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PSI

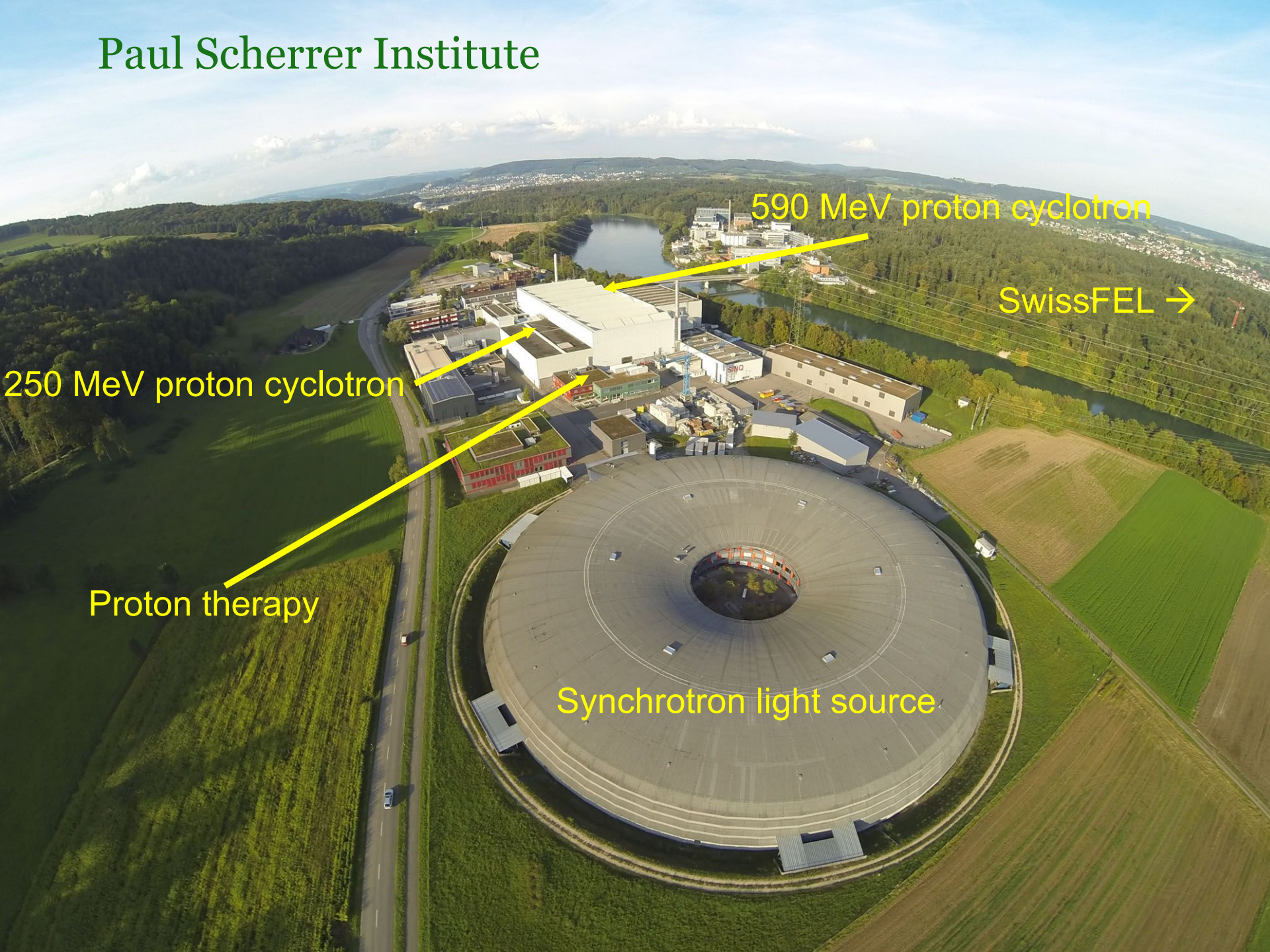
Martin Grossmann

Senior Technical Adviser :: Center for Proton Therapy :: Paul Scherrer Institute

Protontherapy: 30 years experience and current research at PSI


PSI
Island
Schweden
Norwegen
Finnland
Ostsee
Estland
Lettland
Litauen
Moskau
Москва
Nordsee
Dänemark
Irland
Niederlande
Berlin
Polen
Weißrussland
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
Aserbaidschan
Griechenland
Türkei
Turkmenistan
Syrien
Libanon
Tunesien
Mittelmeer
Irak
Afgh
Marokko
Iran
Jordanien
Google

Paul Scherrer Institute



Why Radiotherapy with Protons?

Proton therapy

Mass: ~200 tons

Diameter: ~8 m

Conventional therapy (LINAC)

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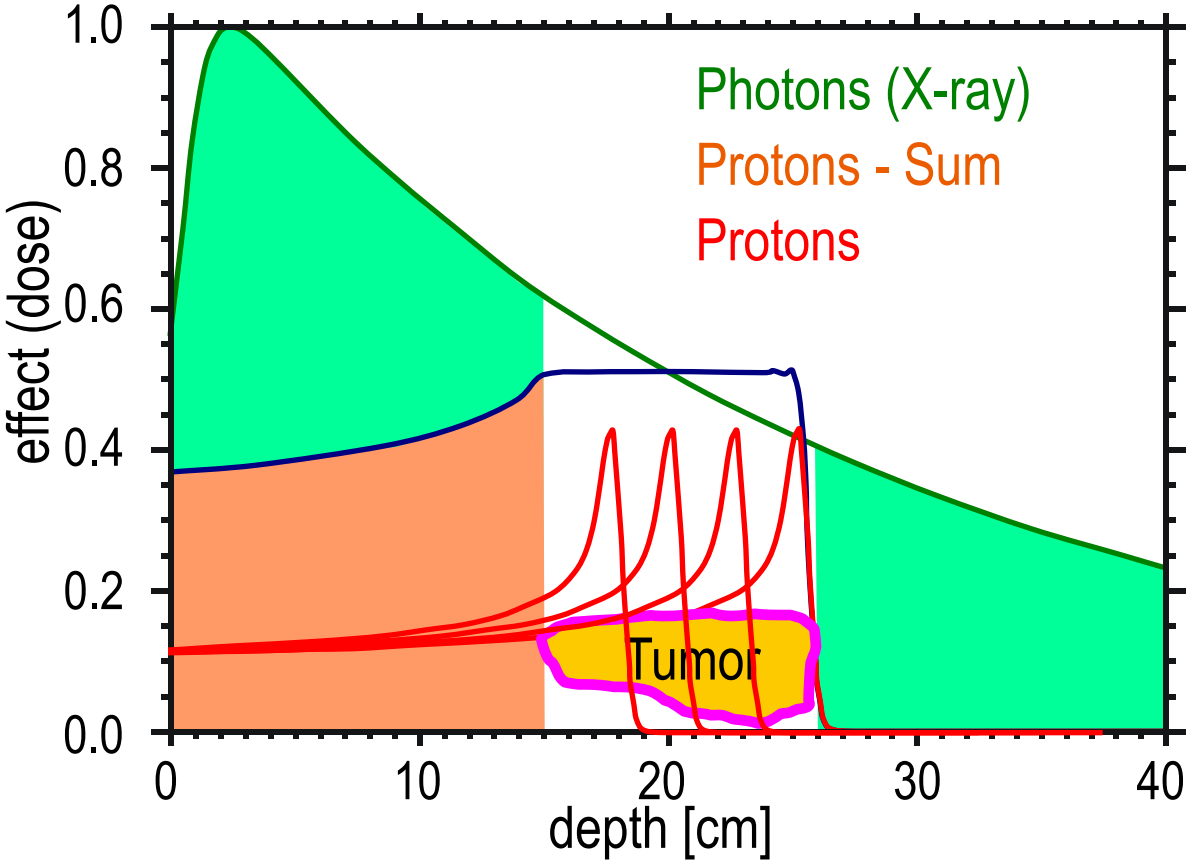
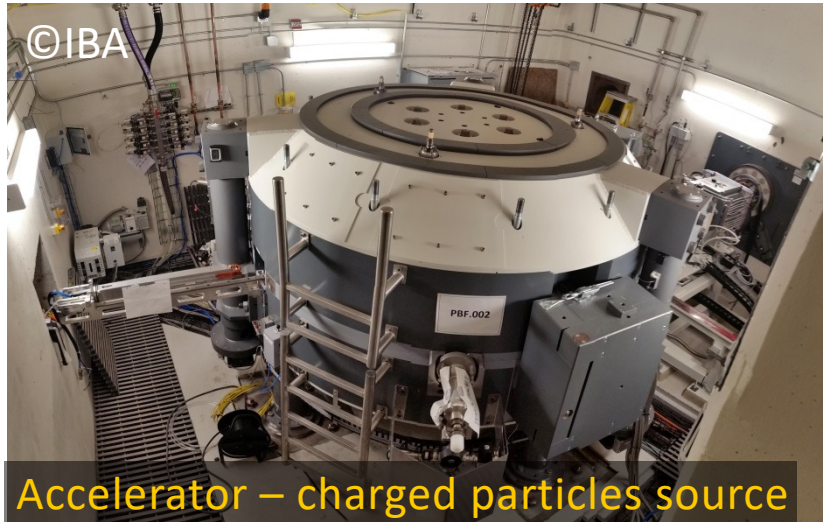
Why Protons?



Dose burden - photons

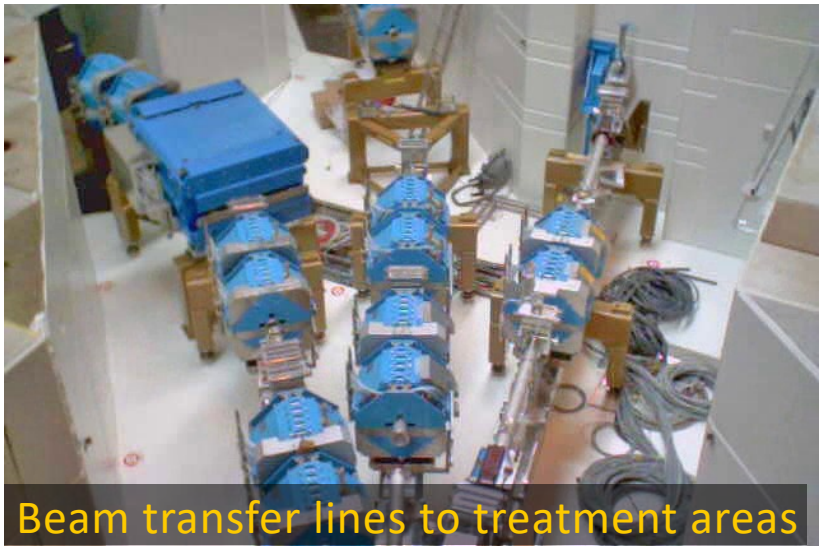
Dose burden - protons

Main parts of a particle treatment facility



Accelerator – charged particles source


Fixed beam line


Beam transfer lines to treatment areas

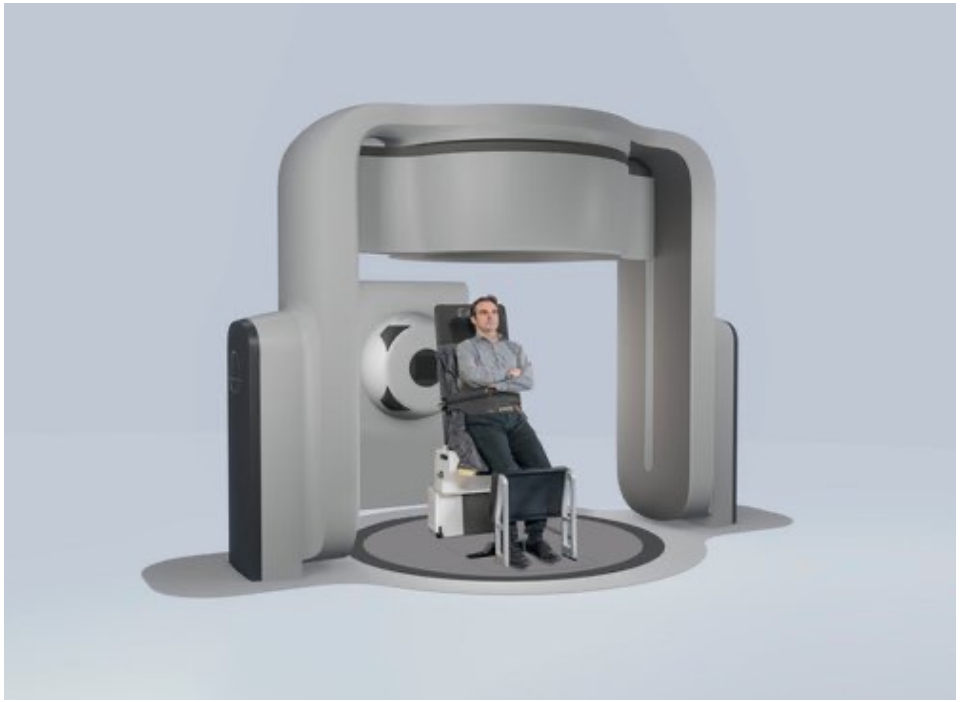

Gantry – rotating beam line

Efforts to reduce cost / increase accesibility

For many cases full flexibility of Gantry is not required:

