OncoRay – National Center for
Radiation Research in Oncology, Dresden

10 years of proton therapy in Dresden: Achievements and outlook of translational medical physics research

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Kutaisi, September 12 2024

OncoRay ZIK
National Center for Radiation Research in Oncology Dresden

TECHNISCHE UNIVERSITÄT DRESDEN

HZDR HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

Universitätsklinikum Carl Gustav Carus

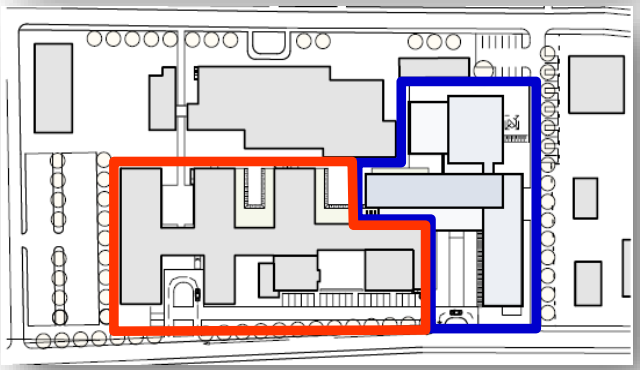
Georgian-German ScienceBRIDGE
CONNECTING PEOPLE AND KNOWLEDGE

OncoRay in Dresden, Germany

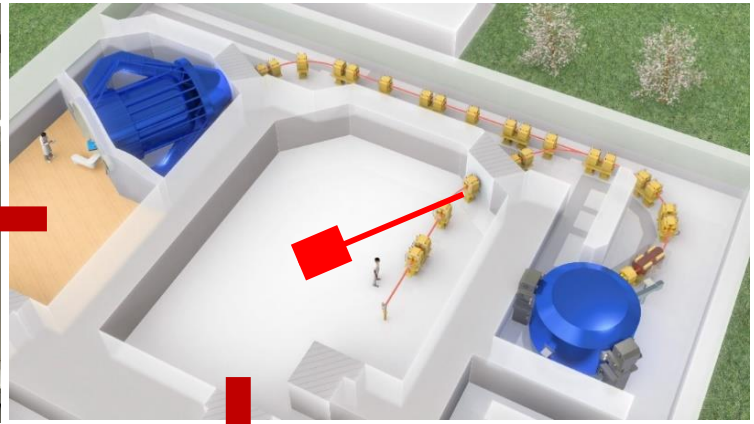
- **Public research institute**
  jointly operated by HZDR, university and university hospital
- **14 Research groups**
  (physics, biology, clinical radiooncology)
- **Focus: Translational research in Radiation Oncology**
- **No borders between clinic and research**

Radiotherapy department:

- **2300 pts / year**
- **110 employees**
- **Photons: 4 ELEKTA linacs + MR-Linac**
- **Protons: 1 clinical treatment room**



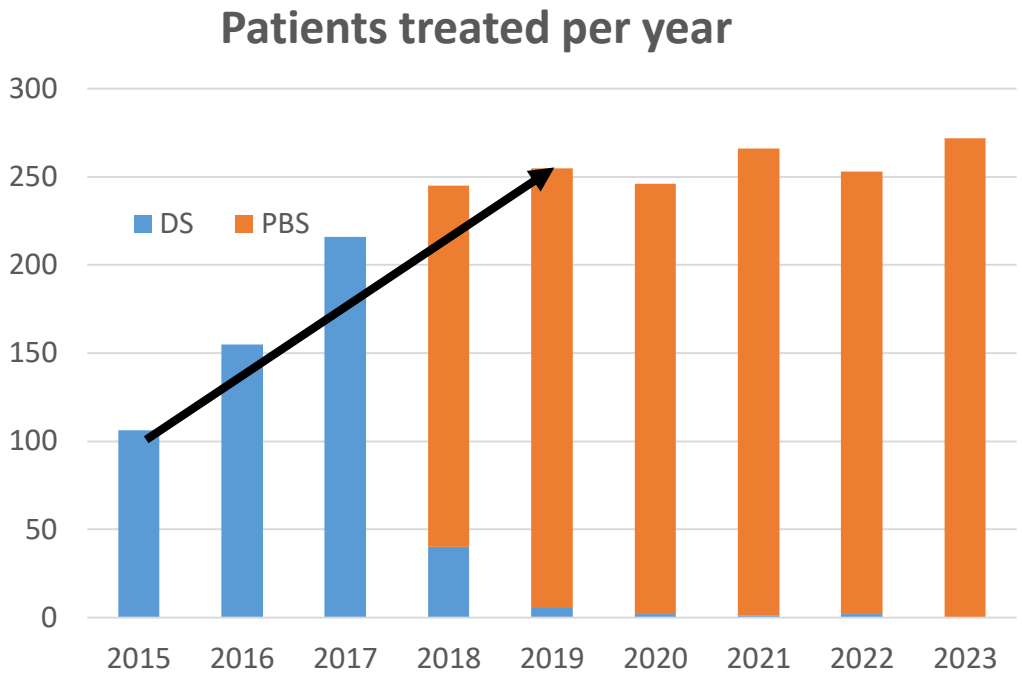
Dresden proton therapy facility (UPTD)



