

# Protontherapy – Technology for the benefit of the patient

Martin Grossmann

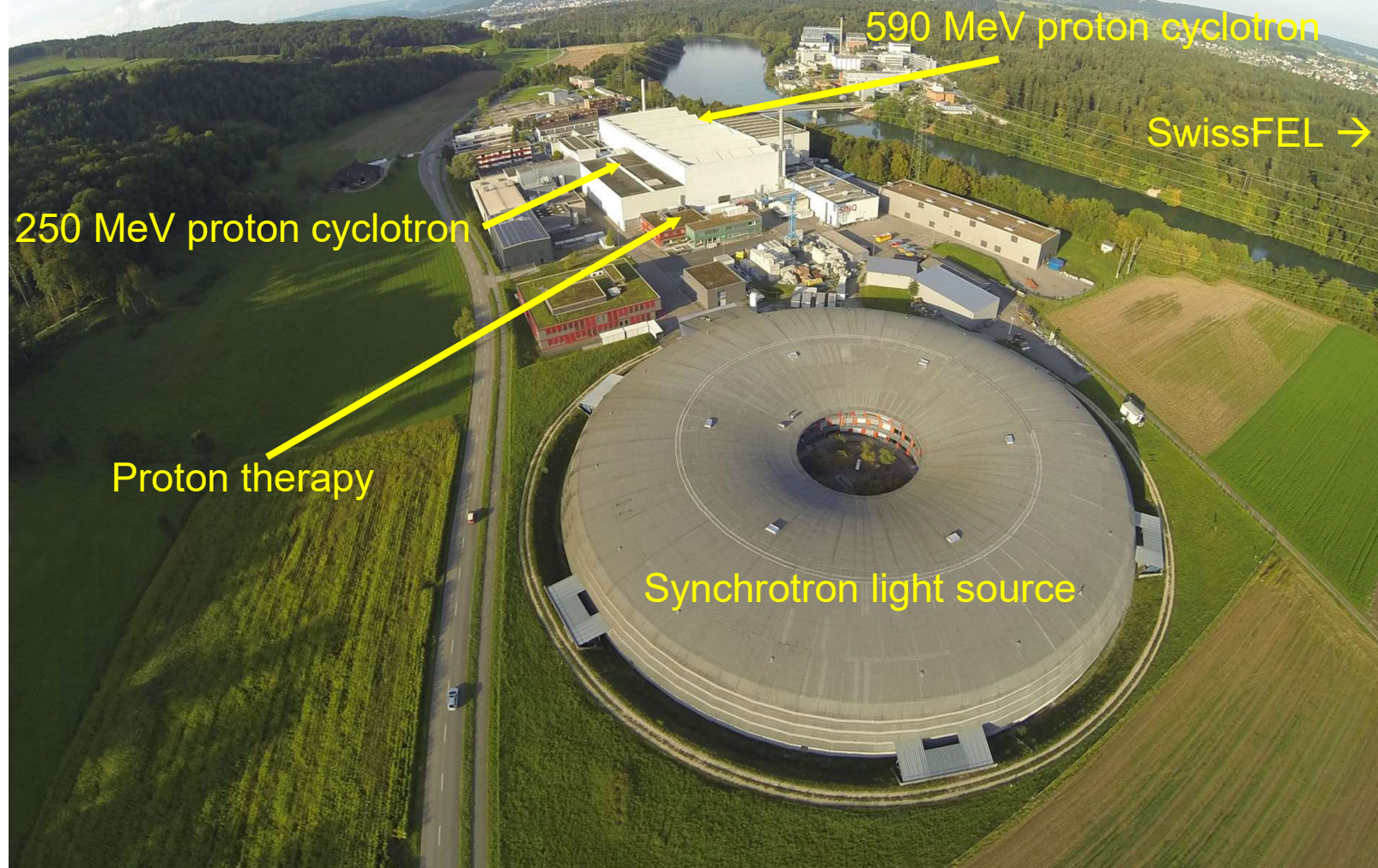
# Agenda



- 1 Why radiotherapy with protons?
- 2 Irradiation techniques
- 3 PSI's clinical program
- 4 FLASH with protons
- 5 Why technology is important



# Paul Scherrer Institute





## About myself...

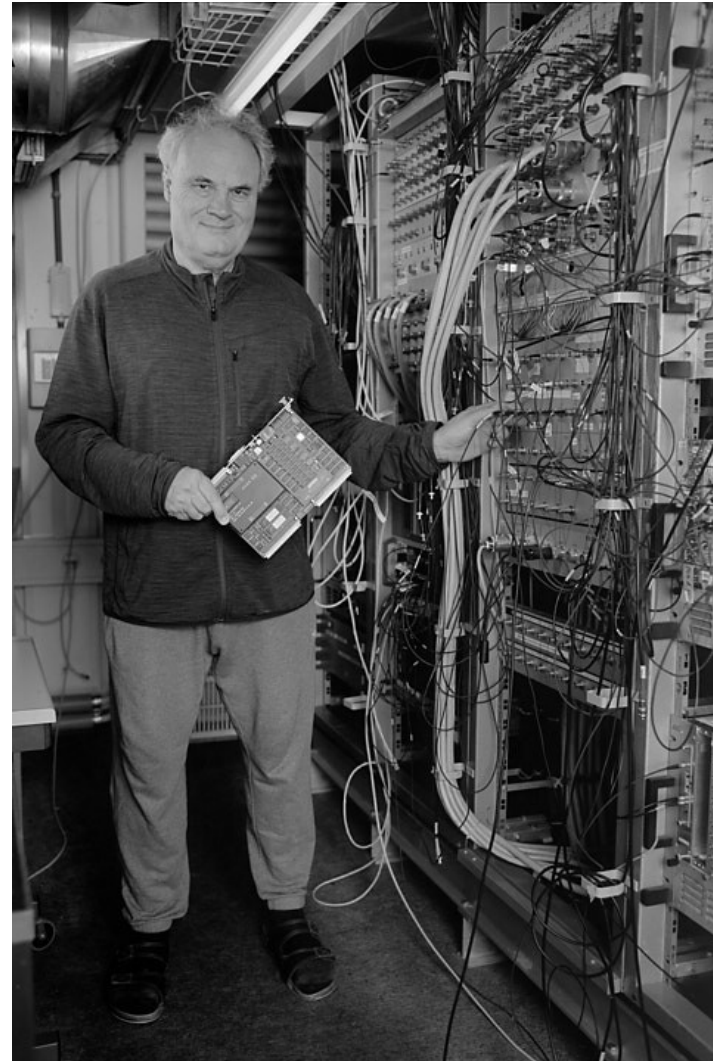
Study physics in Münster & Lausanne

Master thesis CERN

PhD thesis PSI

Protontherapy since 1995

Control and Safety Systems



# Why radiotherapy with protons?

# Why Radiotherapy with Protons?



## Conventional therapy (LINAC)



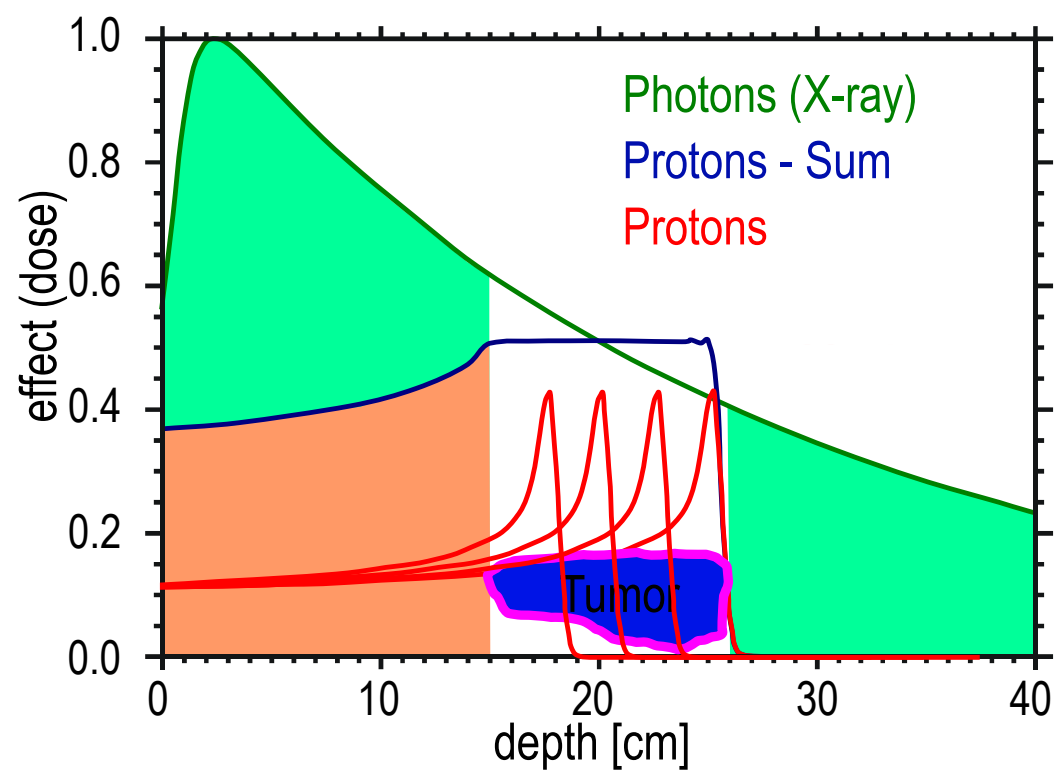
## Proton therapy

Mass: ~200 tons

Diameter: ~8 m



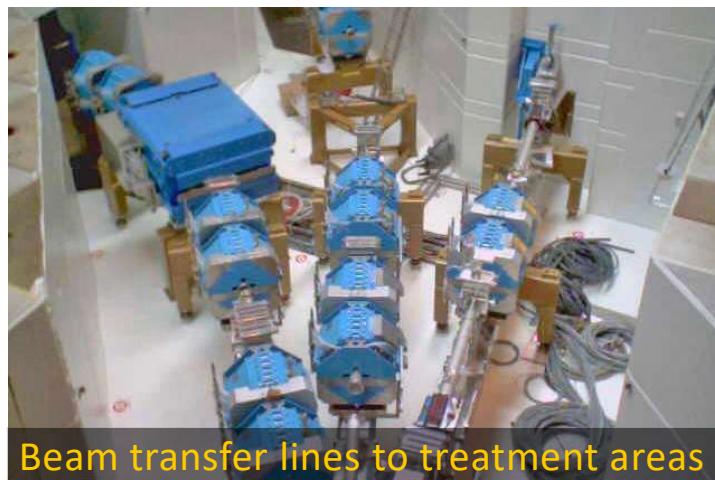
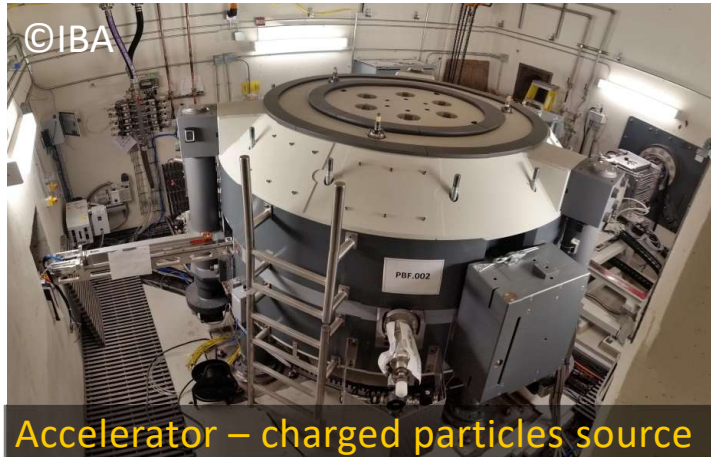
# Why Protons?