- Treatment chair
- Fixed beam
- CT for imaging

LEO Cancer Care



Efforts to reduce cost / increase accesibility

HFCIM, Hefei/China

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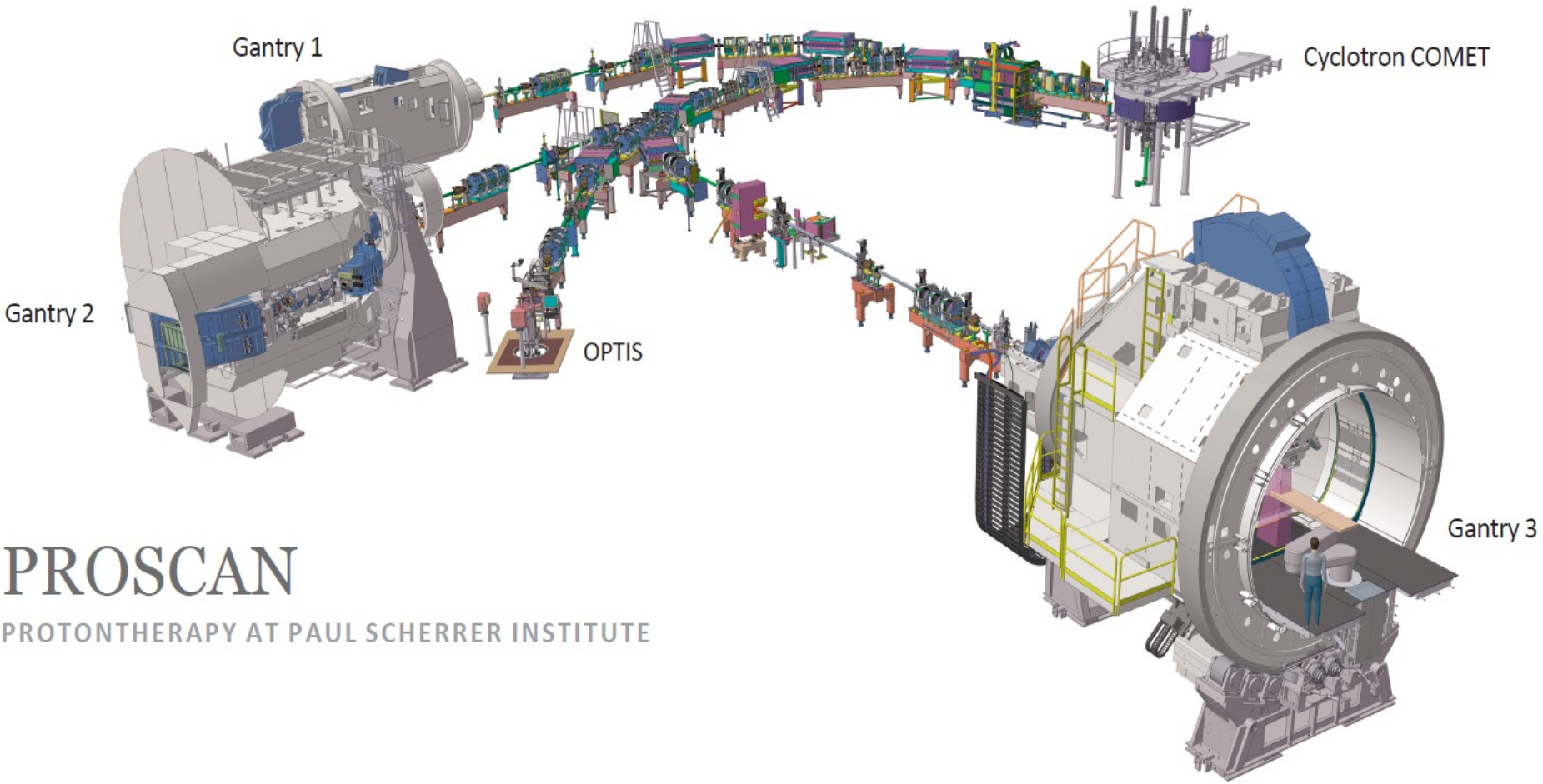

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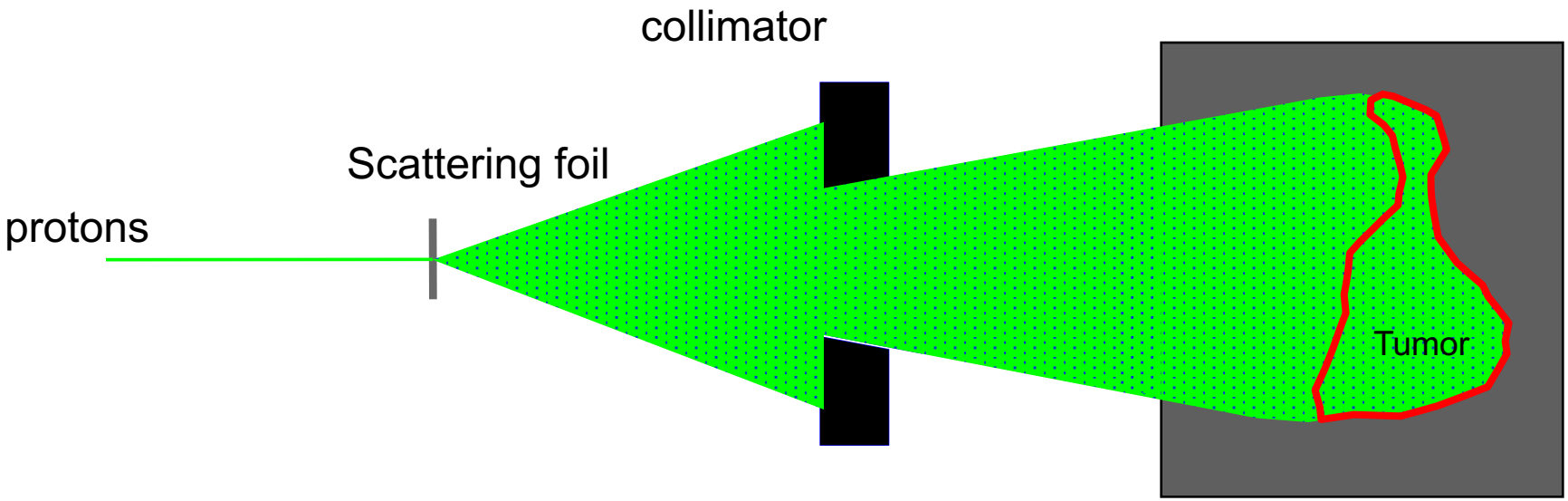
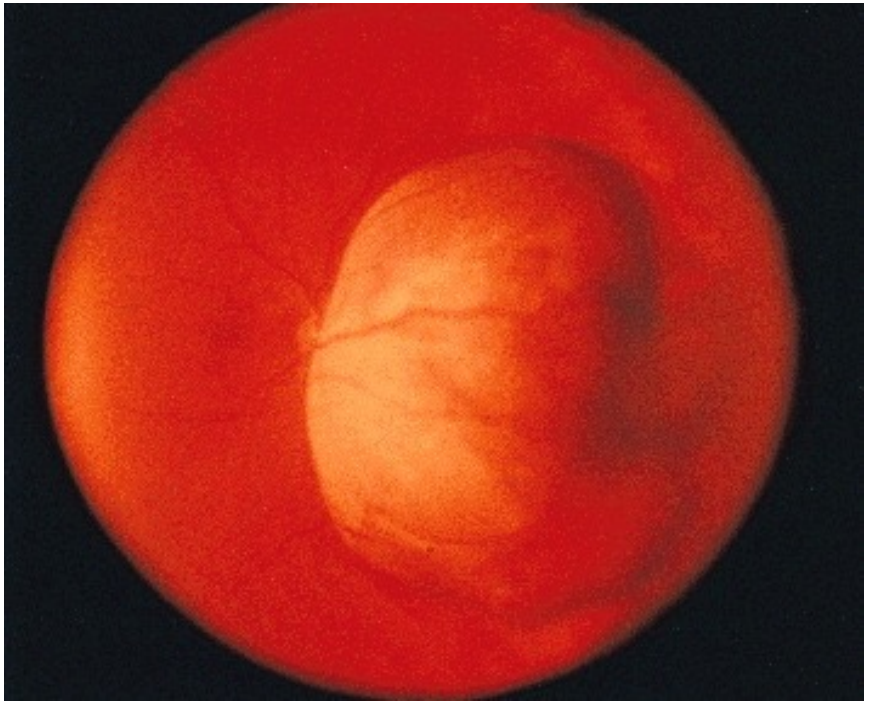
Irradiation technique - classical



PSI's OPTIS program

- Treating Eye Melanoma
- Collaboration with eye clinic in Lausanne

  (Hôpital Ophtalmique Jules Gonin, Prof. L. Zografos)



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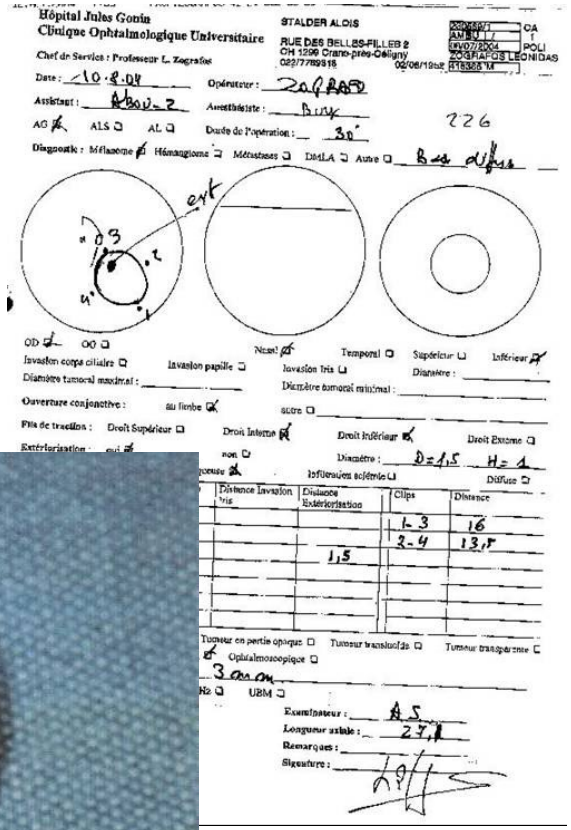
PSI's OPTIS program



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PSI's OPTIS program

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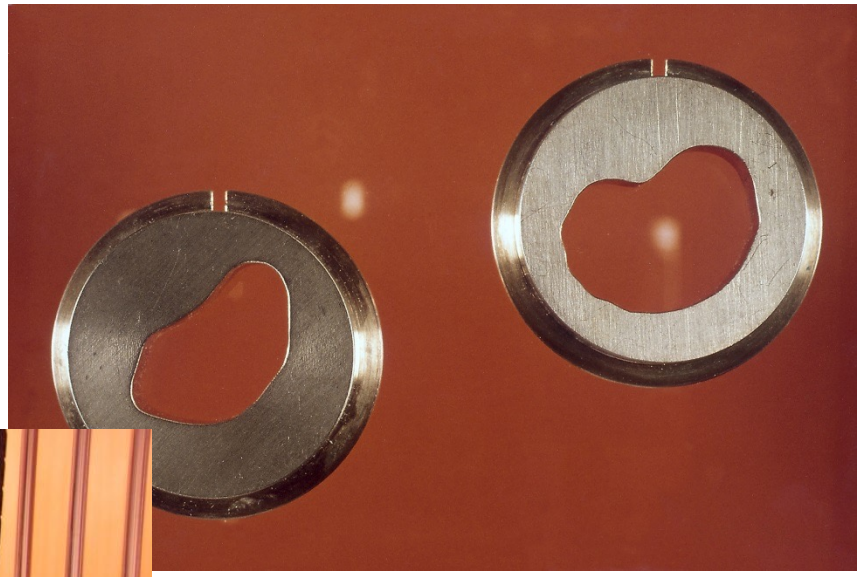
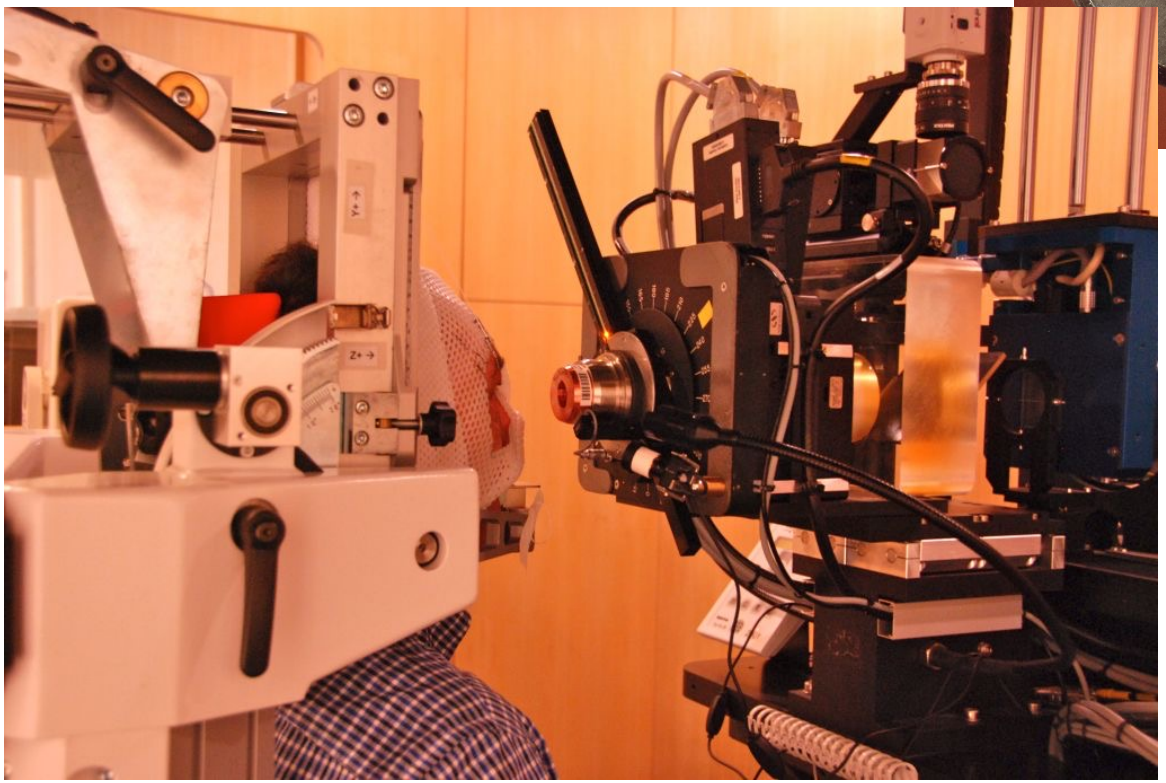
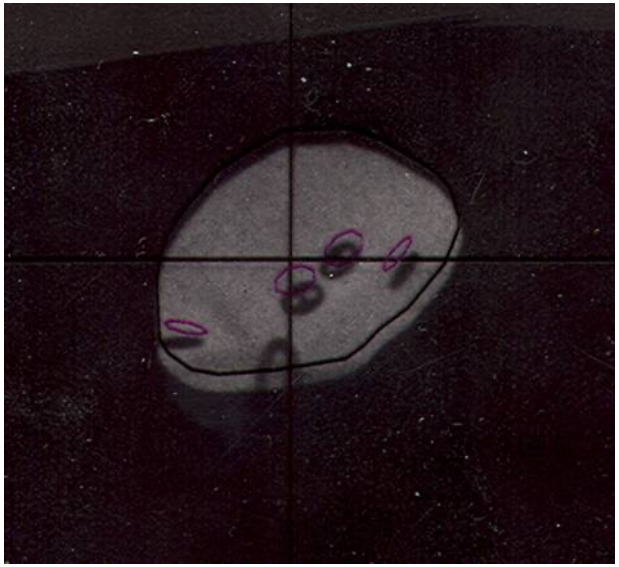
OPTIS





