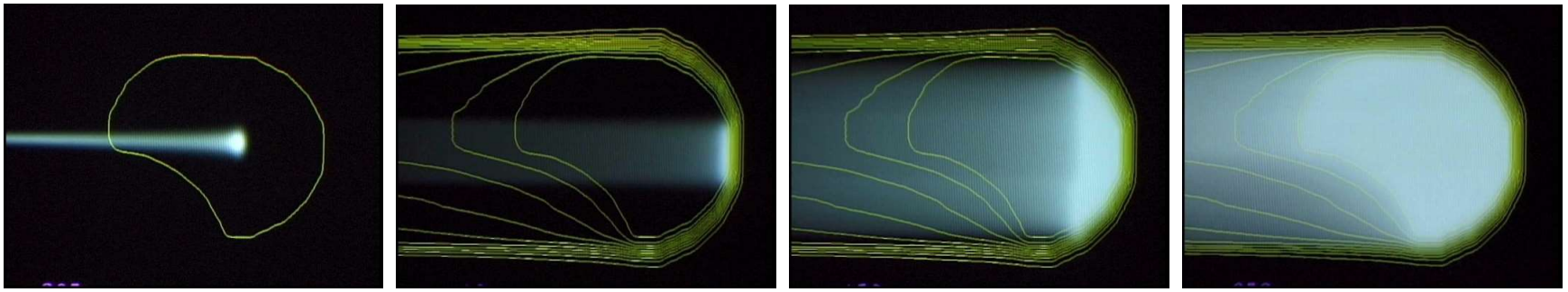
- Since 1984:
  treated more than 7’000 patients
- 98% cure
  (local tumor control)
- Conservation of vision
  100% for small tumors
  90% for big tumors

Protons are the standard!

Irradiation technique – «spot scanning»



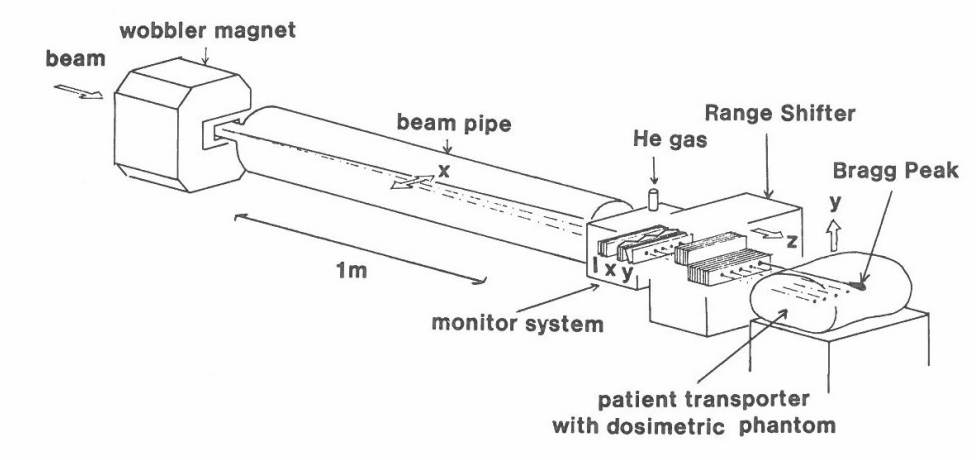
Feasibility demonstrated in 1989



Experimental setup for spot scanning with protons

Horizontal beam line

- Scanning in 1 dimension only
- Range shifter to modifiy proton energy



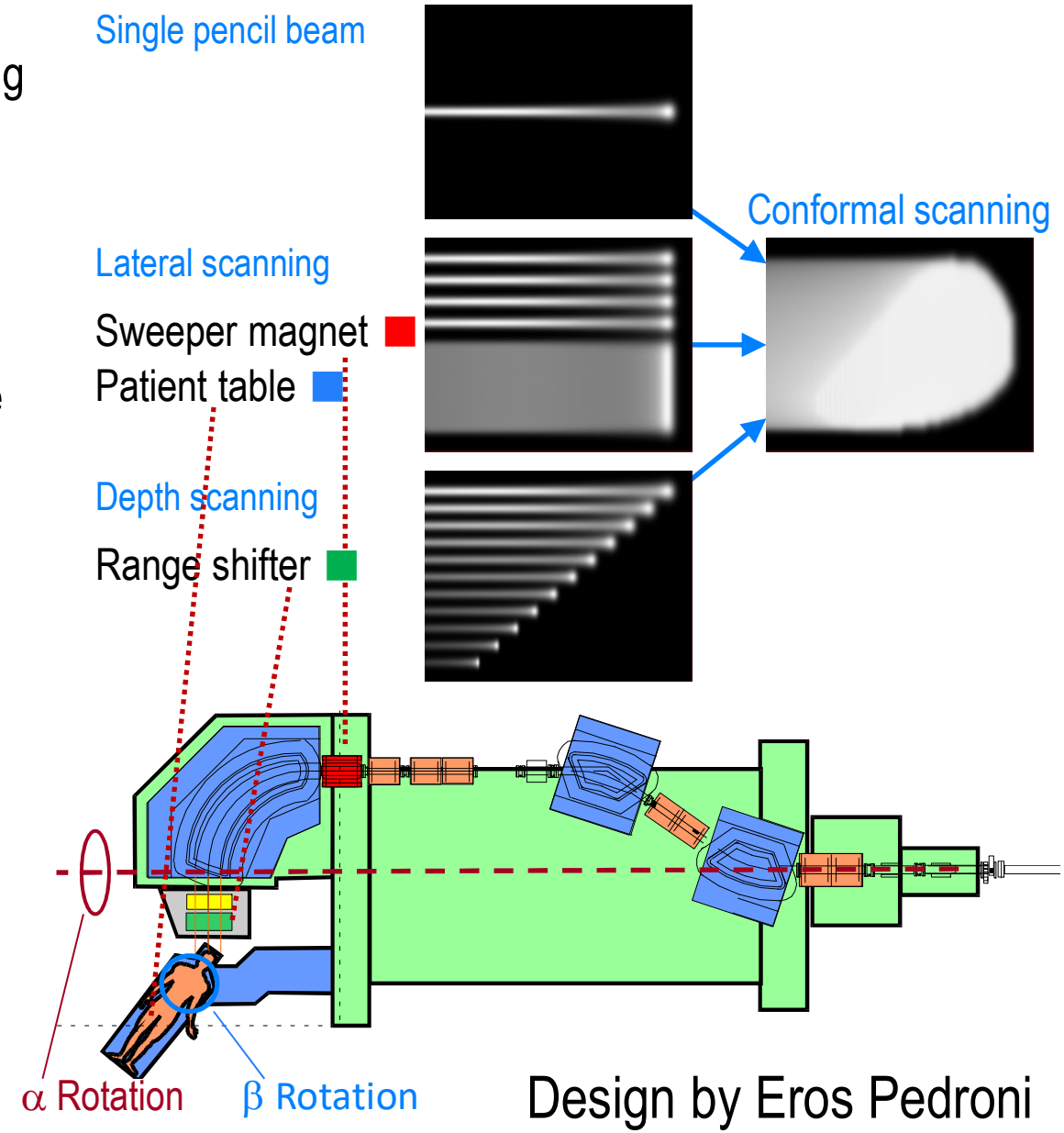
Annex II
Annual Report 1989

Paul Scherrer Institut

Fig. 4: X ray film irradiated with the 200 MeV proton beam using the spot scanning method.

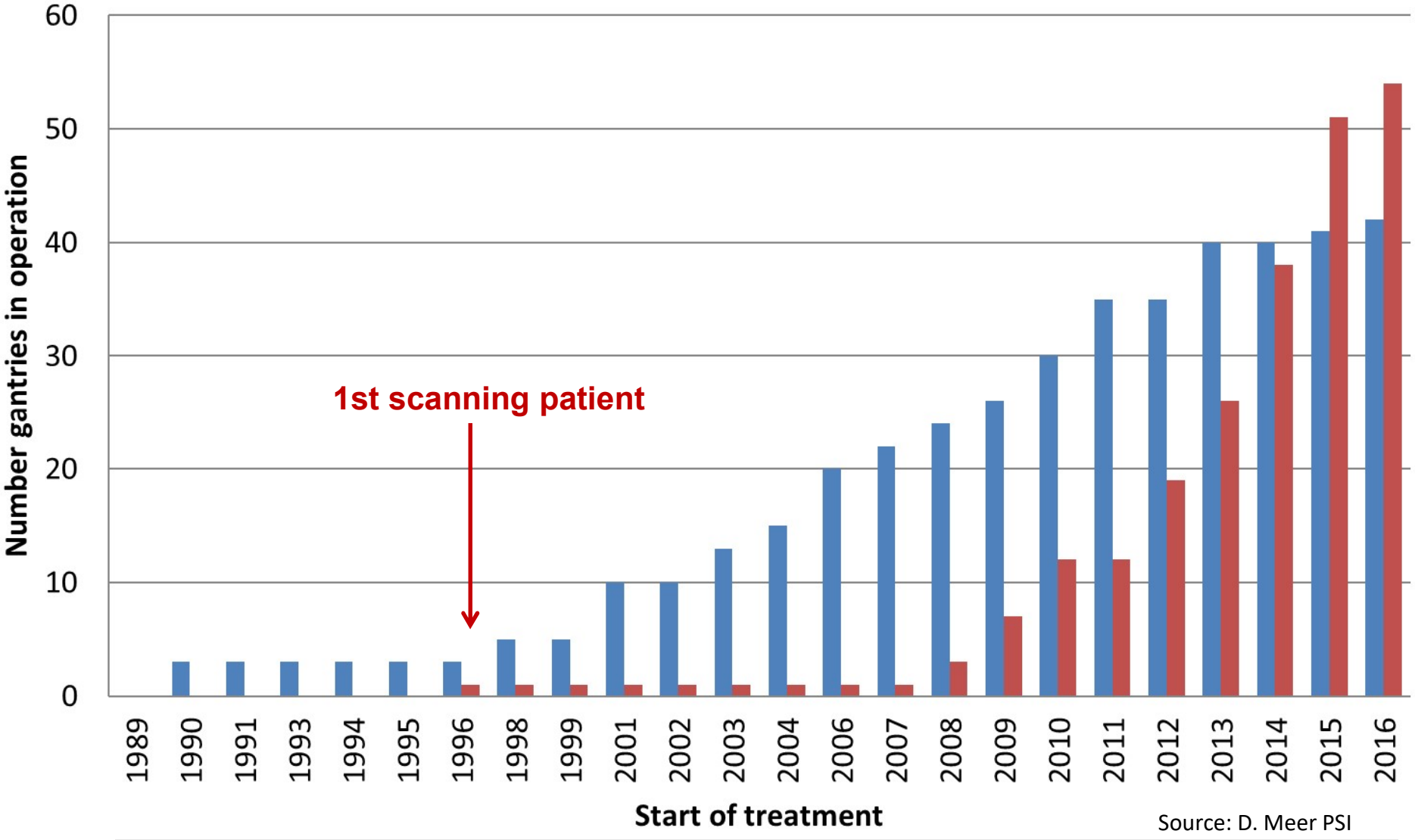
Gantry 1: A compact system for spot scanning

- Implementation of spot scanning technique
- Start patient operation 1996
- During 12 years the only spot scanning gantry worldwide
- Due to eccentric design still the most compact system, r = 2m



Design by Eros Pedroni

Scanning-Technology is today's standard



Source: D. Meer PSI

Gantry 2: next generation spot scanning

Easy access to patient at all times

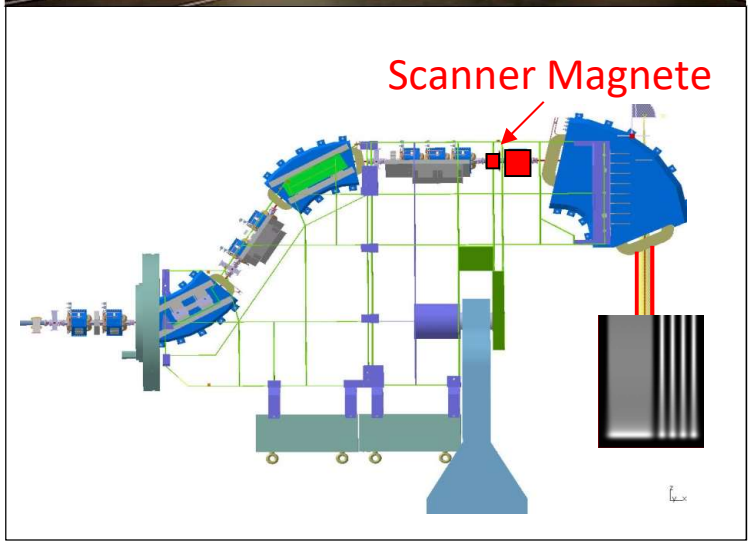
- Rotation limited to 210°
- Patient table rotatable 180°
  (→ still full flexibility)
- No pit

Fast scanning in 2 dimensions

- Re-scanning possible
- Parallel Scanning
- Field size 12 x 20 cm

Fast energy change → 3rd dimension

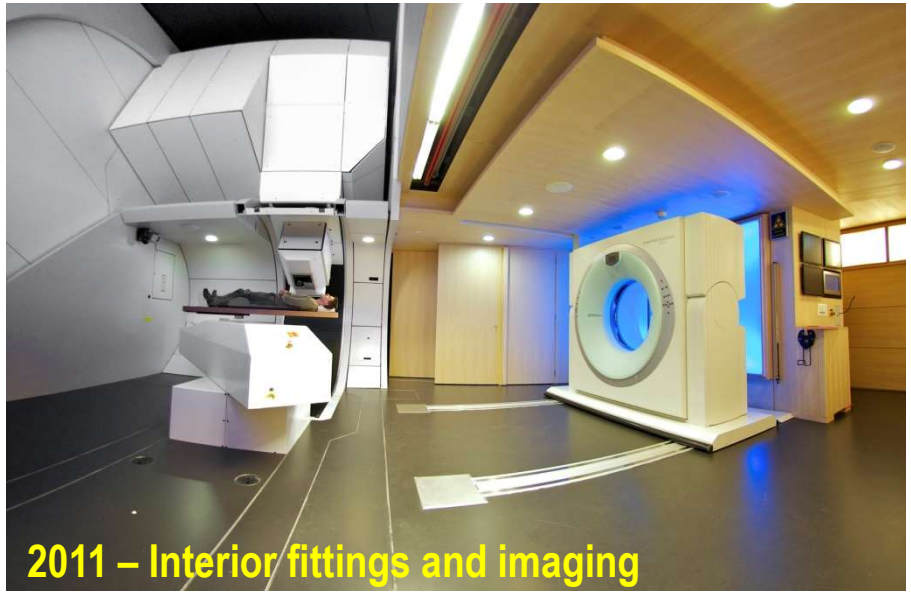
- Energy step < 100 ms
- Re-scanning possible in 3 dimensions