Dose burden - photons

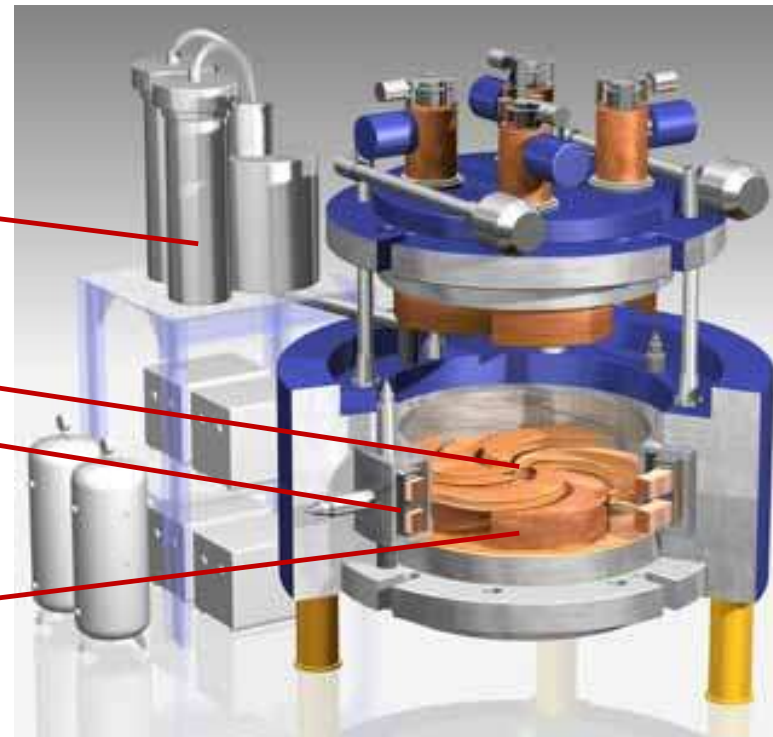
Dose burden - protons

# Main parts of a particle treatment facility



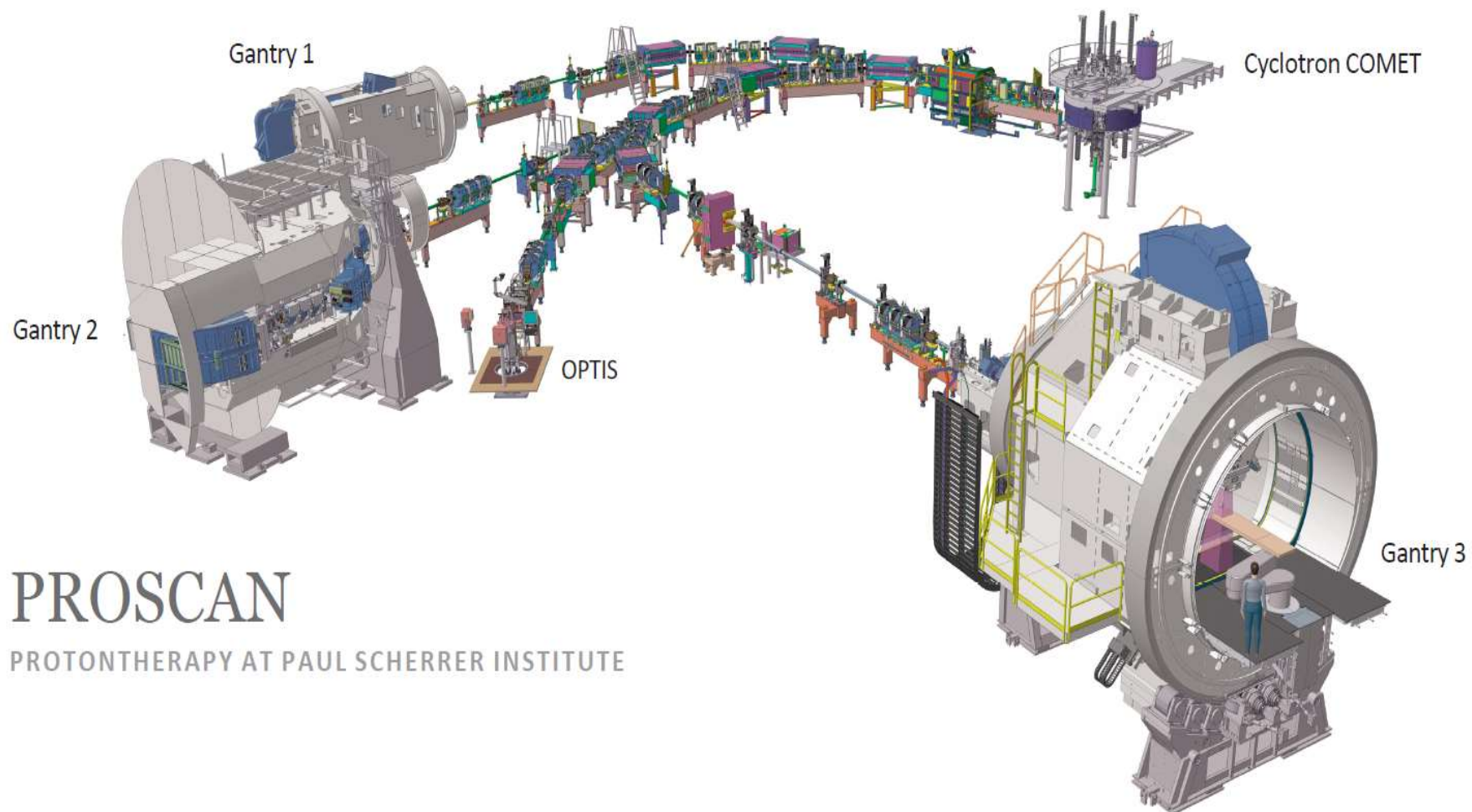
## Superconducting Cyclotron COMET (Accel/Varian)

- 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)



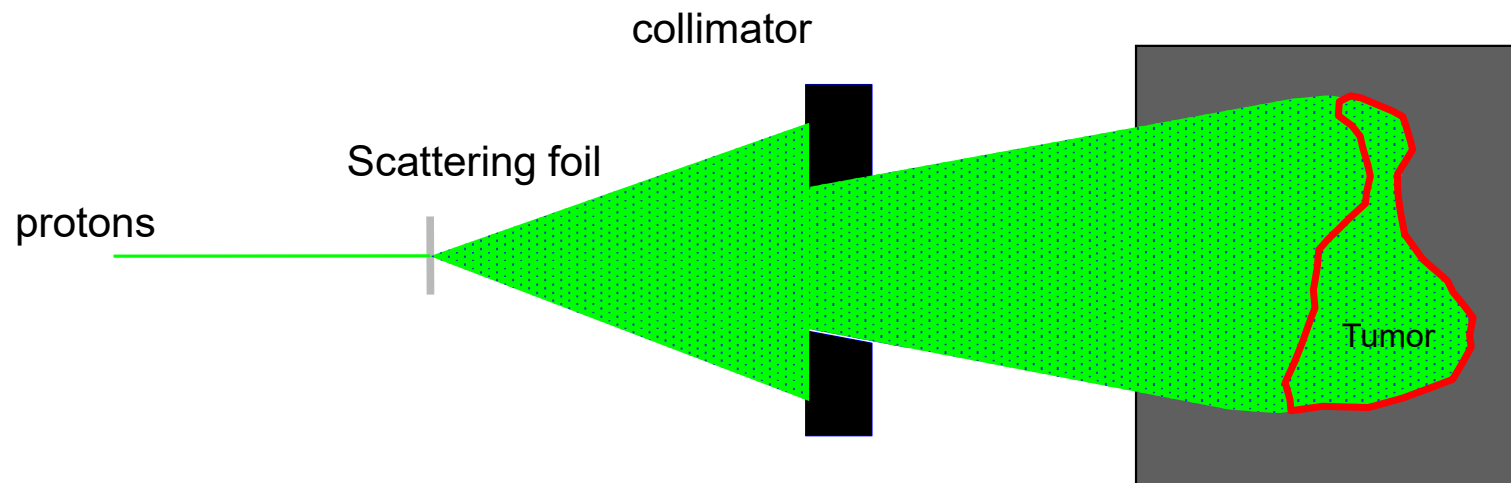


# PROSCAN

PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

# Irradiation Techniques

# Irradiation technique - classical



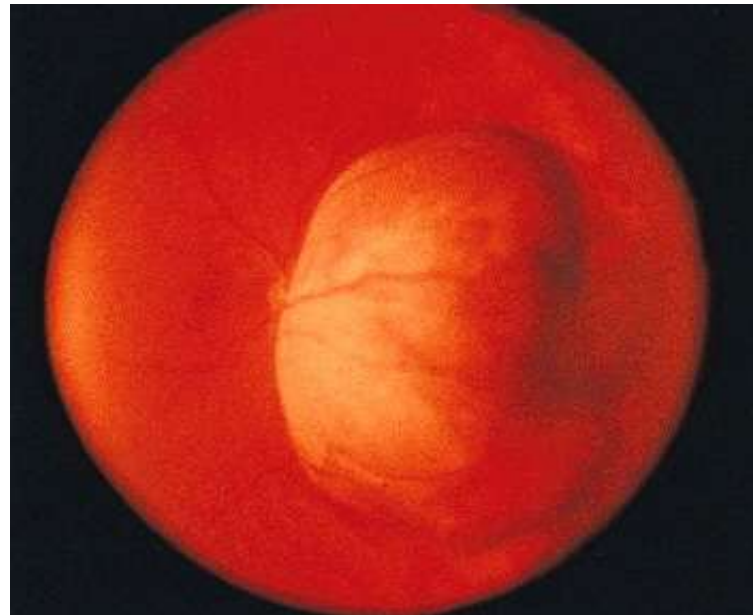
# Irradiation technique - classical



Treating Eye Melanoma

Collaboration with eye clinic in  
Lausanne

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



# Irradiation technique - classical



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

Date : 10.8.04 Opérateur : ZAGRODZKI  
Anesthésiste : B. L. 226  
AO ☒ ALS ☐ AL ☐ Durée de l'opération : 30'  
Diagnostic : Inflammation ☒ Hémangiome ☐ Mélanome ☐ DMLA ☐ Autre ☒ R. de l'op. ☒

OD ☒ OI ☐ Nasal ☒ Temporal ☐ Supérieur ☐ Inférieur ☒

Invasion cornéenne ☐ Invasion pupillaire ☐ Invasion vitréale ☐ Diamètre :  
Diamètre tumoral maximal :  
Ouverture conjonctive : du limbe ☒ autre ☐

Plan de traction : Droit Supérieur ☐ Droit Latéral ☒ Droit Inférieur ☒ Droit Externe ☐

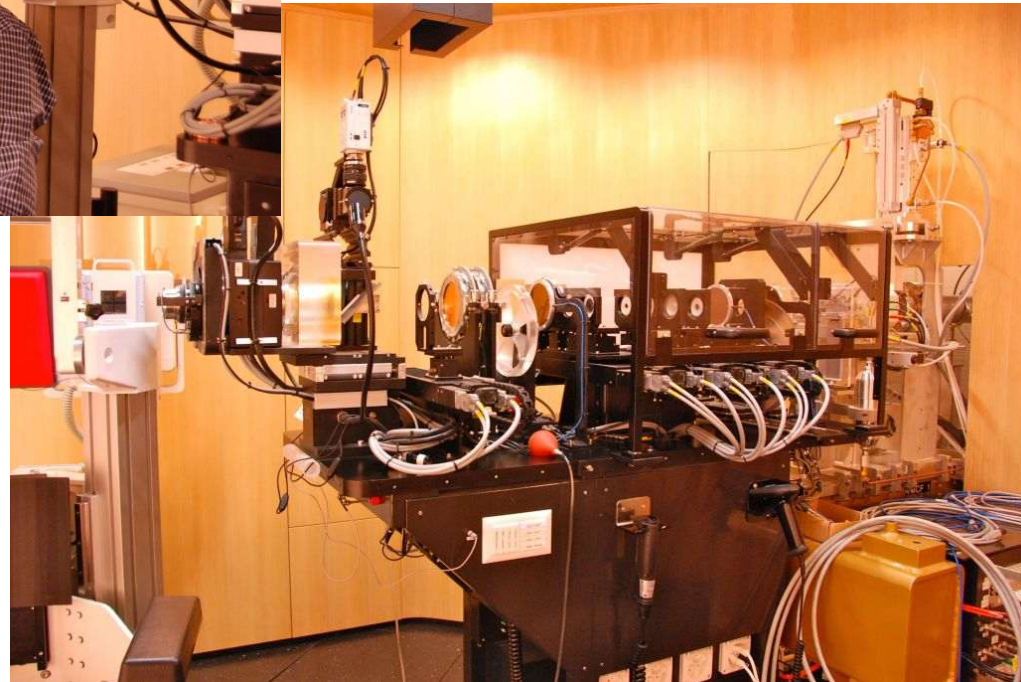
Enterré : ☒ non ☐ Diamètre : D=4.5 H=4  
Infiltration scléro-LA ☐ Diffuse ☐

| Distance Inversion | Distance Infiltration | Clips | Distance |
|--------------------|-----------------------|-------|----------|
|                    |                       | 1-3   | 16       |
|                    |                       | 2-4   | 13.5     |
|                    | 1.5                   |       |          |

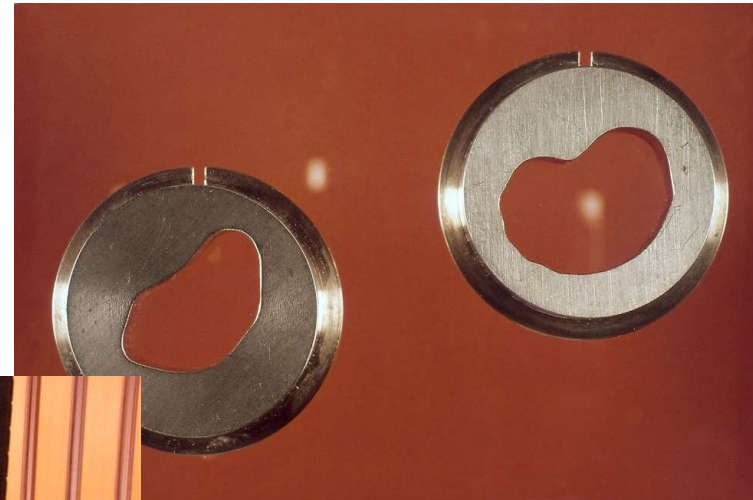
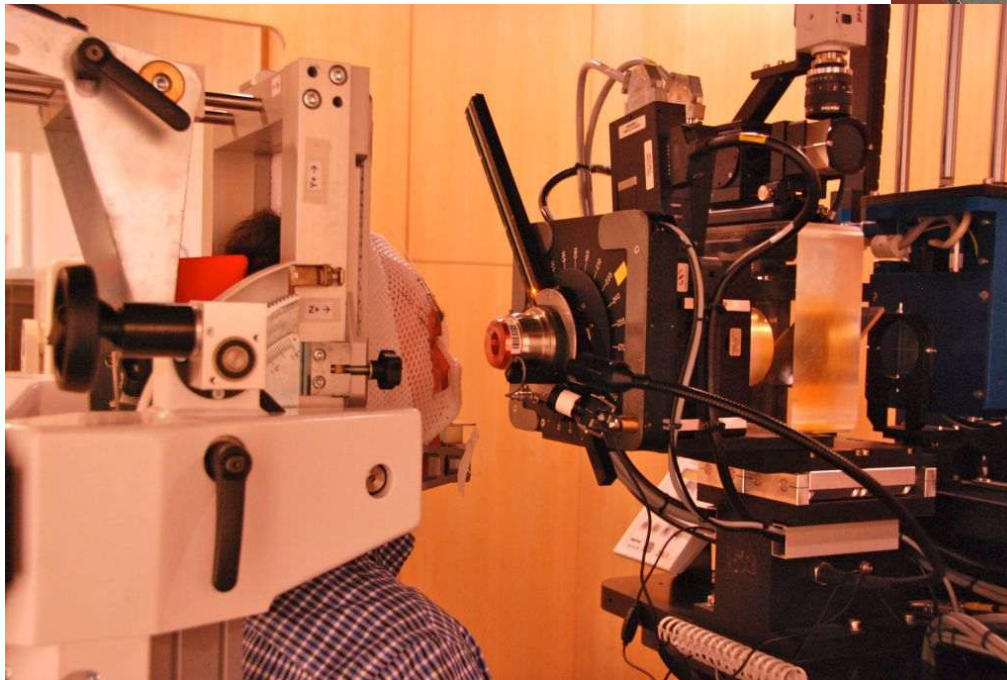
Tumeur en partie opérée ☐ Tumeur vasculaire ☐ Tumeur druse ☐  
☒ Ophtalmologique  
No ☐ URM ☐