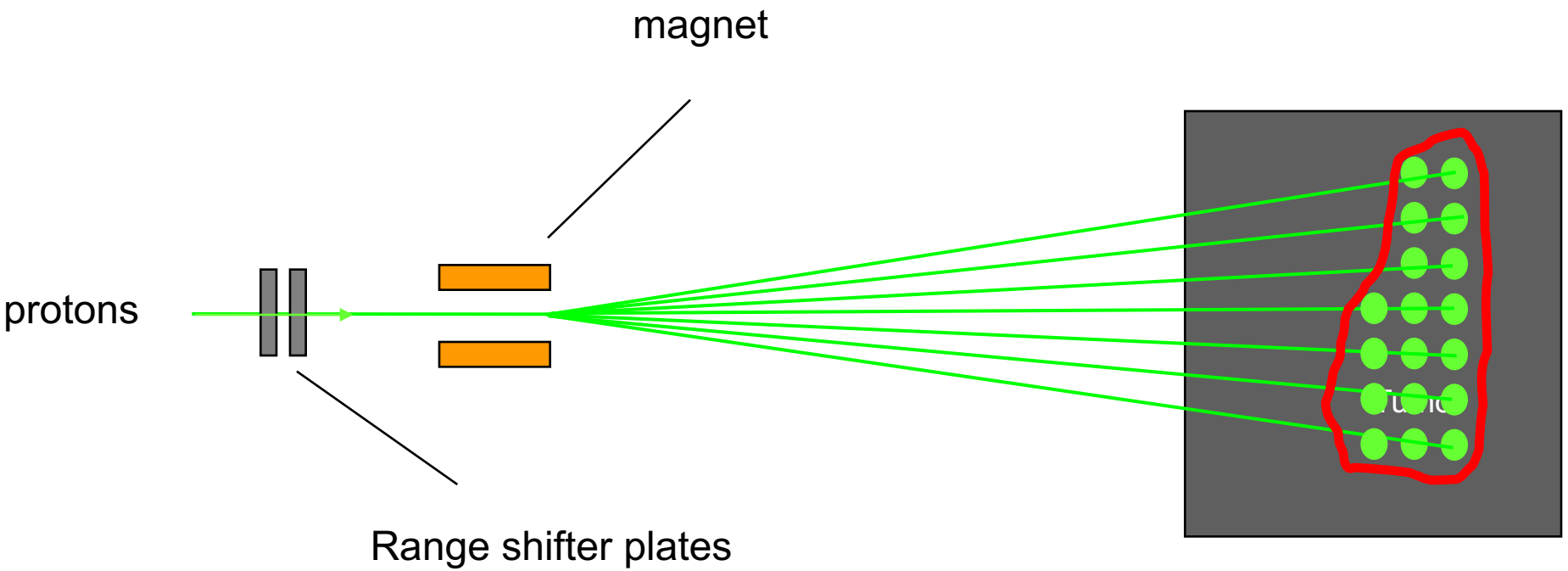


OPTIS – a success story

- Since 1984:
  treated more than 8’500 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»



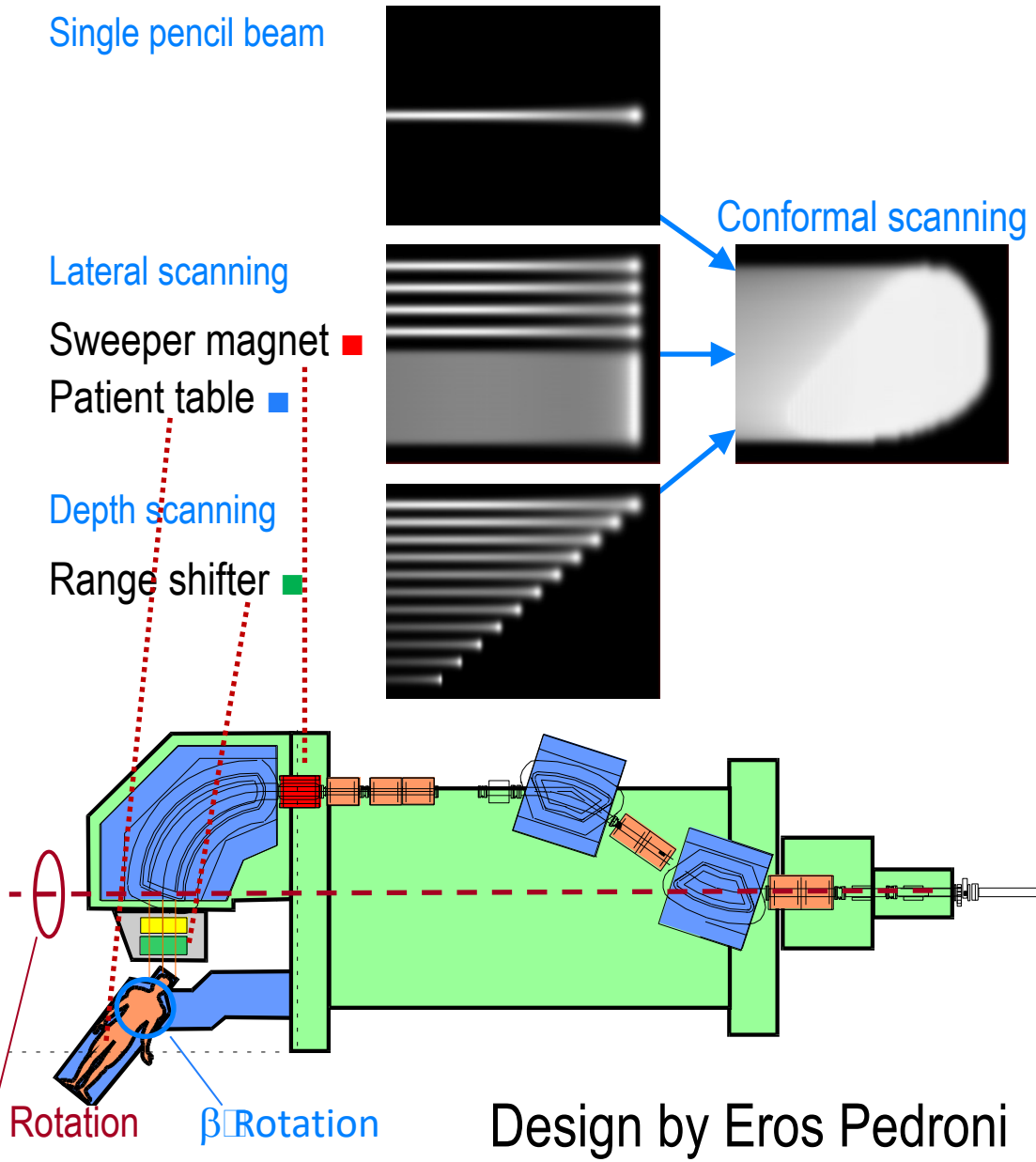
Gantry 1: A compact system for spot scanning

Implementation of spot scanning technique

Start patient operation 1996

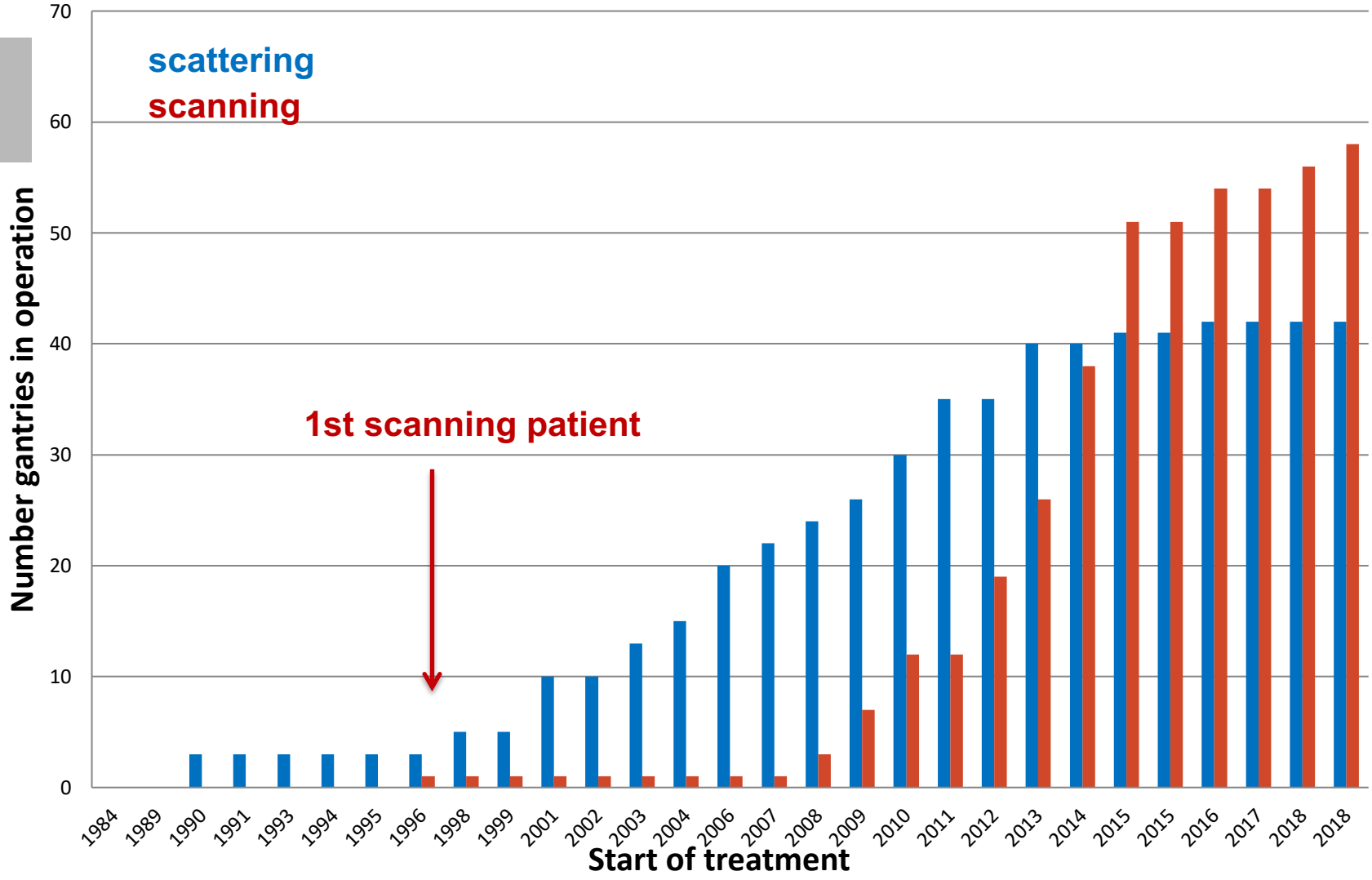
During 12 years the only spot scanning gantry worldwide

Due to eccentric design still the most compact system, r = 2m



Design by Eros Pedroni

Scanning-Technology is today's standard



Source: S. Psoroulas, D. Meer PSI

Gantry 2: next generation spot scanning

Easy access to patient at all times

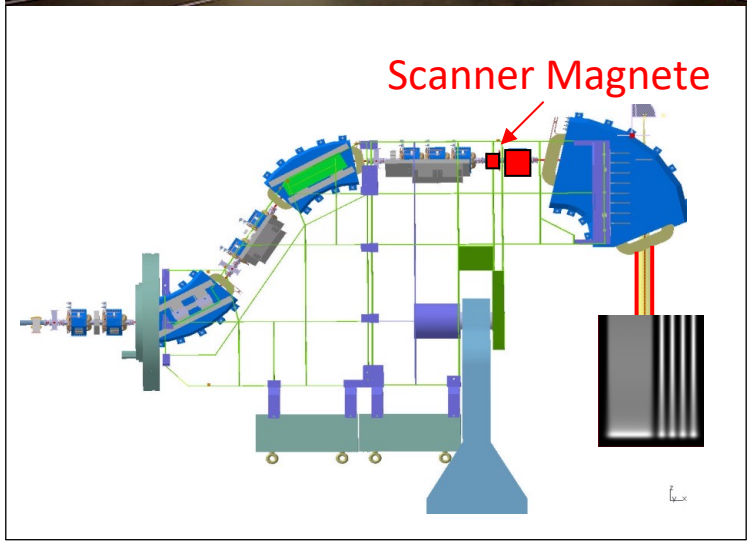
- Rotation limited to 210°
- Patient table rotatable 180°
  (→ still full flexibility)
- No pit