Gantry 2: next generation spot scanning


2006 - Delivery of mechanical structure

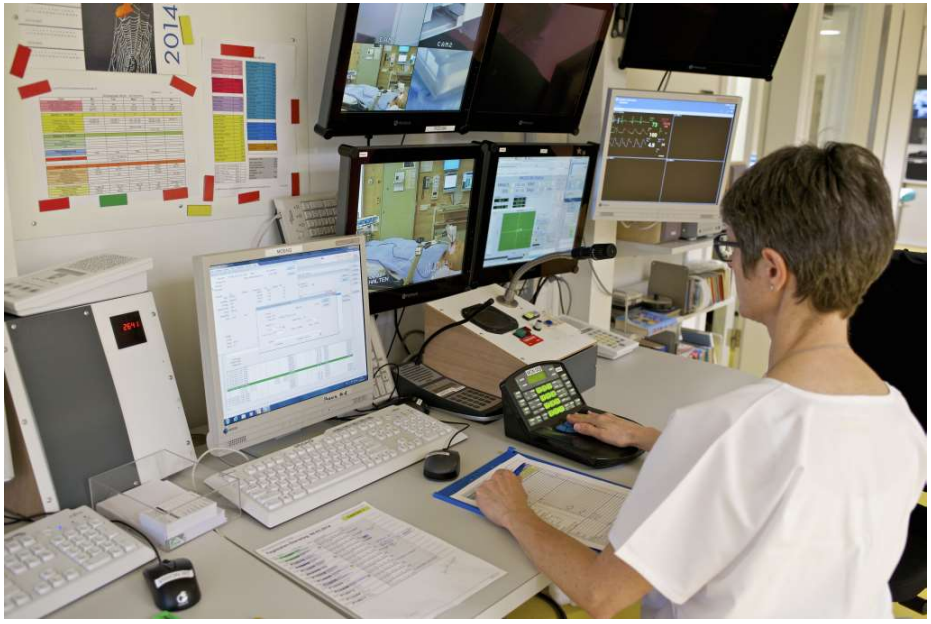

2008 - Beam line with innovative 90° dipole


2011 – Interior fittings and imaging


2013 - 1st patient treated

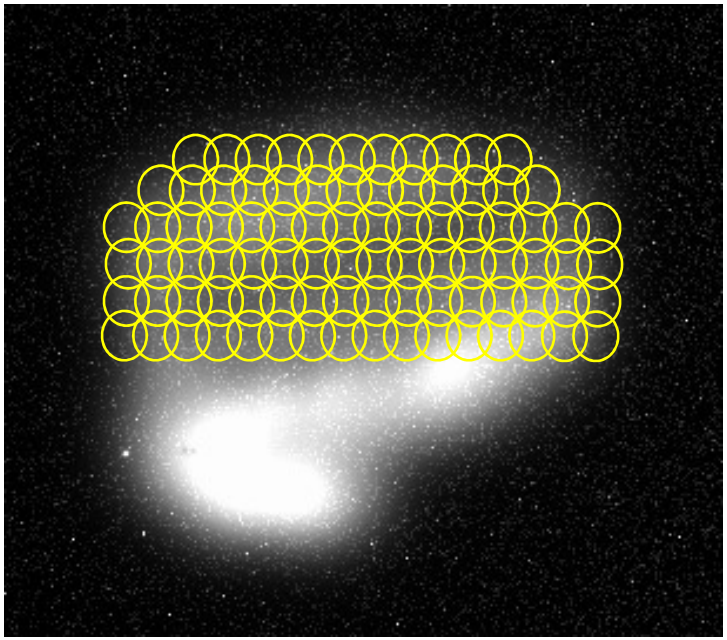
Treating small children

- Since 2004 treatments of small children
  → **anesthesia team from children's hospital in Zurich**
- Ca. 500 patients


2014

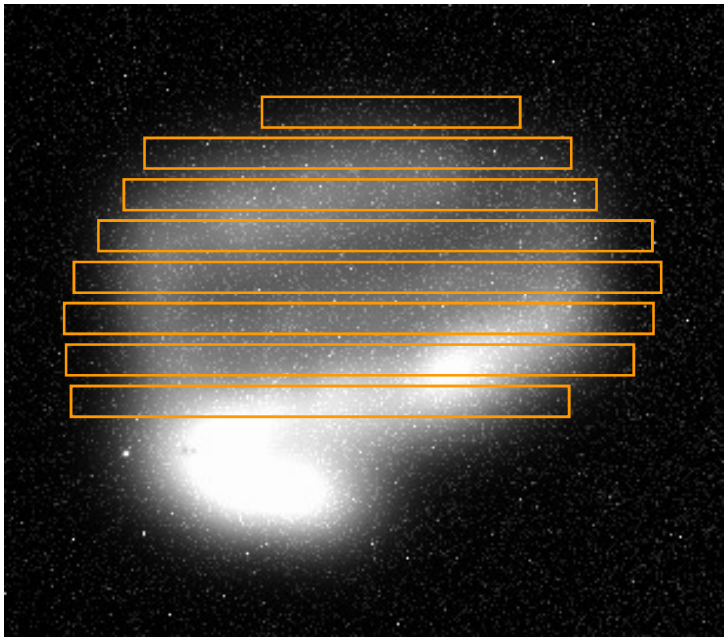

Bair Hugger

Improvements in scanning technology



Discrete spot scanning

- Switching off the beam after each spot
- Dead time per spot ~3 ms.
  Typically field: 10'000 spots
  → 30 s dead time, scales with number of re-scans!
- Accurate dose delivery
- Spot scanning is actual operation mode of Gantry 2

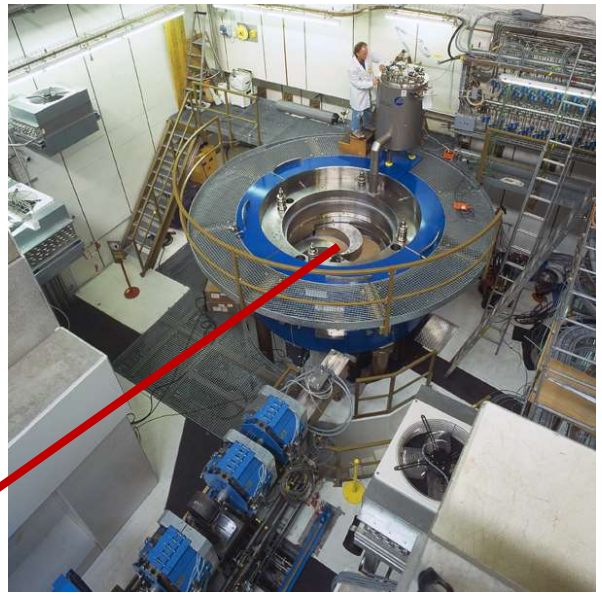


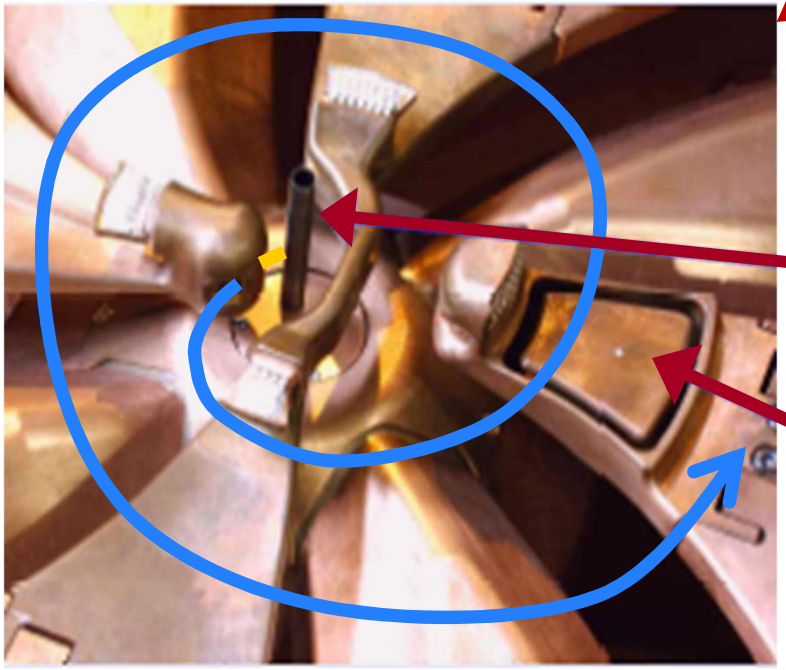
Continuous line scanning

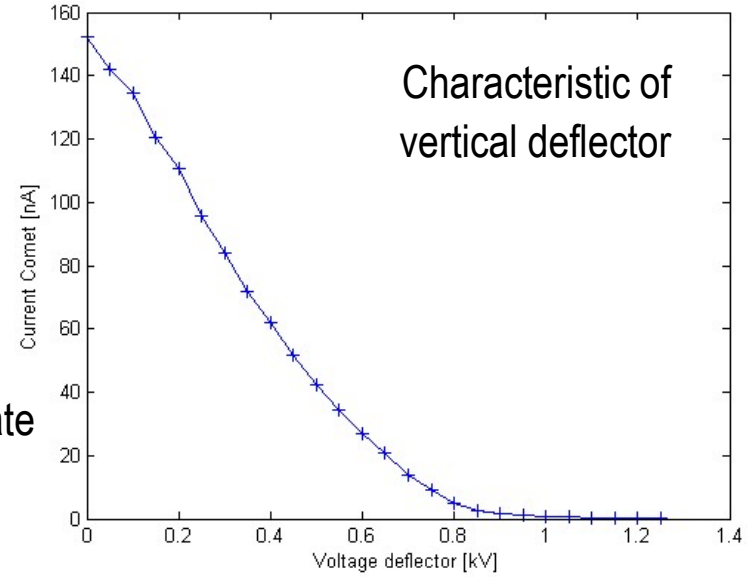
- Paint lines of dose with continuous beam on using
  - Beam intensity modulation
  - Beam motion speed modulation
- For efficient and effective repainting
- Operational in experimental mode, in development

Proton beam intensity modulation

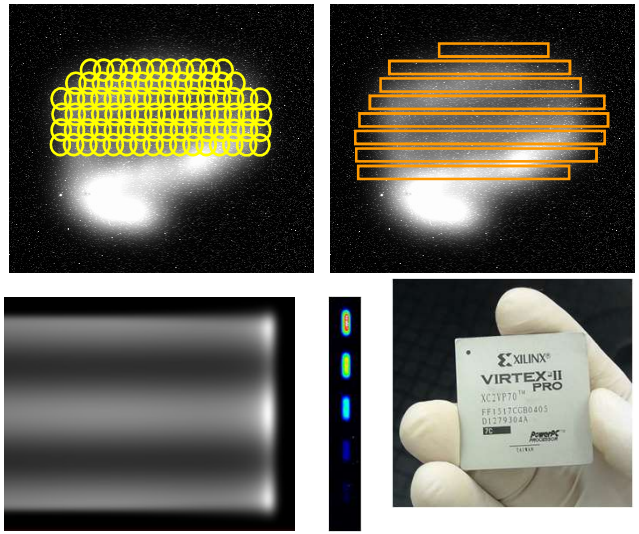
- Fast electrostatic beam deflection inside cyclotron (< 50 μs)
- Switch beam on/off
- Intensity modulation
- Little activation of the cyclotron







A flexible control system for different scanning options



Drive sweeper magnets

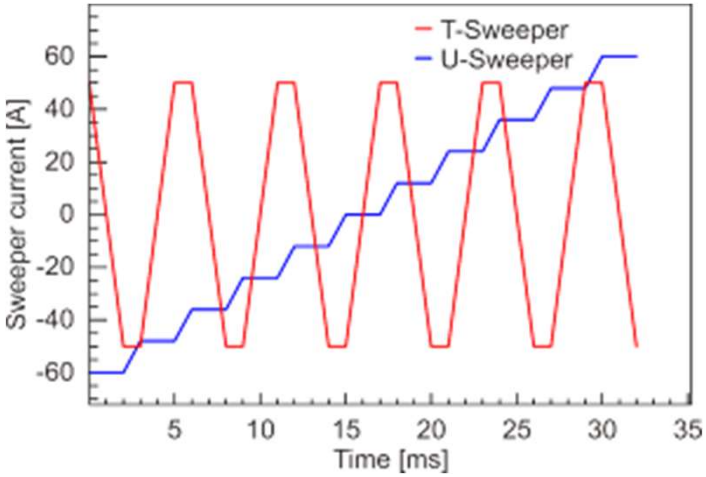
Different modes: *Spot scanning* / *Lines scanning* in the same steering file

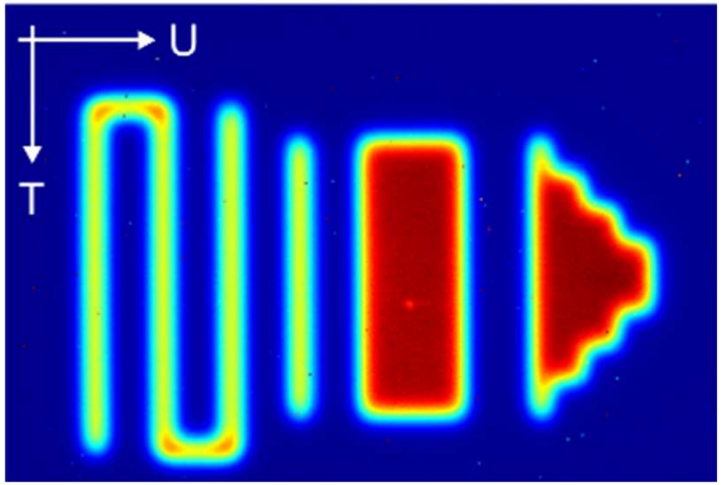
Vertical deflector plate for intensity modulation

