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

Protontherapy:
Technology for the benefit of the patient


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

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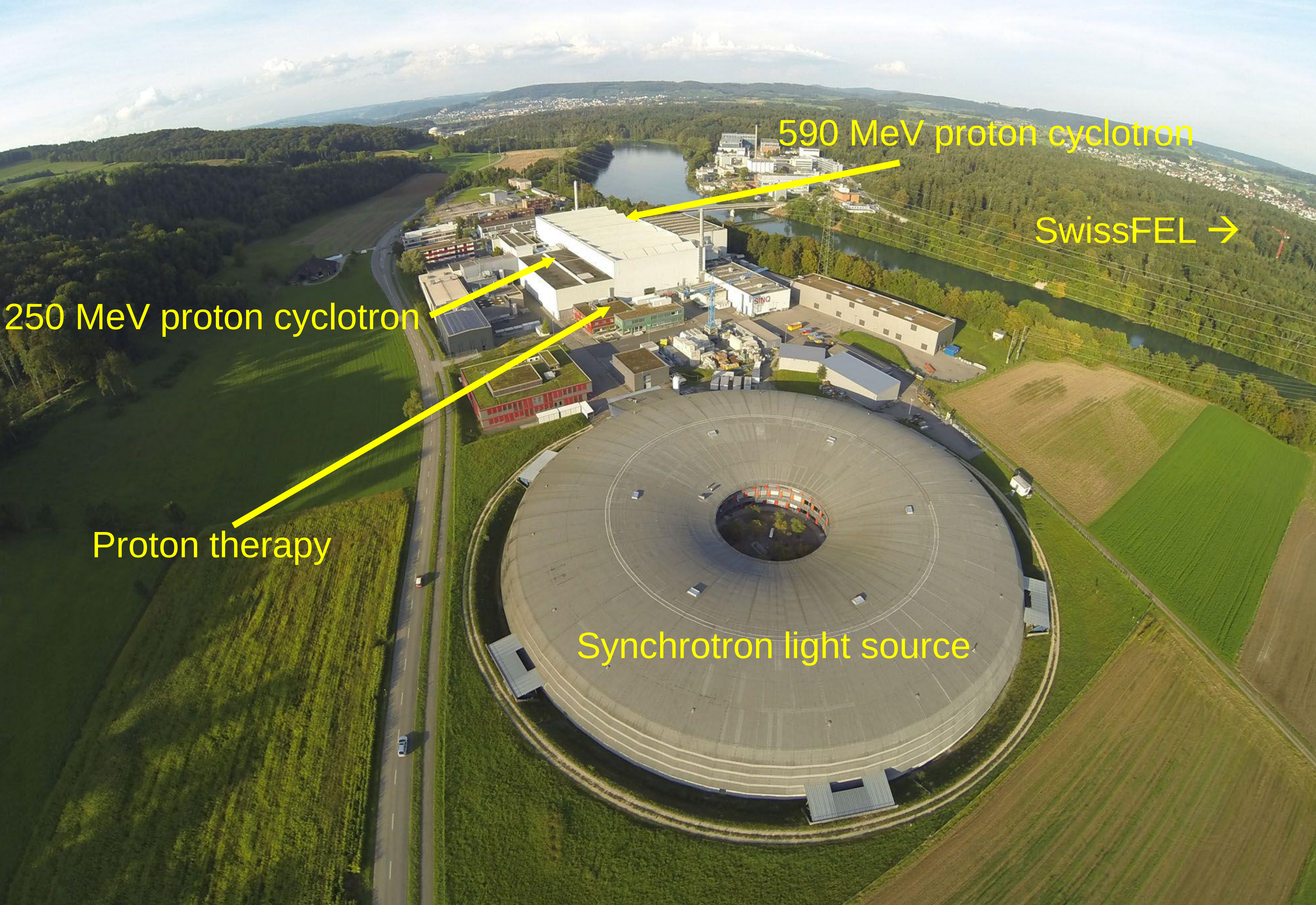


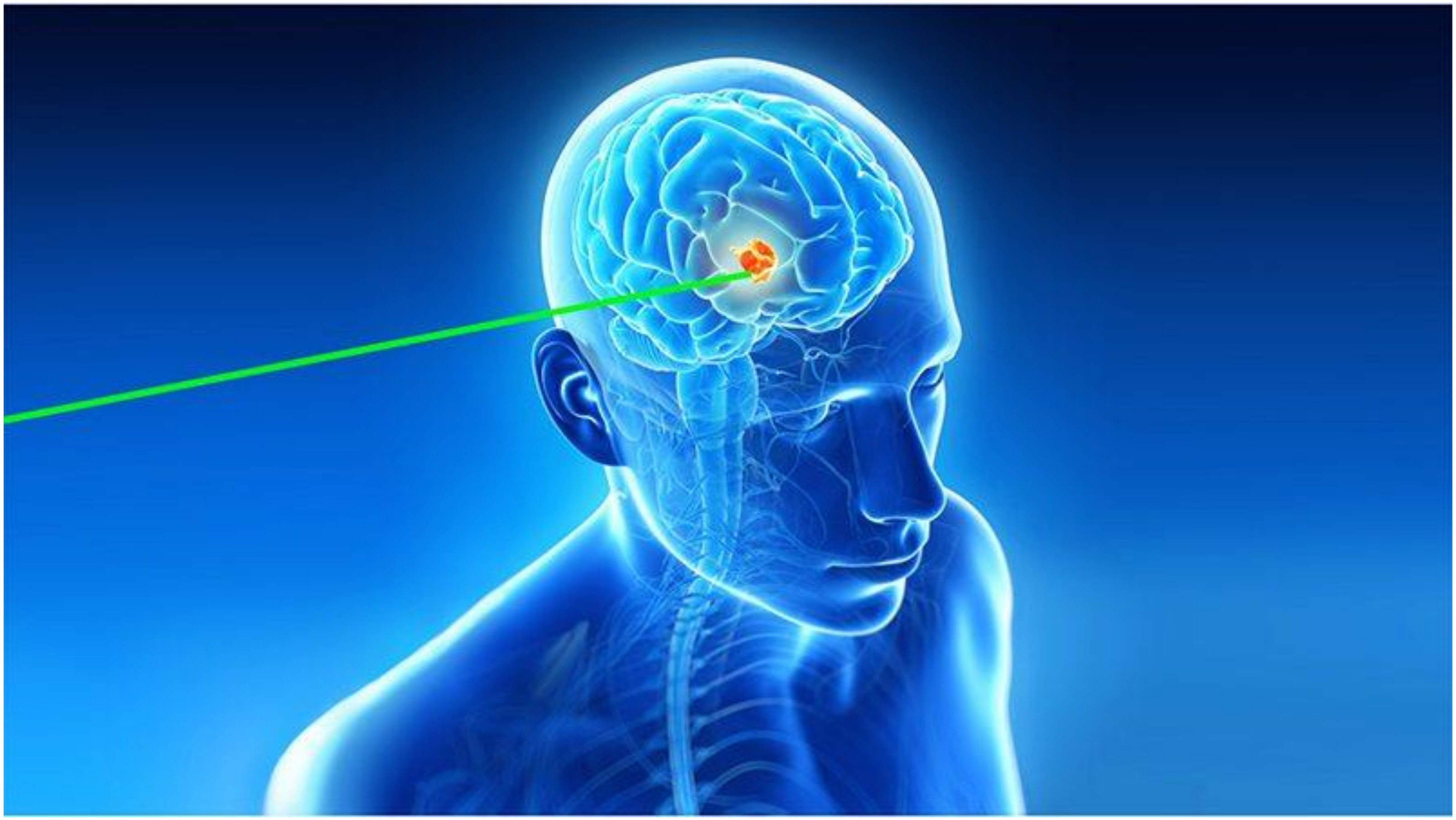
Martin Grossmann

- 1984-1985
  CERN: fixed target experiment (ϒ meson production)
- 1986-1990
  PSI: rare muon decay experiment
- 1991-1994
  PSI: IT department
- 1995-today
  PSI: Protontherapy

- IEEE – NPSS
  Real Time Conference (Program Chair, Chair)
  CANPS Technical Committee (Chair 2018 - 2022)
  Transnational Committee (Chair 2021 - today)

  NPSS International Schools (since 2018)

Radiotherapy with Protons



Why Protons?

Proton therapy

Mass: ~200 tons

Diameter: ~8 m

Conventional therapy (LINAC)

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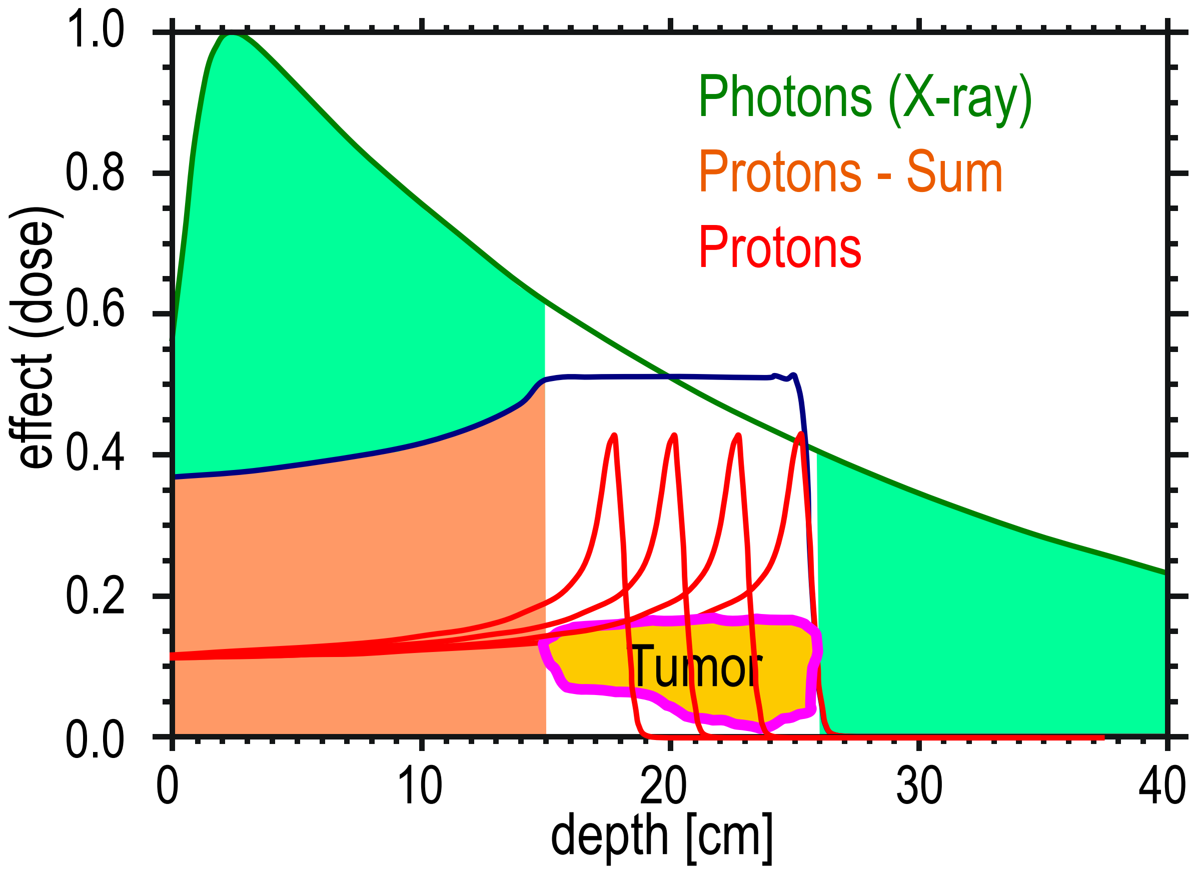
Why Protons?