- 1 Clinical room with in-room DECT
- 1 Experimental room (250 m^2) with PBS nozzle and fixed beam line
- Clinical since **2014**, >2100 patients treated
- Efficient use of clinical room: 260 pts / year

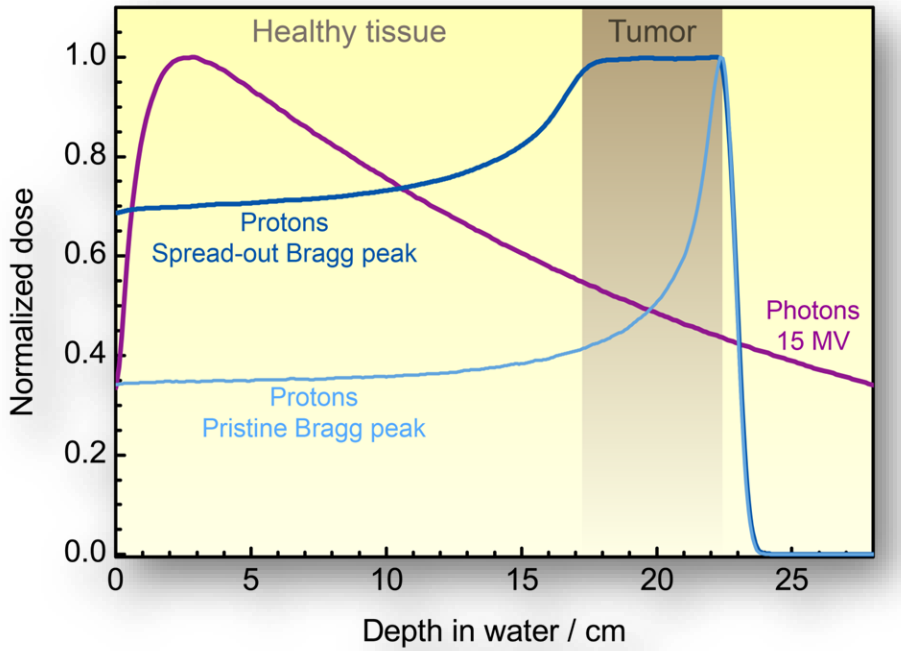
Clinical routine + Translational research

Patient numbers: Reality check



- **95% of patients treated in clinical trials or registries**
- Ramp up over 4 years
- >13 h clinical treatment
- **Case mix:**
  - Brain
  - CSI
  - H&N
  - Lymphoma
  - Lung
  - Esophagus
  - Pediatric
  - Prostate
- Most PT centers worldwide treat <150 patients per room