- Fast intensity control on time scale of 100 µs
- Control dose with feed-back loop

Requires flexible control system

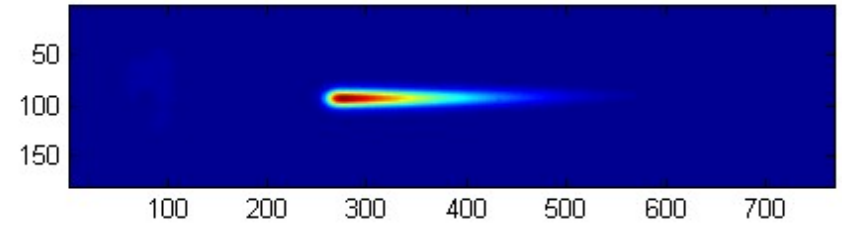
- Synchronous control of fast actuators (sweepers, deflector plate) with 100 kHz
- Tabulated dose delivery based on state-of-the-art electronics (FPGA)
- Example: Painting shaped energy iso-layer



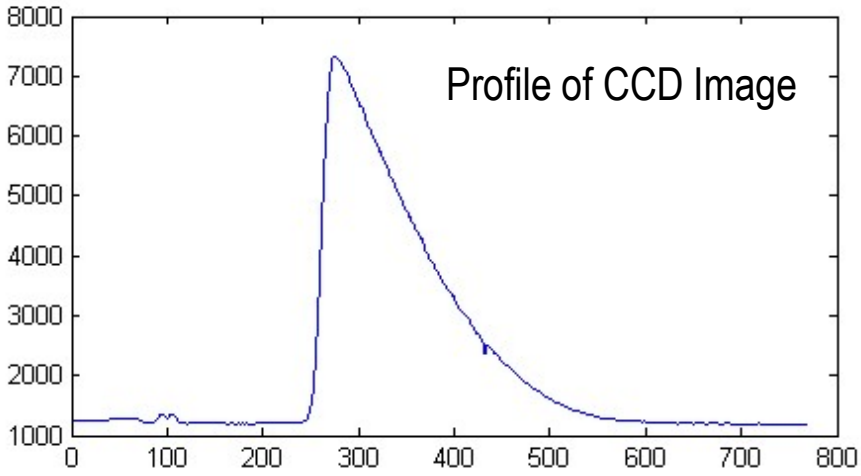


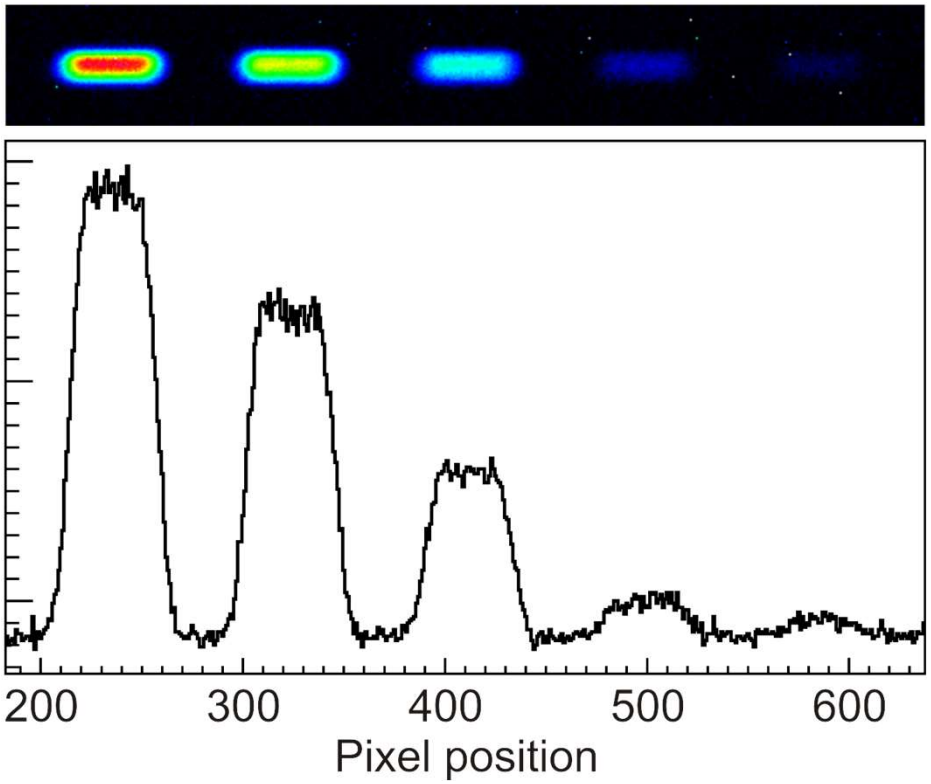
Painting intensity modulated lines

Continuous line (18 cm) with linear increasing vertical deflector voltage



18 cm

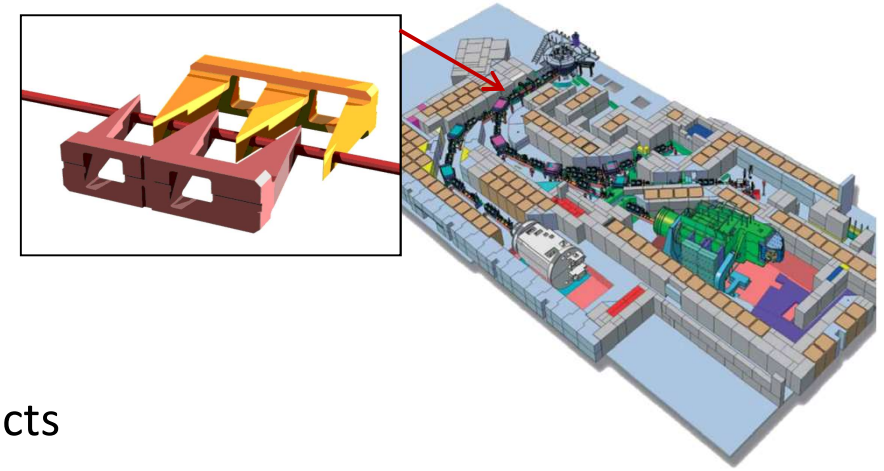




Intensity modulated line segment (15 cm) painted in 30 ms.

Fast changes of the beam energy

- The Gantry 2 and PROSCAN are optimized for fast energy changes:
  - Cyclotron provides fixed energy
  - Fast degrader mechanical
  - Laminated magnets / dedicated power supplies
  - Need to consider magnetization and hysteresis effects
  - On-line correction of “drift” effects

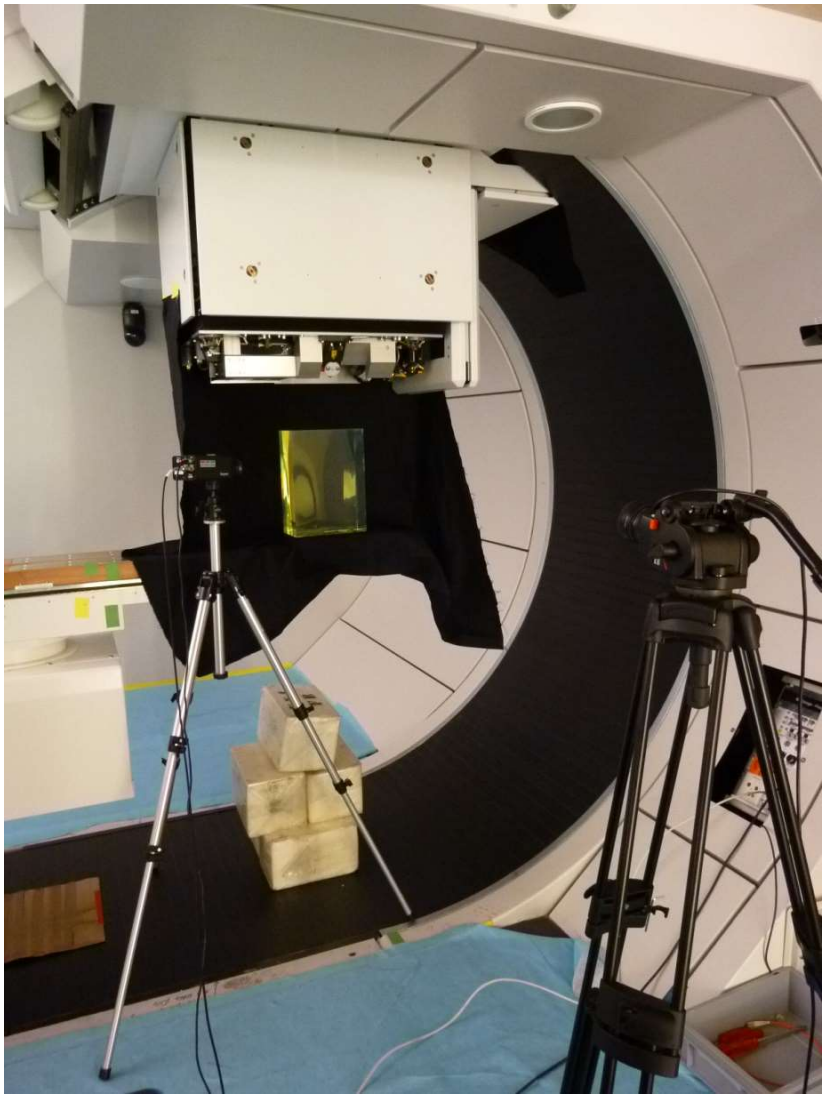


- Realized:
  - **~100 ms** dead time for range steps of 5 mm

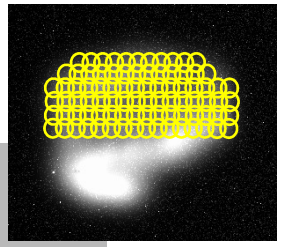
Benefit

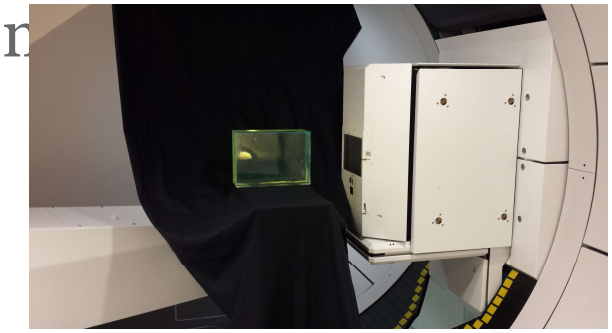
- Faster treatments
- Potential for volumetric repainting

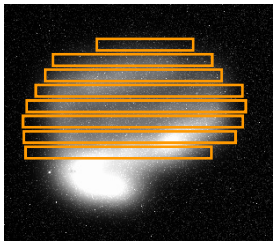

ciclobby



Demonstration to show potential of fast line-scannin







Discrete spot scanning

20412 spots, 28 energy layers

Beam-on time: 17s

Dead time: 80s

Total time: 97s

→ 5 re-scans: ~7min

Cubical target, V = 1l

Spot grid 4 mm

Dose: 0.6 Gy (typical 3 field fraction dose)

Standard dose rate (<6 Gy/s)