Examen : A.S.  
Longueur article : 23.1  
Remarque :  
Signature : 10/15

## PSI's OPTIS program



OPTIS



PSI



## OPTIS – a success story

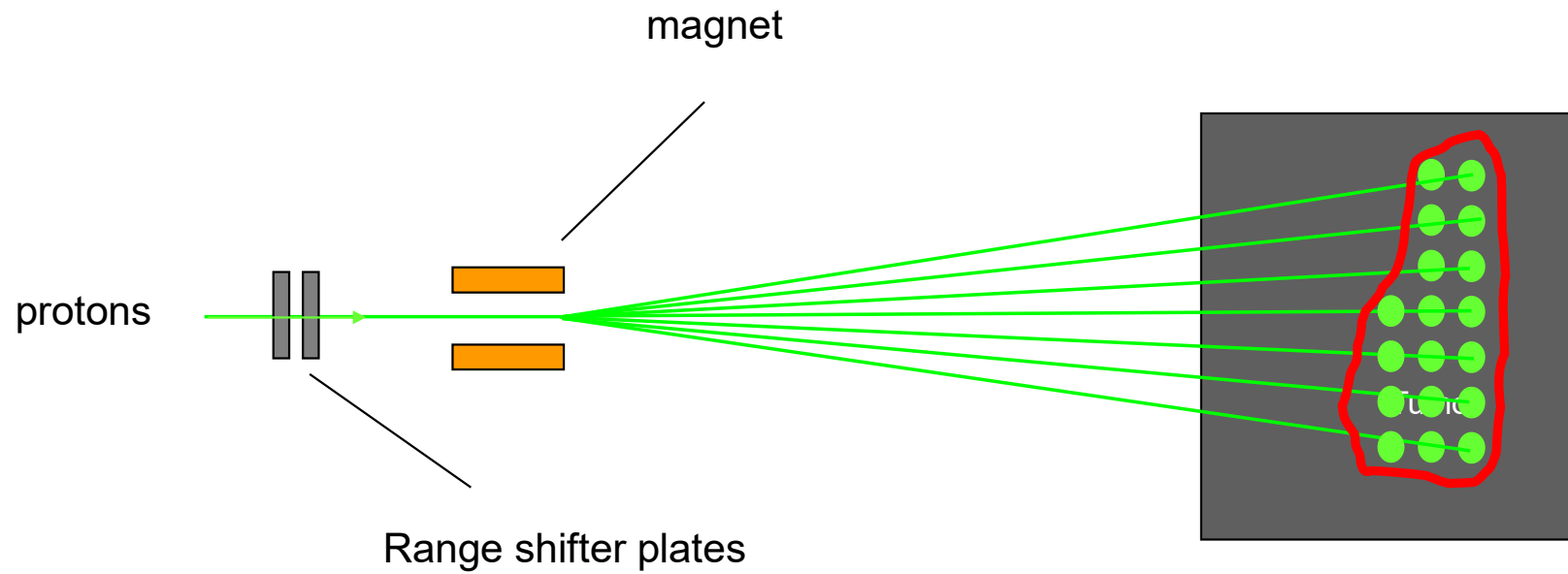


Since 1984:  
treated more than 10'000 patients  
98% cure  
(local tumor control)  
Conservation of vision  
100% for small tumors  
90% for big tumors

Protons  
are the  
standard!



# Irradiation technique – «pencil beam scanning» (PBS)



## Gantry 1: A compact system for PBS



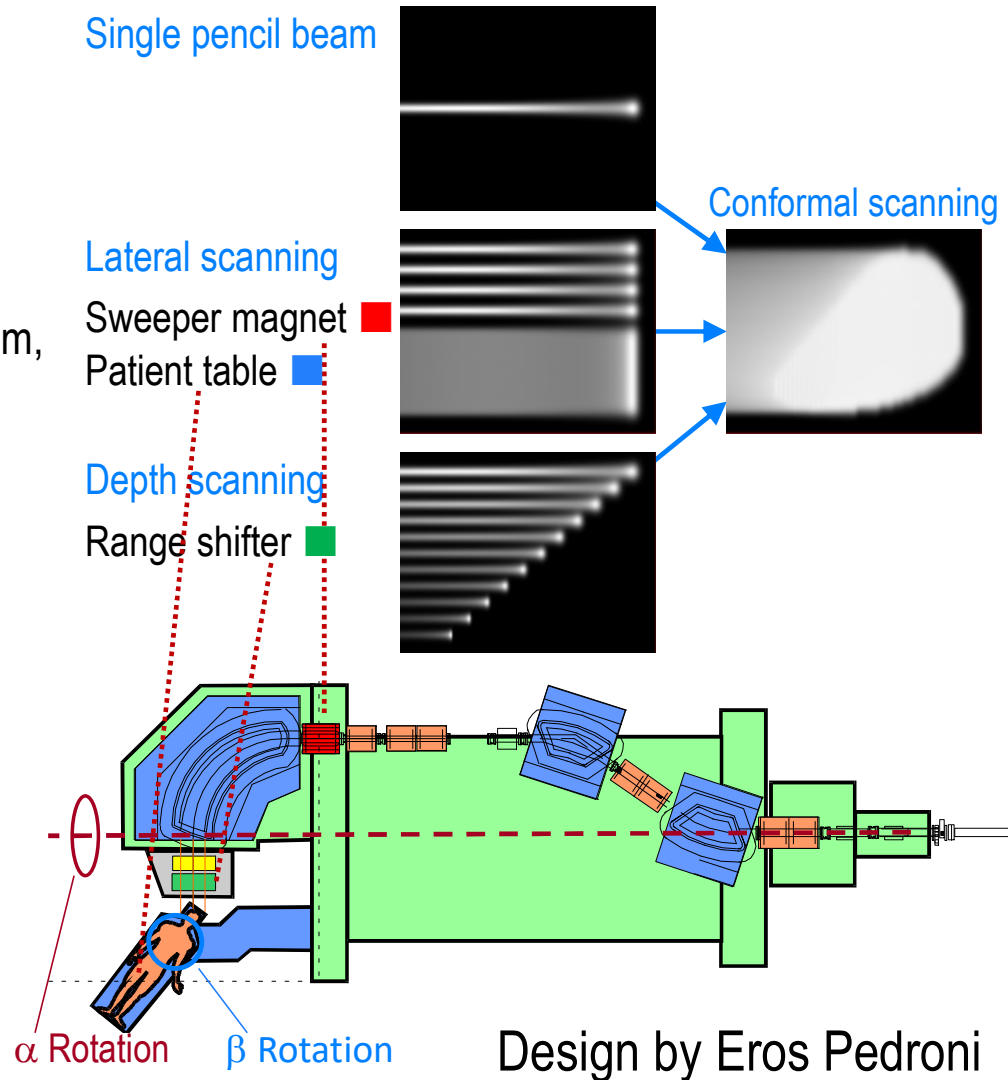
First implementation of PBS

Start patient operation 1996

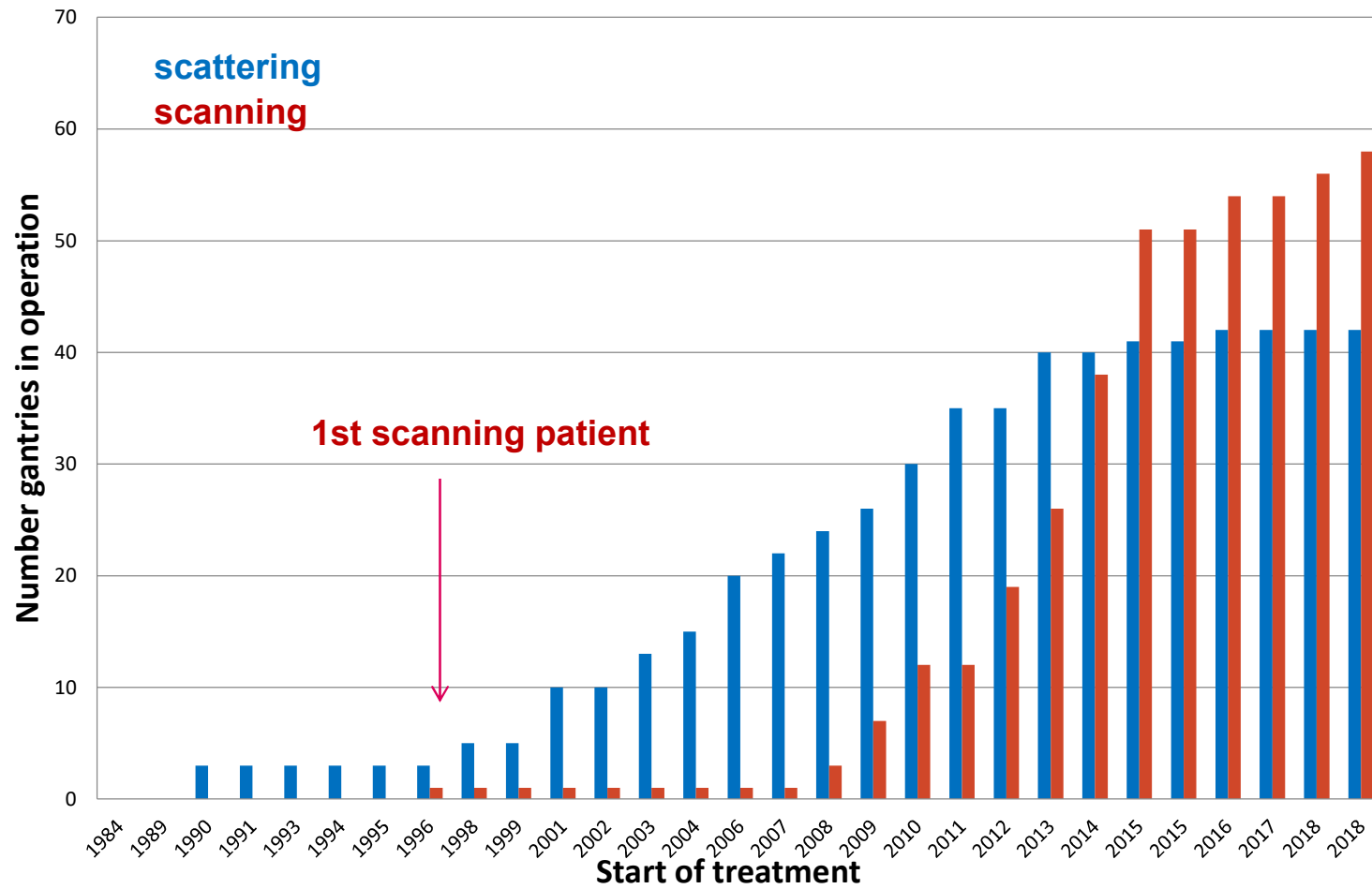
During 12 years the only PBS gantry worldwide

Due to eccentric design still the most compact system,

$r = 2\text{m}$



# 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

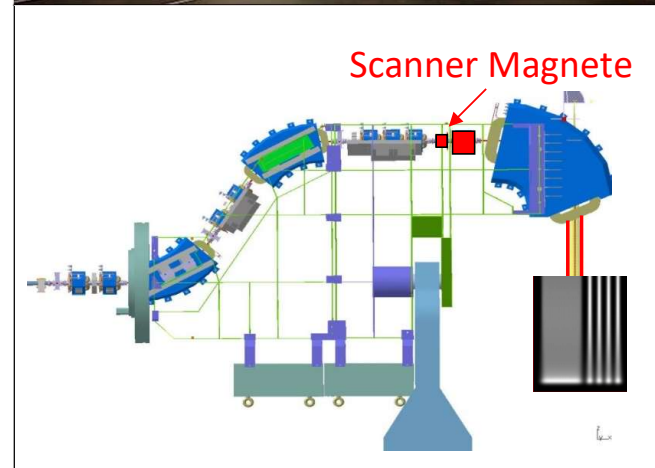
- Rotation limited to  $210^\circ$
- Patient table rotatable  $180^\circ$   
(→ still full flexibility)
- No pit

### Fast scanning in 2 dimensions

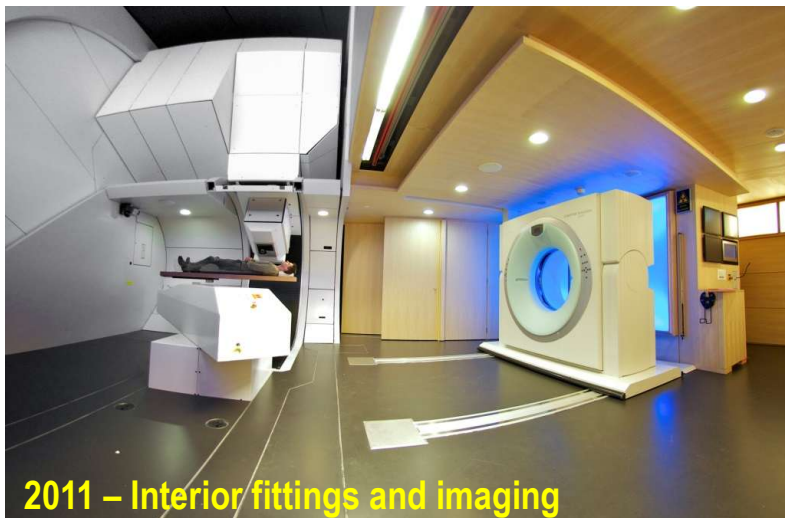
- Re-scanning possible
- Parallel Scanning
- Field size 12 x 20 cm