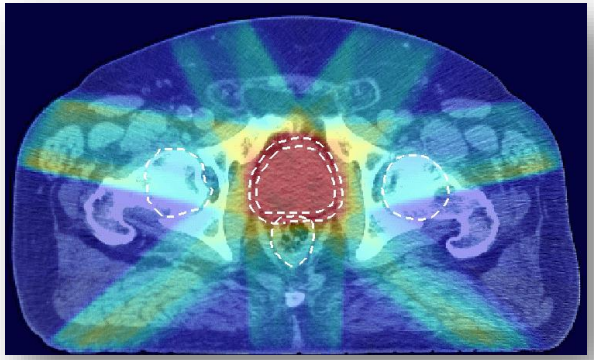
The rationale for proton therapy



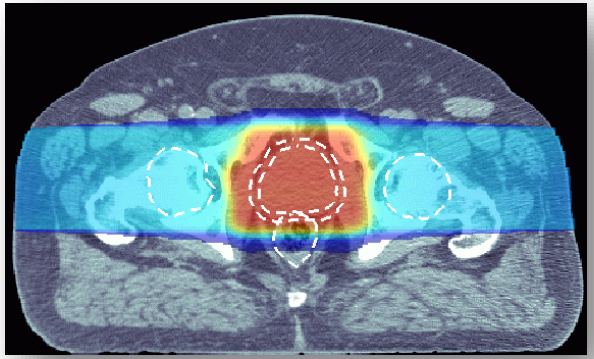
Protons:

- Stop in the patient → **Less dose in normal tissue (-50%)**
- Dose maximum in tumor → **Less beam directions required**