Continuous line scanning

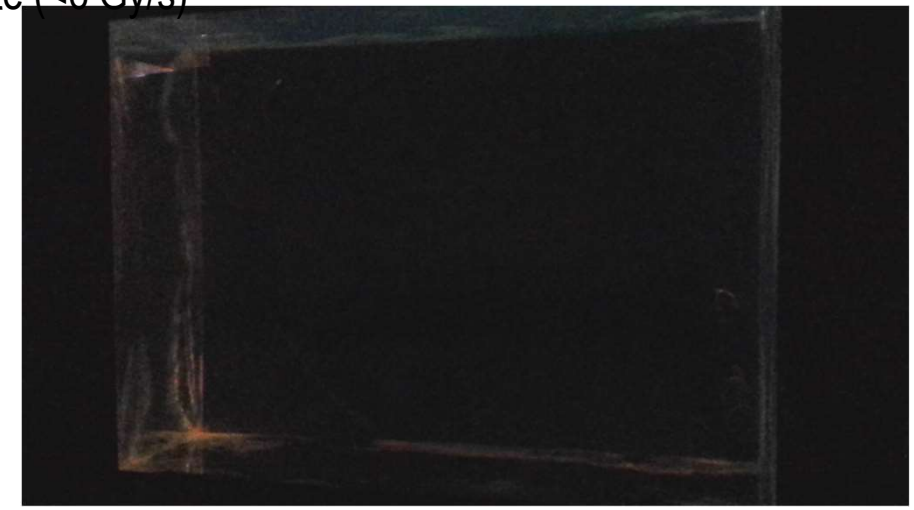
27 lines / energy, 28 energy layers

Beam-on time: 17s

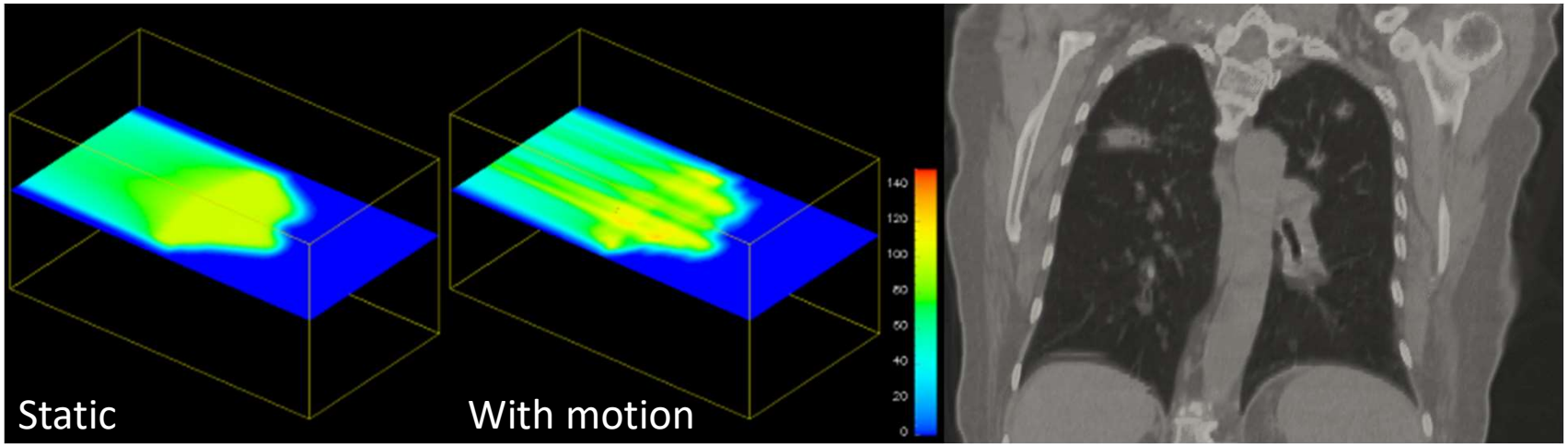
Dead time: 3s

Total time: 20s

→ 5 re-scans: ~30s

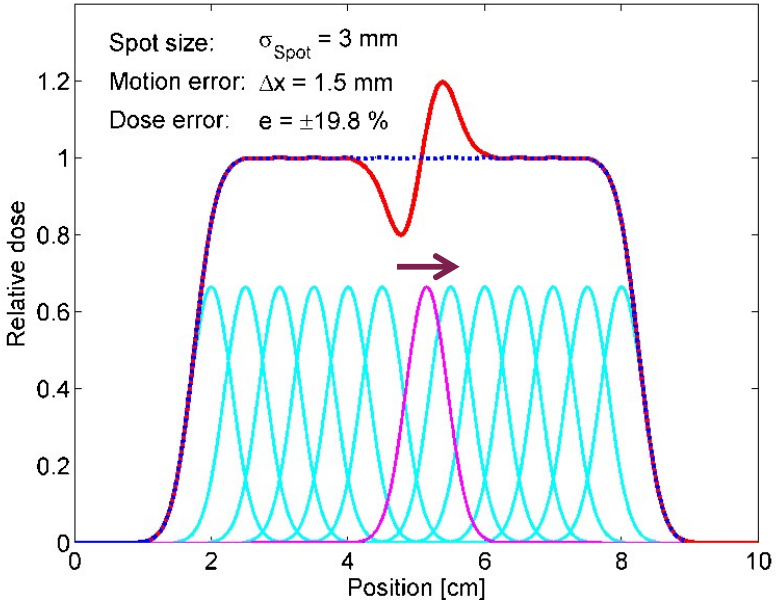


A mayor challenge in PBS: Moving targets / organ motion



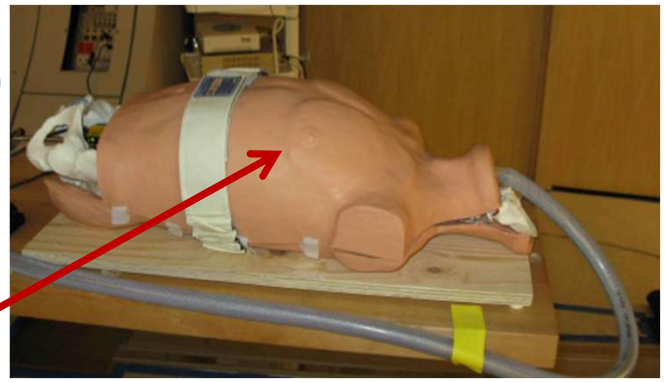
- Interplay effect between beam delivery sequence and organ motions destroys dose homogeneity
- Mitigation techniques:
  - Deliver dose multiple times (Rescanning)
  - Patient hold his/her breath (Breath-hold)
  - Irradiation only in exhaled phase (Gating)

⇨ All approaches require fast beam delivery

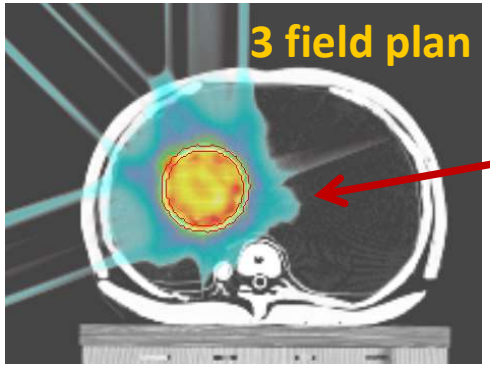


Experimental validation of rescanning

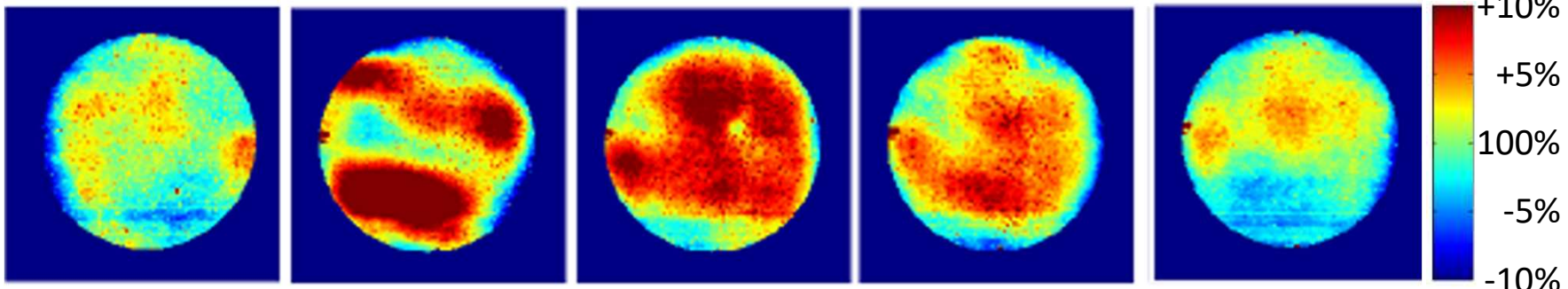
- Anthropomorphic phantom with lung tumour and tissue equivalent materials (bone, skin, lung)
- Simulation of different breathing parameters
- Rescanning to minimize motion interferences
  → Dose homogeneity can be recovered



R. Perrin, PSI



Tumour with insert for dose measurements with film

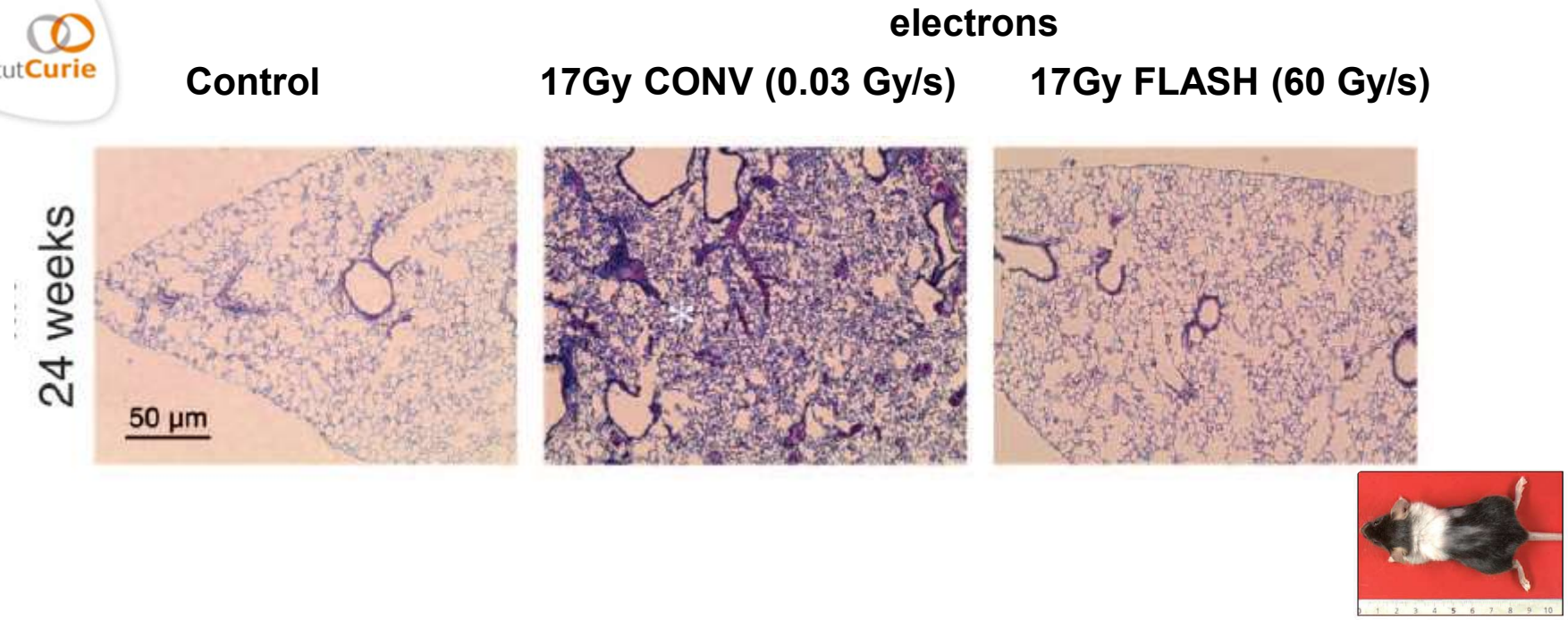


Static | Motion, 1 cm | 2x rescanning | 5x rescanning | 8x rescanning

FLASH radiotherapy

- FLASH: application of therapeutic dose in very short time
- → extremely high dose rates (1000 higher than standard)

- "FLASH-effect": for a given dose, sparing of healthy tissue is better if dose is applied in very short time



V. Favaudon et al., "Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumour tissue in mice", *Science Translational Medicine* 6, 2014

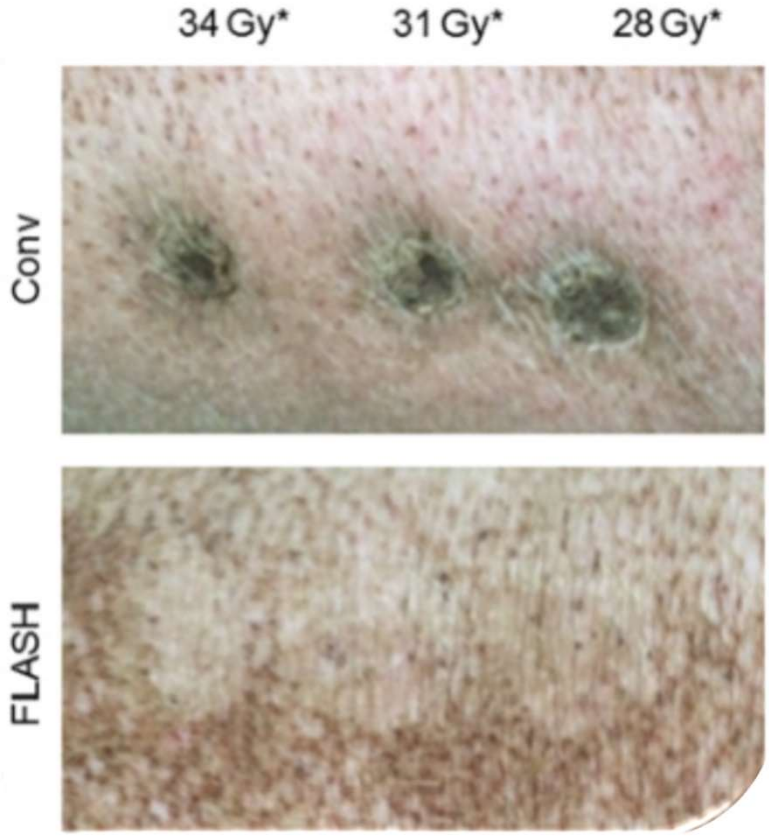
FLASH radiotherapy

FLASH confirmed in larger mammals (mini-pigs)

0.08 Gy/s

electrons

300 Gy/s



Black dots = NECROSIS

Vozenin, et al, The advantage of Flash RT confirmed in mini-pig and cat-cancer patients." Clinical Cancer Research. 2018;

FLASH radiotherapy

First human patient treated with FLASH

lectrons 166 Gy/s

Day 0

5 months

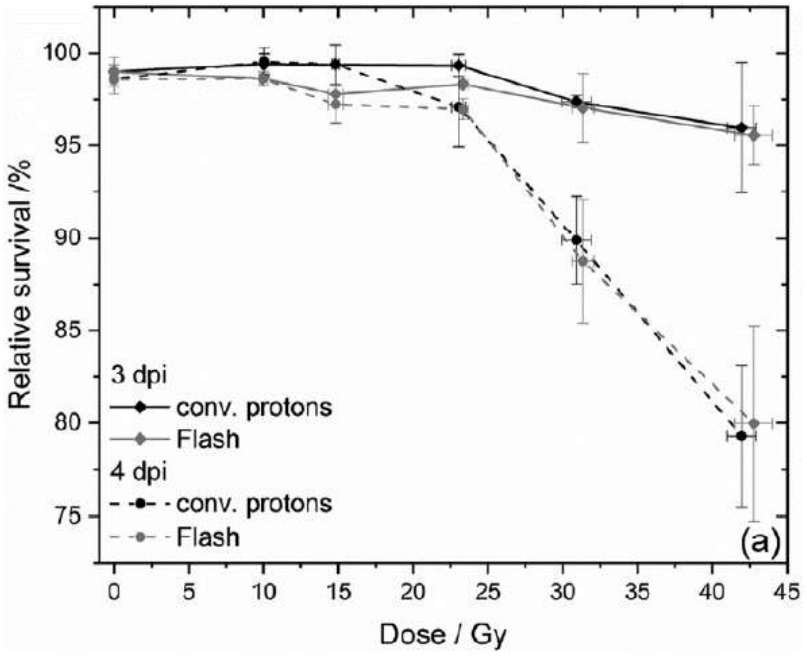
Jean Bourhis et al., «Treatment of a first patient with FLASH-radiotherapy», Radiotherapy and Oncology. 2019

FLASH protontherapy

- Most (important) protontherapy vendors have demonstrated they can reach FLASH dose rates
  - IBA: Groningen, Dresden
  - Varian: Cincinatti
- Biological experiment performed in Dresden
  - Published October 2019
  - No FLASH effect observed ☹