### Fast energy change → 3rd dimension

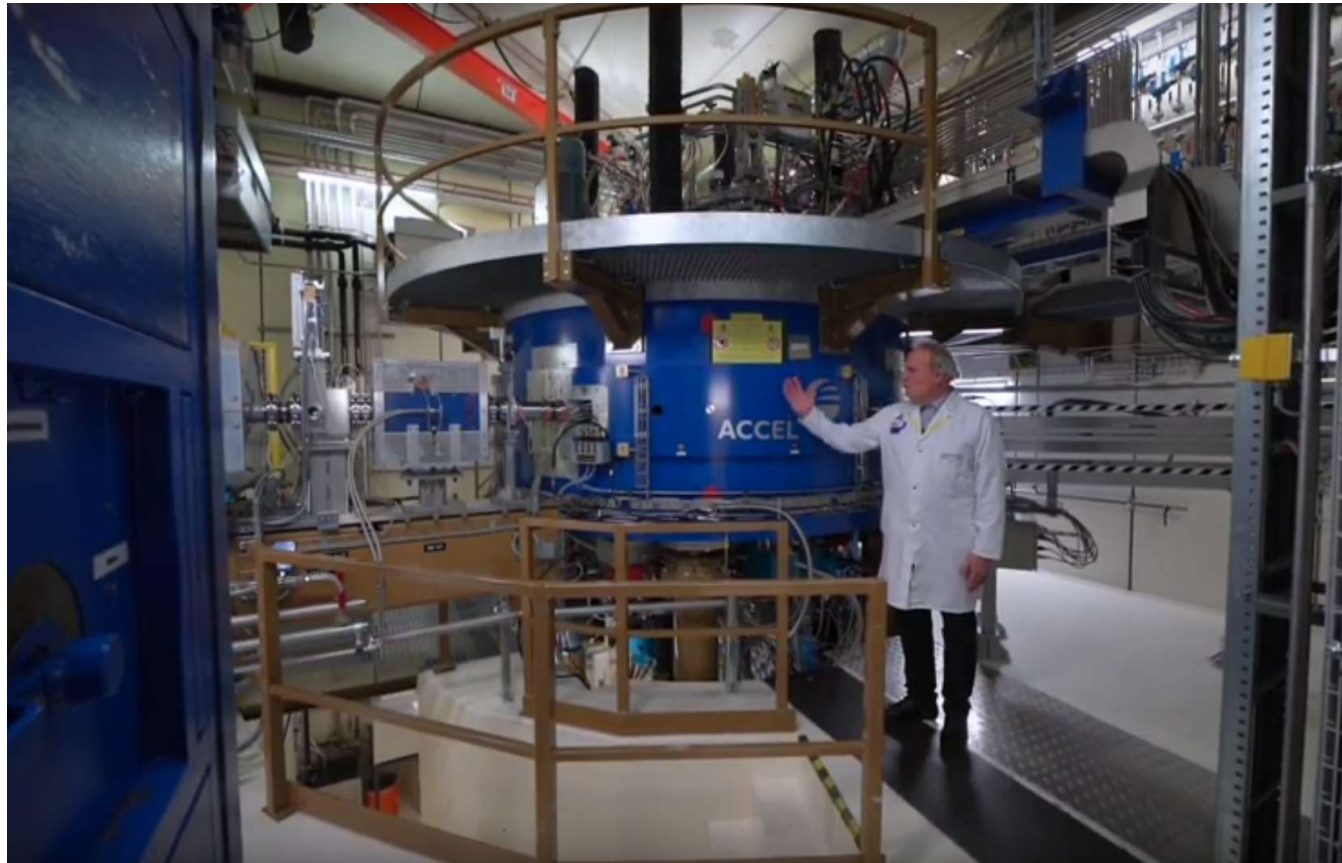
- Energy step < 100 ms
- Re-scanning possible in 3 dimensions



## Gantry 2: next generation spot scanning



## Video: Virtual Tour of PSI Protontherapy



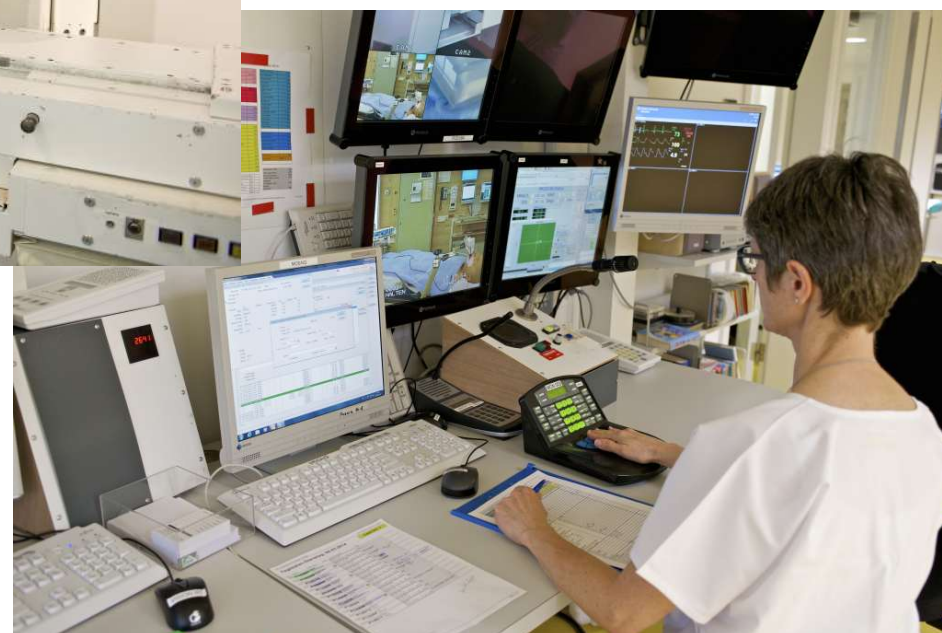
<https://youtu.be/sJOUdAd6QYk>

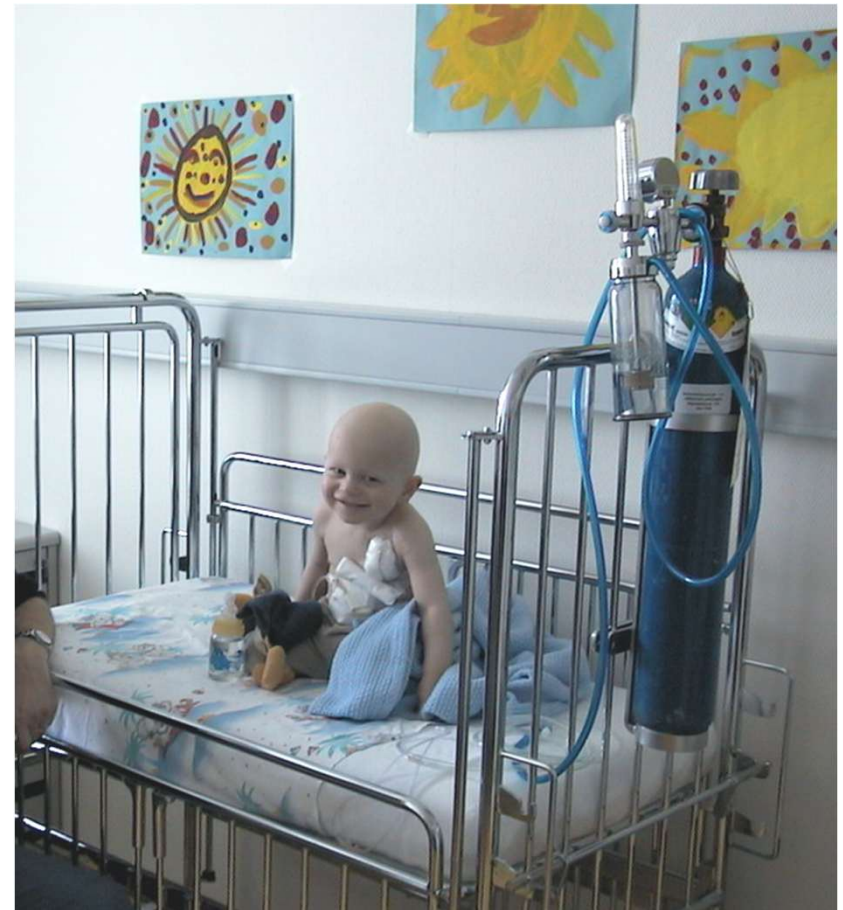
# PSI's clinical program

# Treating small children

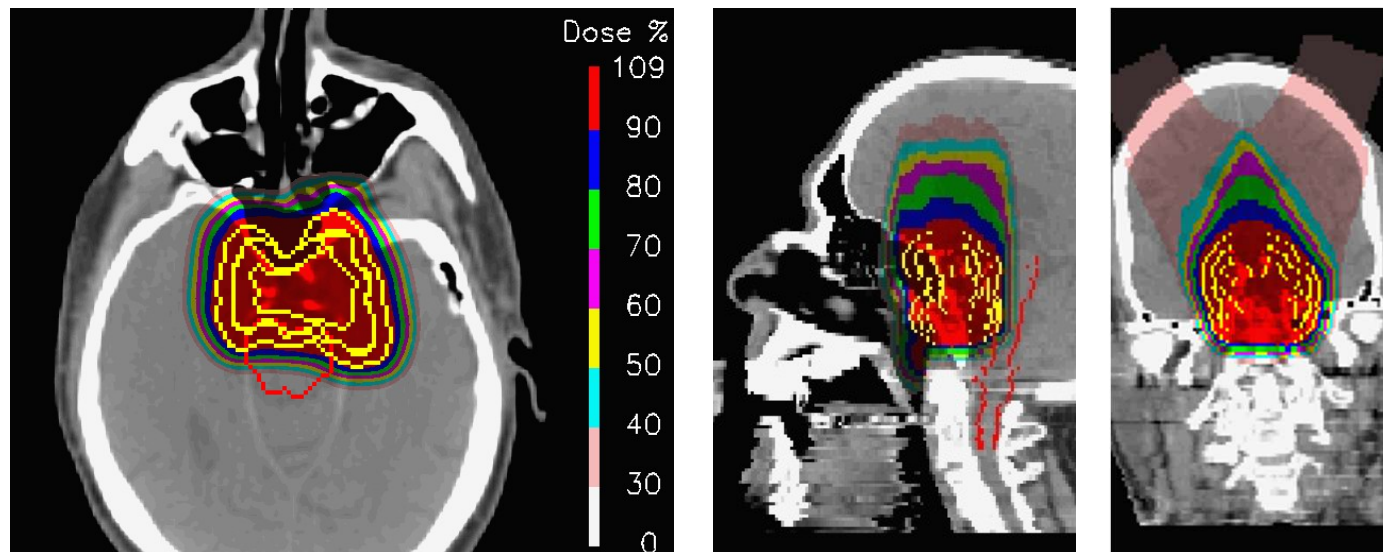
- Since 2004 treatments of small children  
→ **anesthesia team from children's hospital in Zurich**
- Ca. 1000 patients



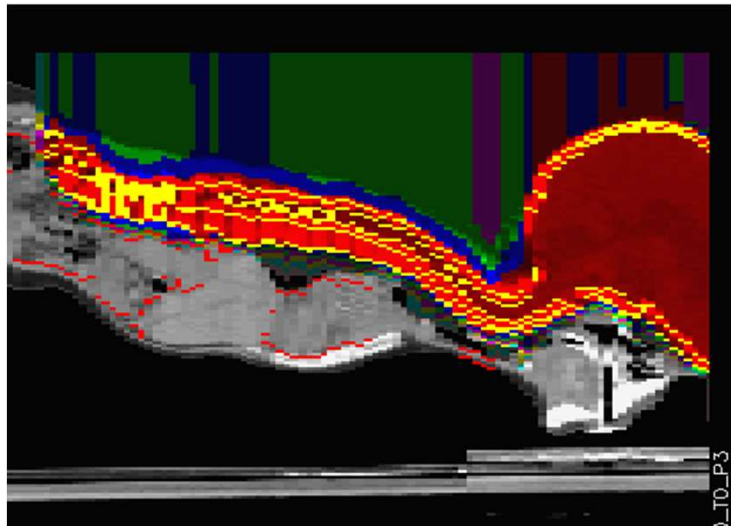




## Base of the skull Chordoma



# Medulloblastoma



## Patient treatments

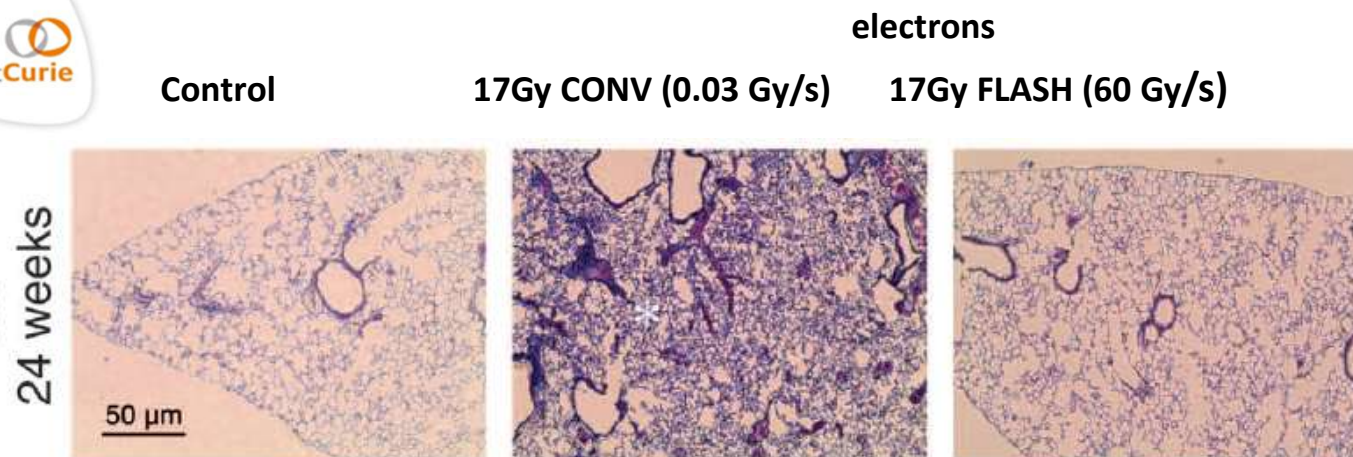


- Per year 400-500 patients
- 80% Switzerland
  - We do accept patients from abroad!
- Eye treatments 8'000 EUR, Gantry treatments 50'000 EUR
- Types of cancer treated at PSI:
  - Meningioma
  - Low-grade glioma
  - Head & Neck tumors
  - Sarcoma
  - Chondrosarcoma and chordoma
  - ALL pediatric tumors
- Covered by basic health insurance
  - Switzerland and EU
- Prostate is a good indication for protons
  - But we don't treat for economic reasons