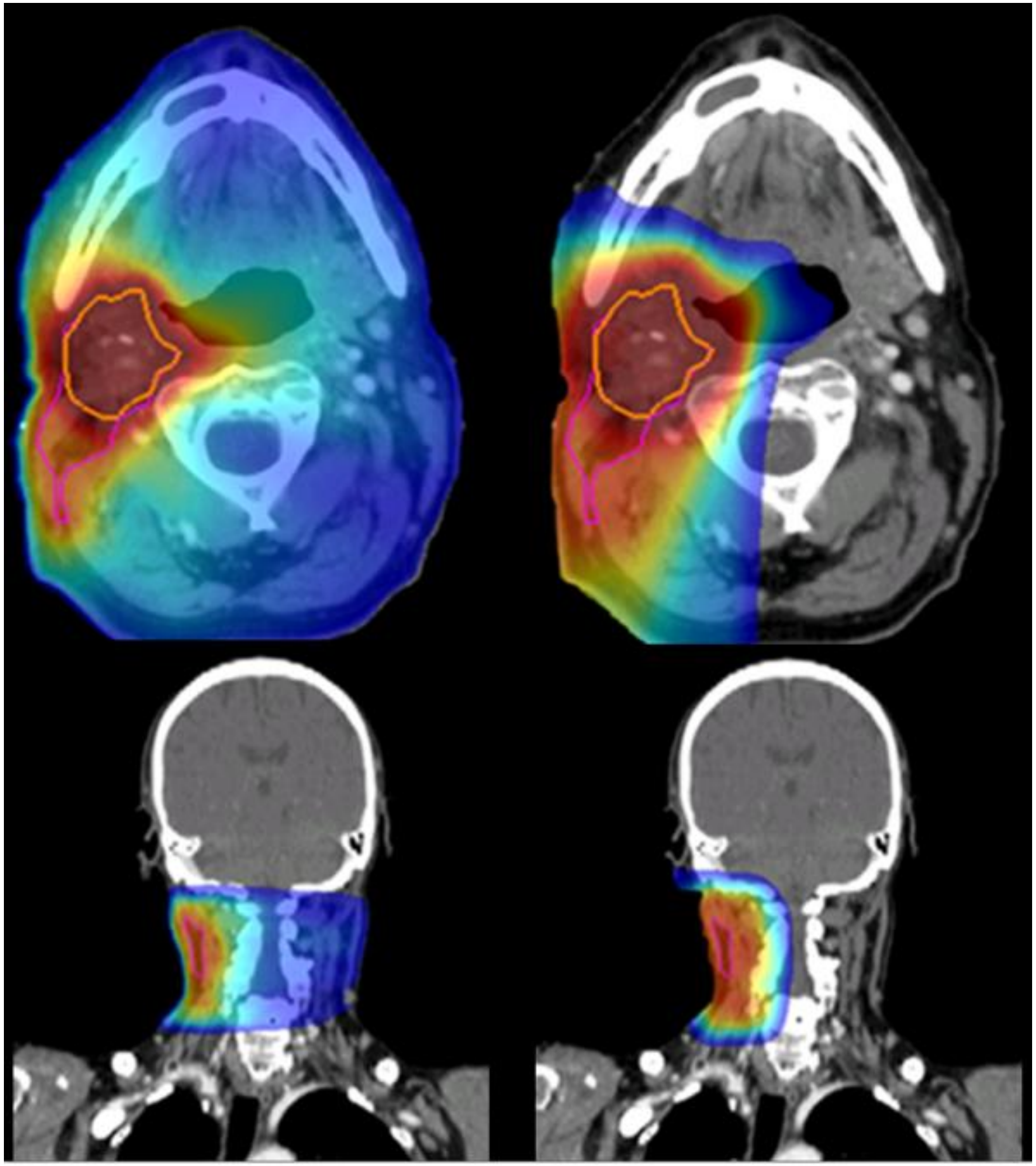


Dose burden - photons

Dose burden - protons

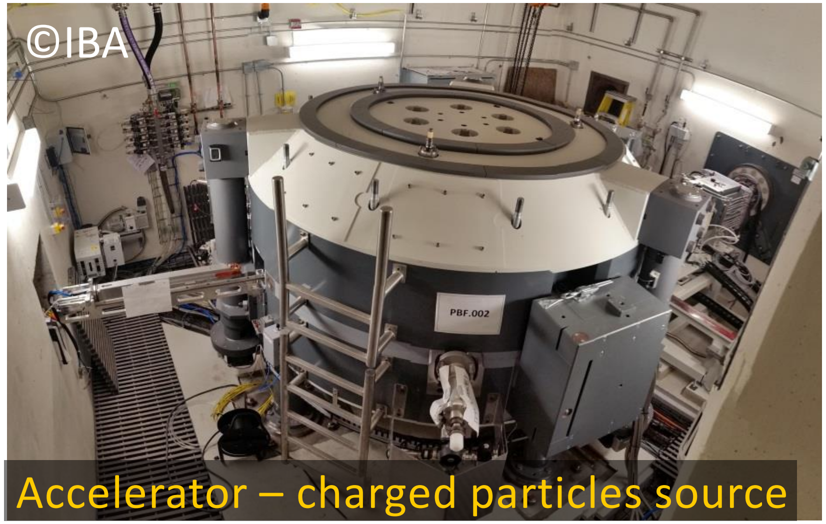
Why Protons?

Photons



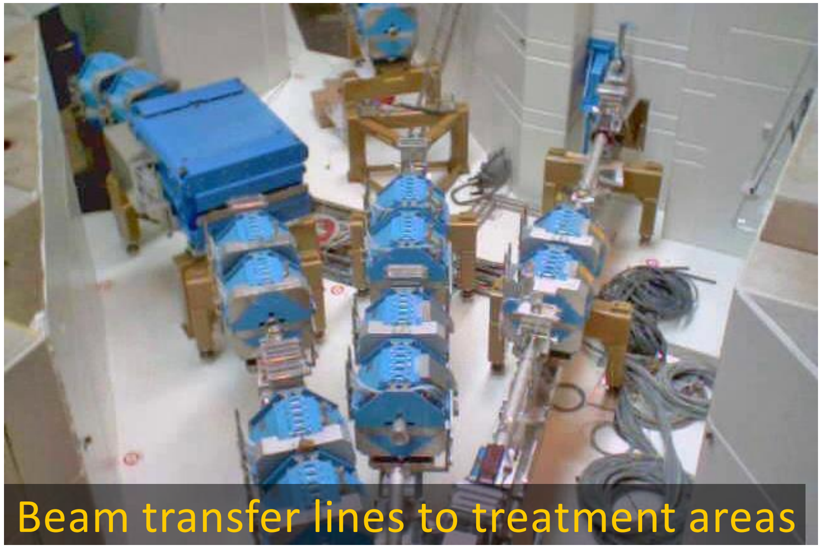
Protons

Main parts of a particle treatment facility



Accelerator – charged particles source

Fixed beam line



Beam transfer lines to treatment areas

Gantry – rotating beam line

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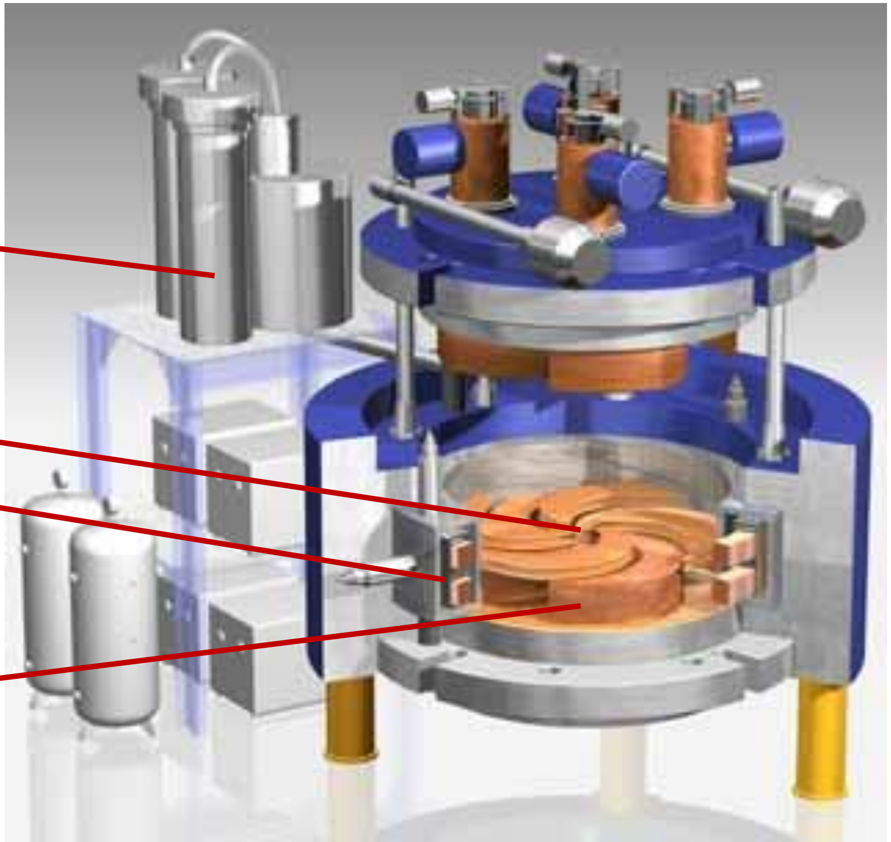
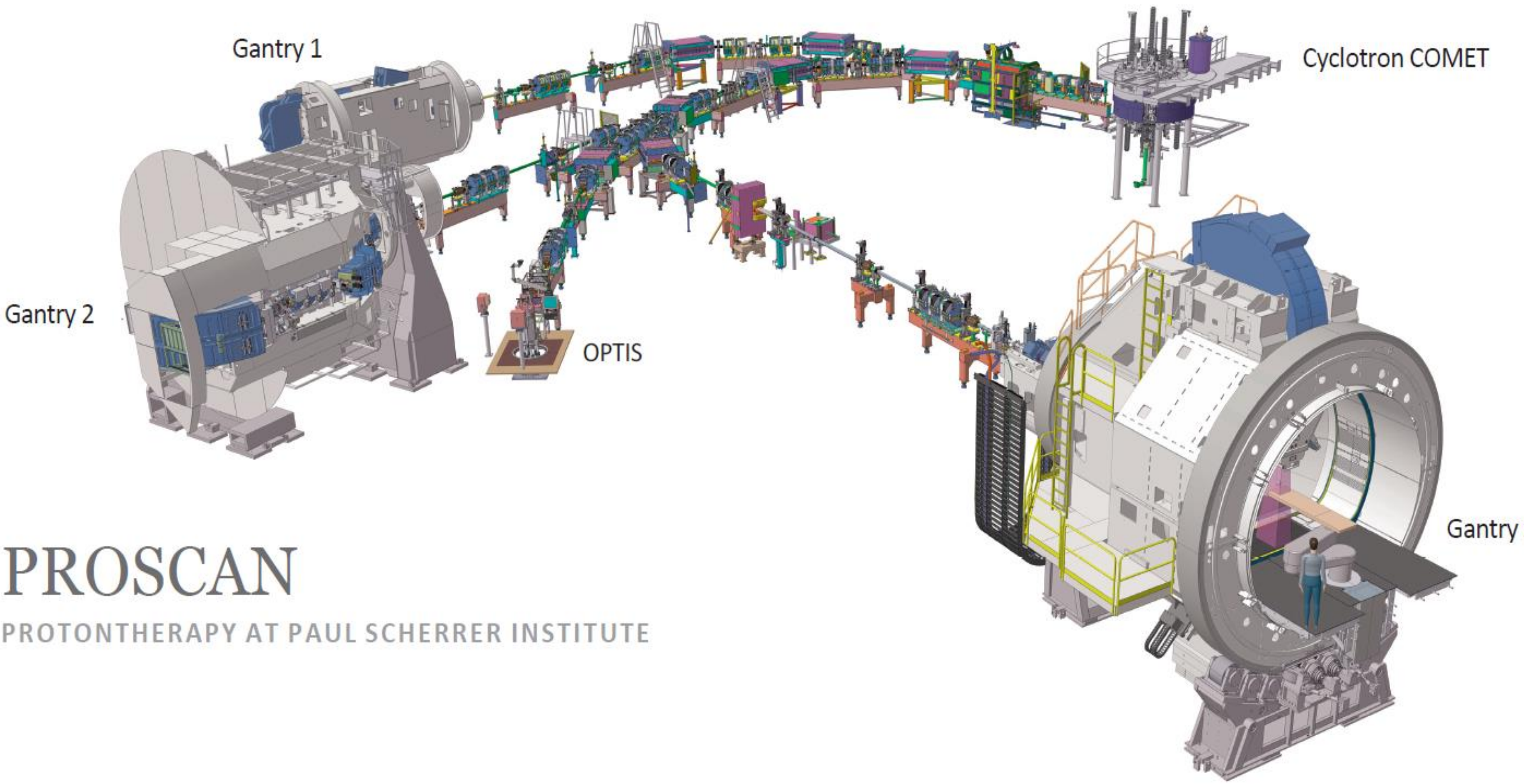
Superconducting Cyclotron COMET (Accel/Varian)