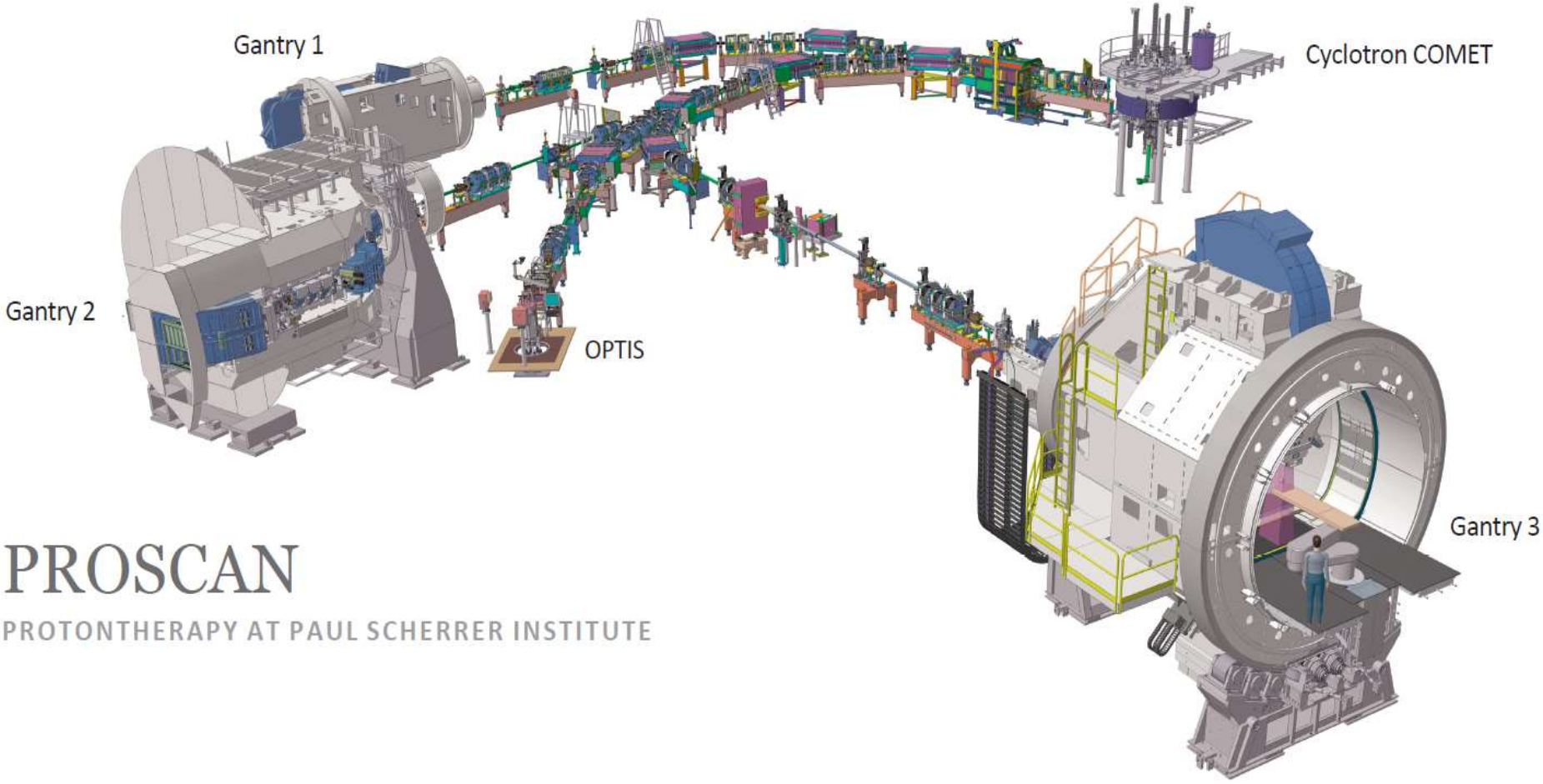
Universitäts Protonen Therapie Dresden

→ More experiments required!



E. Beyreuther et al., "Feasibility of proton FLASH effect tested by zebrafish embryo irradiation", *Radiotherapy and Oncology 139*, 2019

Beamline Transmission

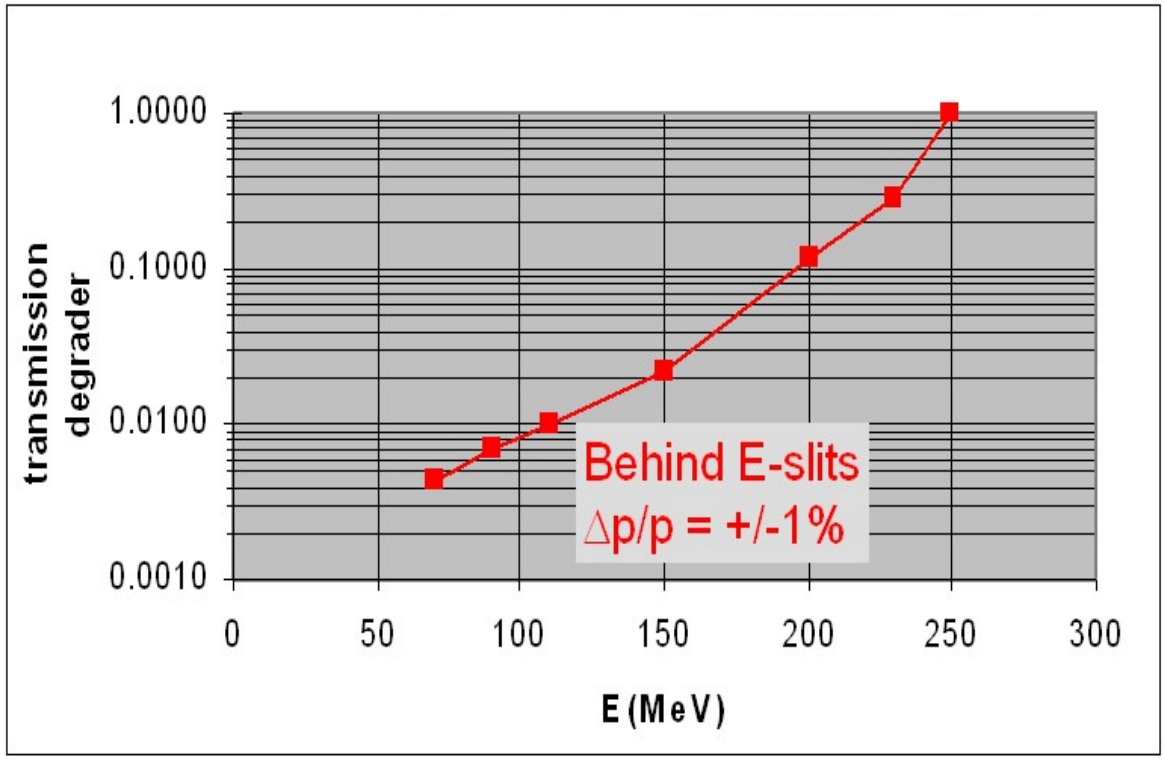


PROSCAN

PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

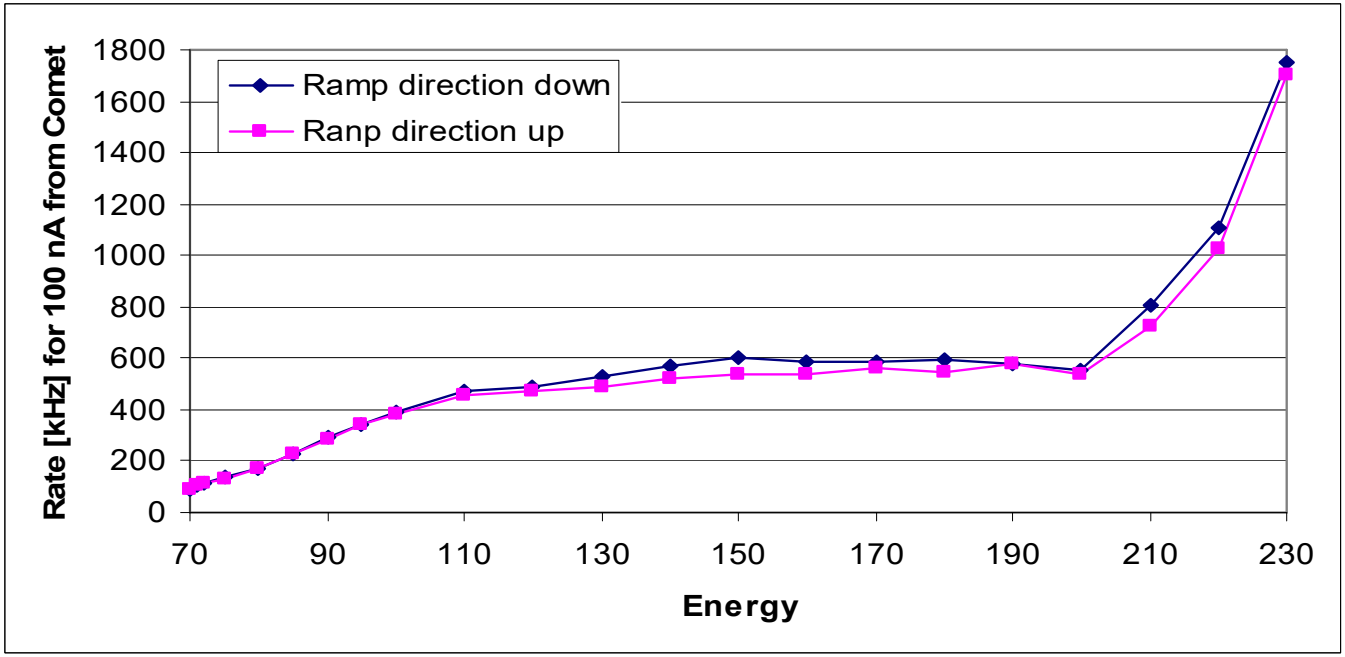
Beamline Transmission

- Transmission is highly energy dependent



Beamline Transmission

- Normal operation: defocus beam ON PURPOSE with quadrupoles
- → Equalisation between 100 – 200 MeV



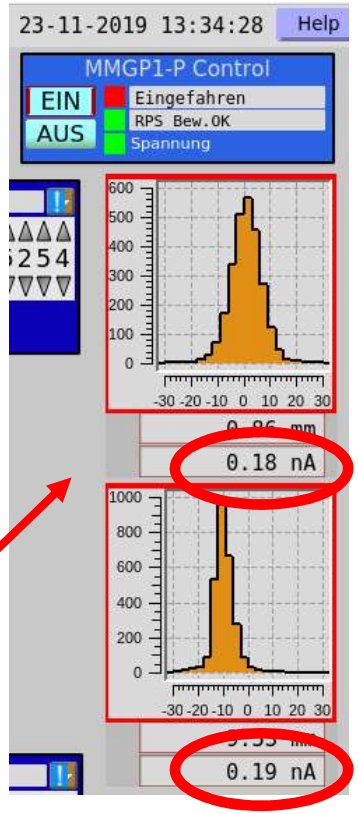
FLASH @ Gantry1

- We CAN operate at high energies with full transmission
- Gantry 1 is designed to transport high energies (250 MeV)
- Gantry 1 can provide energy modulation
- → bring full current from cyclotron (800 nA) to isocentre
- → Dose rate >1000 higher as in standard operations

- Gantry 1 “resurrection”: restart after 10 months shutdown
  - Everything still working ☺
- First experiments with high-transmission beam tunes
  - We are very close to 100% transmission

- Challenges
  - Control dose application
  - Scanning possible?
  - Legal permit

- Plan for biological experiments in 1st half of 2020



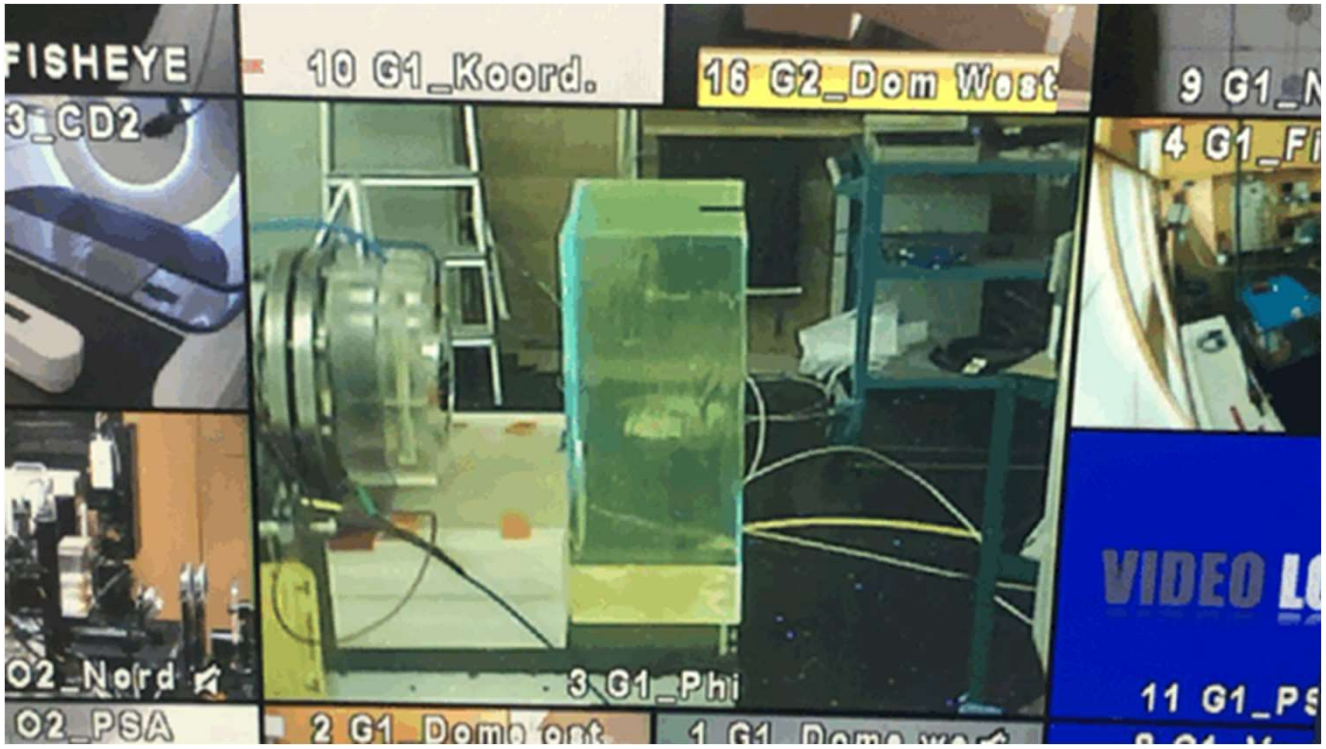
Input current from cyclotron 0.2 nA

X&Y profile monitor on Gantry 1, integrated current


ciclobby
Cal

Flash @ Gantry 1

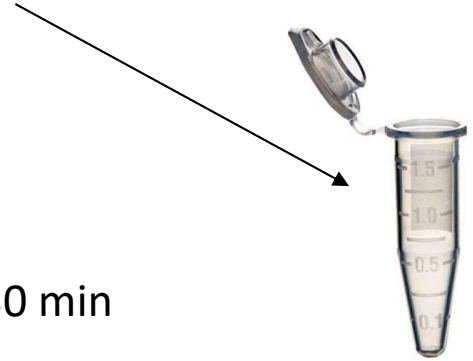
- Demo experiment January 2020
  → reach dose rates up to 9’000 Gy/s