# FLASH with protons

# 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



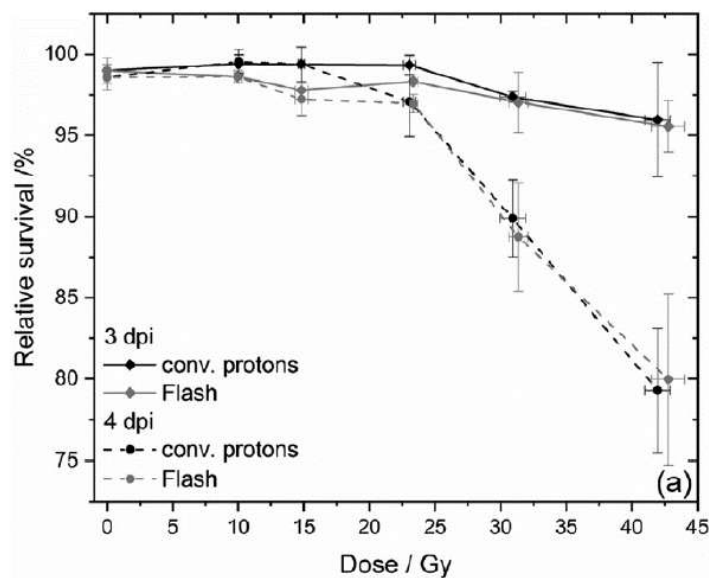
V. Favaudon et al., “Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumour tissue in mice”, *Science Translational Medicine* 6, 2014

# FLASH protontherapy

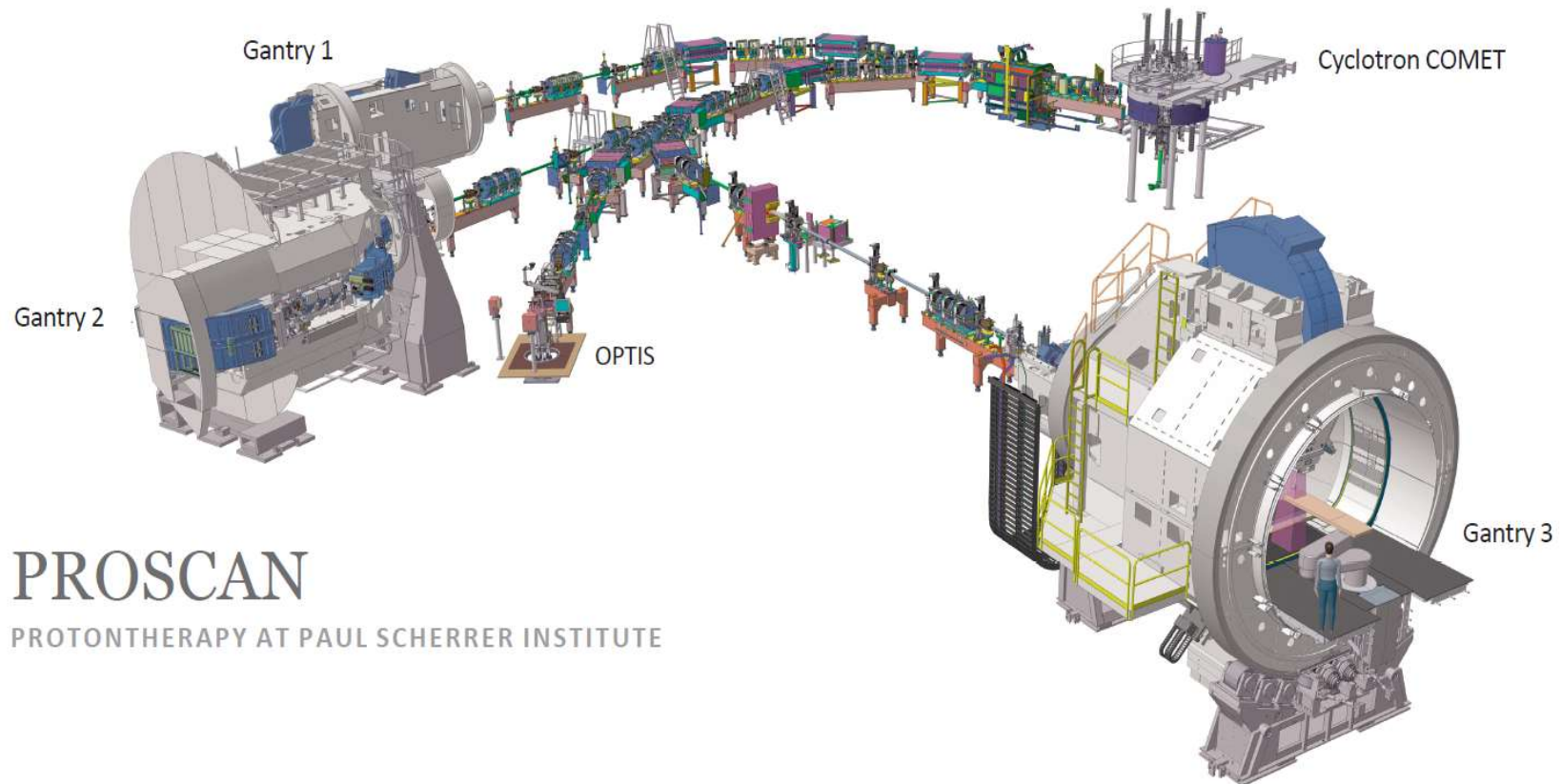
- Most (important) protontherapy vendors have demonstrated they can reach FLASH dose rates
  - IBA: Groningen, Dresden
  - Varian: Cincinatti
- Biological experiment performed in Dresden
  - Published October 2019
  - No FLASH effect observed ☹️



→ More experiments required!



# Beamline Transmission



PROSCAN

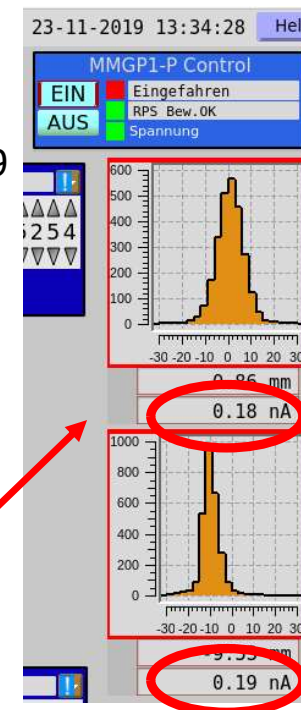
PROTONTHERAPY AT PAUL SCHERRER INSTITUTE

# 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 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

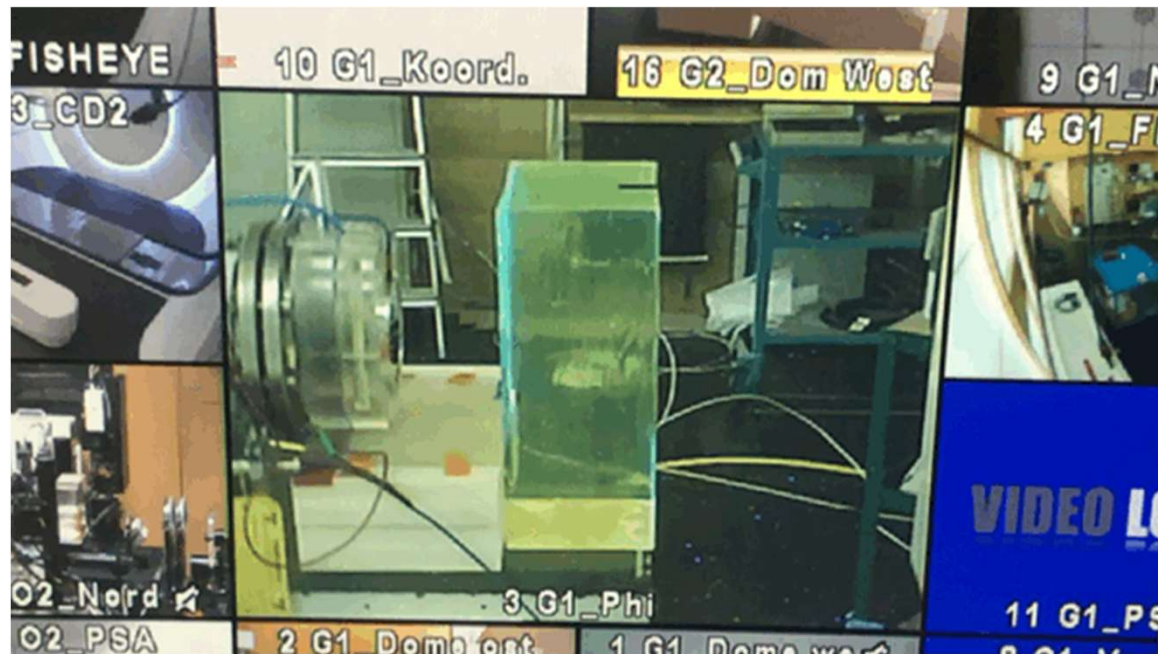


# Flash @ Gantry 1



Demo experiment January 2020

→ reach dose rates up to 9'000 Gy/s



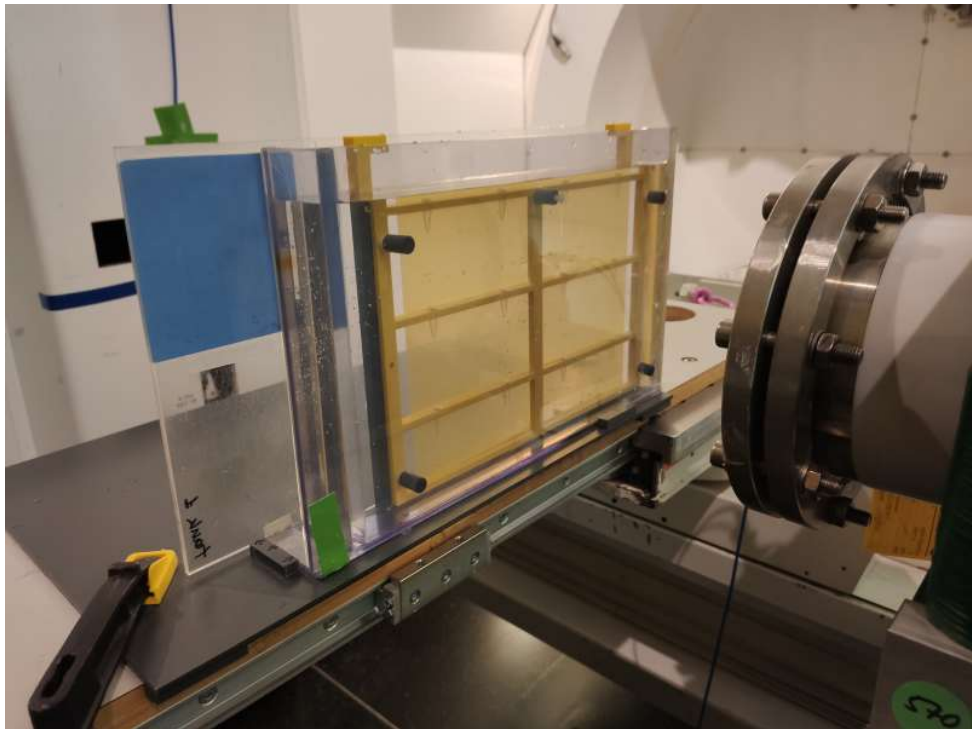
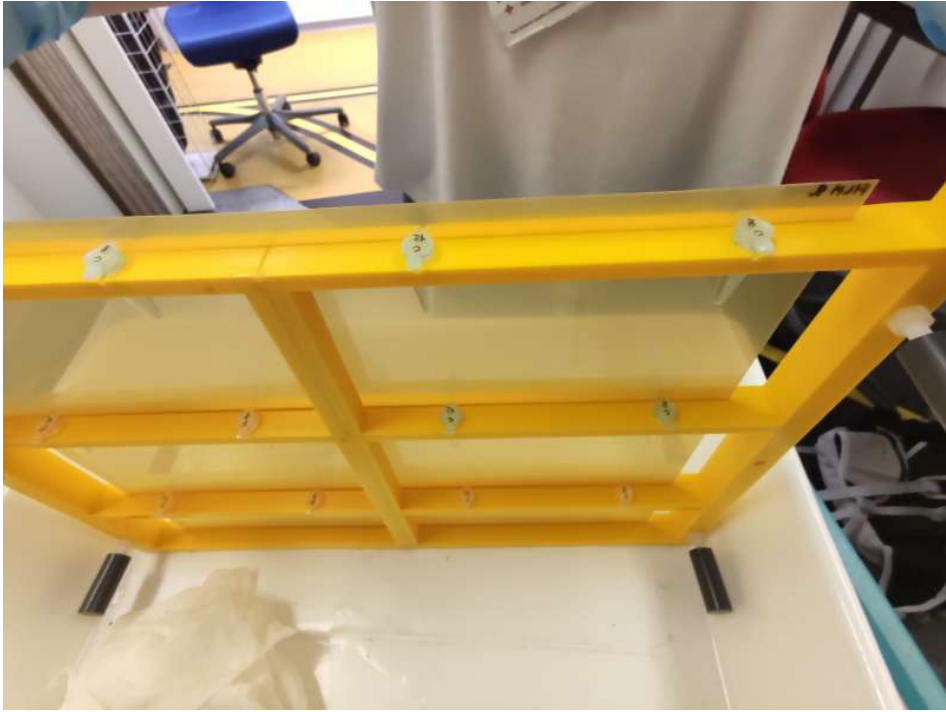
Nesteruk et al., Medical Physics 2021