Fast scanning in 2 dimensions

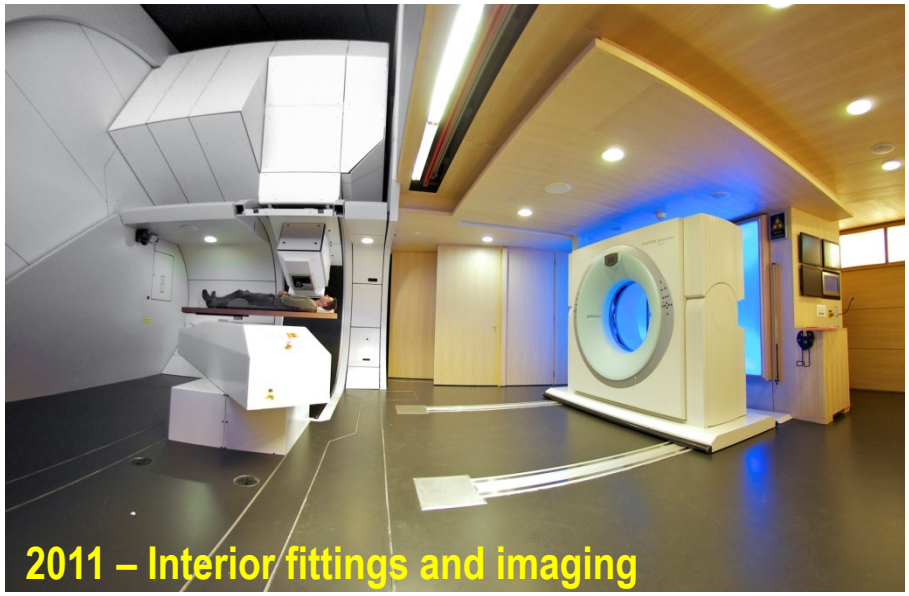
- Re-scanning possible
- Parallel Scanning
- Field size 12 x 20 cm

Fast energy change → 3rd dimension

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



Gantry 2: next generation spot scanning



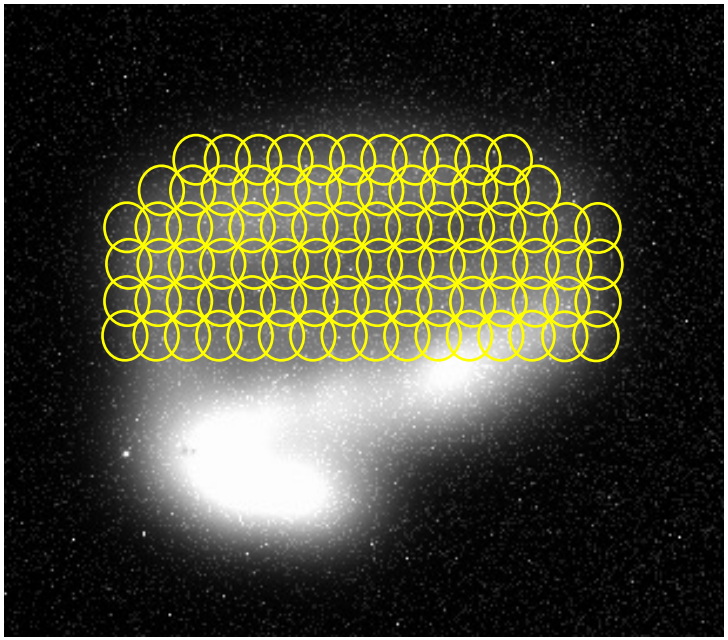
Treating small children

- Since 2004 treatments of small children
  → **anesthesia team from children's hospital in Zurich**
- Ca. 700 patients


2014

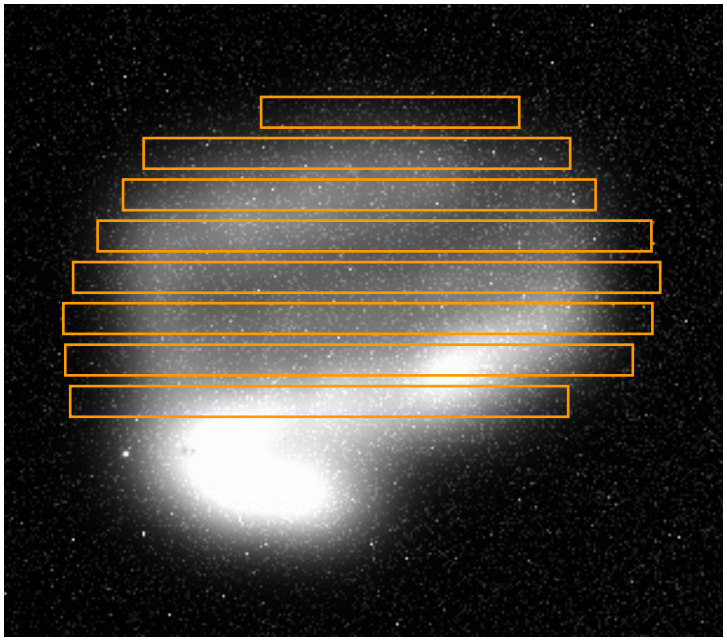

Bair Hugger

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

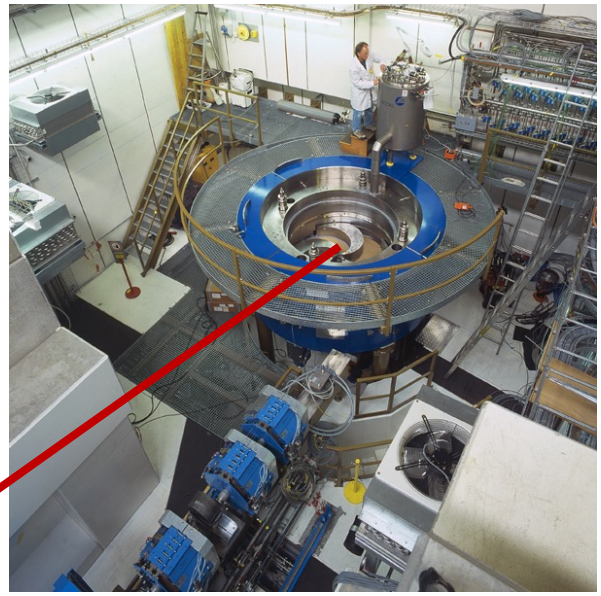


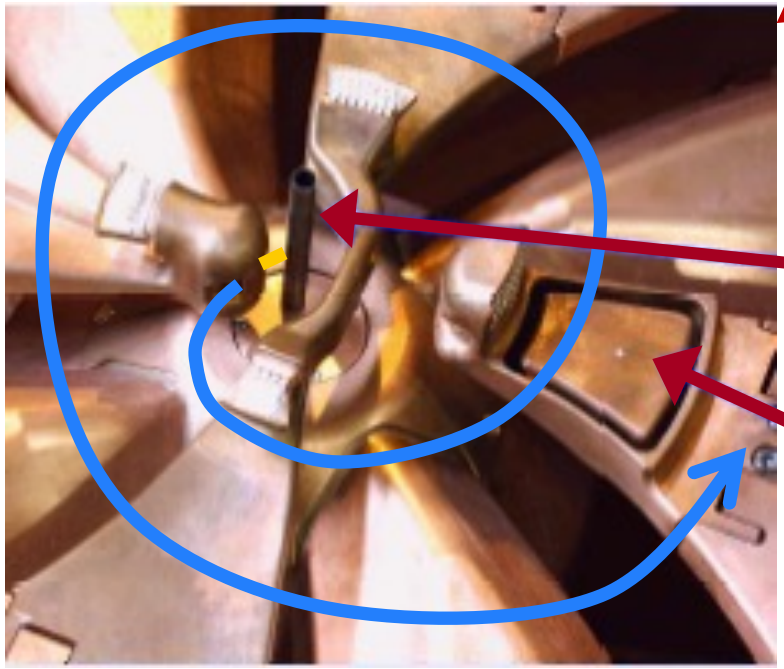
Continuous line scanning

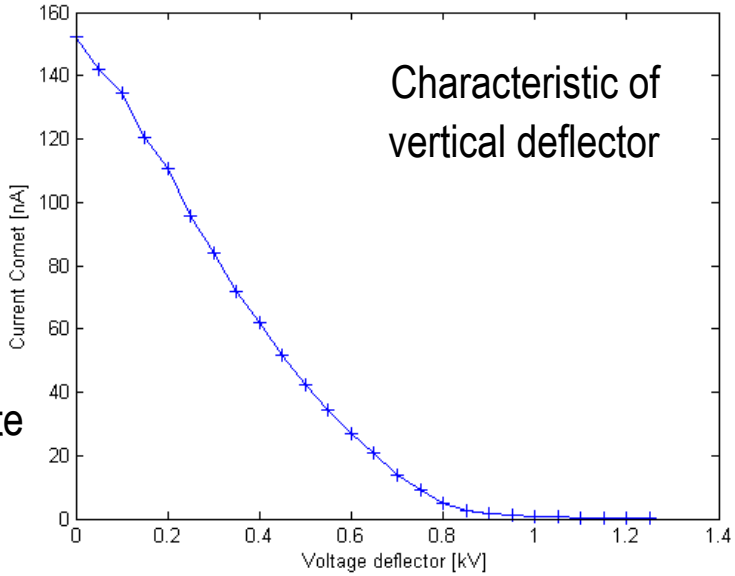
- Paint lines of dose with continuous beam on using
  - Beam intensity modulation
  - Beam motion speed modulation
- For efficient and effective repainting
- Operational in experimental mode, in development