Photons

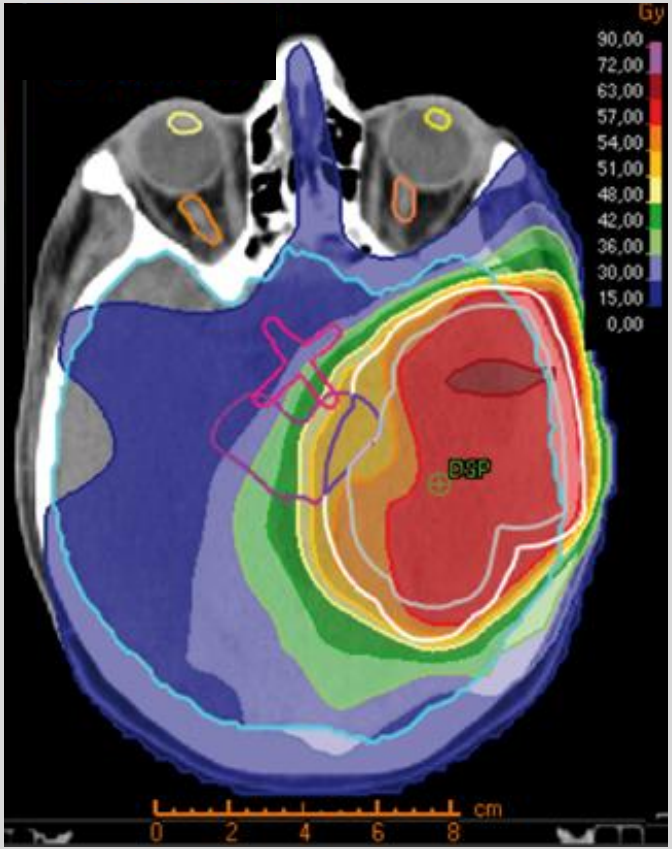


Protons



The rationale for proton therapy

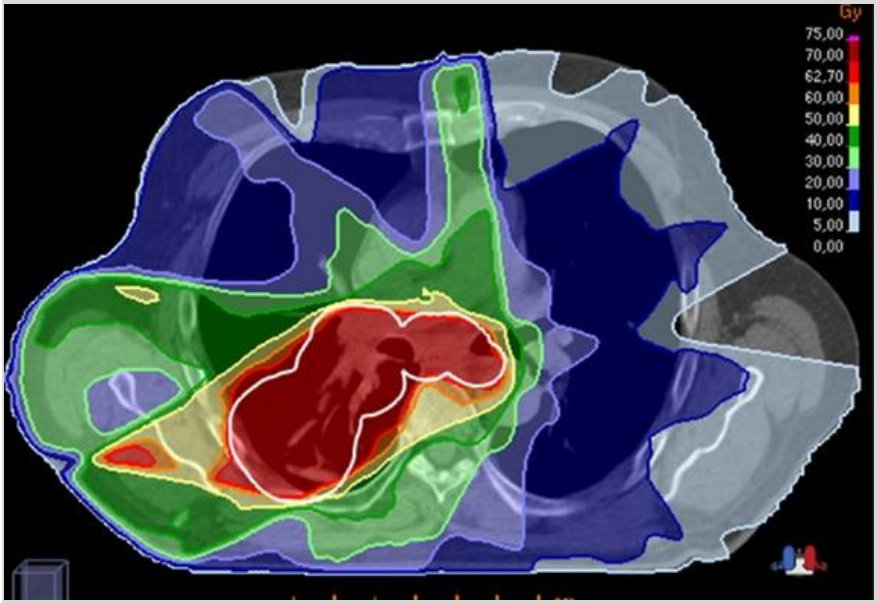
Photons



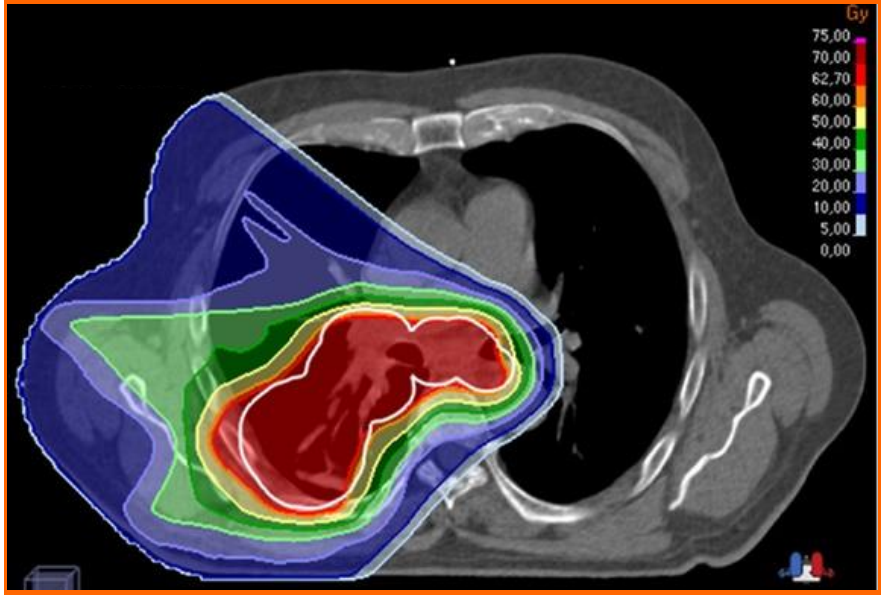
Protons

The rationale for proton therapy

Photons

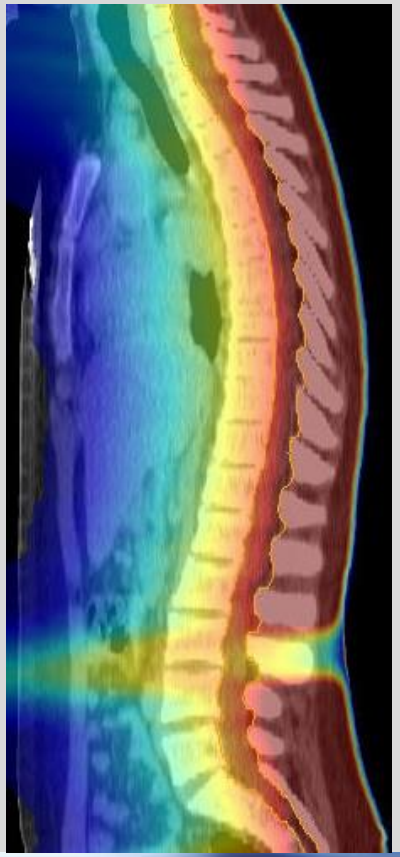


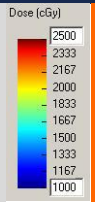
Protons