Radiobiological experiments with CHUV

- Irradiation of zebrafish embryos

- First experiments
  - Shoot-through only
  - Maximum dose rate (1000 Gy/s), standard dose rate (10 Gy/s)
  - 20 eggs in each 0.2 mL sample with water
  - 2-3 mm beam with a constant dose rate (within 5 %)
  - Total dose uncertainty < 5%
  - Irradiation 6h and 24h post-fertilization
  - All the samples must be irradiated within 30 min



- Endpoint – development of the embryos

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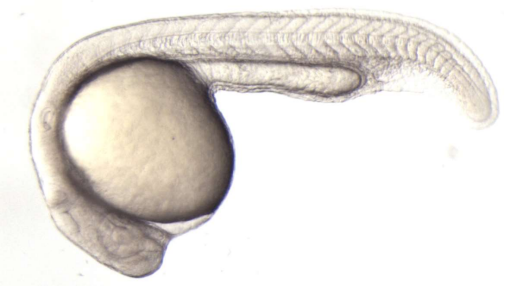

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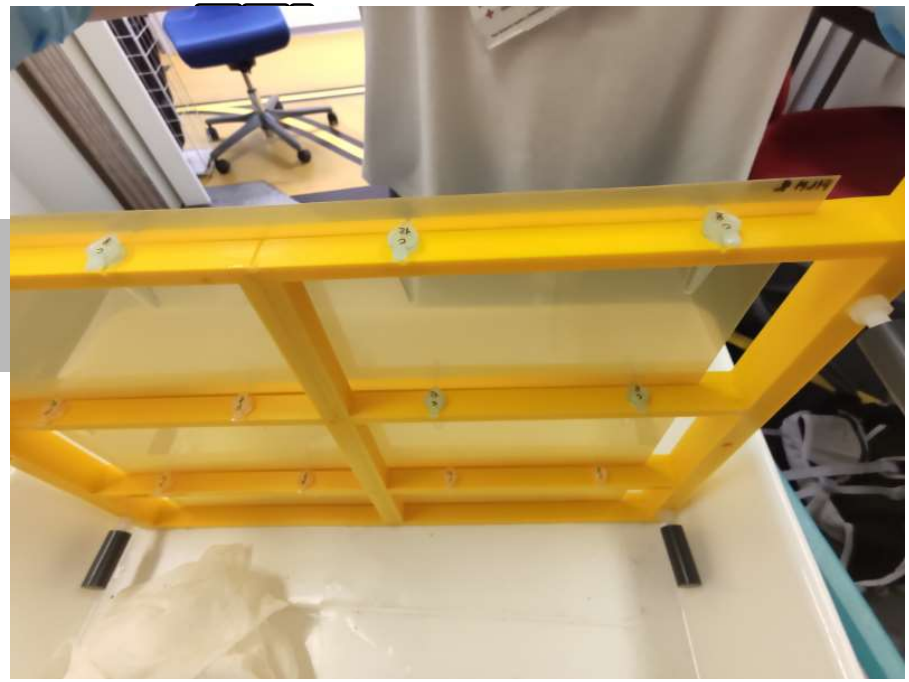