Proton beam intensity modulation

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

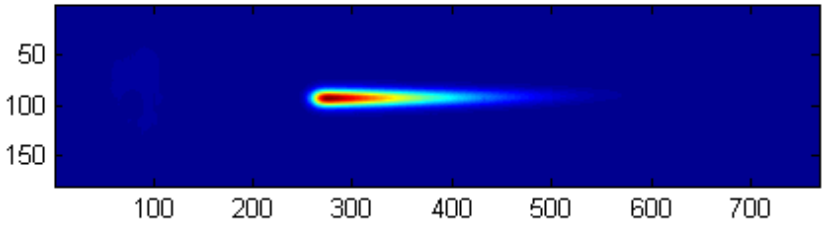




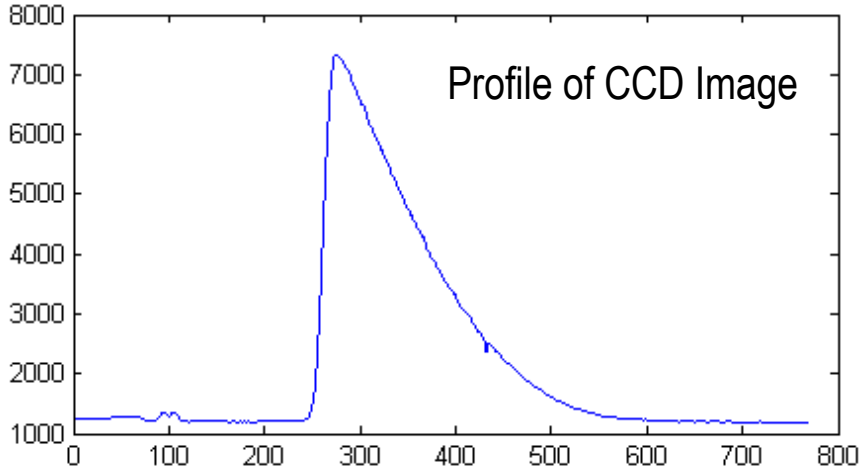


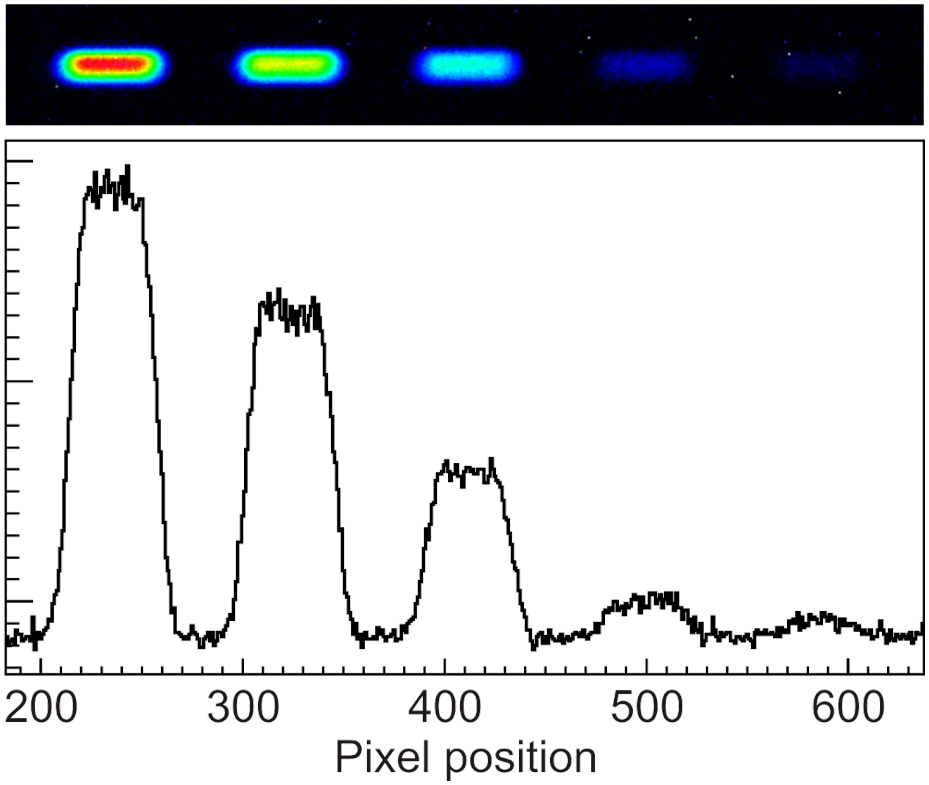
Painting intensity modulated lines

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



18 cm





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

Video: Virtual Tour of PSI Protontherapy

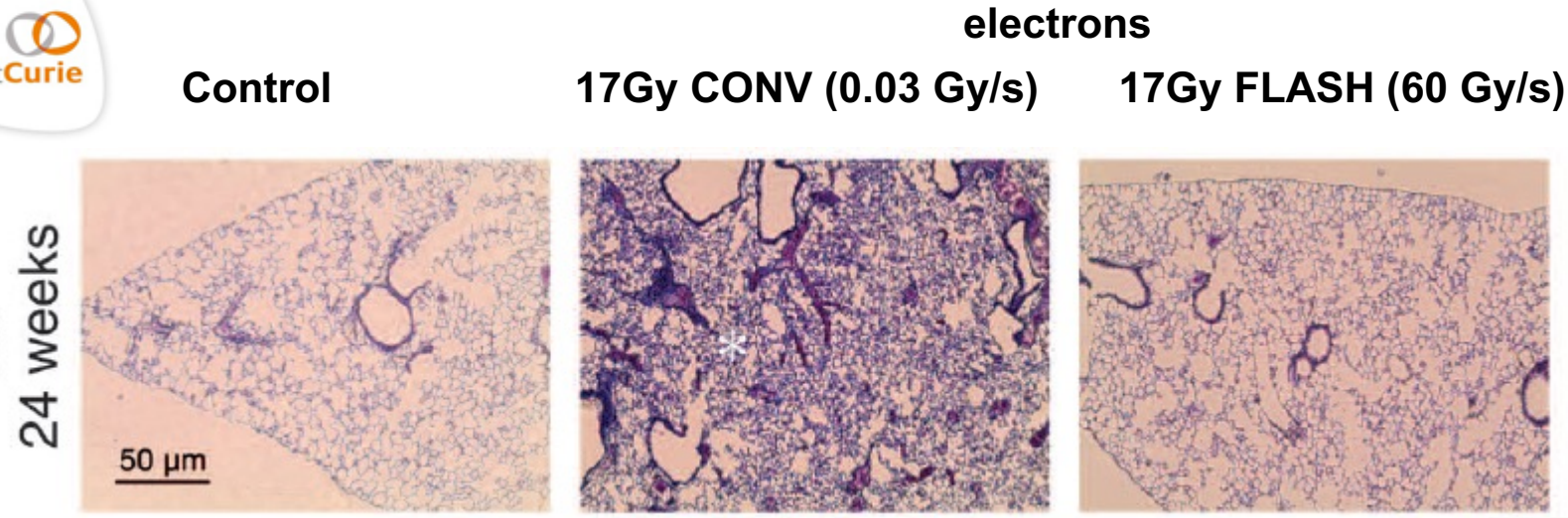
in YouTube: search «psi protontherapy»

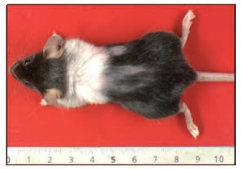
https://www.bilibili.com/video/BV1cQ4y1d7po

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

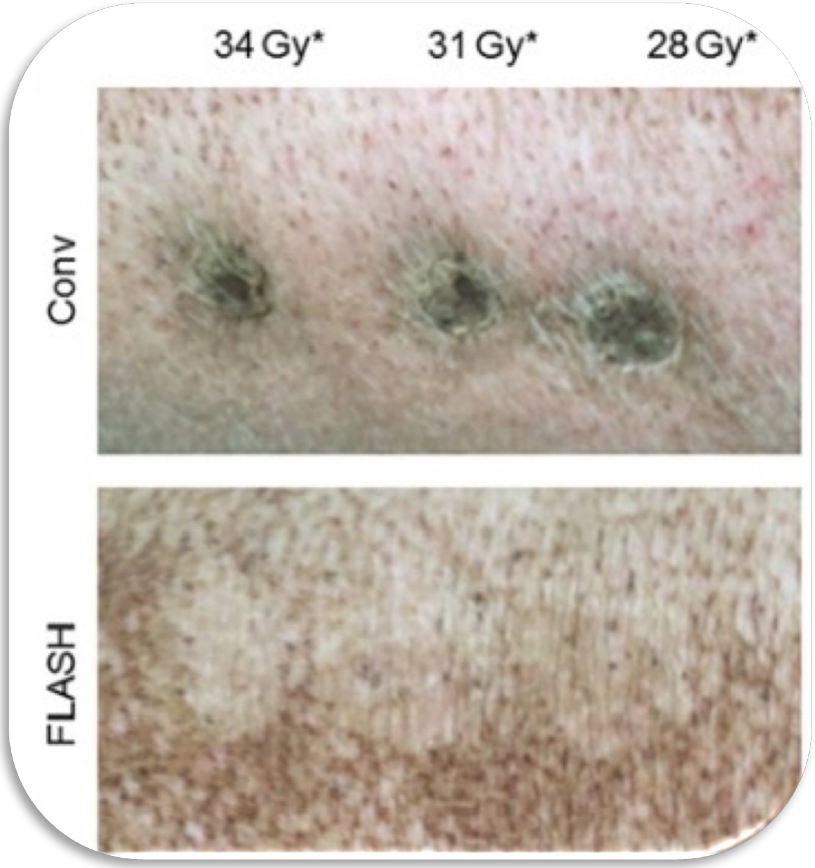
FLASH radiotherapy

FLASH confirmed in larger mammals (mini-pigs)

0.08 Gy/s

electroncs

300 Gy/s



Black dots = NECROSIS

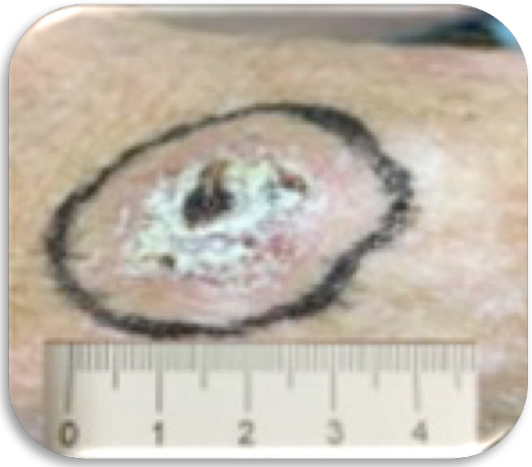
Vozenin, et al, The advantage of Flash RT confirmed in mini-pig and cat-cancer patients." Clinical Cancer Research. 2018;

FLASH radiotherapy

First human patient treated with FLASH

Electrons 166 Gy/s

Day 0



5 months

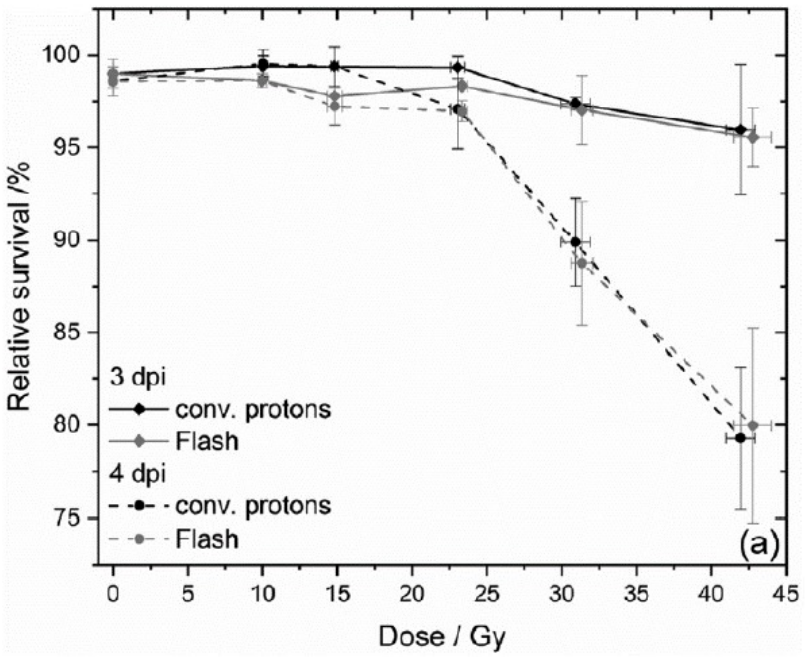
Jean Bourhis et al., «Treatment of a first patient with FLASH-radiotherapy», Radiotherapy and Oncology. 2019

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 ☹

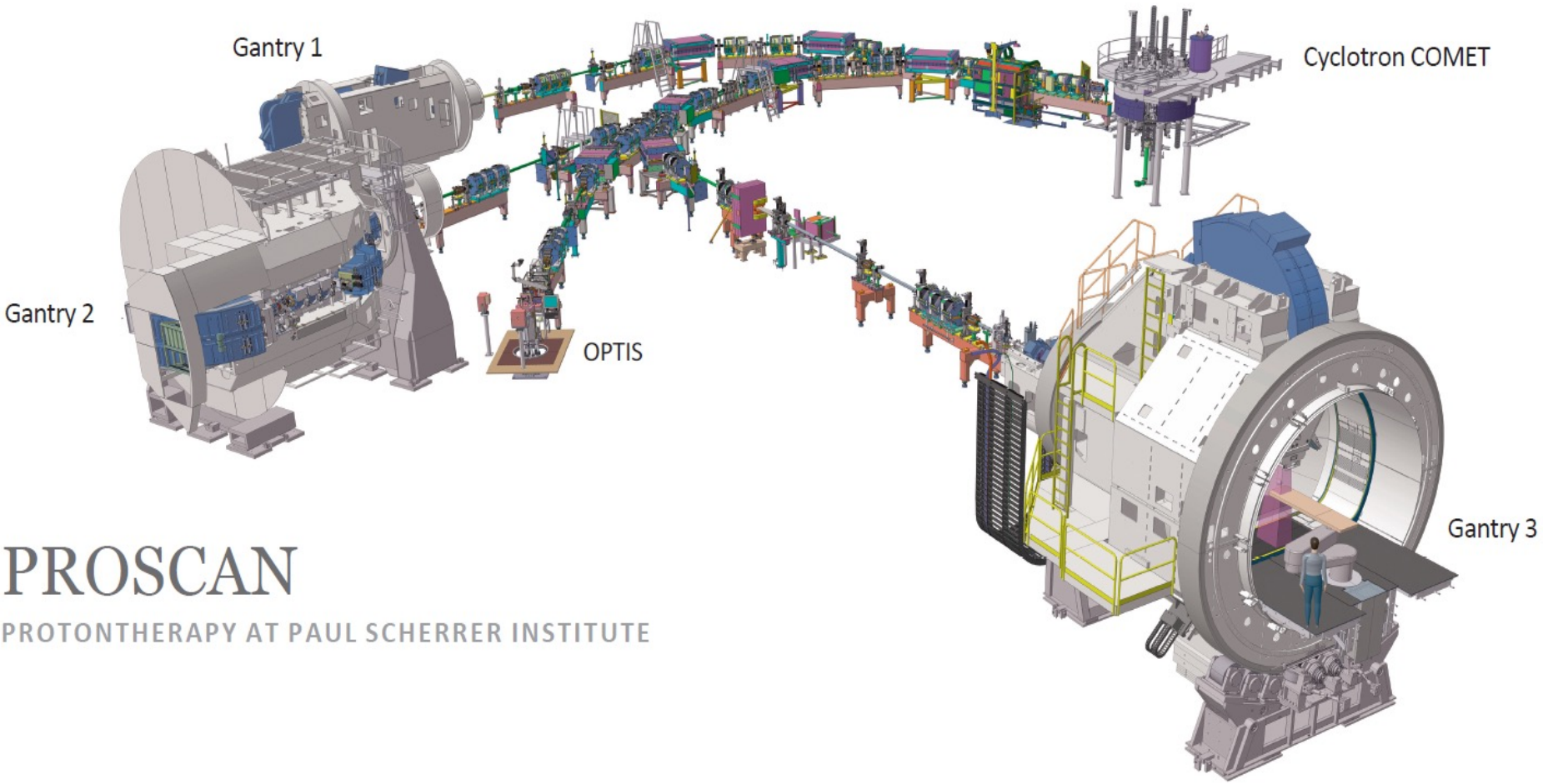
Universitäts Protonen Therapie Dresden

→ More experiments required!