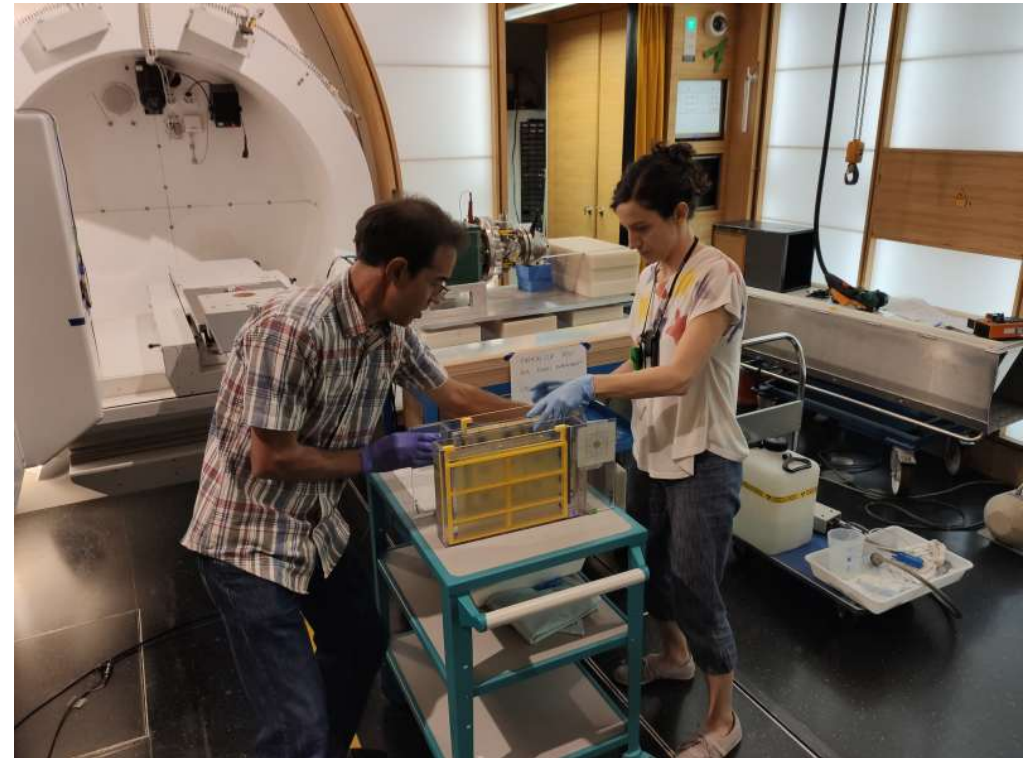
<https://doi.org/10.1002/mp.14933>

Togno et al., Physica Medica 2022

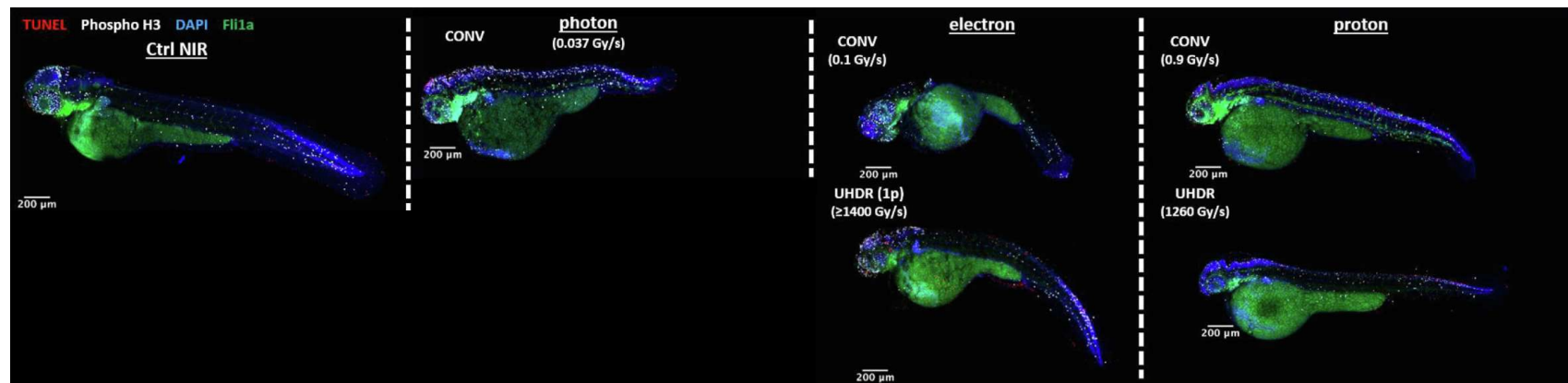
<https://doi.org/10.1016/j.ejmp.2022.10.019>







# Results



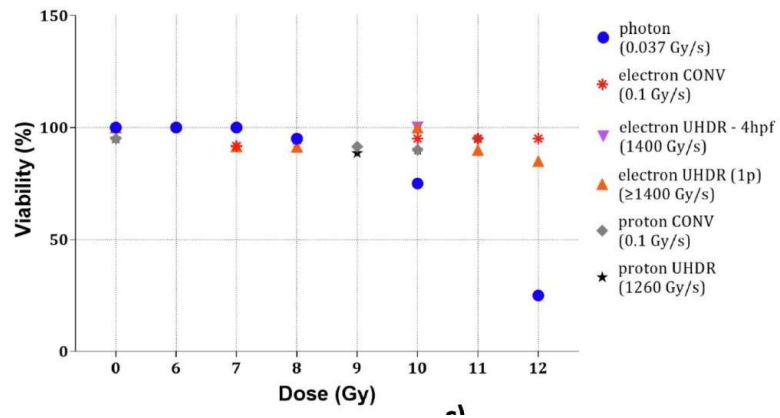
Dose rate effect for electrons, but not so much for protons

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

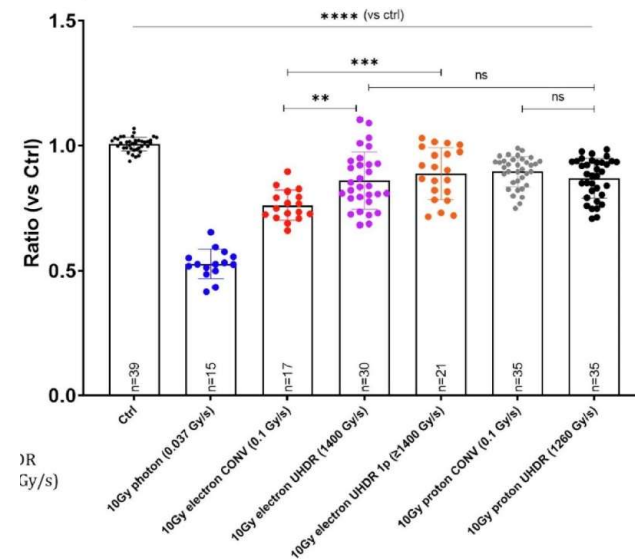
# Zebrafish embryos: Morphological analysis



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>

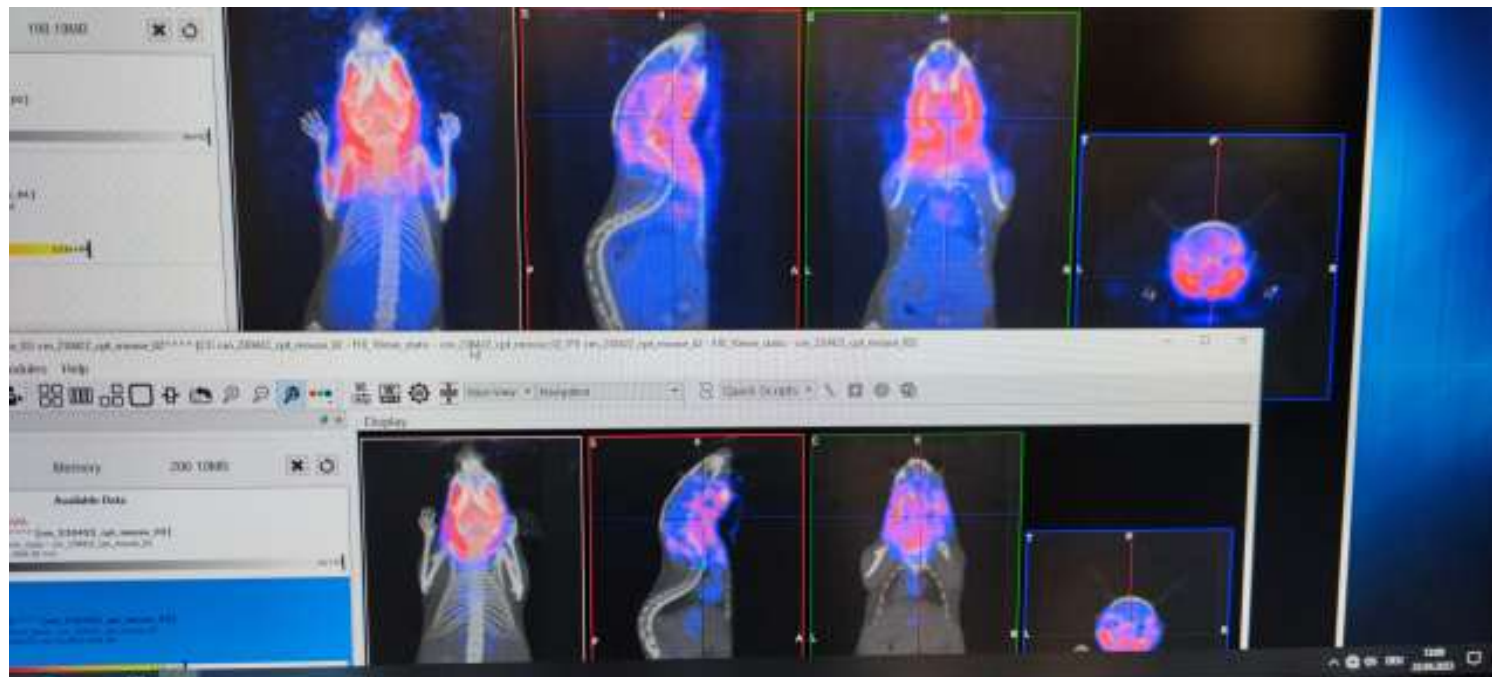
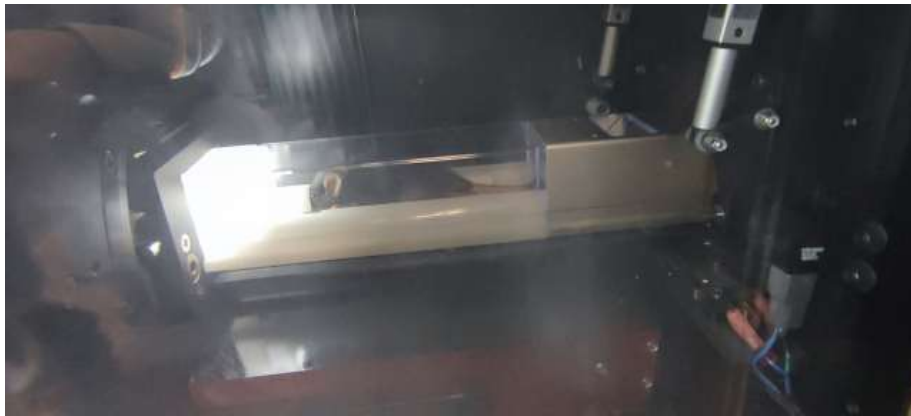
# Proton FLASH irradiations of mice