- 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



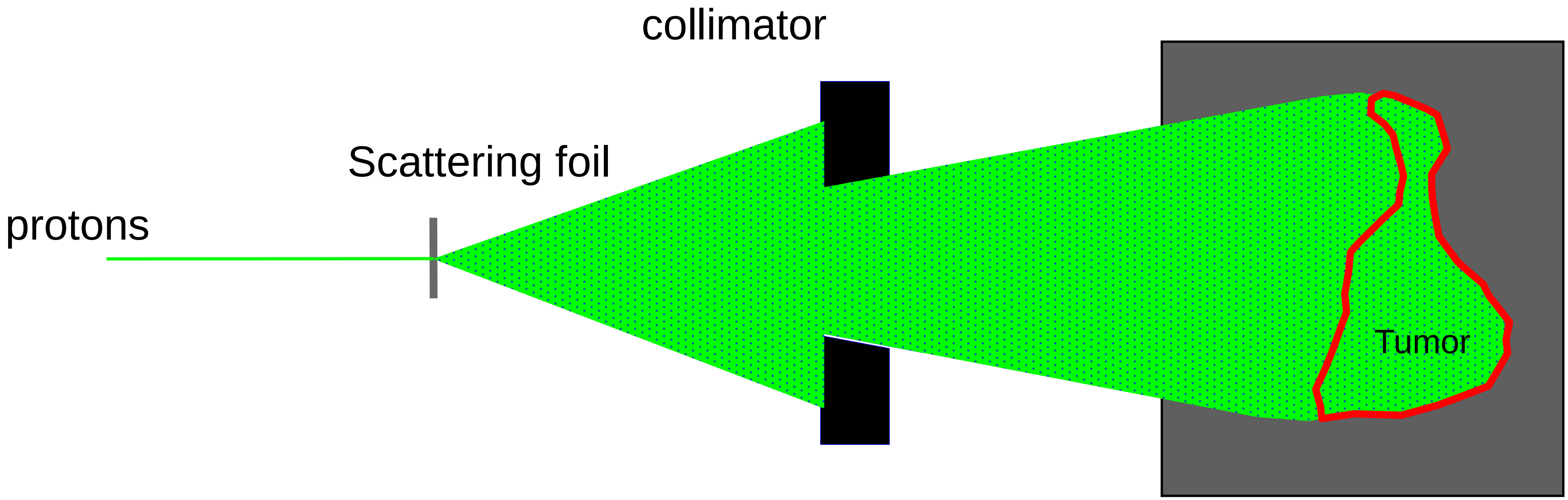
Superconducting Cyclotron COMET (Accel/Varian)



PROSCAN

PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

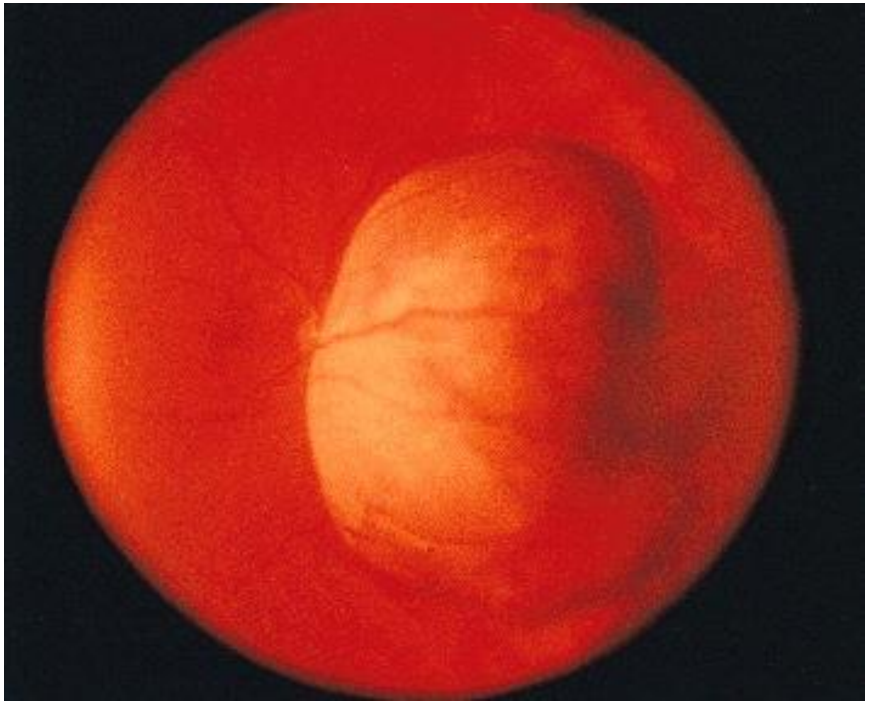
Irradiation technique - classical



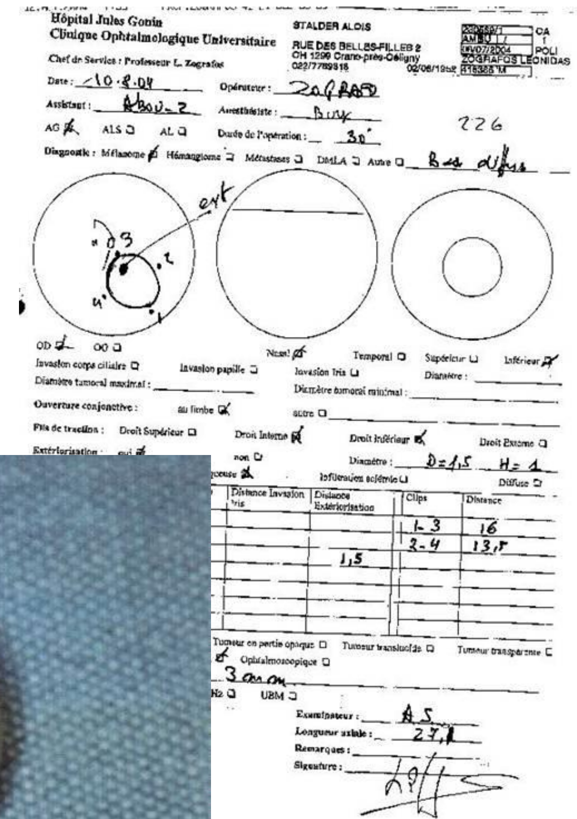
PSI's OPTIS program

- Treating Eye Melanoma

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



PSI's OPTIS program


Hôpital Jules Gonin
Clinique Ophtalmologique Universitaire
Chef de Service : Professeur L. Zografos

STALDER ALOIS
RUE DES BELLES-FILLES 2
CH 1299 Crans-près-Céligny
022/7789818
02/06/1958

CA
1
POLI
ZOGRAFOS LEONIDAS

Date : 10.8.04
Opérateur : ZOGRAFO
Assistant : Abou-Z
Anesthésiste : Buy
226
AG ☒ ALS ☐ AL ☐
Durée de l'opération : 30'
Diagnostic : Mélanome ☒ Hémangiome ☐ Métastases ☐ DMLA ☐ Autre ☐ B-a diffus

ext
3
2
4
1

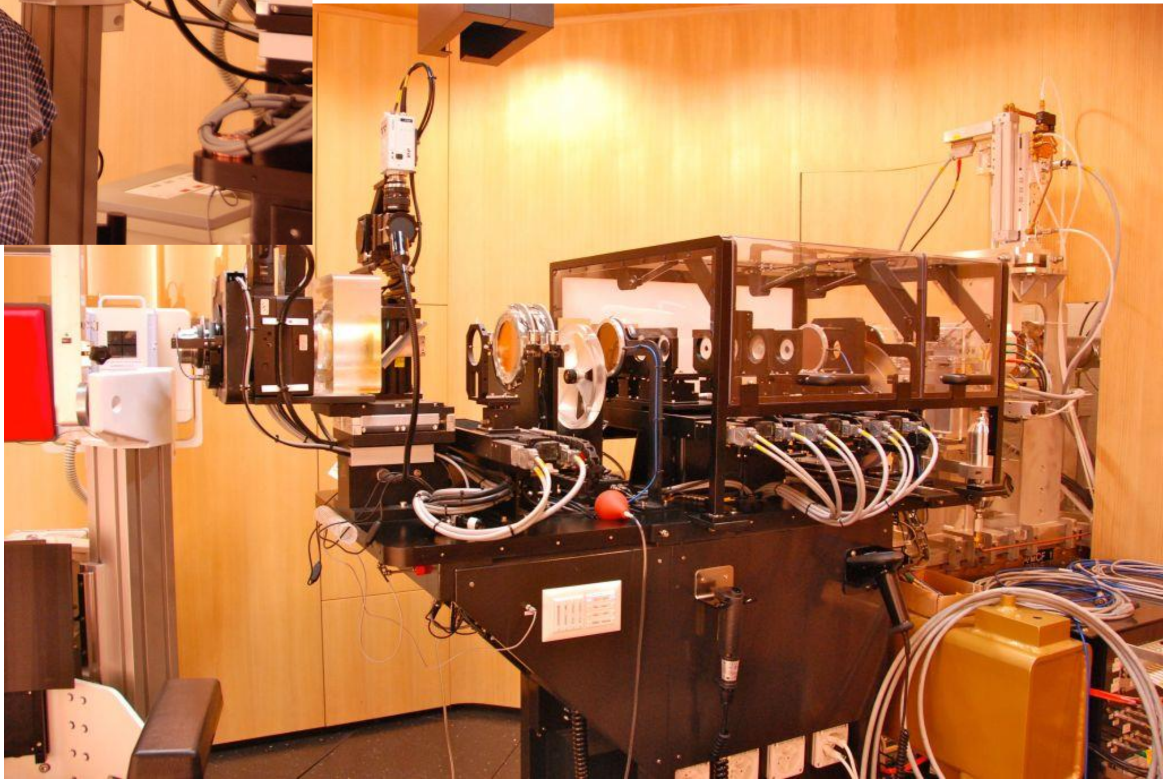
OD ☒ OG ☐
Nasal ☒ Temporal ☐ Supérieur ☐ Inférieur ☒
Invasion corps ciliaire ☐ Invasion papille ☐ Invasion Iris ☐
Diamètre :
Diamètre tumoral maximal :
Diamètre tumoral minimal :
Ouverture conjonctive : au limbe ☒ autre ☐
Fils de traction : Droit Supérieur ☐ Droit Interne ☒ Droit Inférieur ☒ Droit Externe ☐
Extériorisation : oui ☒ non ☐
Diamètre : D=1,5 H=1
Infiltration sclérale ☐
Diffuse ☐

Distance Invasion Iris	Distance Extériorisation	Clips	Distance
		1-3	16
		2-4	13,5
	1,5		

Tumeur en partie opaque ☐ Tumeur translucide ☐ Tumeur transparente ☐
Ophtalmoscopique ☐
3 mm
UBM ☐