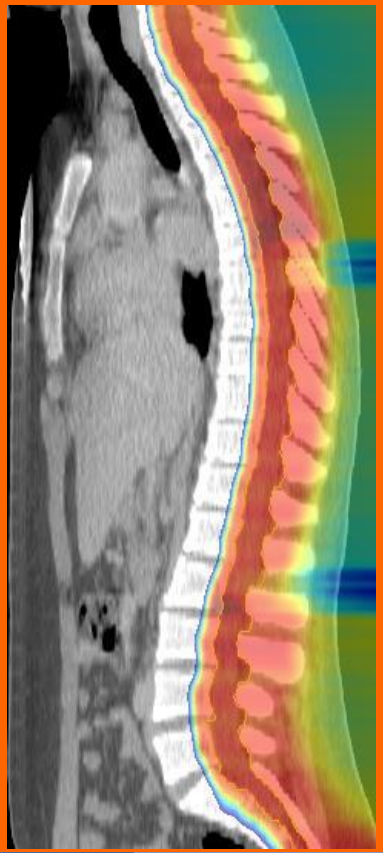
The rationale for proton therapy

Photons





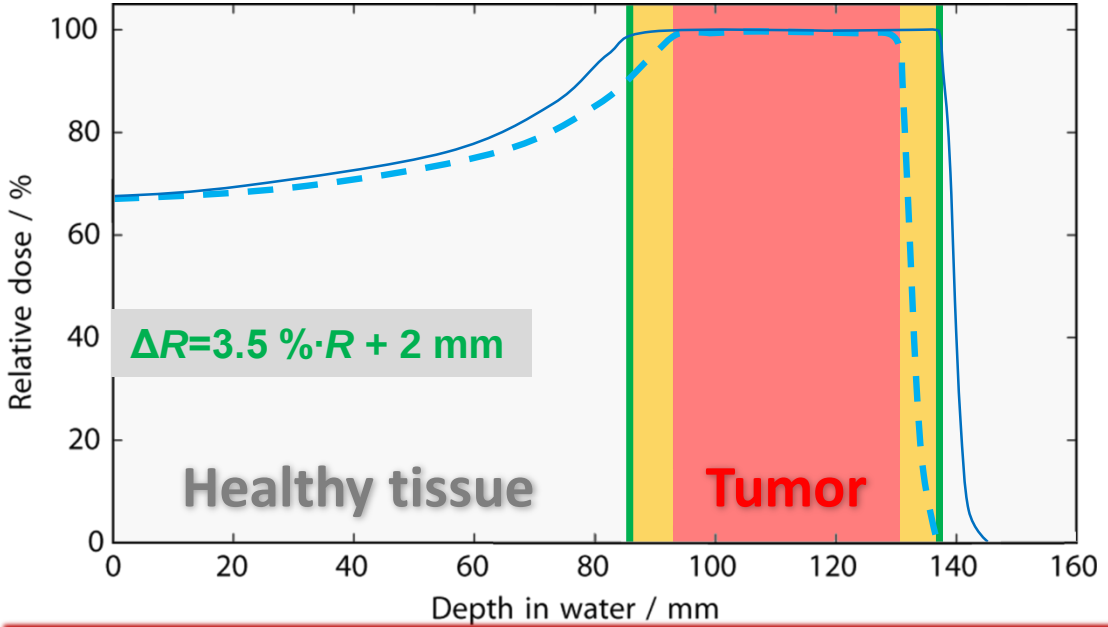
Protons



Challenges

1. Range uncertainty in treatment planning

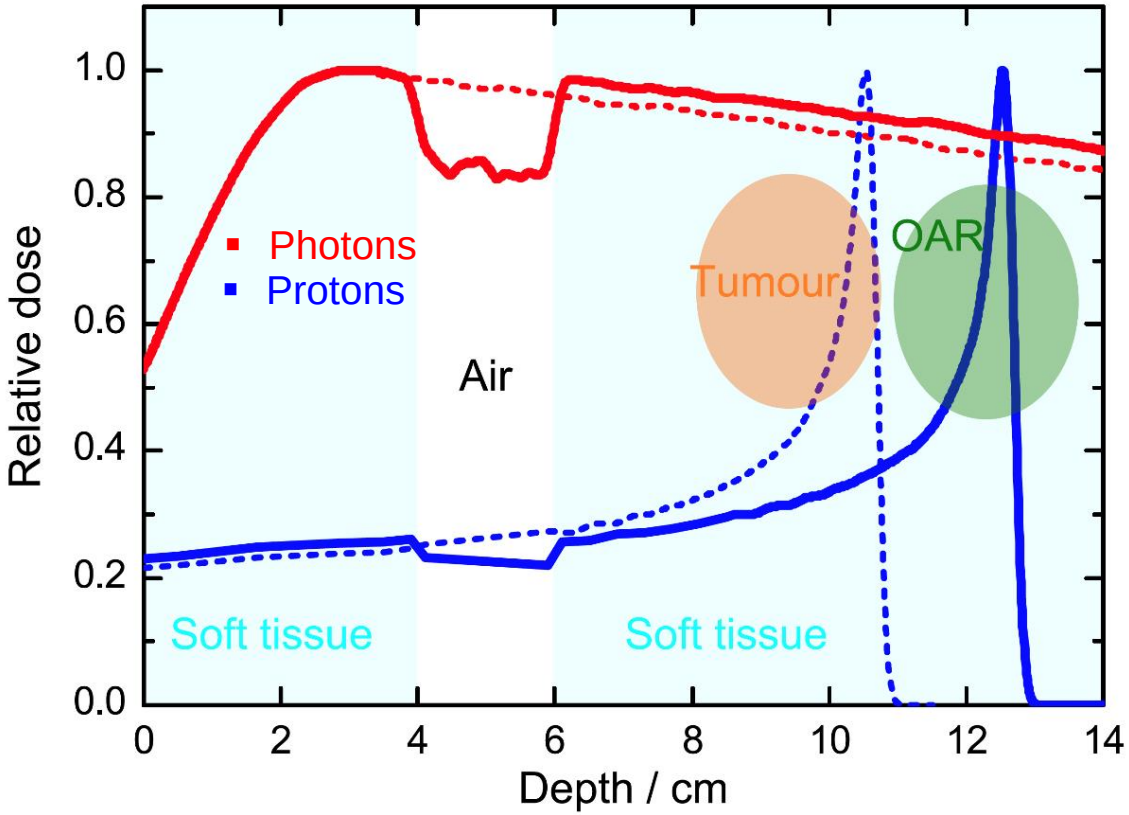
"The big advantage of **protons** is that they **stop**, **but** the problem is **we don't know** exactly **where**." (T. Lomax)