- Experiments at PSI ongoing since 2021



# Proton FLASH irradiations of mice





## Clinical Trial: Cats



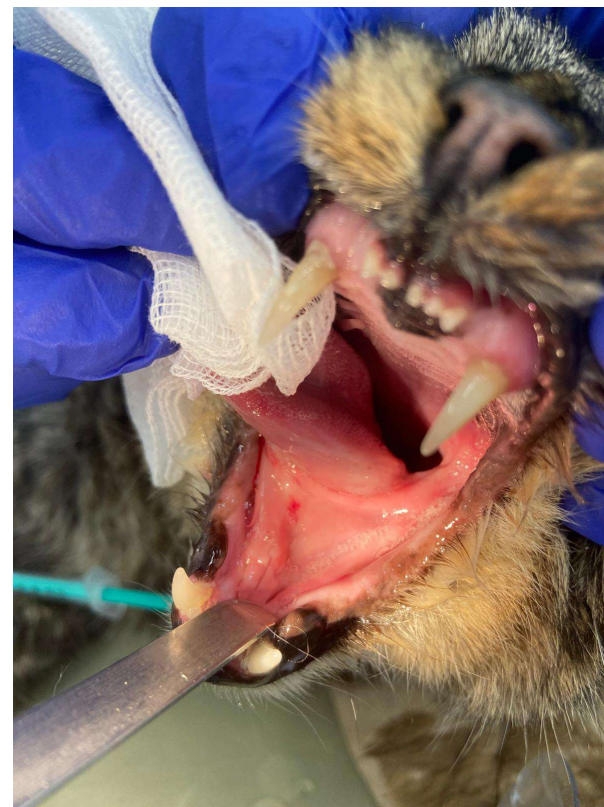








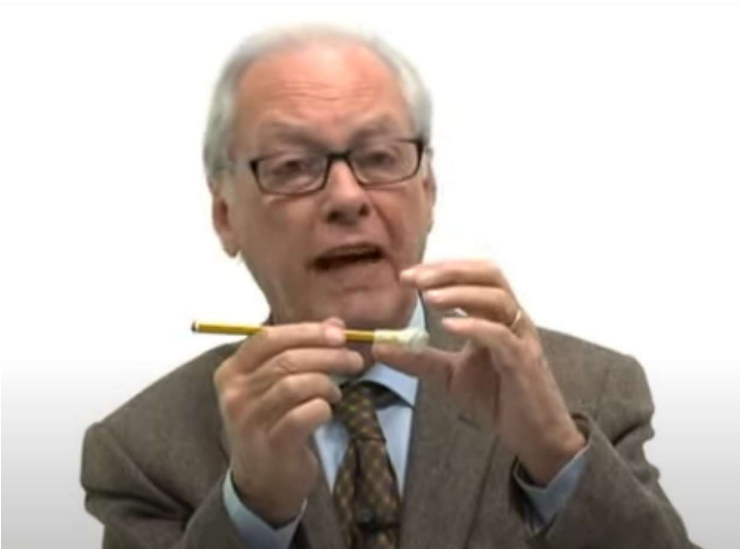
**03.06.2024**



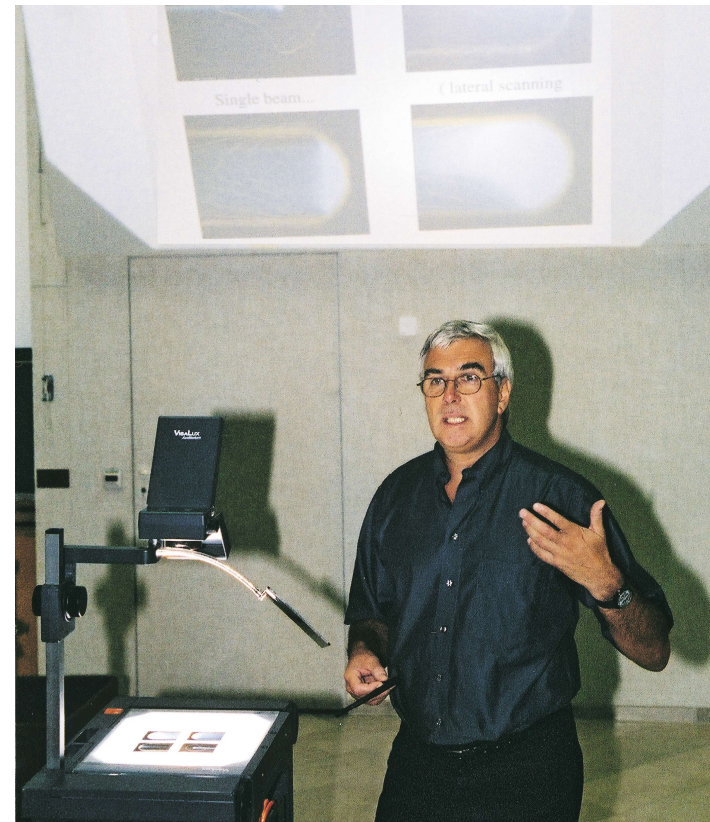
**12.06.2024**

# Why technology is important

## A new idea: pencil beam scanning



Ugo Amaldi CERN



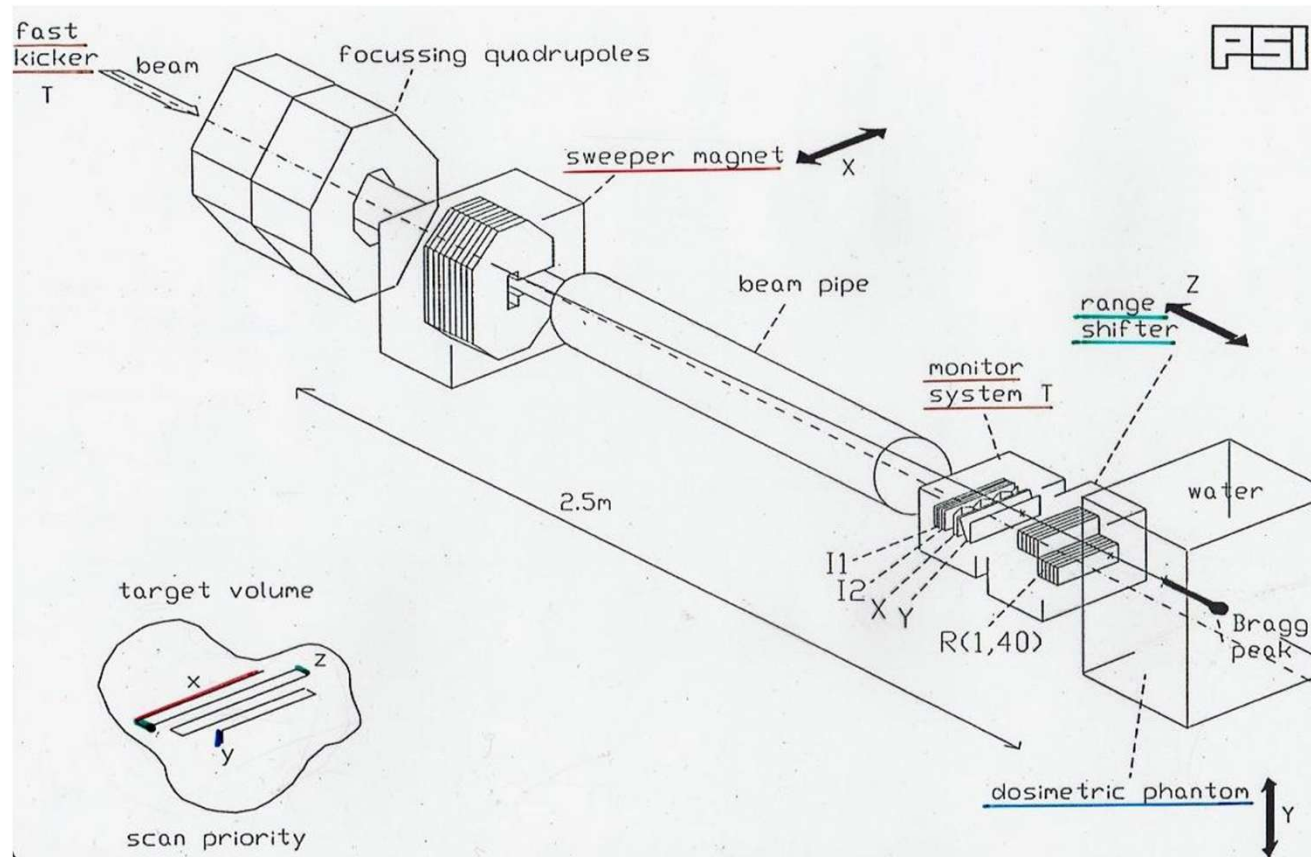
Eros Pedroni PSI

# From the idea to the implementation



- Pencil beam scanning requires:
  - Fast magnets
  - Fast position-sensitive detectors
  - Fast electronics
  - Fast control systems
  - Medical Imaging (CT, MRI)
  - Fast computers (preparation of therapy plans)
- All these technologies became available in the 1970s/1980s
- Proton therapy is *applied particle physics!*

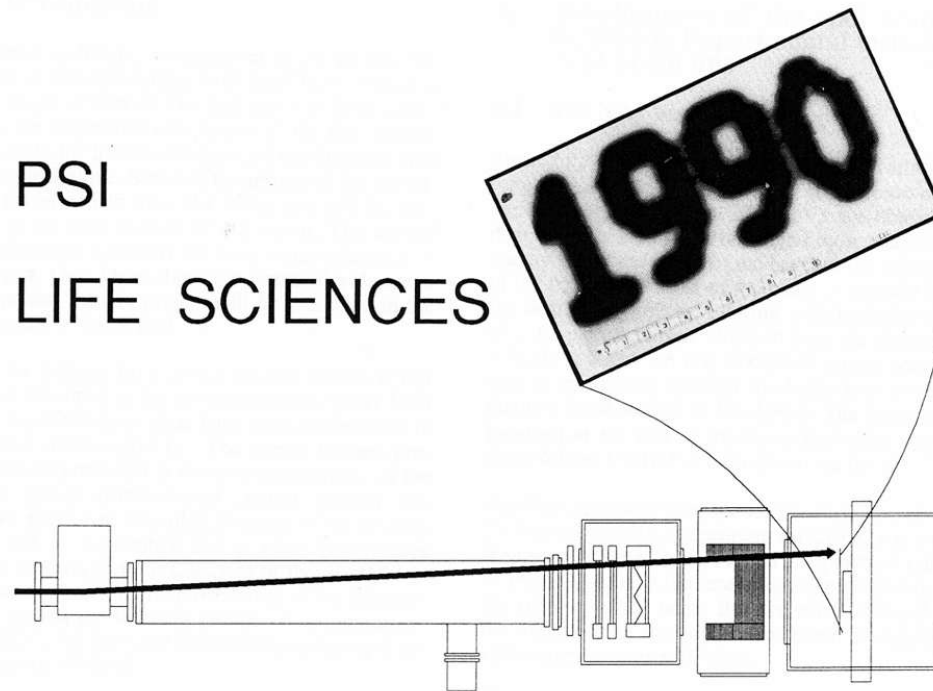
# Demonstration experiment at PSI 1989



It worked!

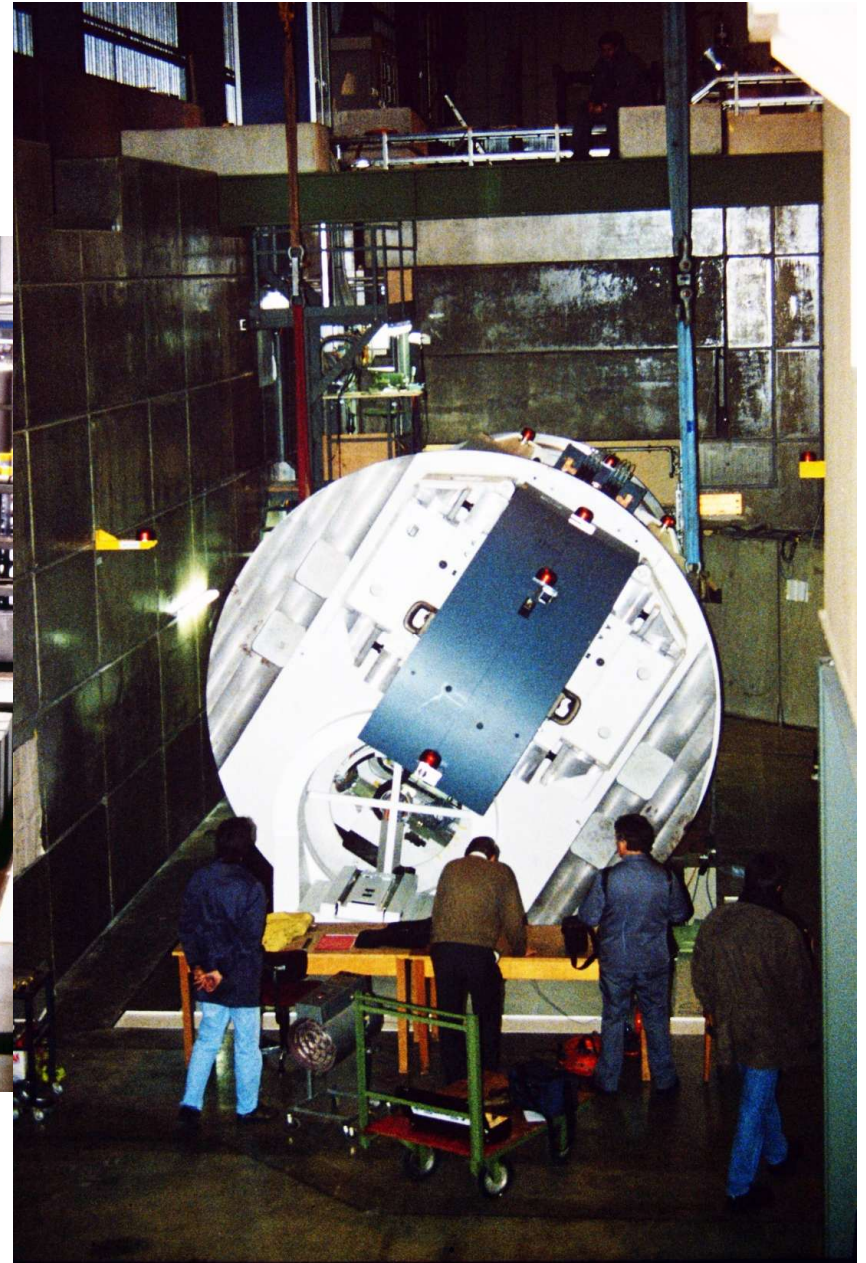


PSI  
LIFE SCIENCES



NEWSLETTER 1989 / 90

1994



# «Machine Ready» Signal



Pencil beam scanning proceeds spot by spot

Between spots individual «devices» are modified:

- configuration of dose monitor units
- Setting of scanning magnets
- Energy setting
- Patient table motion

→ «Ready» Signal ok when all devices reached nominal value

New signals can easily be added

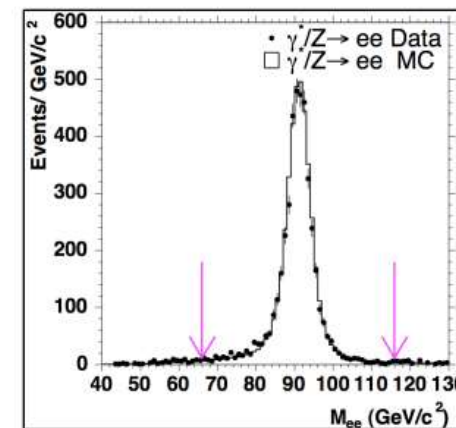
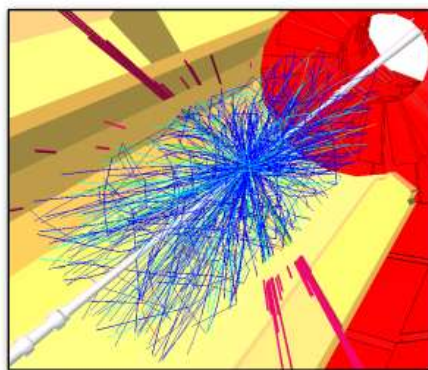
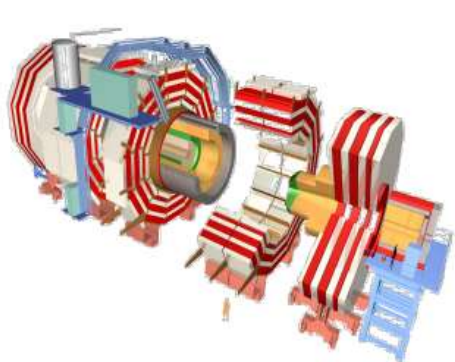
- Gating for organ motion: automatically pause therapy when patient is breathing