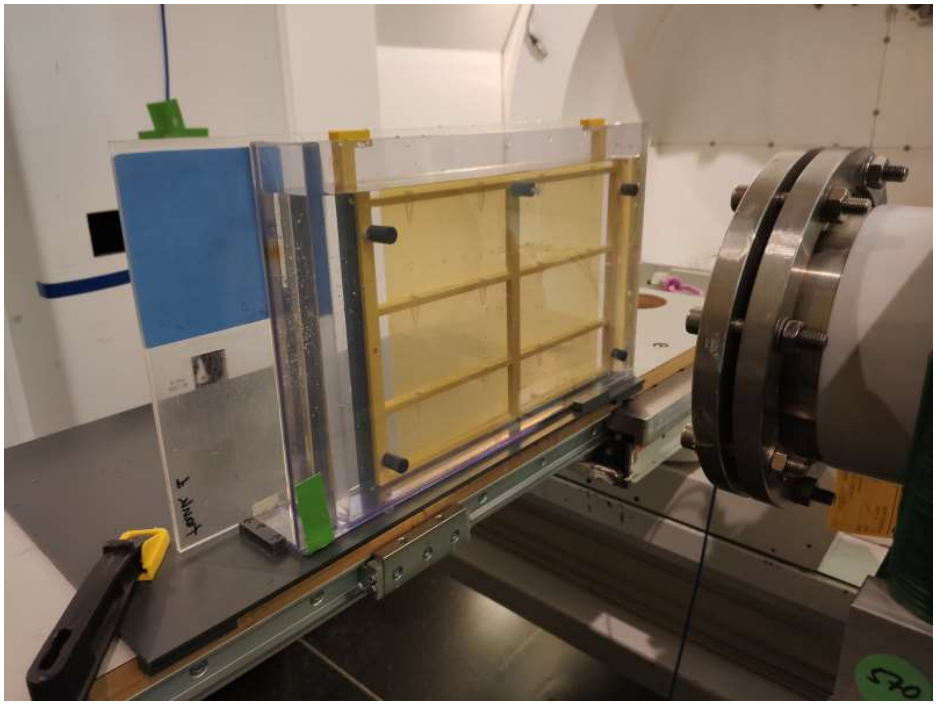

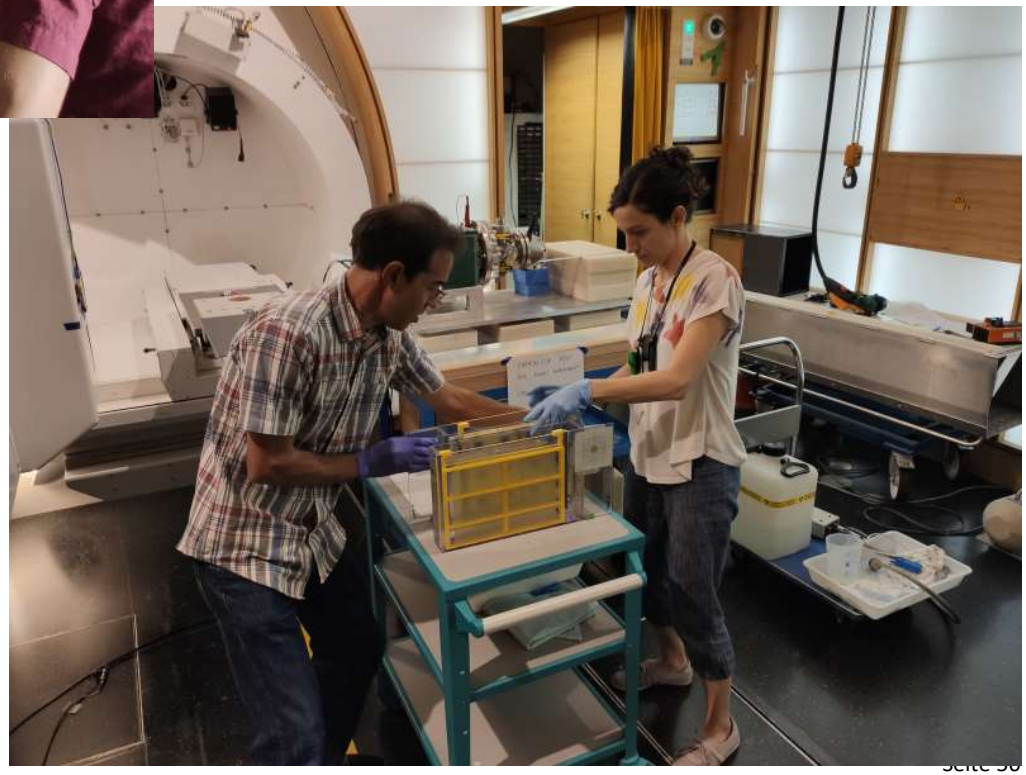

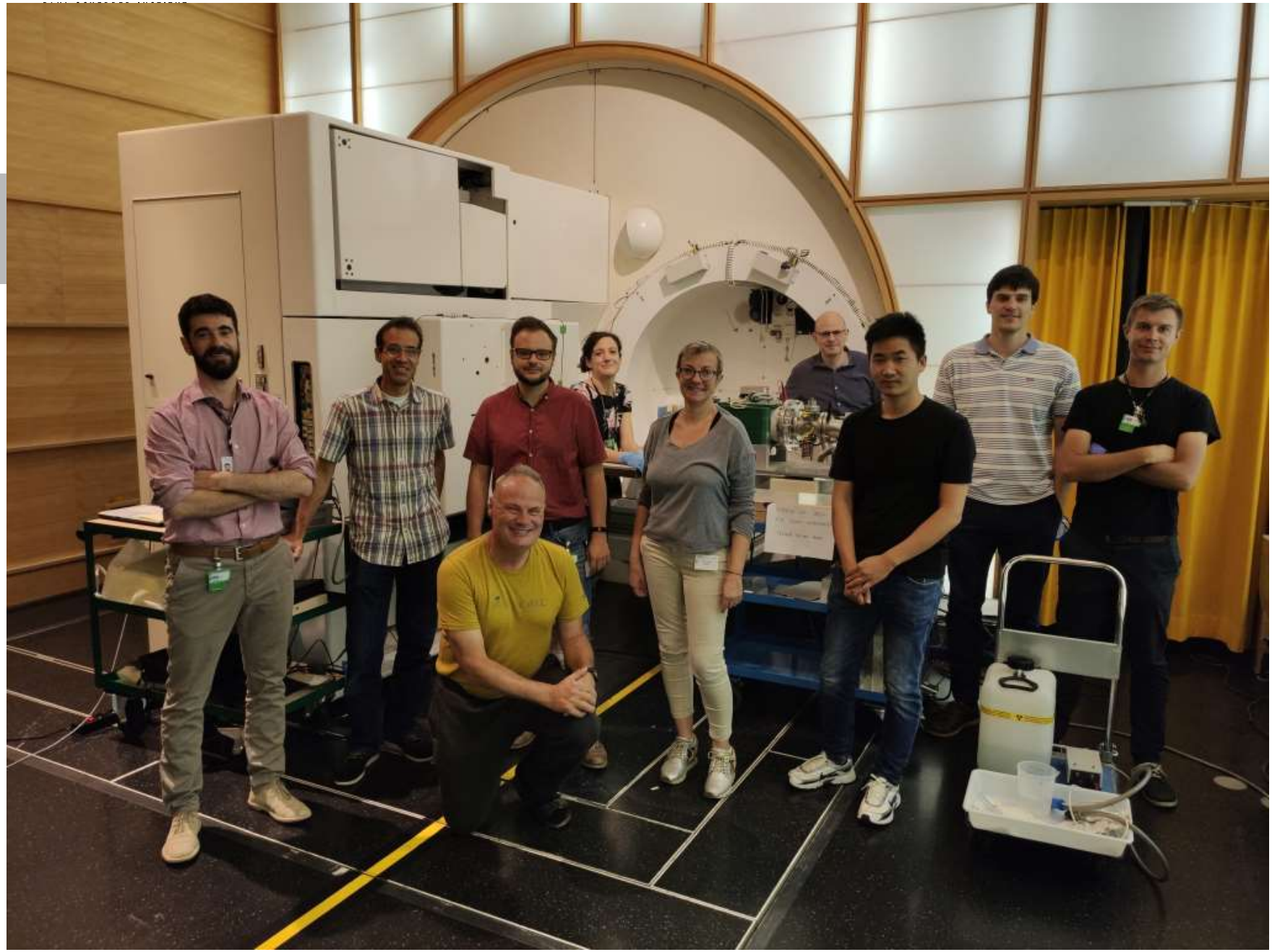

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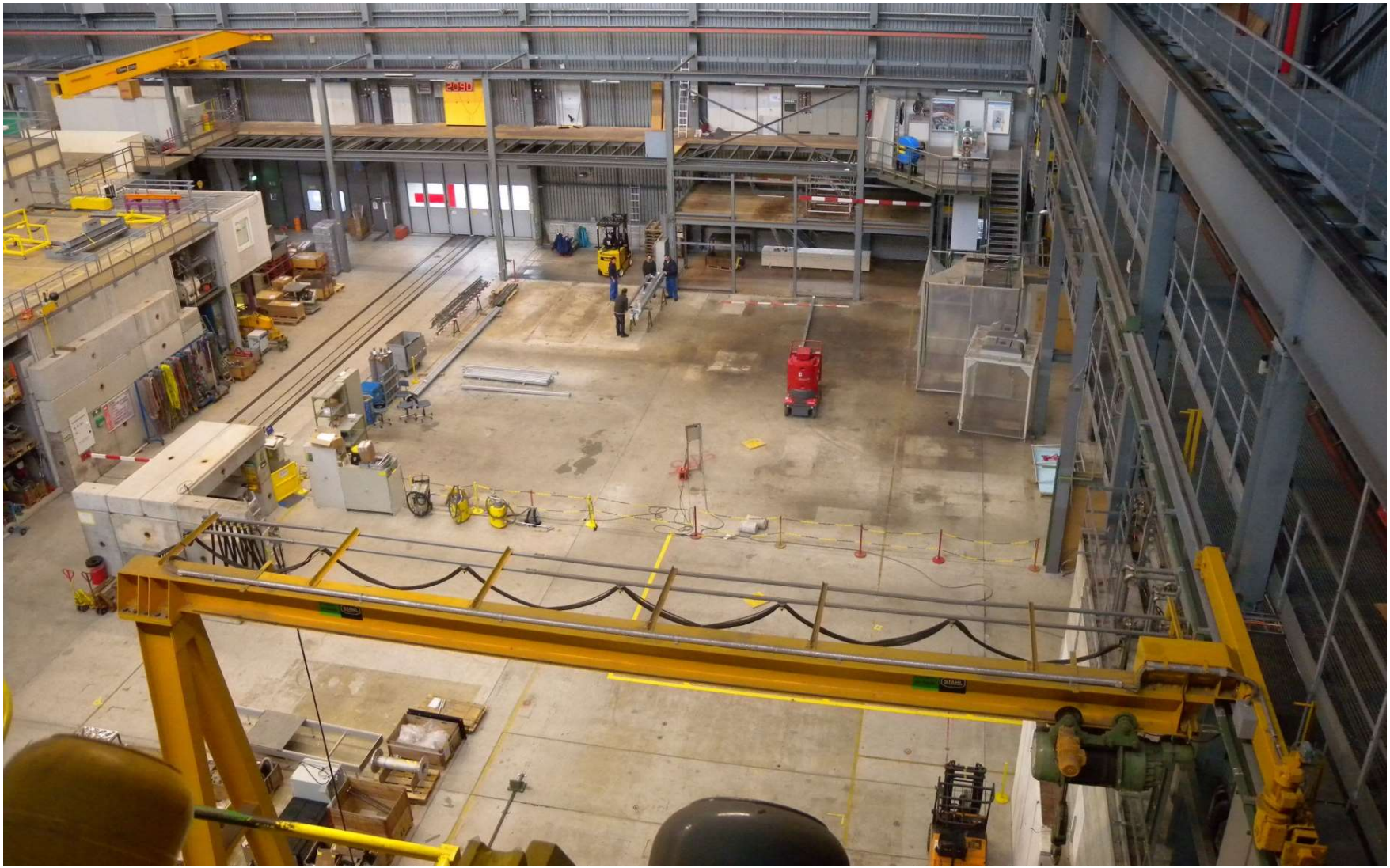
Some impressions from construction of Gantry 3

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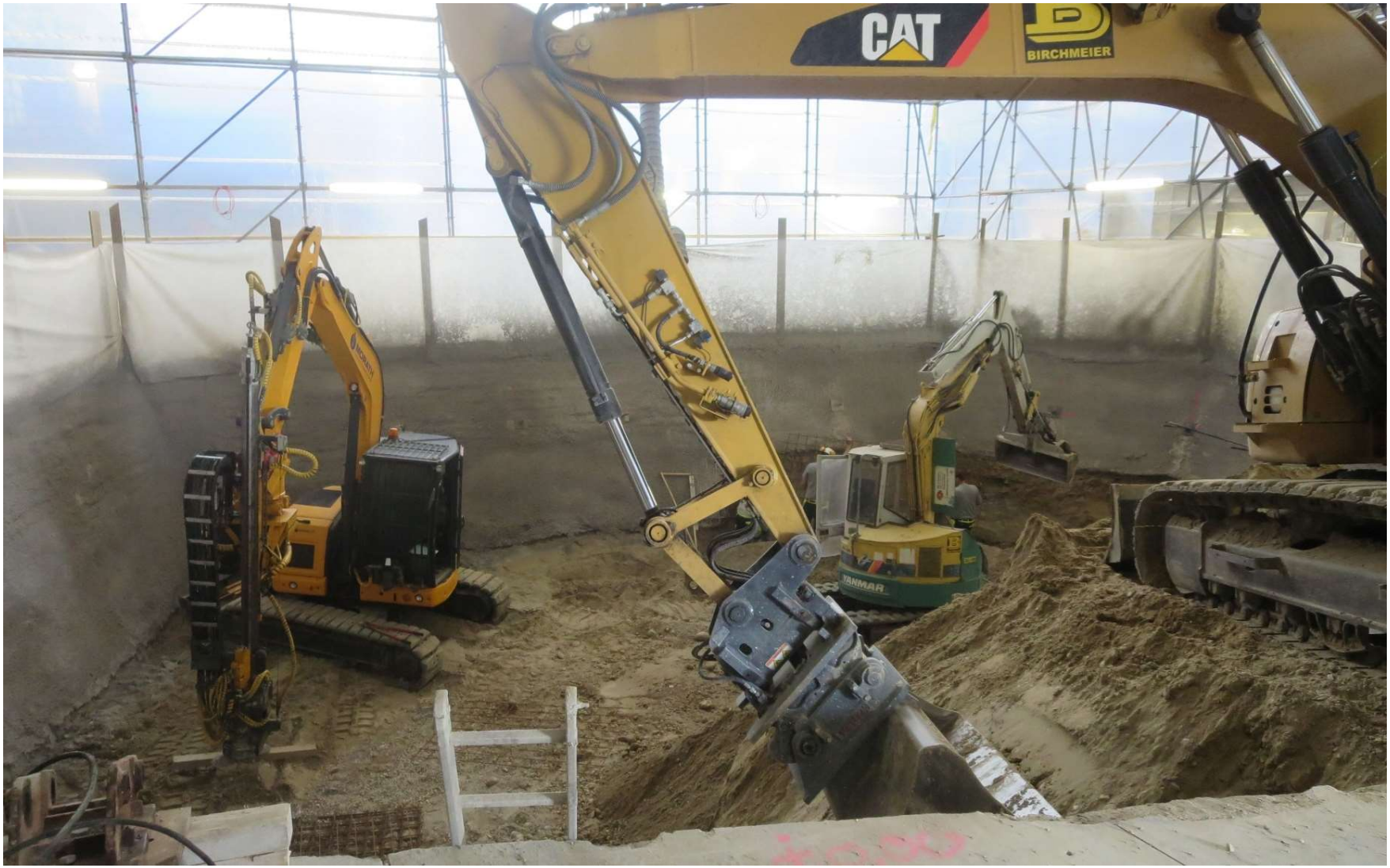
CAT


CAT
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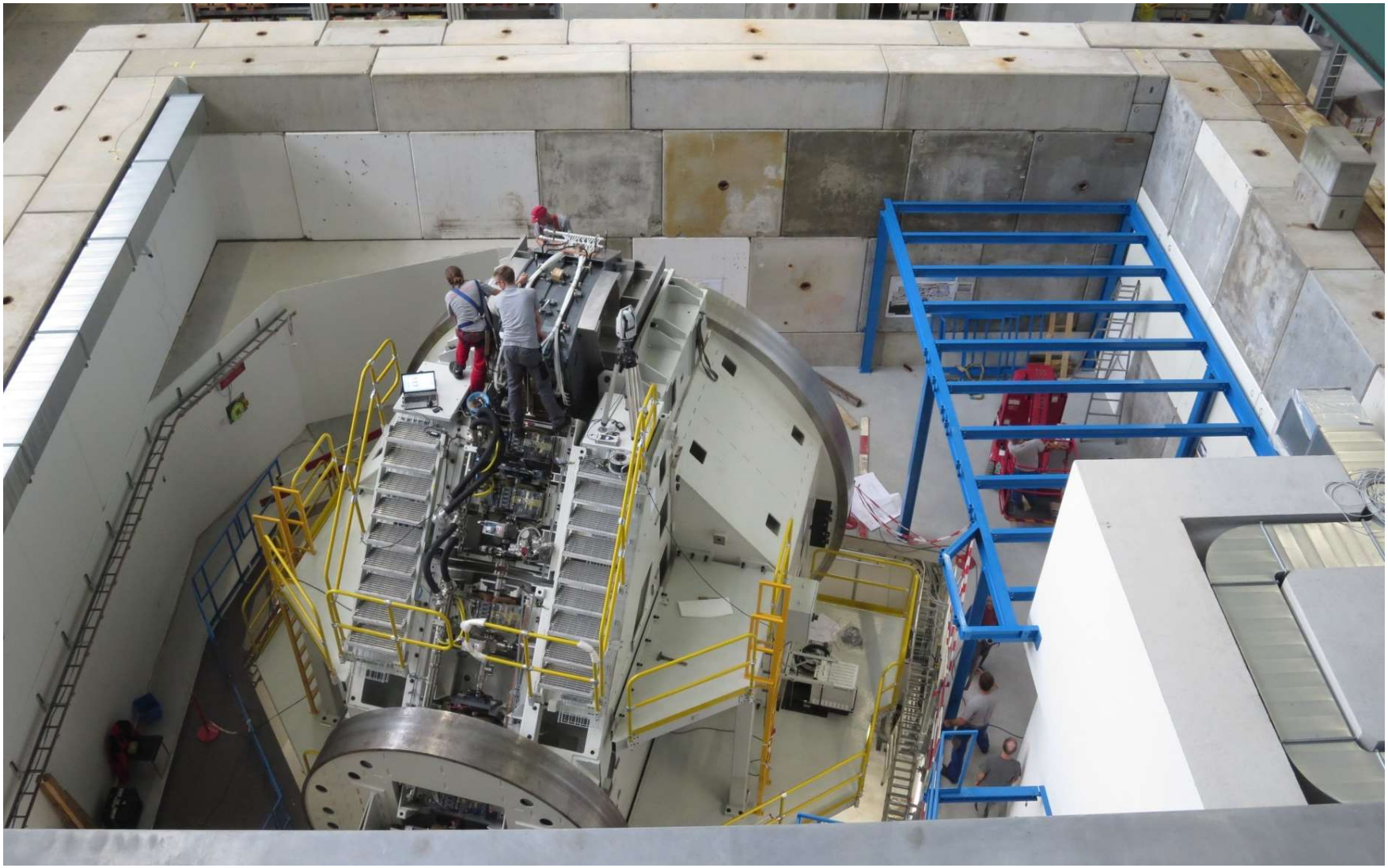