Solution: Uncertainty margin surrounding target volume

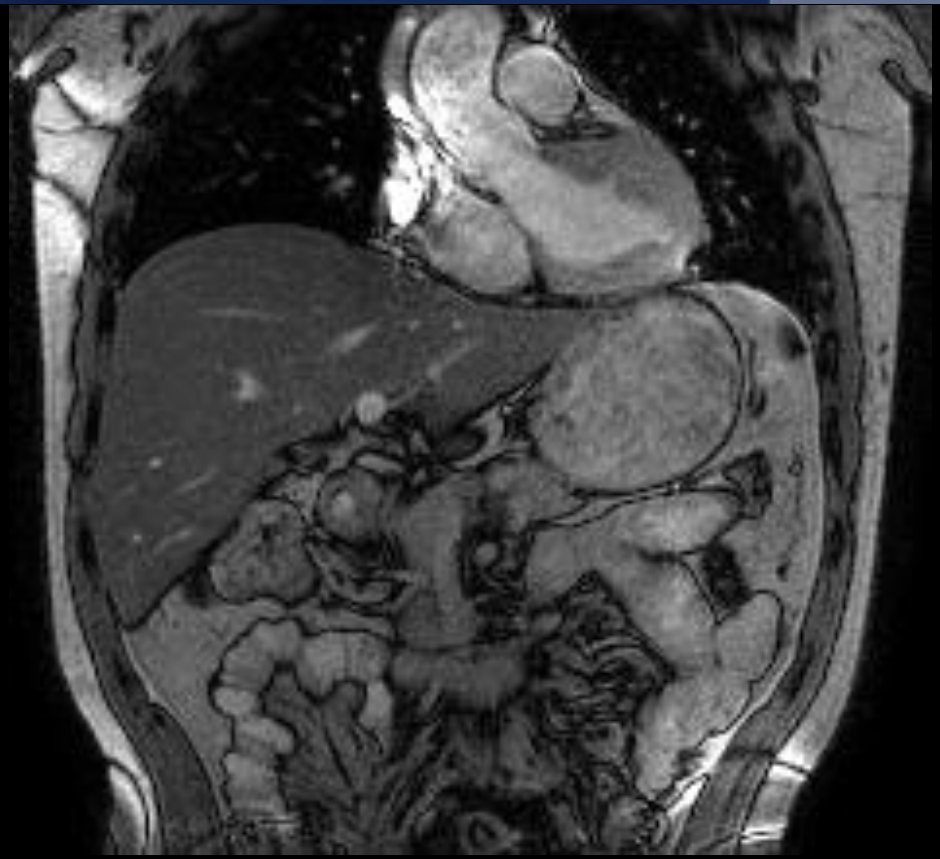
Range margins practically unchanged over the last 3 decades