Examinateur : A.S.
Longueur axiale : 27,1
Remarques :
Signature :

PSI's OPTIS program



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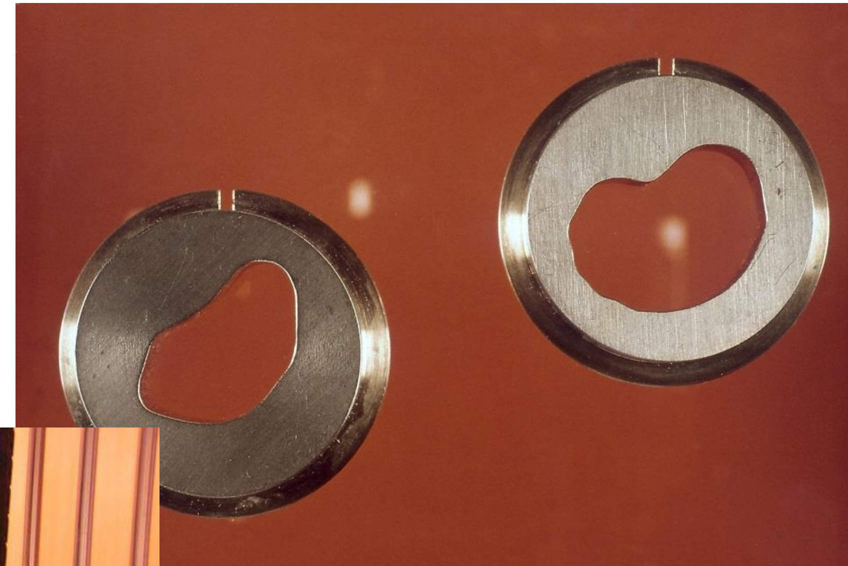
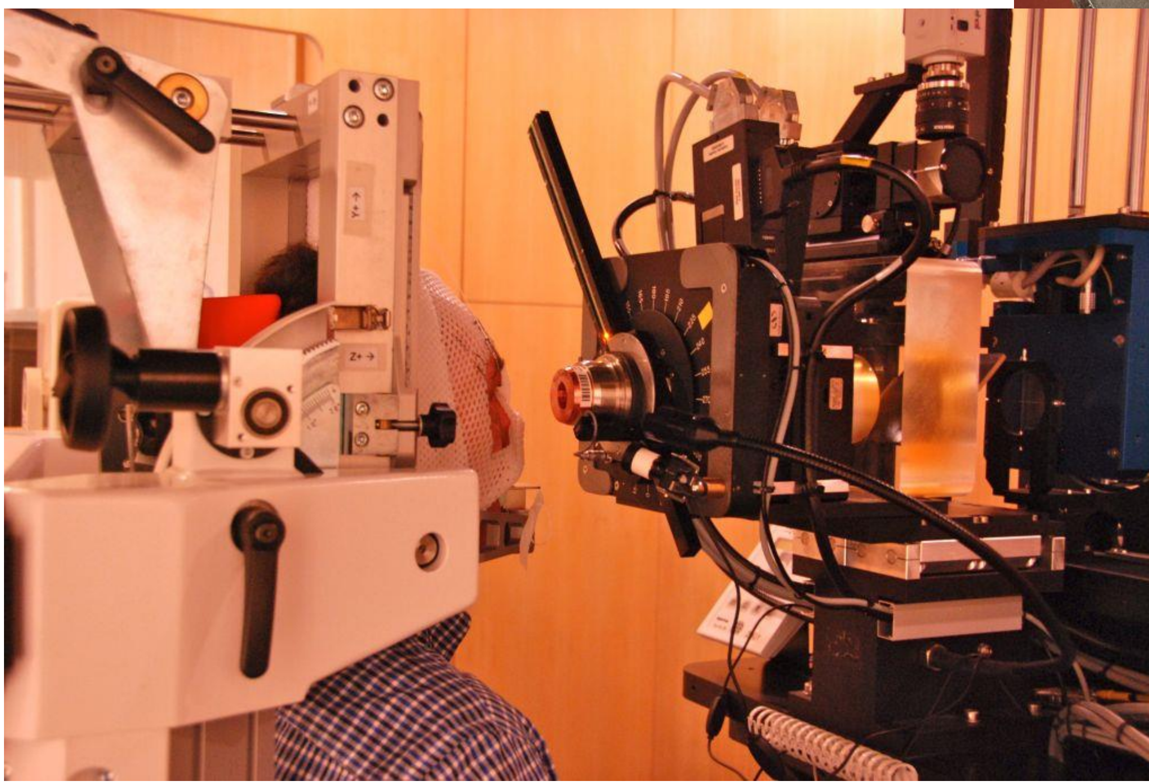
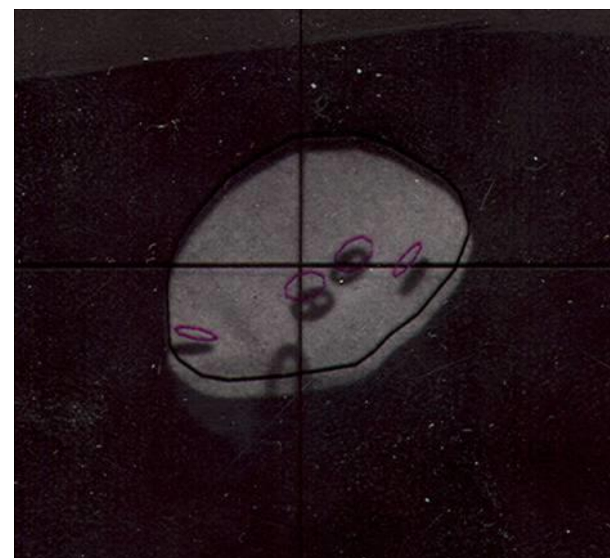
OPTIS







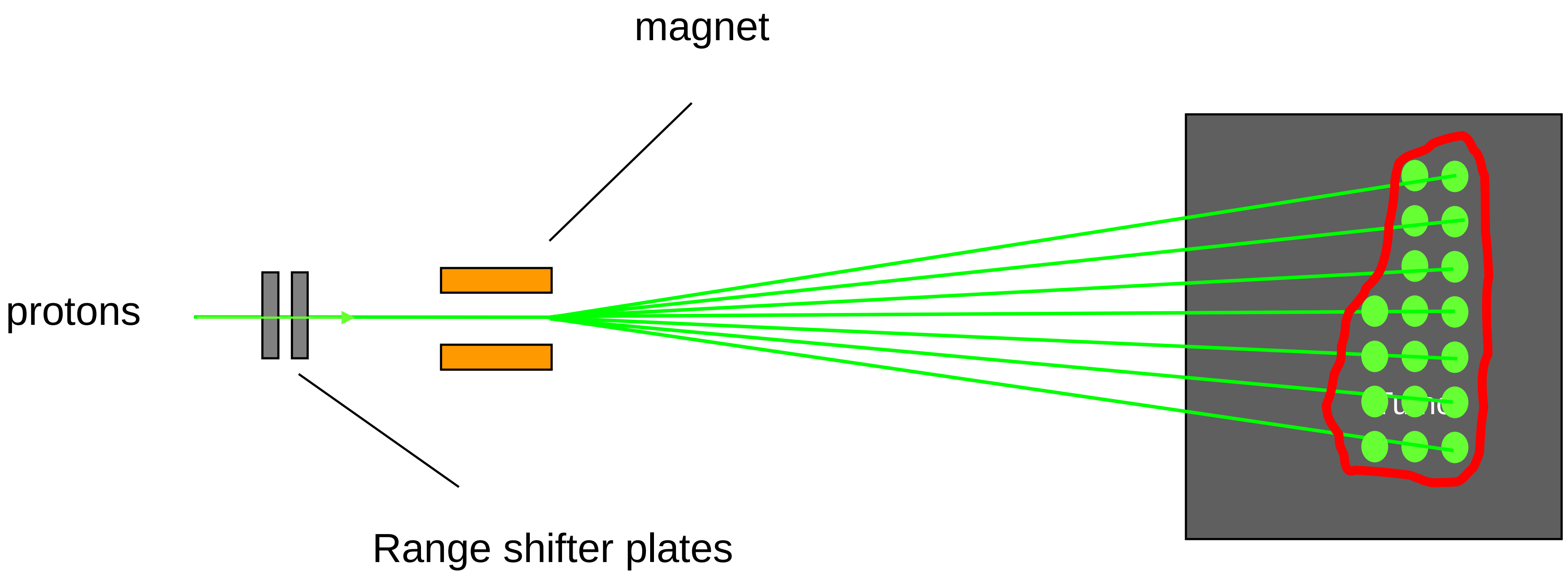
OPTIS – a success story

- Since 1984:
  treated more than 7’500 patients
- 98% cure
  (local tumor control)
- Conservation of vision
  100% for small tumors
  90% for big tumors


5 J., retinoblastoma, left eye,
18 months after treatment

Protons are the standard!

Irradiation technique – «spot scanning»



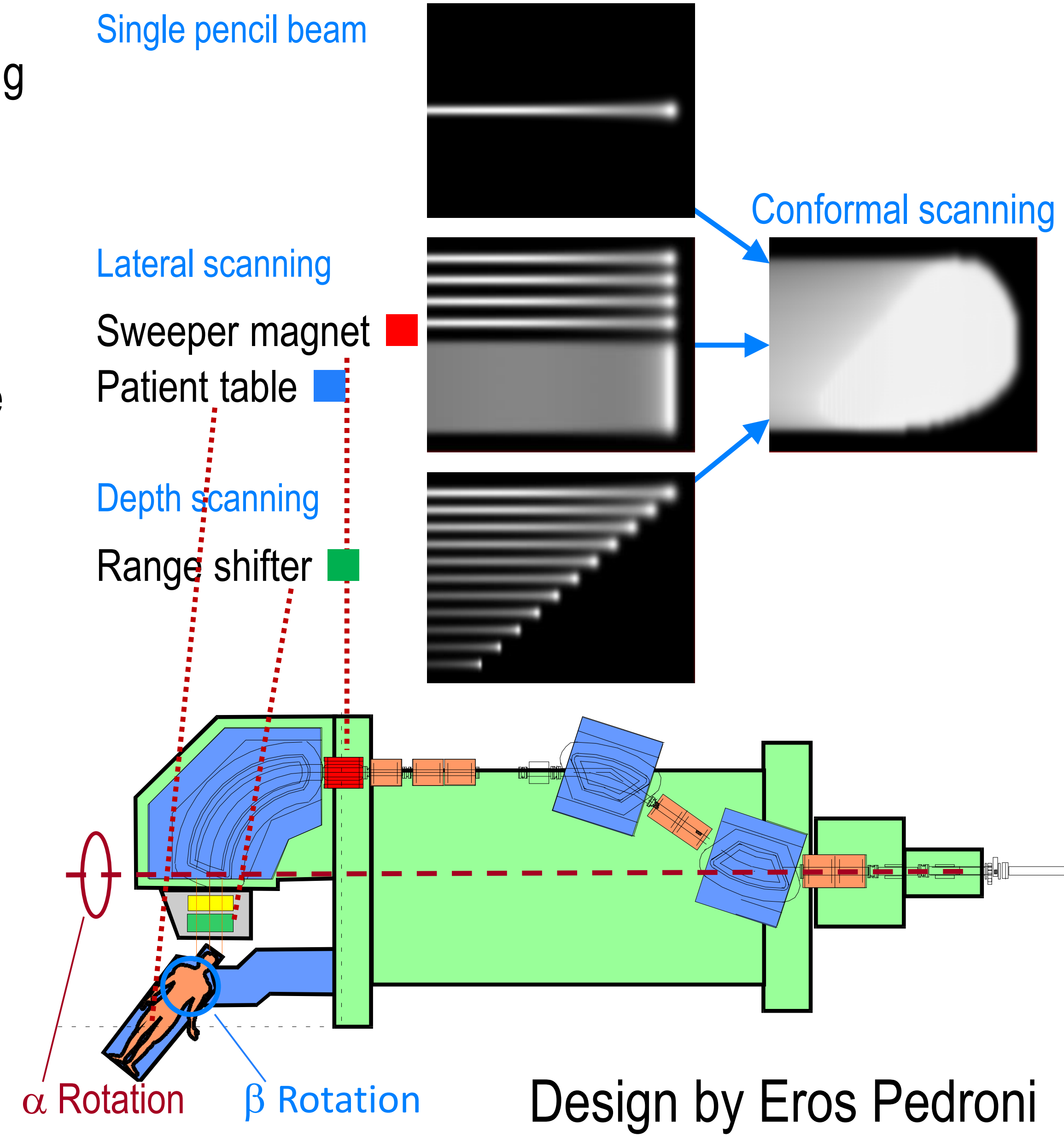
Gantry 1: A compact system for spot scanning