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

Beamline Transmission



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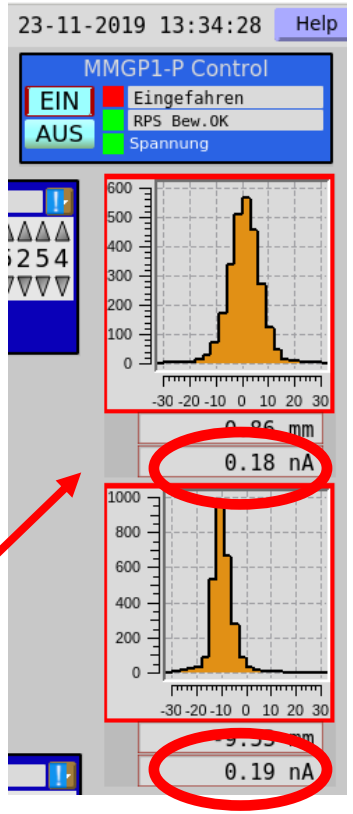
PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

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 Nov 2019
  - We are very close to 100% transmission

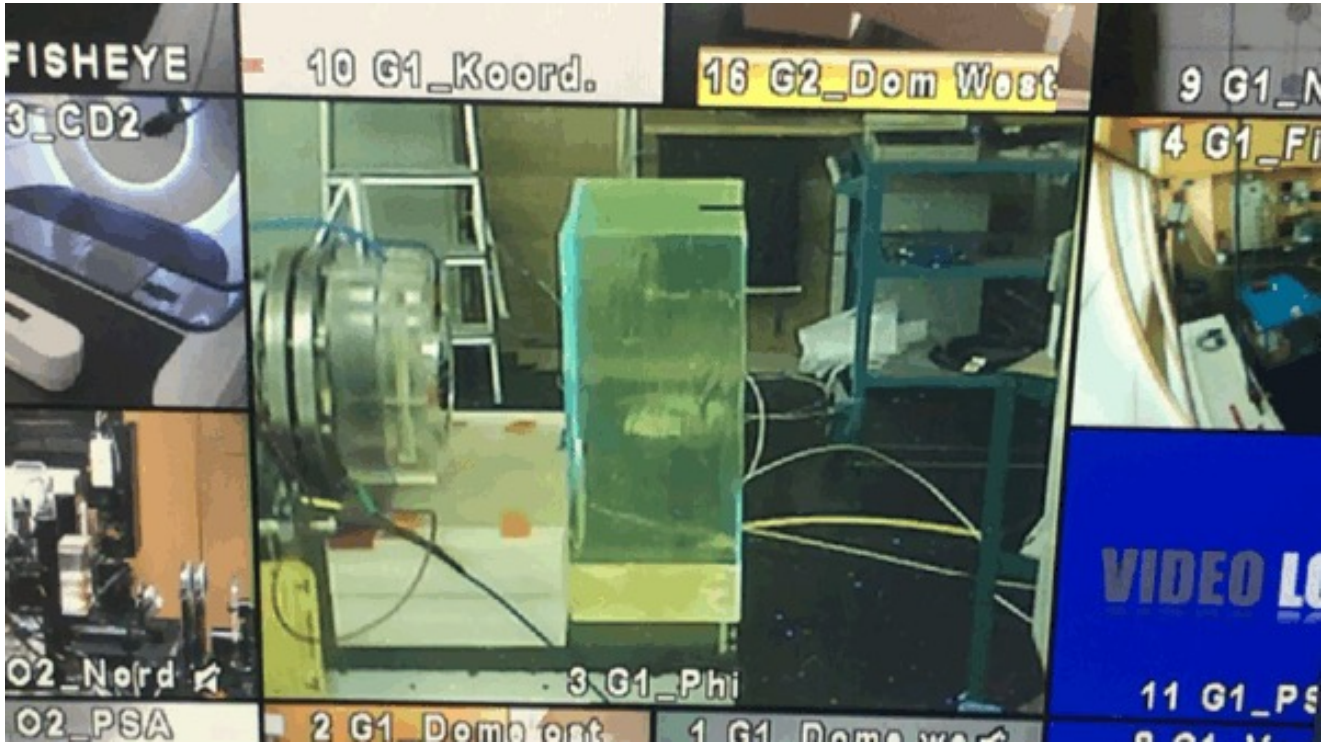


Input current from cyclotron 0.2 nA

X&Y profile monitor on Gantry 1, integrated current

Flash @ Gantry 1

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



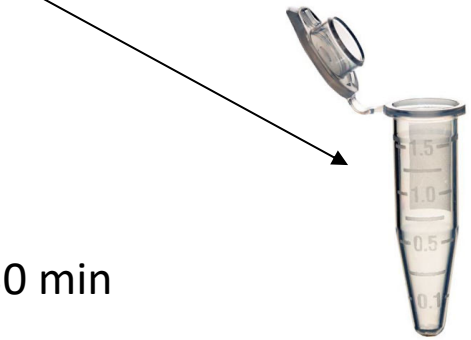
Nesteruk et al., Medical Physics 2021
https://doi.org/10.1002/mp.14933

Togno et al., Physica Medica 2022
https://doi.org/10.1016/j.ejmp.2022.10.019

Radiobiological experiments with CHUV

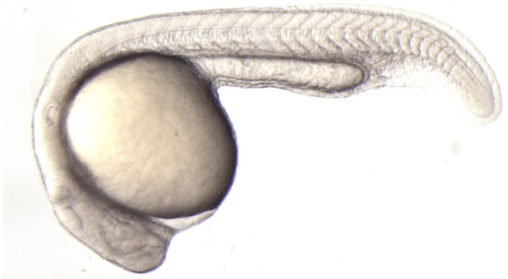
- Irradiation of zebrafish embryos

- Experiments conducted 2020 - 2021
  - 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

©U of Washington



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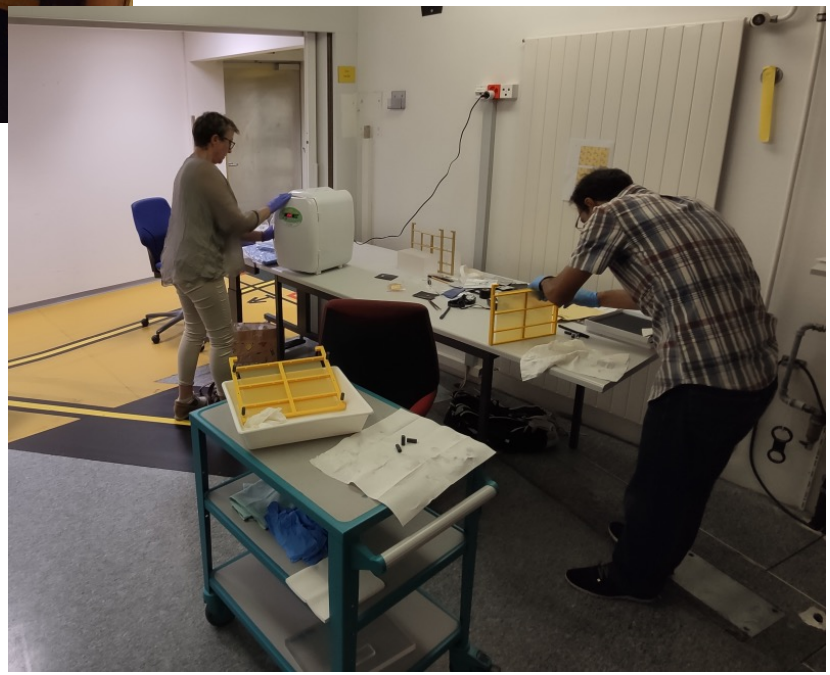
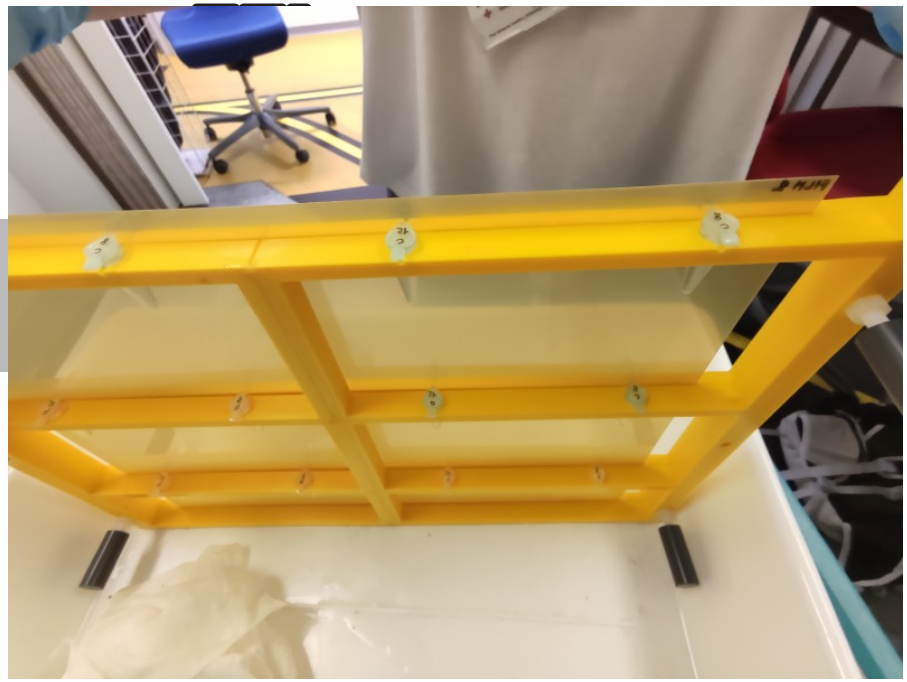
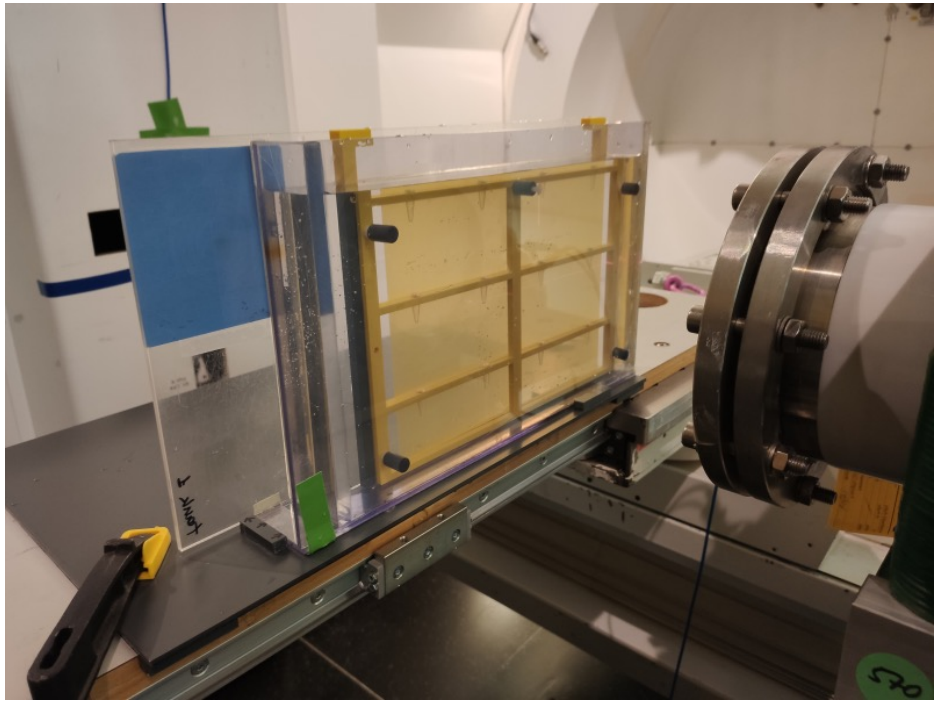
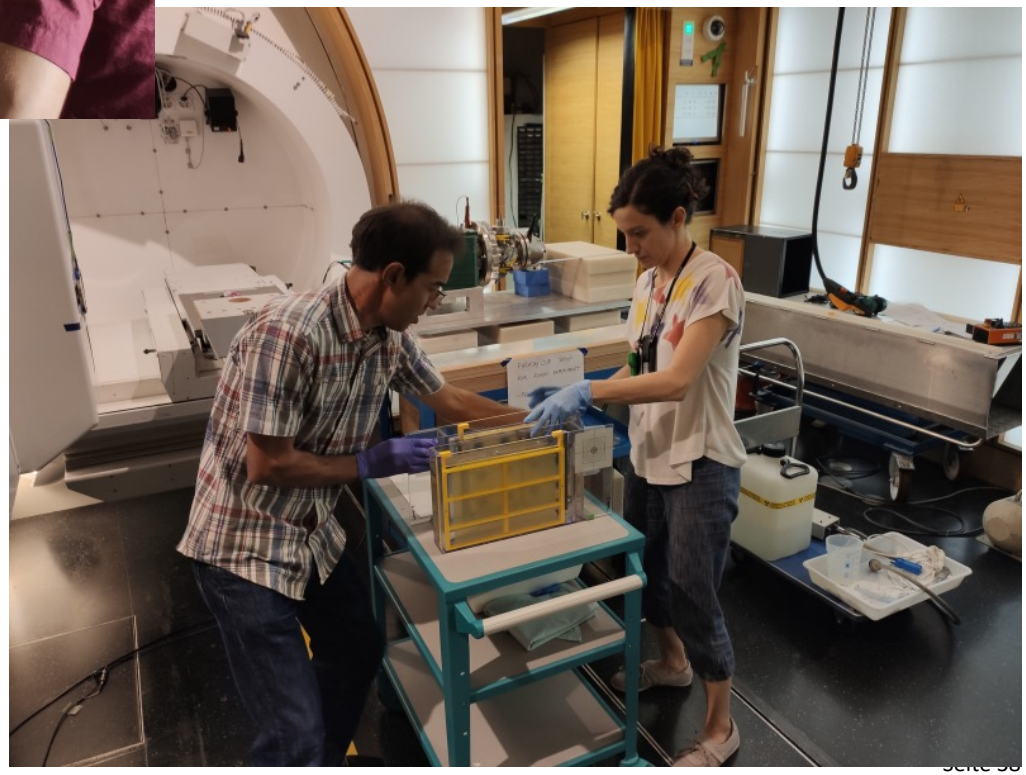