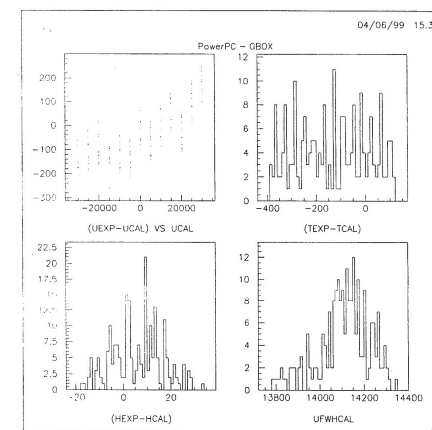
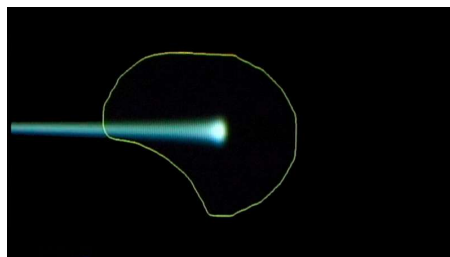
# Optimizing a pencil beam scanning system using tools from high energy physics



HEP: Detector → Single event → Analysis of many events



Pencil beam scanning: Gantry → Single spot → Analysis of many spots



→ Write logfiles with per-spot-data

# CERN: HBOOK → PAW → ROOT



CERN Program Library Long Writup Q121

## PAW

Physics Analysis Workstation

The Complete Reference

Version 1.14 (July 1992)

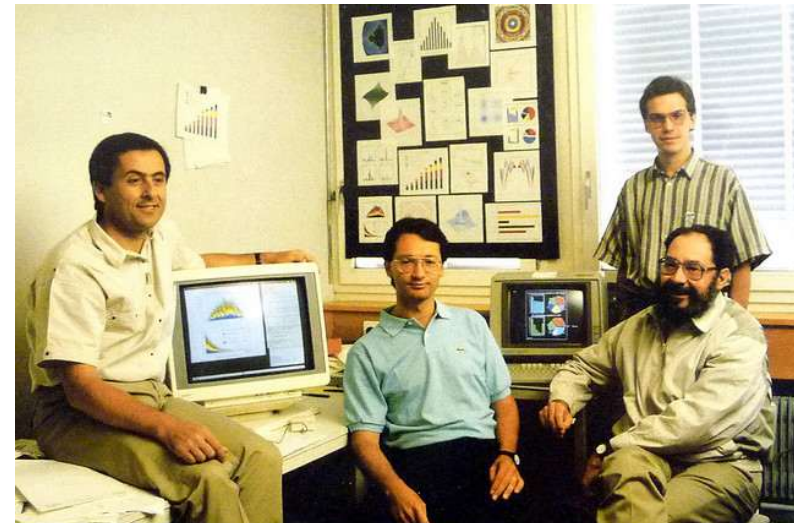
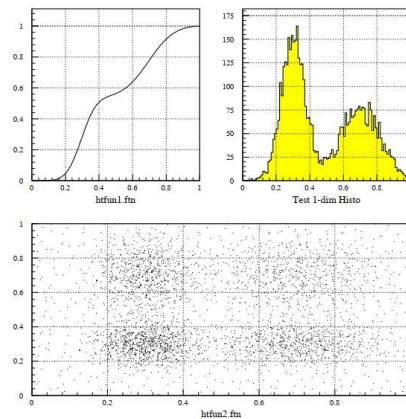
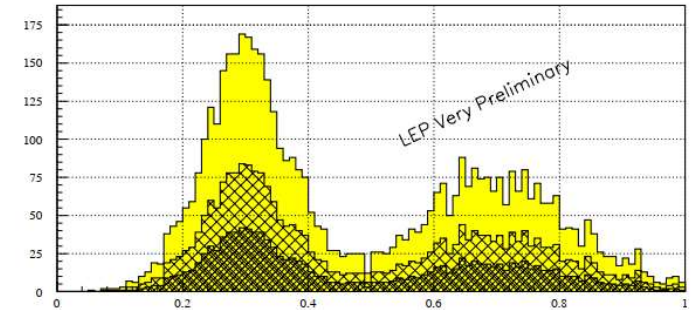
Application Software Group

Computing and Networks Division

CERN Geneva, Switzerland

```
PAW > NT/SCAN 10 nation=NATFR.and.division=DIVEP ! ! 5 age service children grade step
```

```
*****
* ENTRY * AGE * SERVICE * CHILDREN * GRADE * STEP *
*****
! 48 ! 56.000 ! 34.000 ! 0.00000 ! 7.0000 ! 8.0000 !
! 194 ! 62.000 ! 27.000 ! 0.00000 ! 7.0000 ! 13.000 !
! 213 ! 56.000 ! 26.000 ! 0.00000 ! 6.0000 ! 13.000 !
! 214 ! 45.000 ! 26.000 ! 0.00000 ! 6.0000 ! 12.000 !
! 216 ! 56.000 ! 19.000 ! 0.00000 ! 5.0000 ! 13.000 !
! 266 ! 63.000 ! 26.000 ! 0.00000 ! 13.000 ! 10.000 !
! 267 ! 59.000 ! 32.000 ! 0.00000 ! 13.000 ! 10.000 !
! 273 ! 55.000 ! 26.000 ! 1.0000 ! 12.000 ! 13.000 !
! 275 ! 53.000 ! 26.000 ! 1.0000 ! 11.000 ! 13.000 !
! 279 ! 51.000 ! 30.000 ! 0.00000 ! 6.0000 ! 13.000 !
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! 316 ! 54.000 ! 26.000 ! 0.00000 ! 6.0000 ! 13.000 !
*****
```



<https://ep-news.web.cern.ch/content/interview-rene-brun>

# Logging information per spot



\*\*\*\*\*

contents of output buffer:

| index | contents                              |
|-------|---------------------------------------|
| 0     | spotnumber                            |
| 1     | Preset Monitor 2                      |
| 2     | delay_to_add for Preset Monitor 2     |
| 3     | Monitor1 single gated                 |
| 4     | Monitor2 single ungated               |
| 5     | dose measured by U strip chambers     |
| 6     | dose measured by T strip chambers     |
| 7     | U center nominal                      |
| 8     | U center actual                       |
| 9     | T center nominal (should always be 0) |
| 10    | T center actual                       |
| 11    | U FWHM nominal                        |
| 12    | U FWHM actual                         |
| 13    | T FWHM nominal                        |
| 14    | T FWHM actual                         |
| 15    | sweeper hall probe nominal            |
| 16    | sweeper hall probe actual             |

contents of output buffer:

| index   | contents                                  |
|---------|-------------------------------------------|
| 17      | gantry position X                         |
| 18      | gantry position Y                         |
| 19      | gantry position Z                         |
| 20      | actual range shifter plate settings plate |
| 01...24 |                                           |
| 21      | actual range shifter plate settings plate |
| 25...40 |                                           |
| 22      | 10 kHz clock ungated single               |
| 23      | 10 kHz clock gated single                 |
| 24      | ADG3 hallprobe nominal value [0.1 mV]     |
| 25      | ADG3 hallprobe actual value [0.1 mV]      |
| 26      | 10 kHz clock summed gated                 |
| 27      | 10 kHz clock summed ungated               |
|         | . . .                                     |

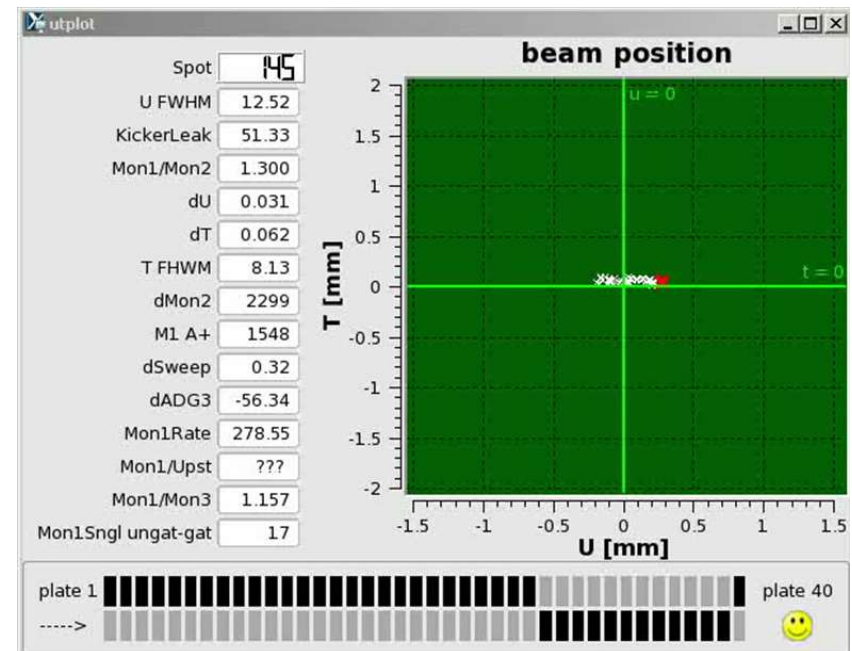
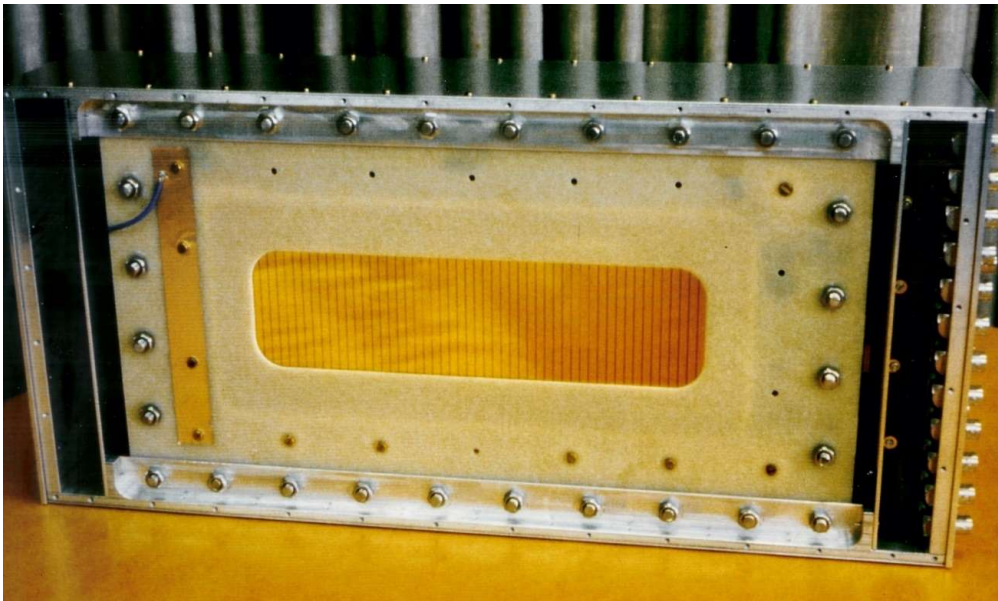
128 parameters per spot

# Pencil beam scanning needs to control dose AND position



Position sensitive IC (Kapton foil with 4mm aluminium strips)

Measure beam position and shape

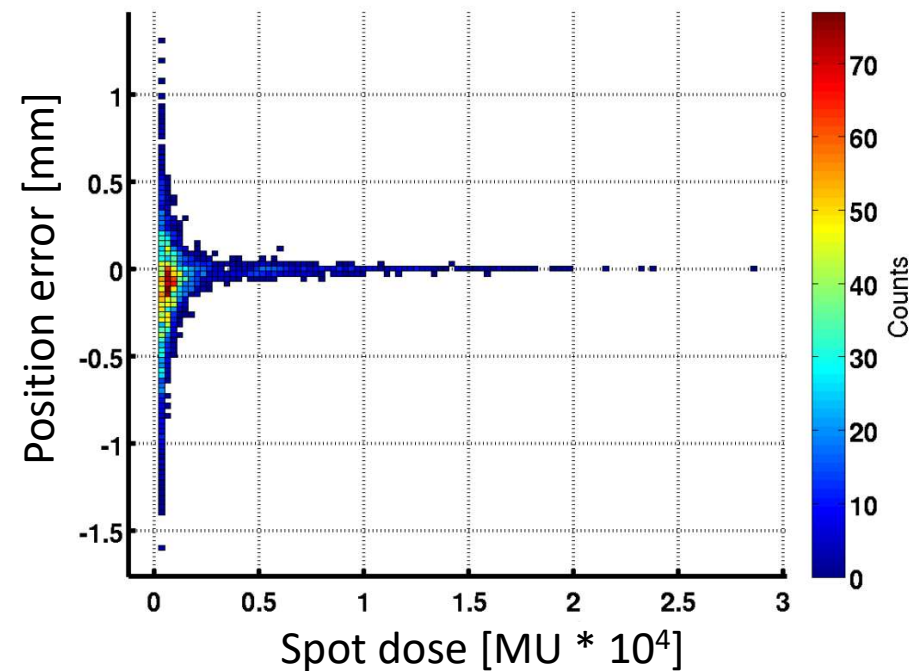


## Use HEP tools to analyze proton therapy data



During commissioning of Gantry 1: interlocks due to spot position error  
(difference nominal/actual position out of tolerance)

→ Introduce dose dependent tolerance!



# A useful tool for Quality Assurance



Logfiles proved to be a valuable tool for Patient Specific Quality Assurance

- Back calculation of dose and dose distribution from monitor units, table position, beam settings etc. (PhD thesis; now a routine tool)
- Current project: retrospective analysis of PSI Gantry treatments
  - «Modeling of proton RBE variations in patients: Retrospective analysis of 20 years of treatment of chordoma and chondrosarcoma cancer patients»

RBE is hypothesized to be affected by numerous factors, among which dose averaged LET. Other, more "exotic" quantities that have sparked interest in the last years are Dose rates ... Thanks to the logfiles we can reconstruct all these quantities and get as close as possible to the actual delivered physics quantities.

We can approximate the dose rate because the timings of the spots were recorded (timestamps and durations)



*Bastien Golomer, PSI PhD student*