Implementation of spot scanning technique

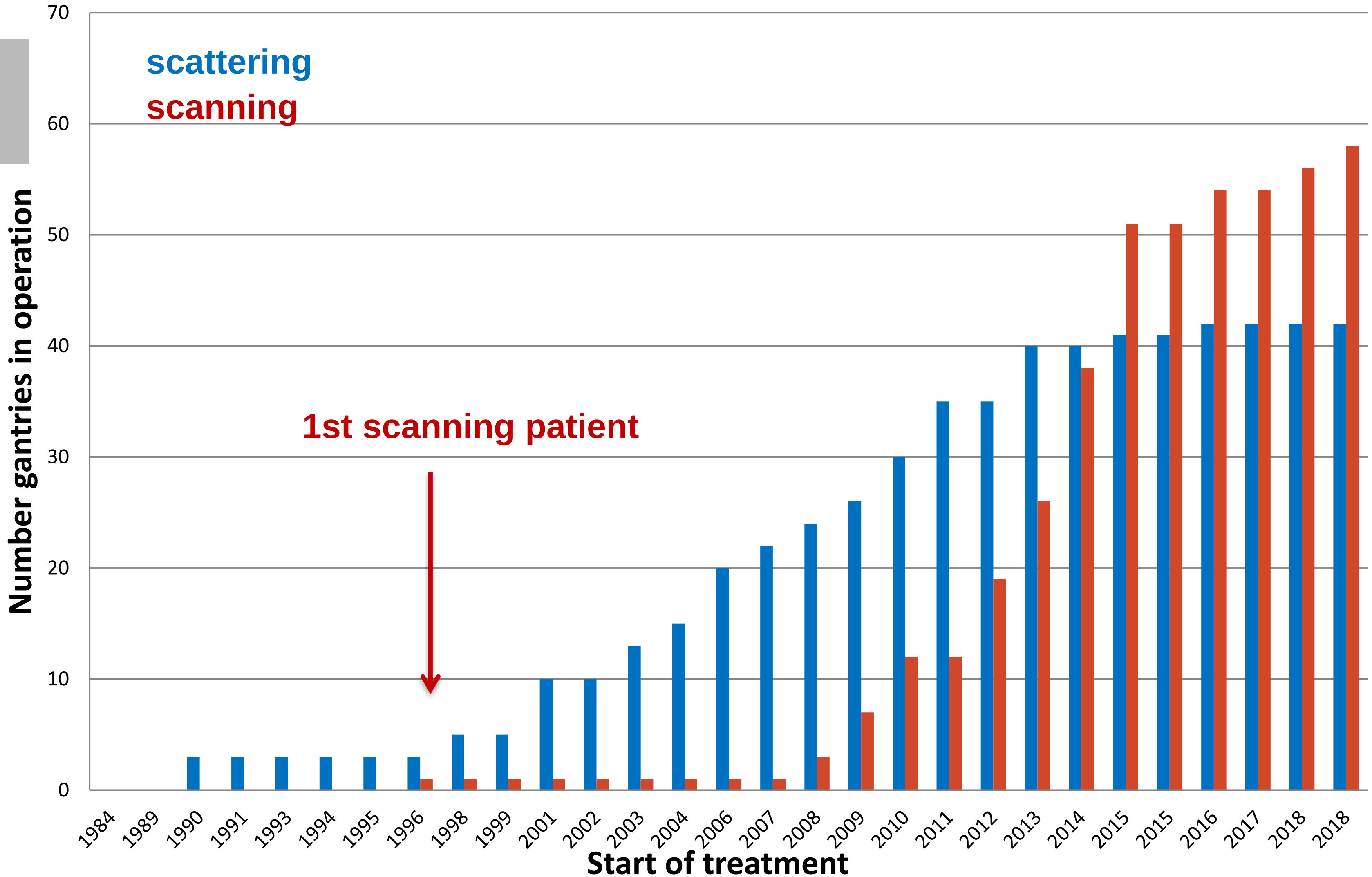
Start patient operation 1996

During 12 years the only spot scanning gantry worldwide

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



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

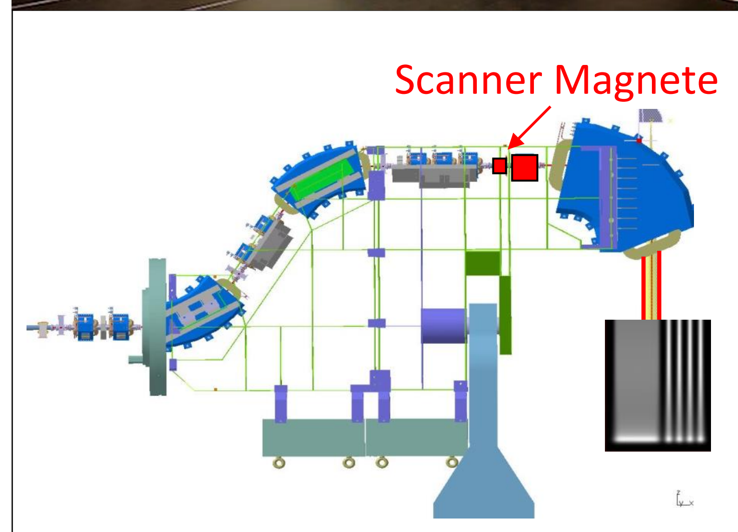
- Rotation limited to 210̊
- Patient table rotatable 180̊
  (→ still full flexibility)
- No pit

Fast scanning in 2 dimensions

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

Fast energy change → 3rd dimension

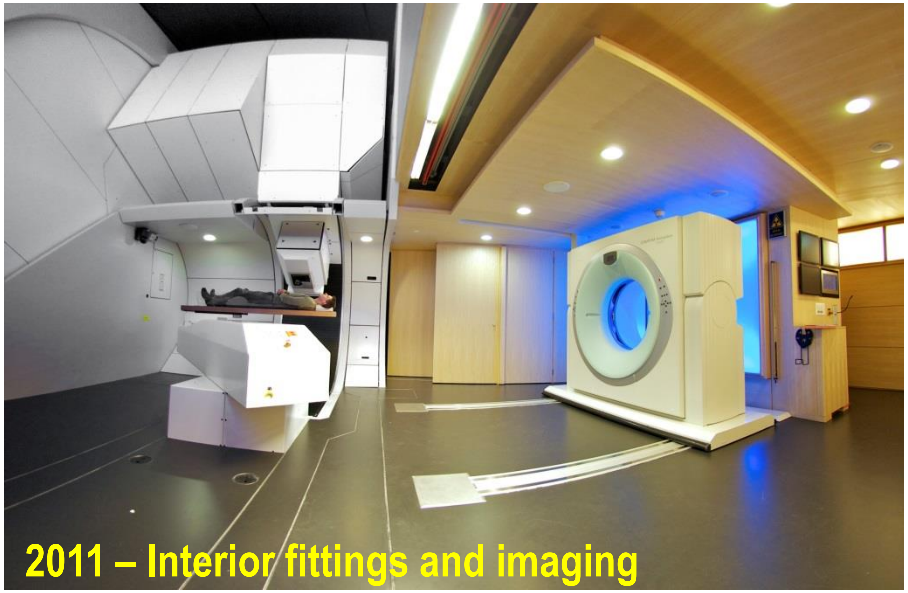
- Energy step < 100 ms
- Re-scanning possible in 3 dimensions