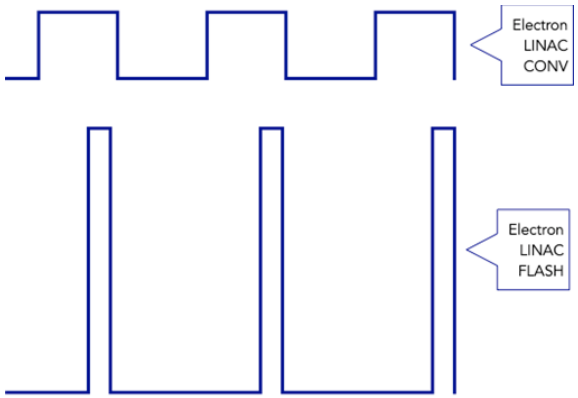


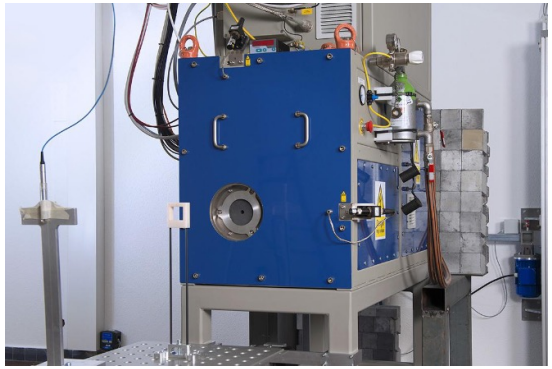




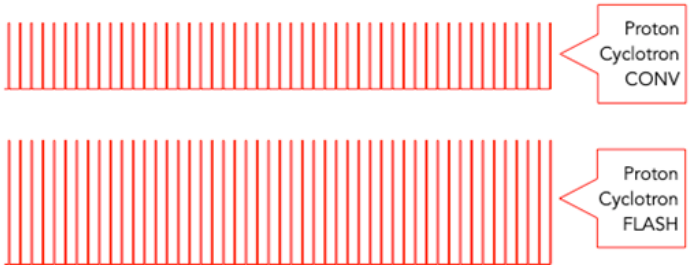
Beam structures

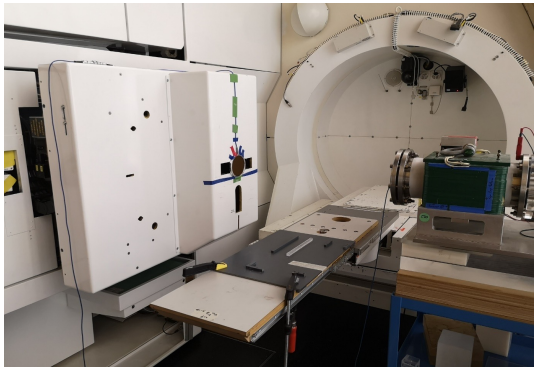
Electrons





Protons





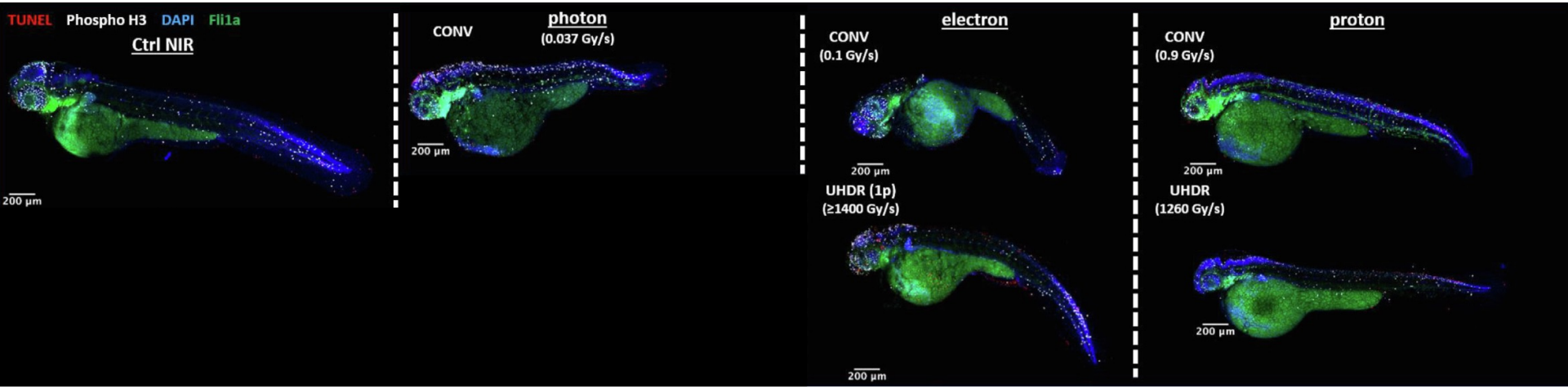
Results

ZF embryos as rapidly-responding in-vivo model (acute toxicity)

Measurements of

1. Survival
2. radiation-induced alteration estimated with measurements 5 day post fertilization

Results

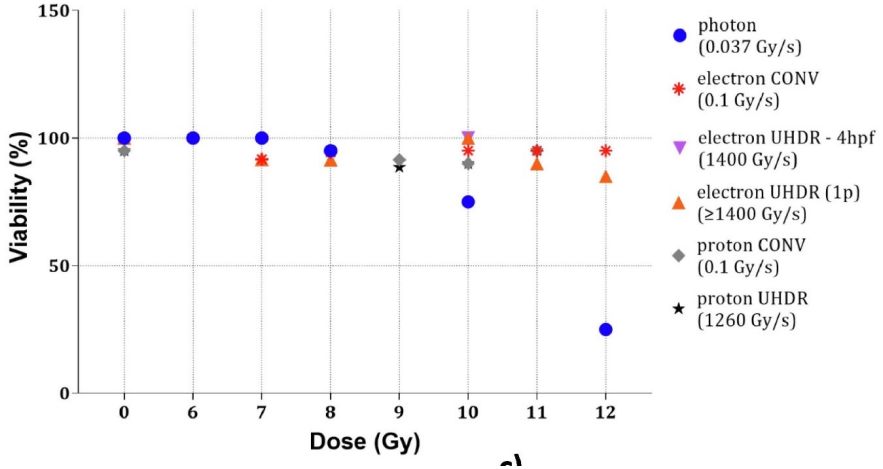


Dose rate effect for electrons, but not so much for protons

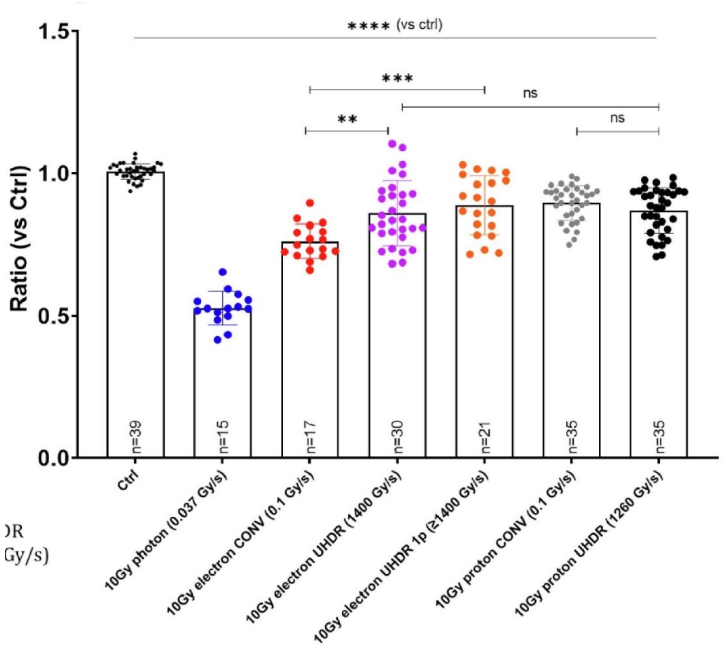
Kacem et al., *Radiotherapy and Oncology*, in press
https://doi.org/10.1016/j.radonc.2022.07.011

Zebrafish embryos: Morphological analysis

1



2

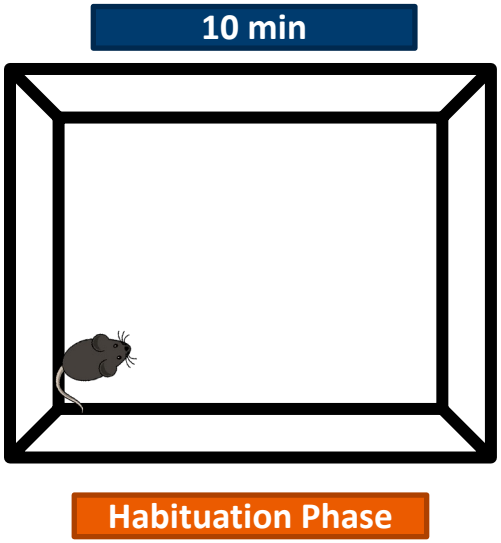


Protons have minimal impact on growth and survival

Kacem et al., *Radiotherapy and Oncology*, in press
https://doi.org/10.1016/j.radonc.2022.07.011

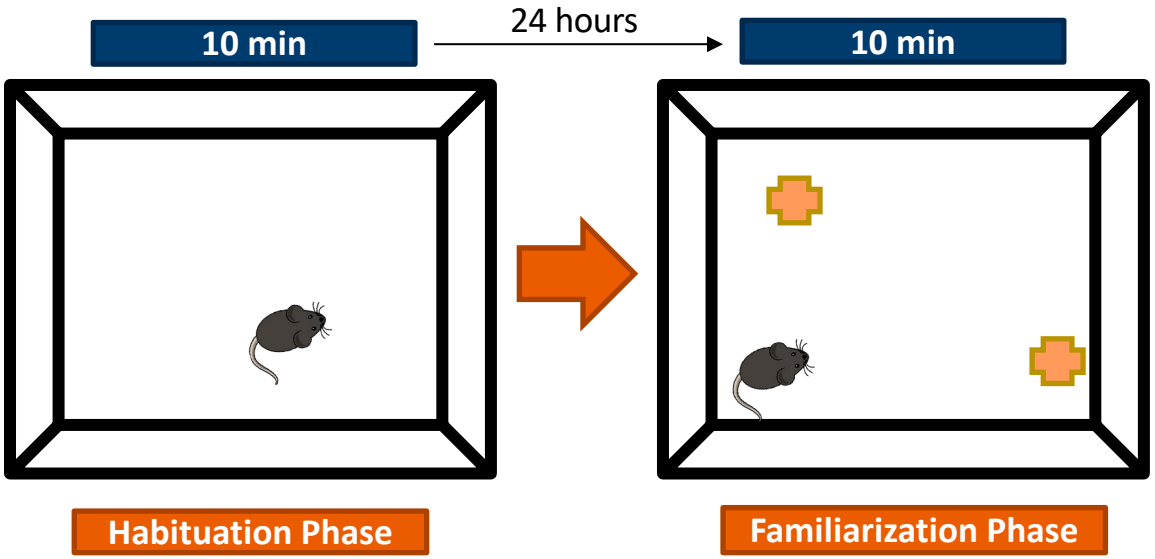
Neurocognitive response

- Novel Object Recognition (NOR)



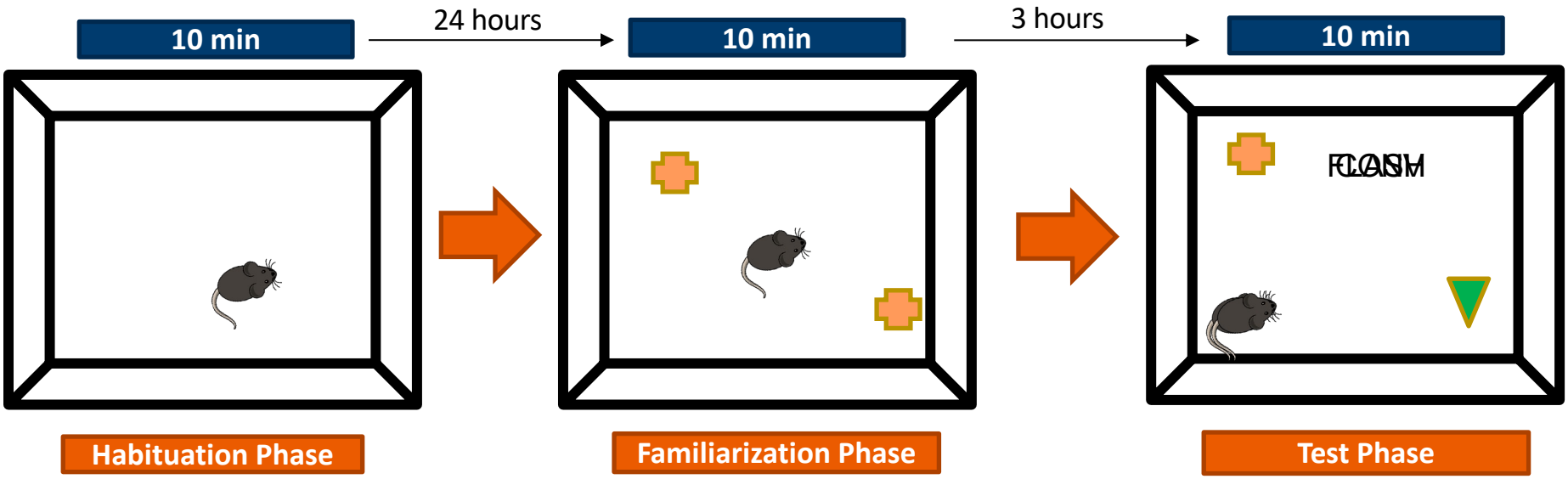
Neurocognitive response

- Novel Object Recognition (NOR)