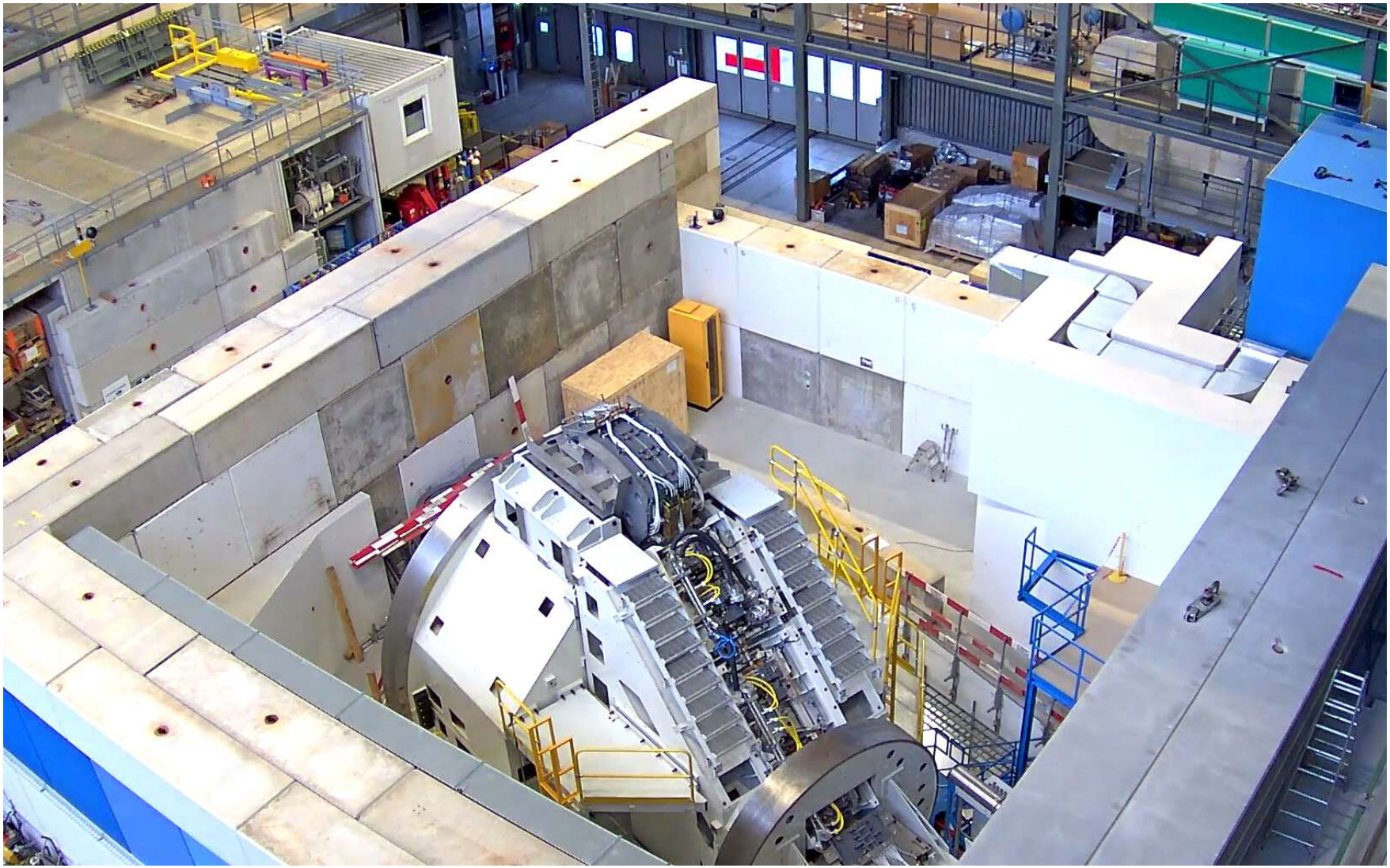

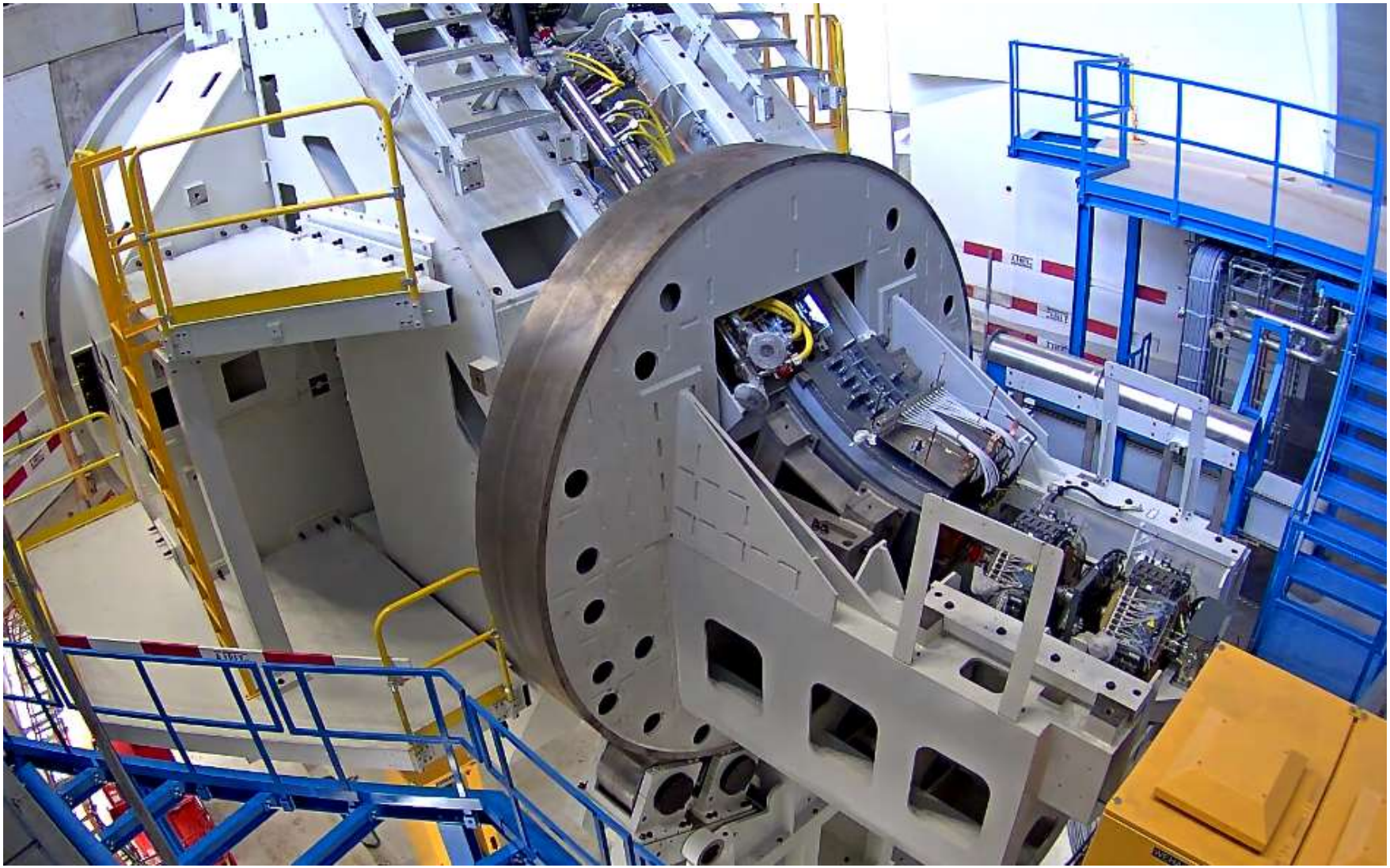


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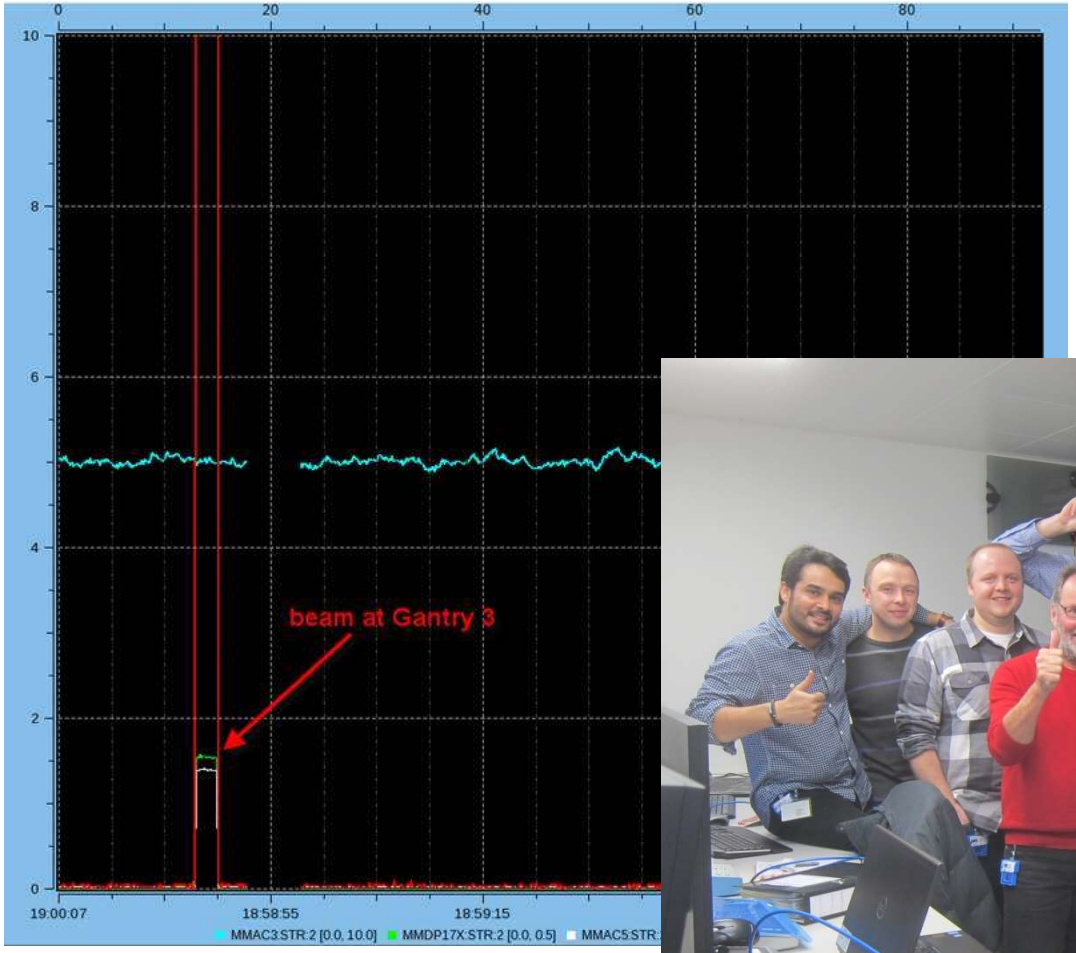
First beam 01.12.2015 19:00:20




O.D. 102X32X75
FRAGILE

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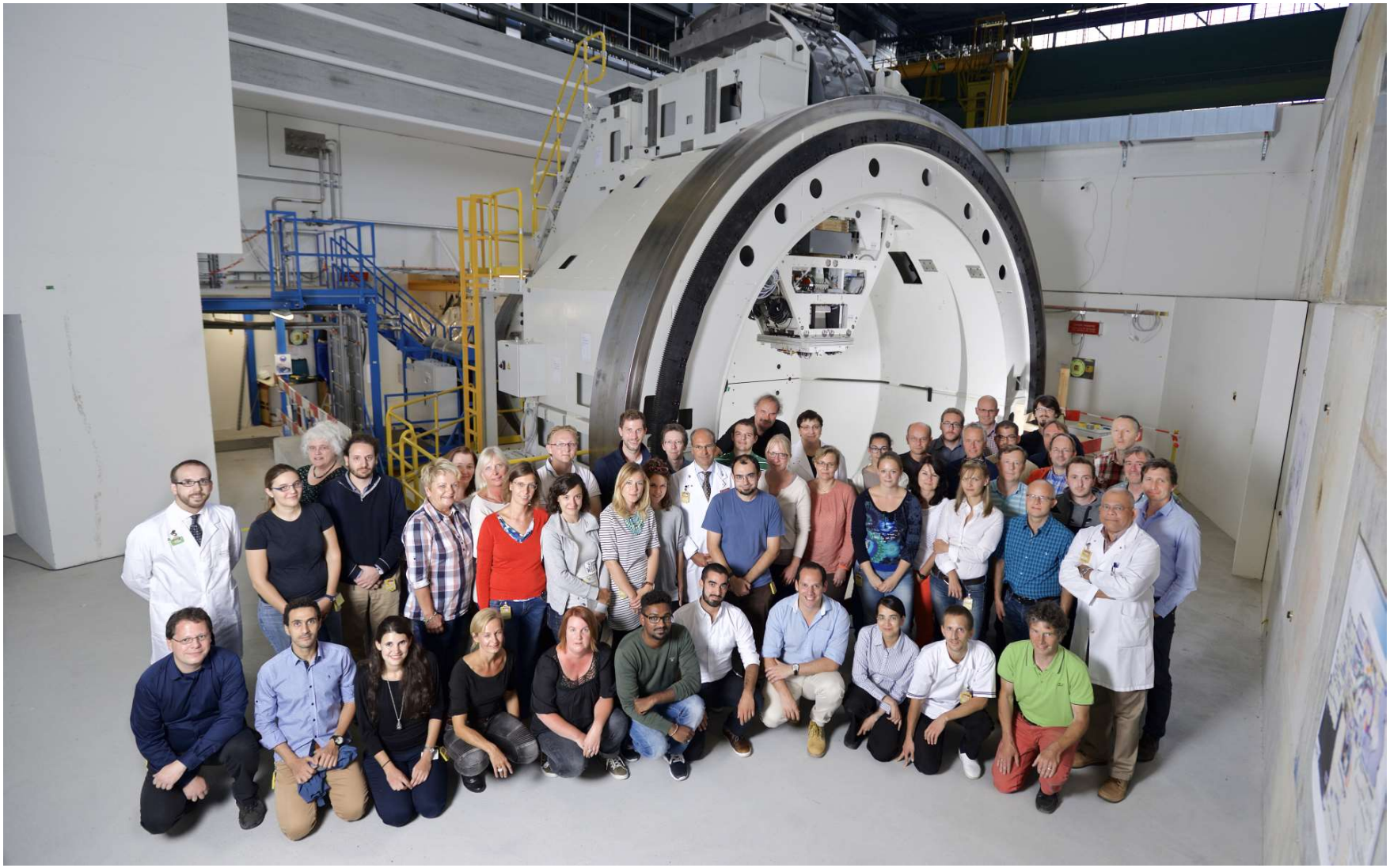
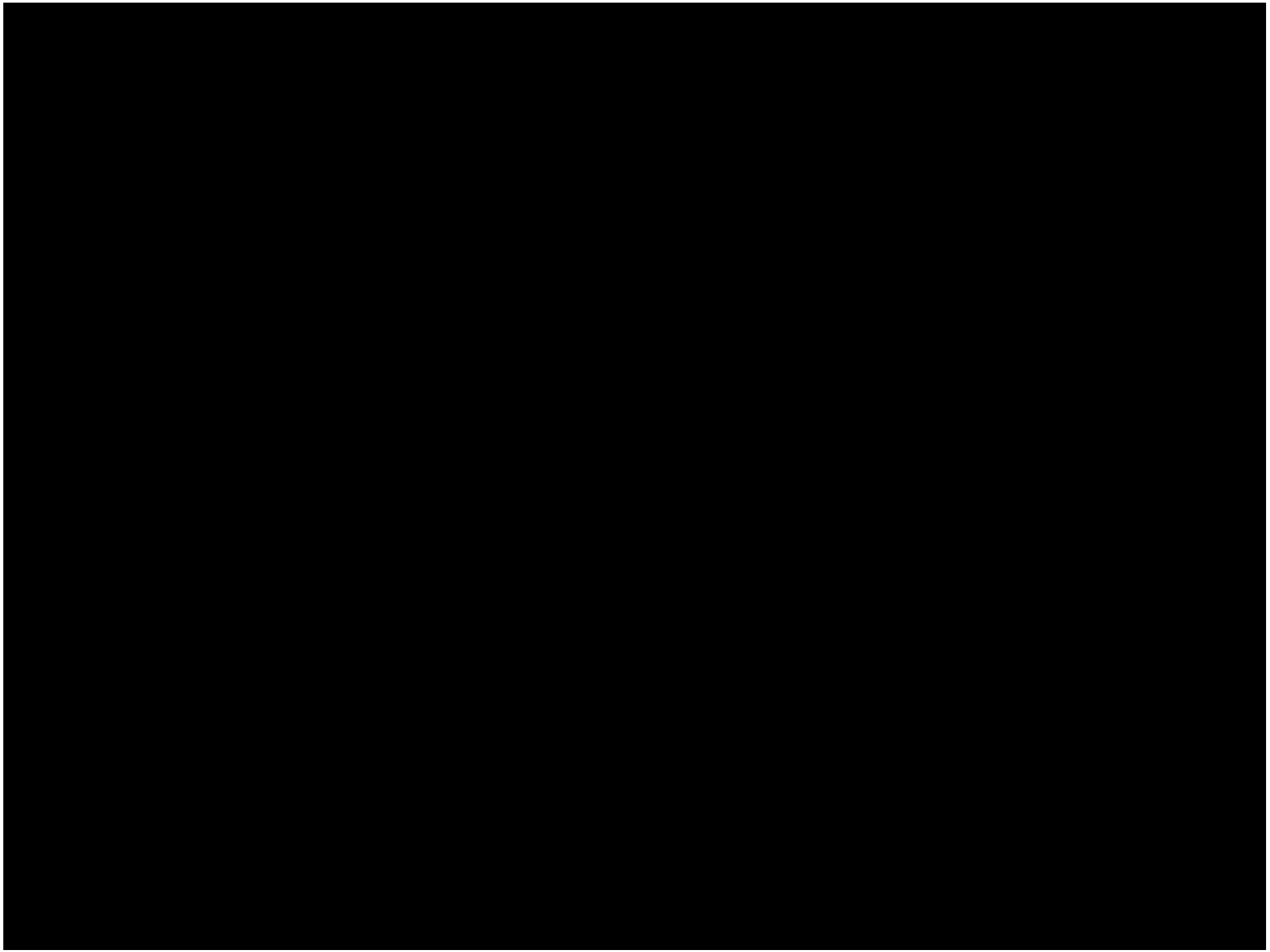
07.2018





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