Gantry 2: next generation spot scanning


2006 - Delivery of mechanical structure

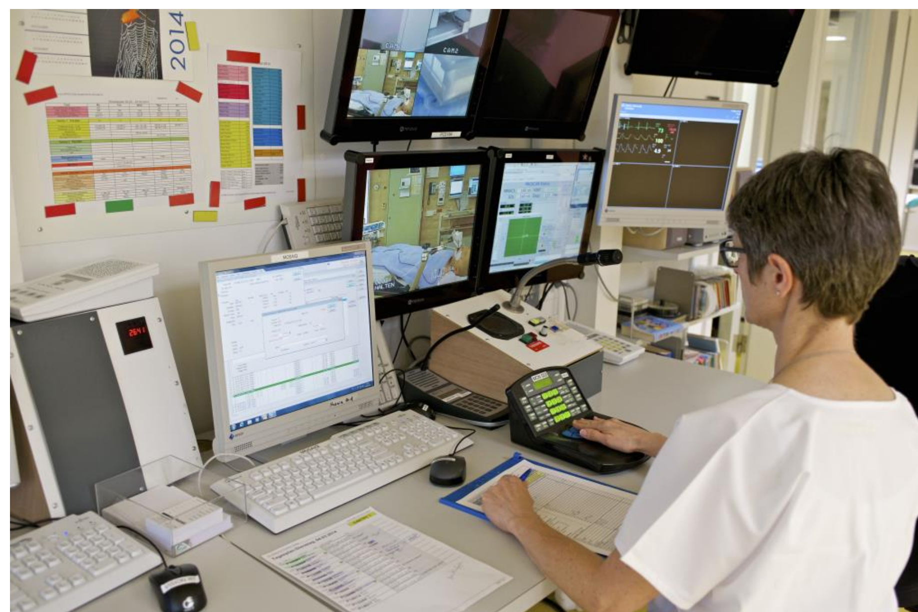

2008 - Beam line with innovative 90° dipole


2011 – Interior fittings and imaging

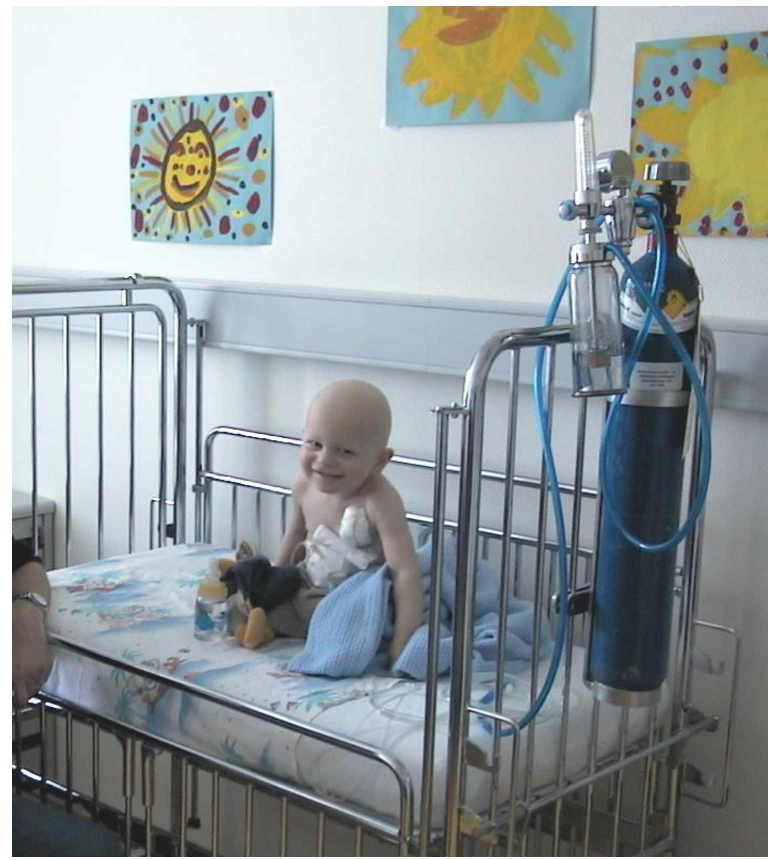

2013 - 1st patient treated

Treating small children

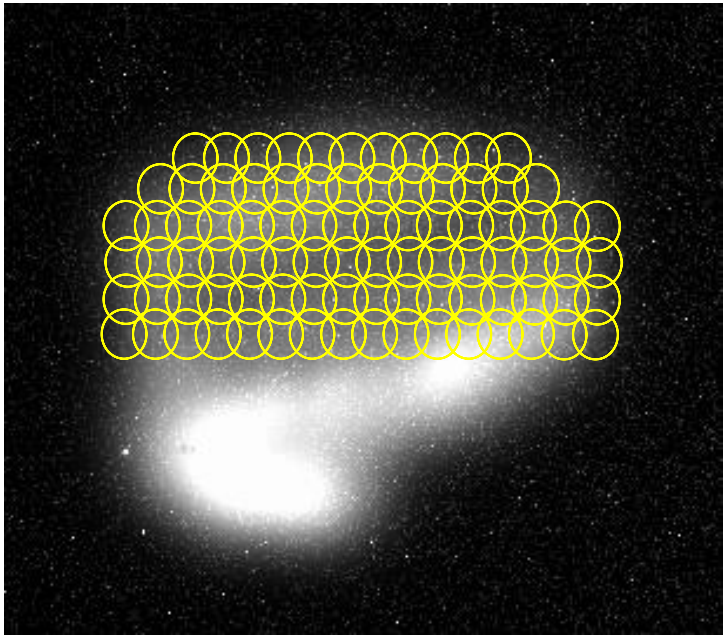
- Since 2004 treatments of small children
  → anesthesia team from children's hospital in Zurich
- Ca. 500 patients

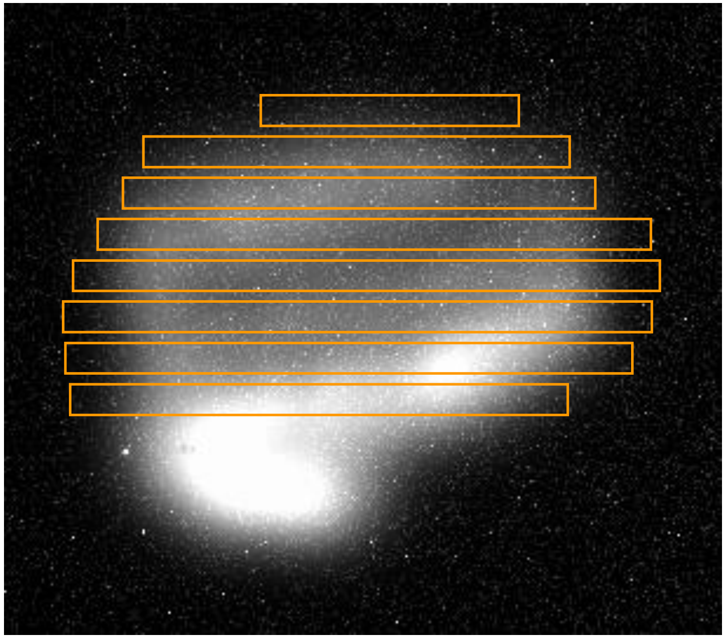

2014


Bair Hugger



Improvements in scanning technology





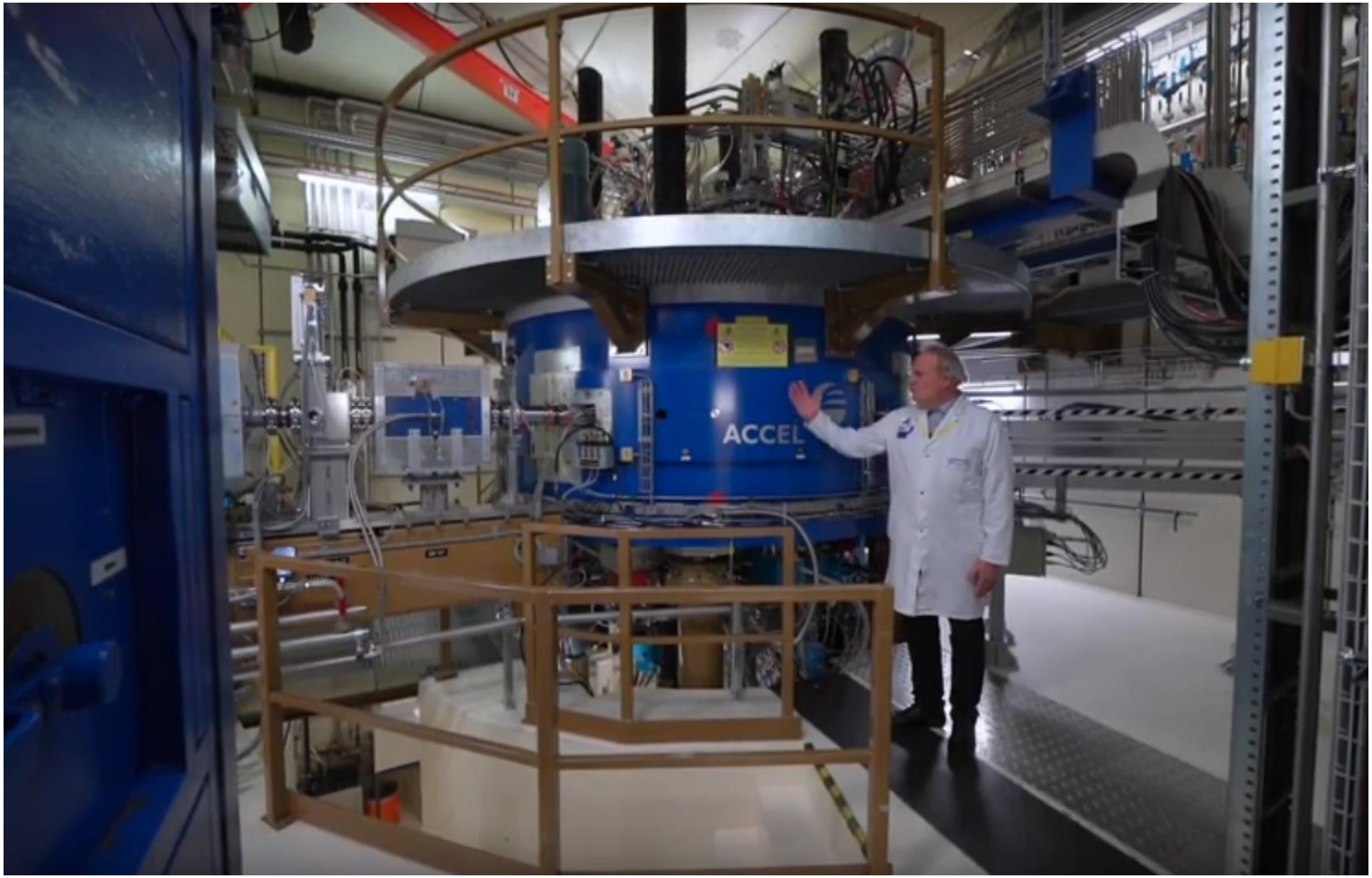
Discrete spot scanning

- 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

Video: Virtual Tour of PSI Protontherapy



https://youtu.be/sJOUdAd6QYk

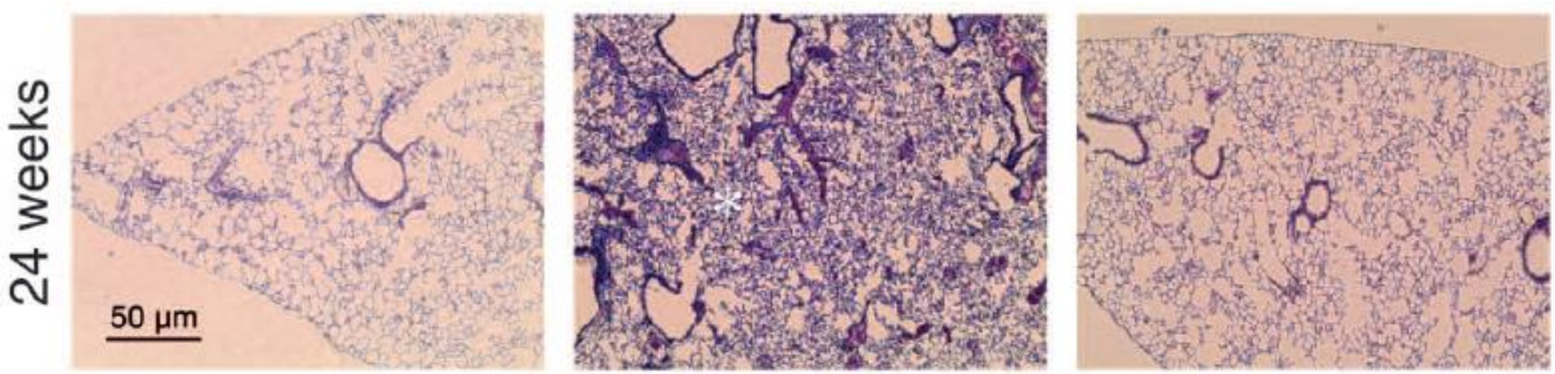
FLASH radiotherapy

- 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

electrons

Control **17Gy CONV (0.03 Gy/s)** **17Gy FLASH (60 Gy/s)**



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

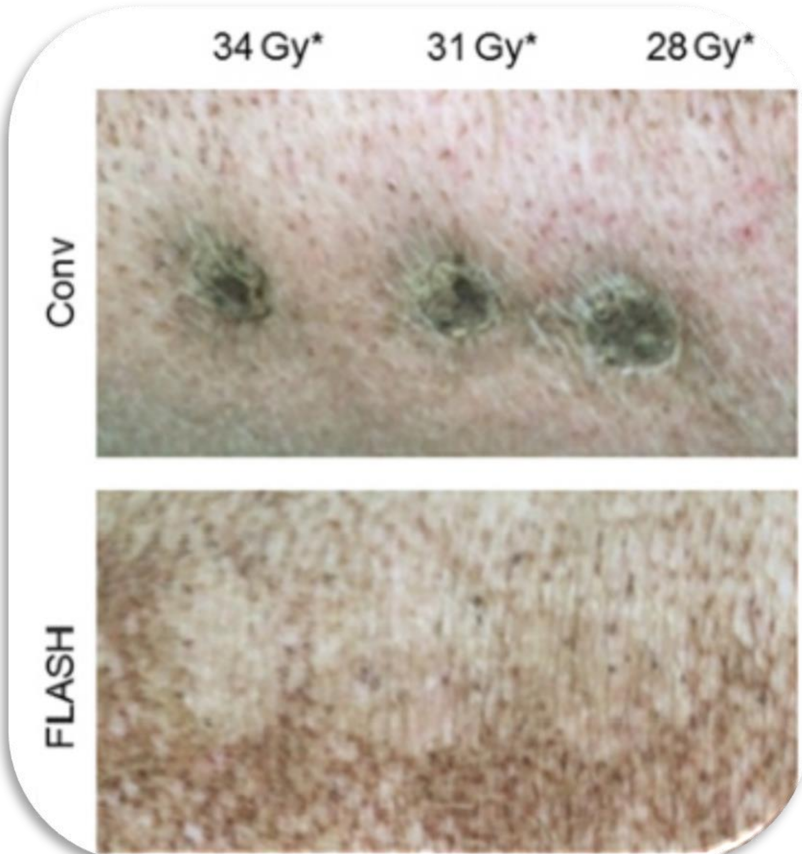
FLASH radiotherapy

FLASH confirmed in larger mammals (mini-pigs)