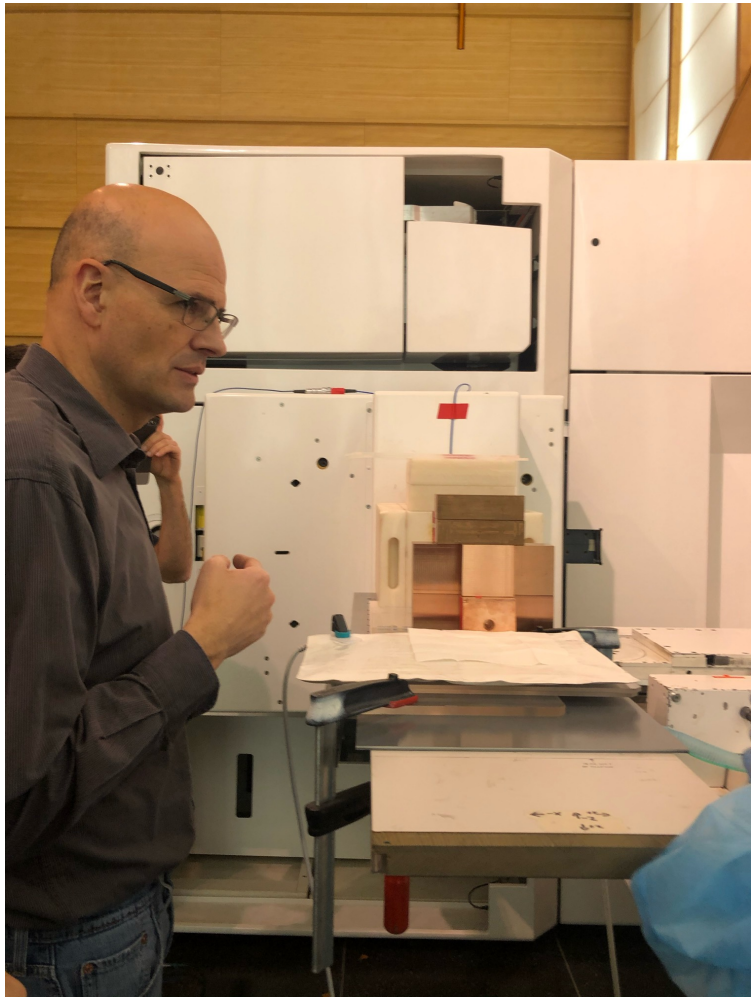
Neurocognitive response

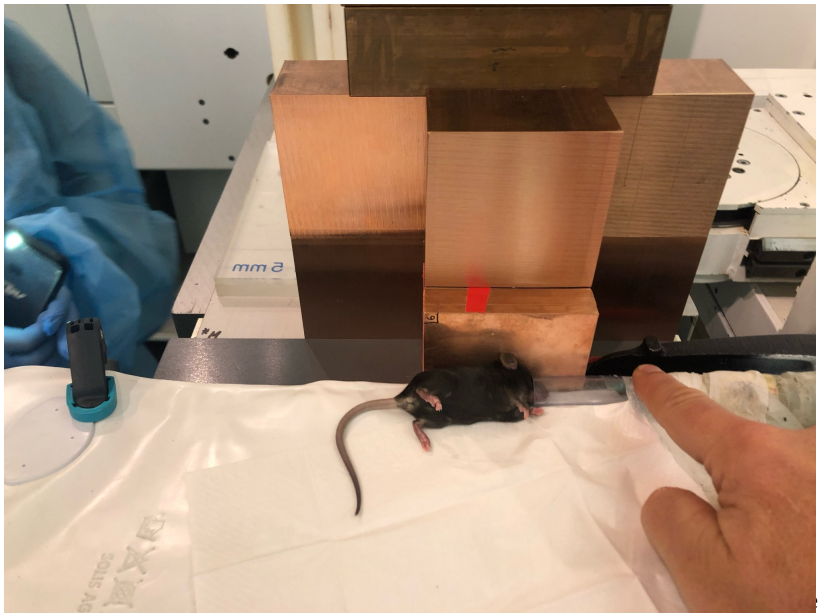
- Novel Object Recognition (NOR)



Proton FLASH irradiations of mice

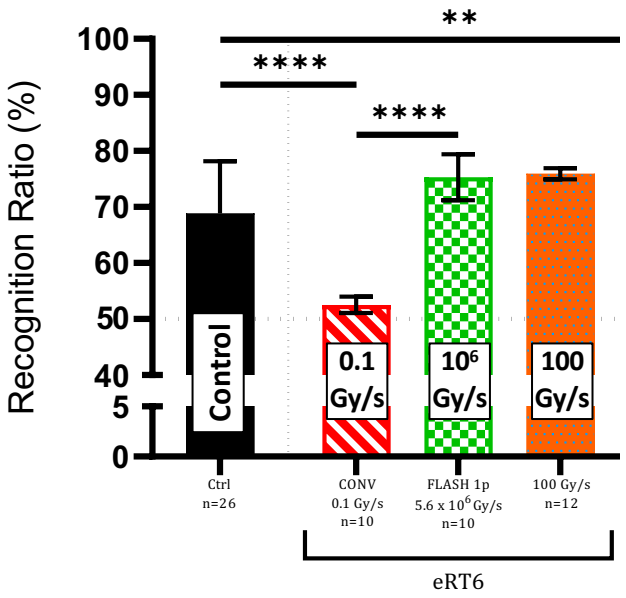
- Experiments at PSI ongoing since November 2021





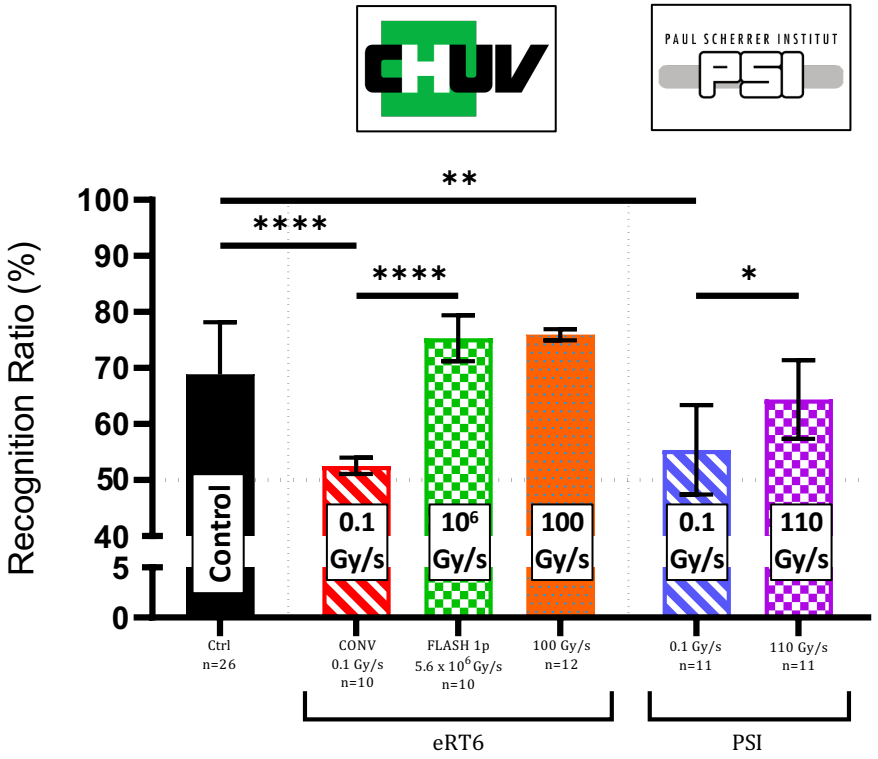
Neurocognitive response

- NOR 2 months post-RT (10Gy)



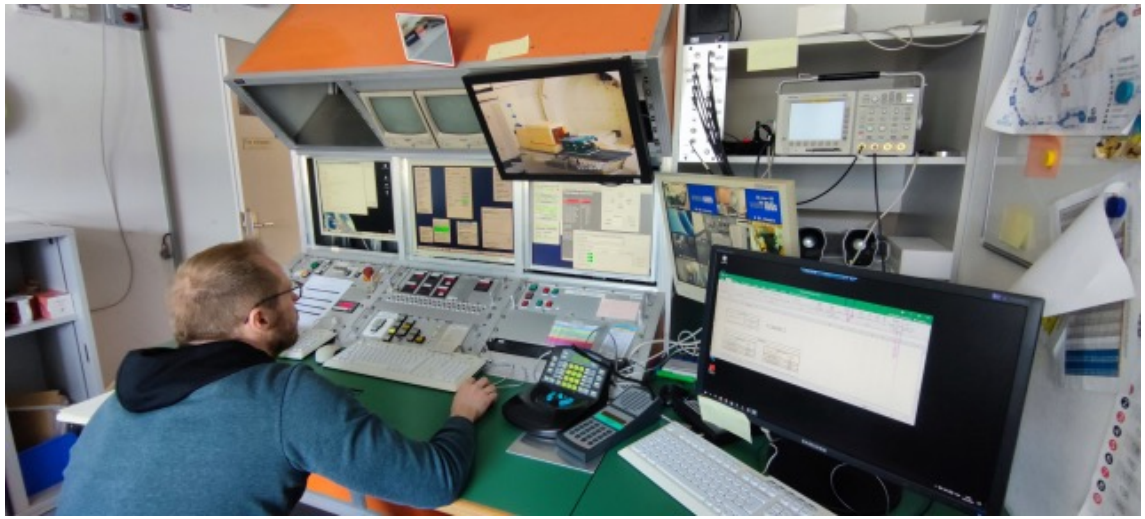
Neurocognitive response

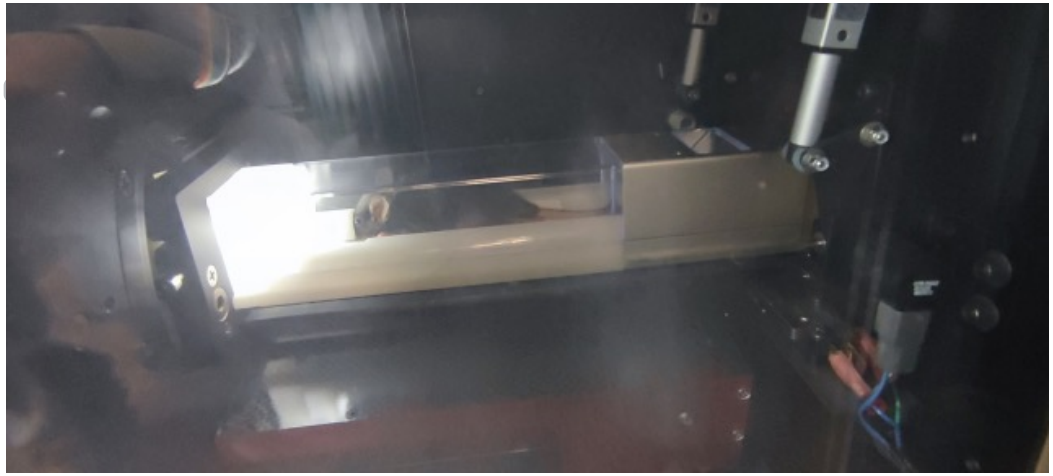
- NOR 2 months post-RT (10Gy)

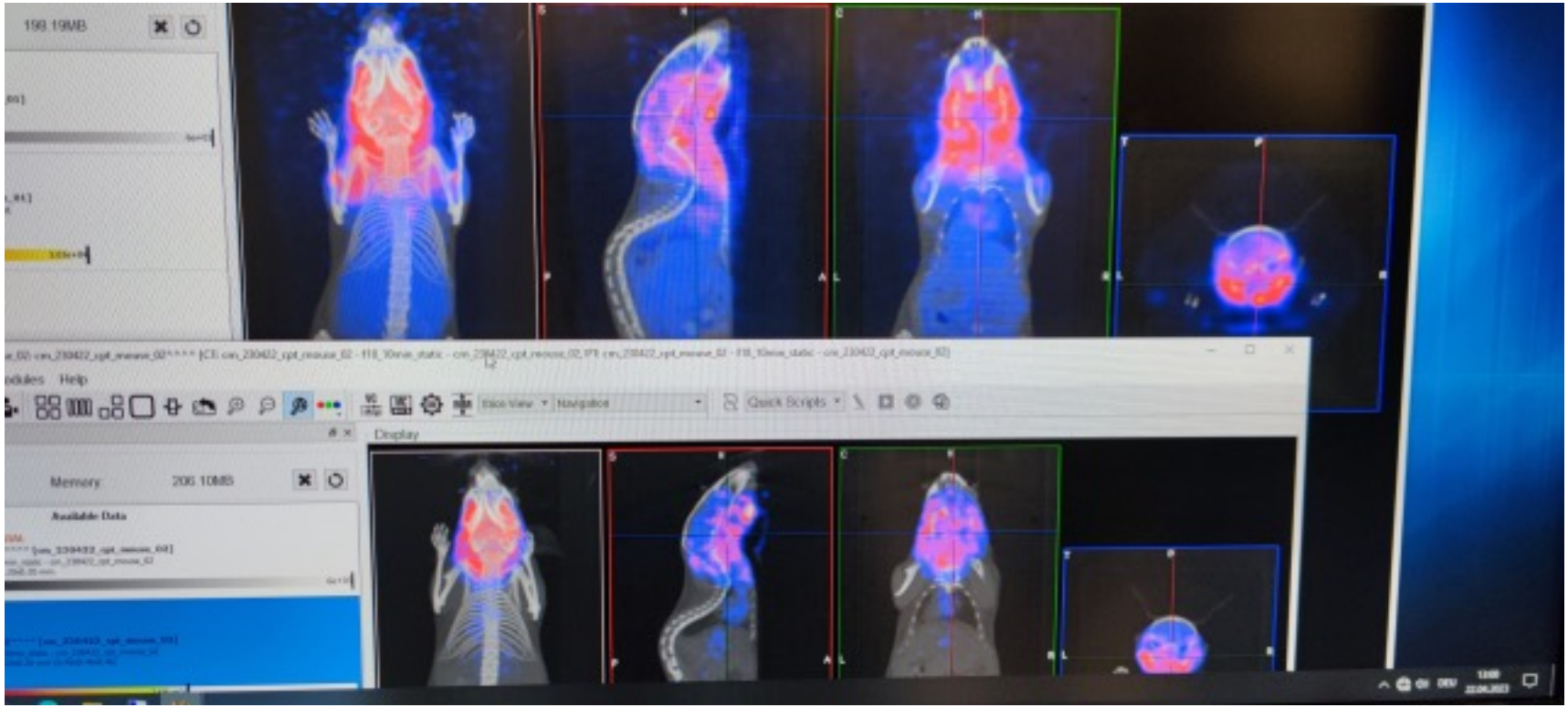


→ PET/CT

Proton FLASH irradiations of mice



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