0.08 Gy/s

electroncs

300 Gy/s



Black dots = NECROSIS

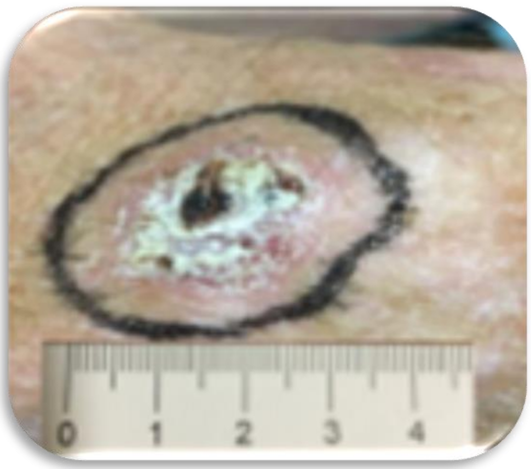
Vozenin, et al, The advantage of Flash RT confirmed in mini-pig and cat-cancer patients." Clinical Cancer Research. 2018;

FLASH radiotherapy

First human patient treated with FLASH

Electrons 166 Gy/s

Day 0 **5 months**

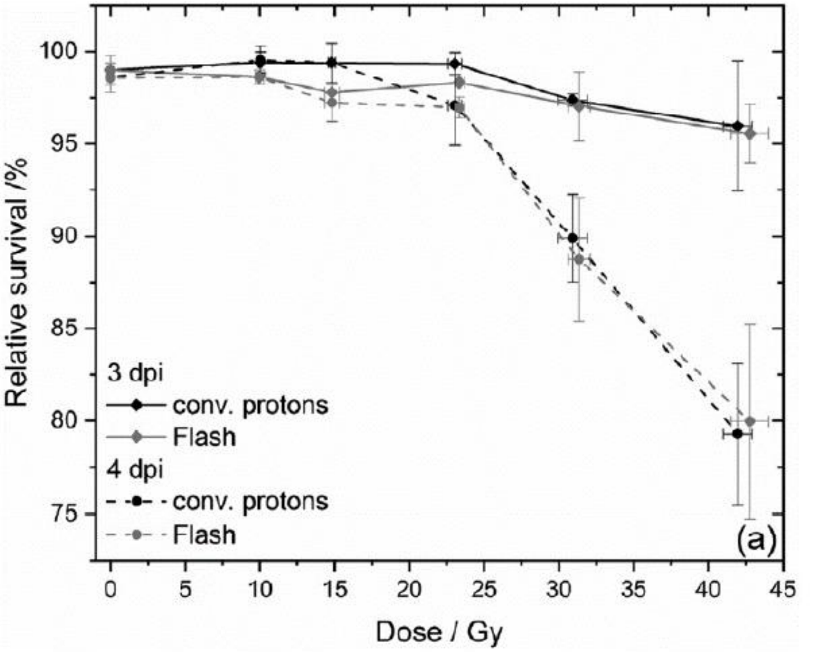


Jean Bourhis et al., «Treatment of a first patient with FLASH-radiotherapy», Radiotherapy and Oncology. 2019

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 ☹

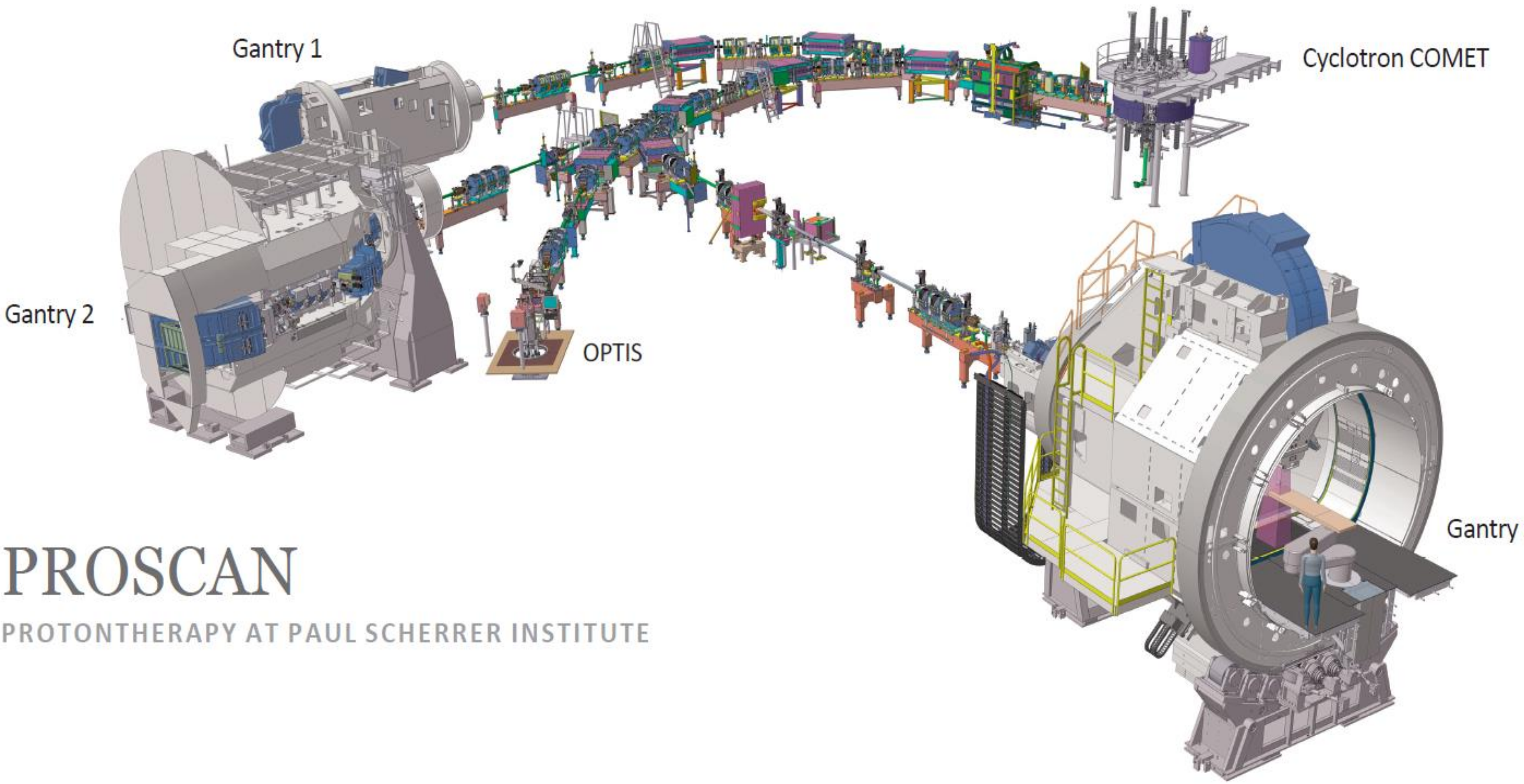
Universitäts Protonen Therapie Dresden



→ More experiments required!

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

Beamline Transmission



PROSCAN

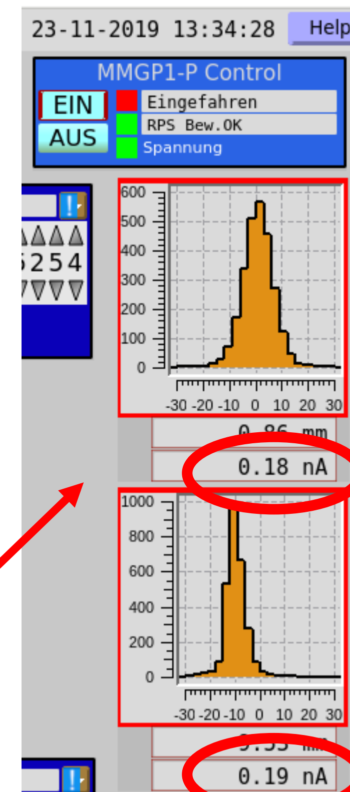
PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

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
  - We are very close to 100% transmission

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



Input current from cyclotron 0.2 nA
X&Y profile monitor on Gantry 1, integrated current

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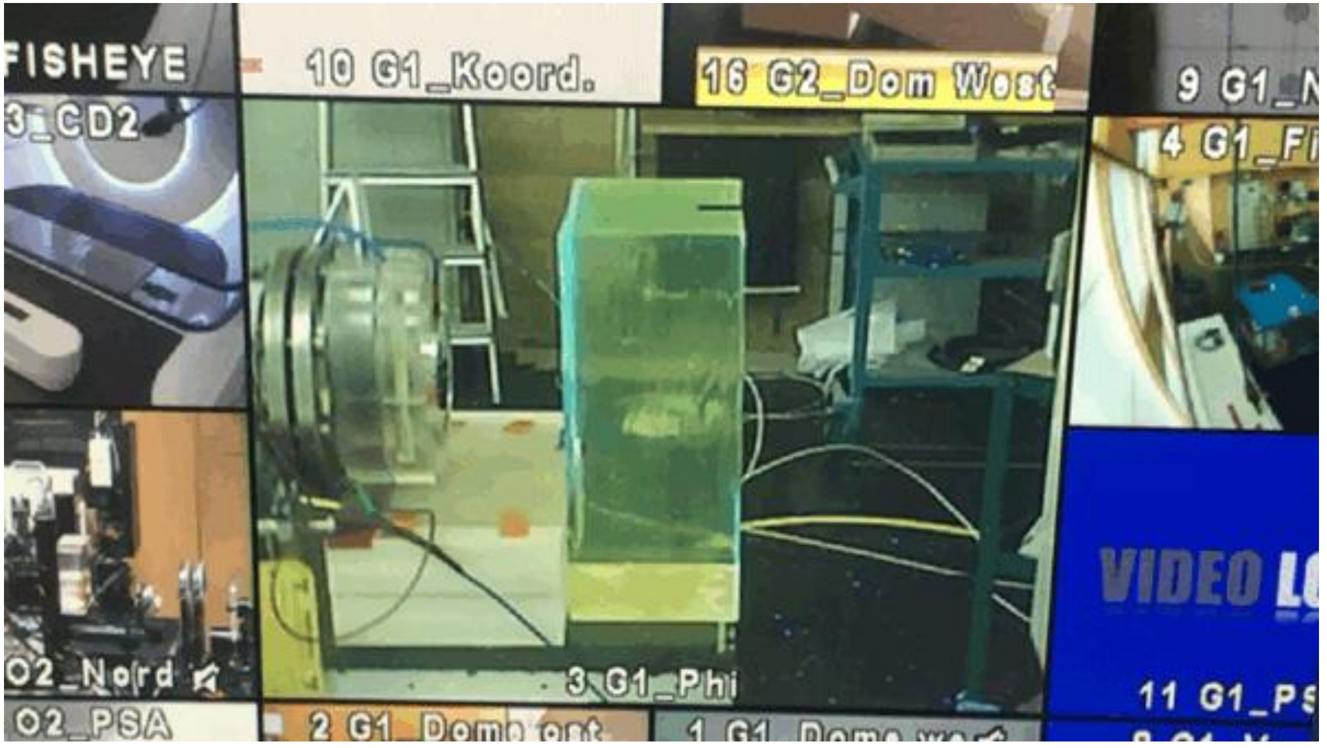
Flash @ Gantry 1

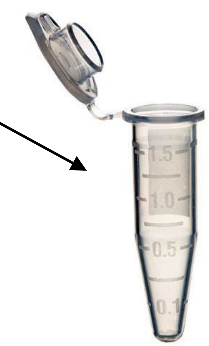
- Demo experiment January 2020
  → reach dose rates up to 9'000 Gy/s



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

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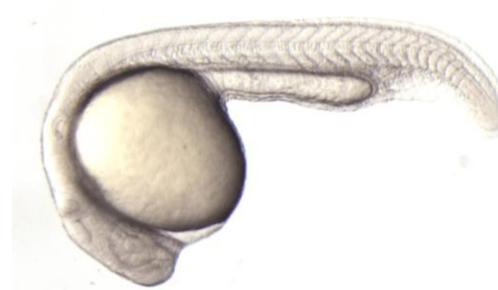

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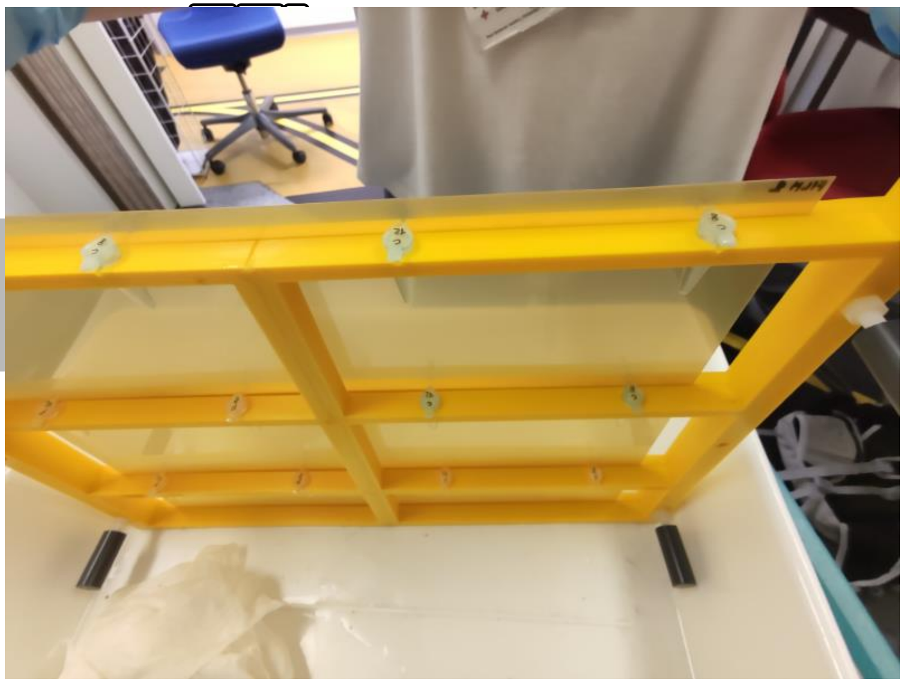

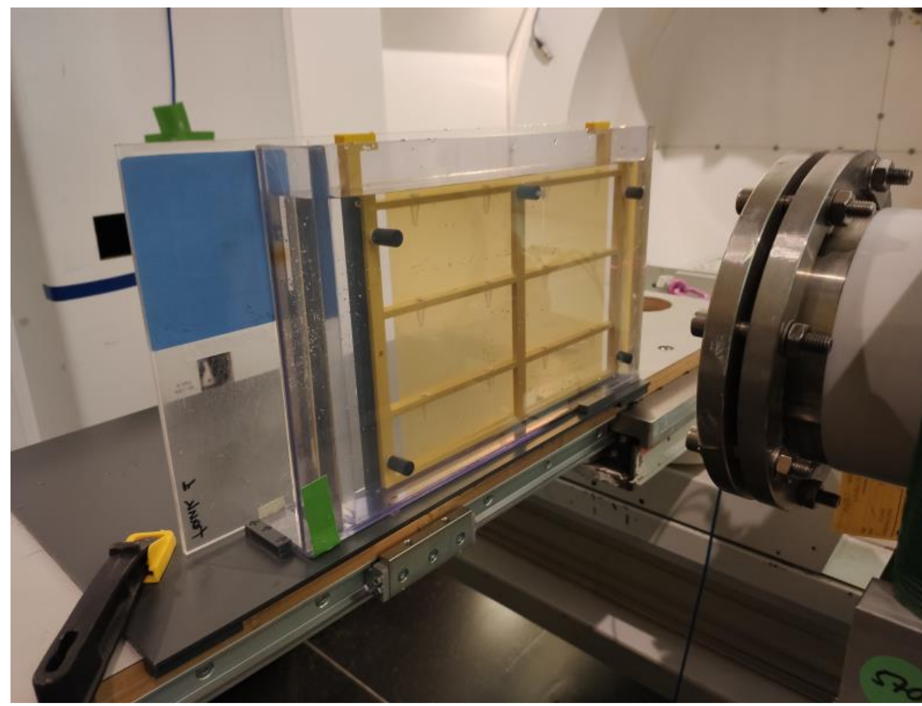


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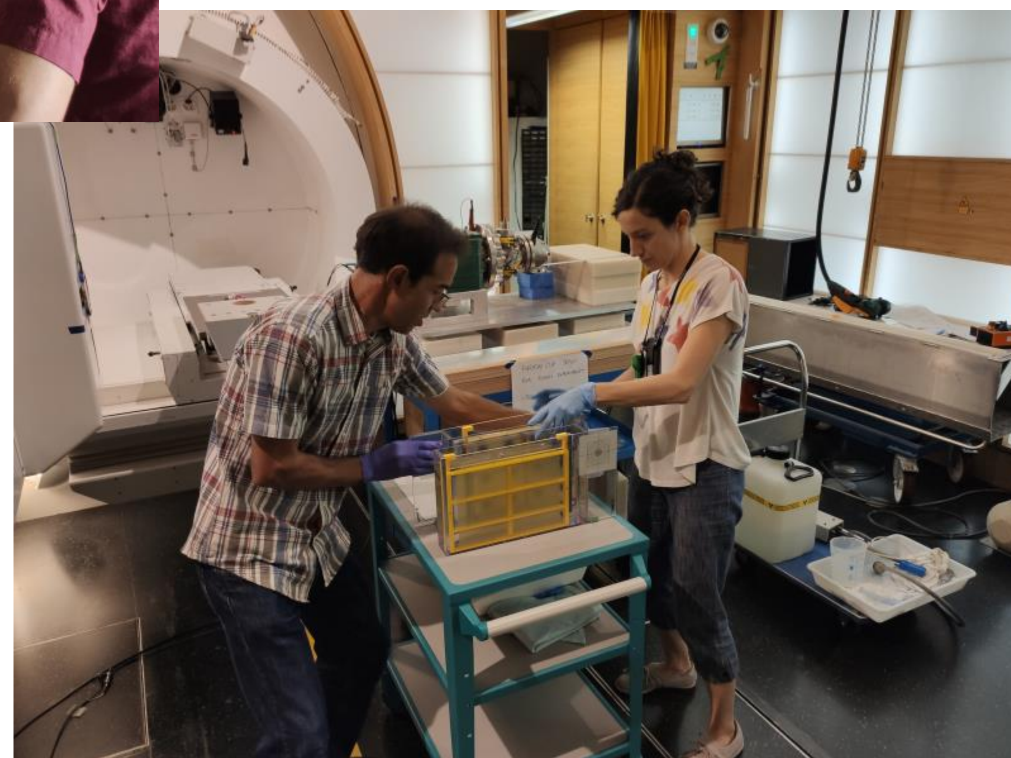

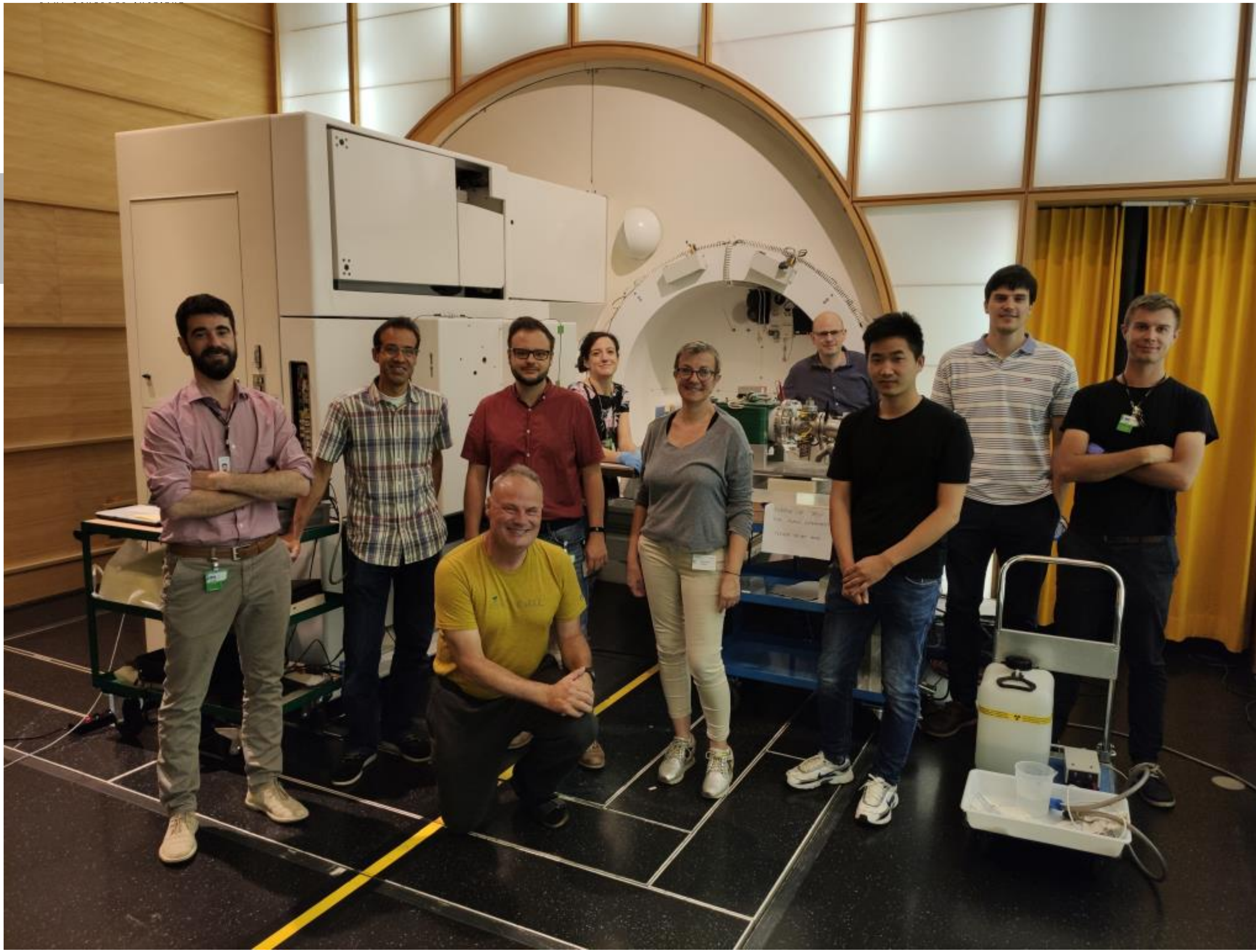

Proton FLASH irradiations of mice

- Effect seen in mice with electron beams:

Hypofractionated FLASH-RT as an Effective Treatment against Glioblastoma that Reduces Neurocognitive Side Effects in Mice

Pierre Montay-Gruel [#] [1], Munjal M Acharya [#] [2], Patrik Gonçalves Jorge [1] [3], Benoît Petit [1], Ioannis G Petridis [1], Philippe Fuchs [1], Ron Leavitt [1], Kristoffer Petersson [1] [3], Maude Gondré [1] [3], Jonathan Ollivier [1], Raphael Moeckli [3], François Bochud [3], Claude Bailat [3], Jean Bourhis [1], Jean-François Germond [3], Charles L Limoli [#] [2], Marie-Catherine Vozenin [#] [4]

Affiliations + expand

PMID: 33060122 PMCID: PMC7854480 DOI: 10.1158/1078-0432.CCR-20-0894

Free PMC article

Abstract

Purpose: Recent data have shown that single-fraction irradiation delivered to the whole brain in less than tenths of a second using FLASH radiotherapy (FLASH-RT), does not elicit neurocognitive deficits in mice. This observation has important clinical implications for the management of invasive and treatment-resistant brain tumors that involves relatively large irradiation volumes with high cytotoxic doses.

Proton FLASH irradiations of mice

- Experiments at PSI ongoing since November 2021