2. Anatomical changes during therapy



Anatomical changes can have severe influence on dose deposition in the patient

2. Anatomical changes during therapy



@ Sergej Schneider, OncoRay

Challenges hinder optimal use of PT

We do not use the full potential of the technology

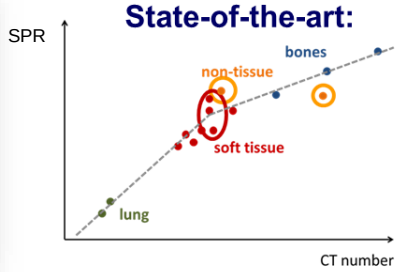
Translational medical physics research at OncoRay

1. Dual-energy CT for range prediction
2. Prompt-gamma based treatment verification
3. MR integrated proton therapy

Range prediction: Problem & Answer

Main problem:
CT-based prediction of proton stopping

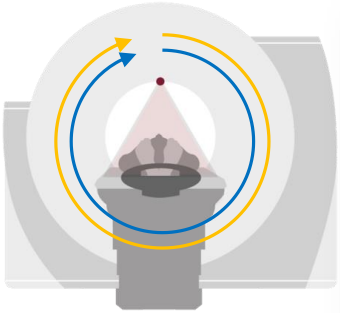
CT measures **X-ray** absorption → Treatment with **charged particles**

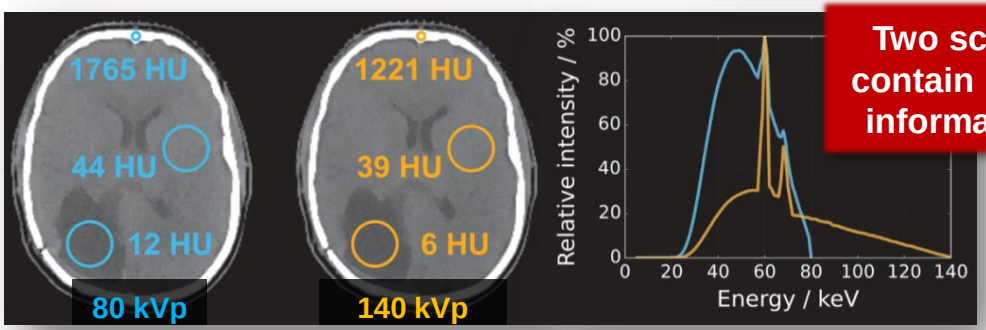


Improvement:

Dual-energy CT for treatment planning

Universal Studios





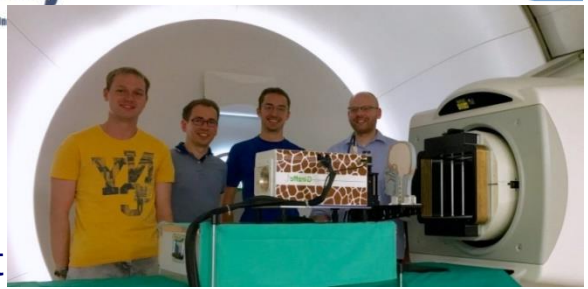
Two scans contain more information

Better tissue characterization for prediction of particle stopping

Dual-energy CT for accurate range prediction

2014: Translation of Dual-Energy CT into application in PT

OncoRay + dkfz.



Patrick Wohlfahrt

Christian Möhler

Cooperation with SIEMENS Healthineers

DirectSPR Approach

Scan 1

Scan 2

Electron density ρ_e

Effective atomic number Z_{eff}

Stopping power relative to water (SPR)

Dual-energy CT for accurate range prediction

2019

2017

2015

2014

SIEMENS Healthineers

RaySearch Laboratories

Step 1:
Clinical
DECT scans

Step 2:
DirectSPR based
HLUT adaption

Step 3:
DirectSPR clinical
implementation

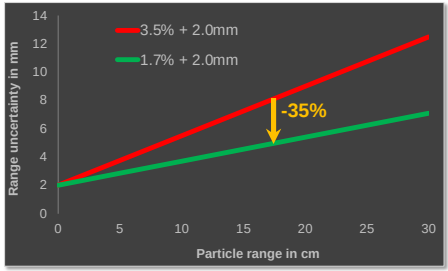
Optimized DECT imaging protocol

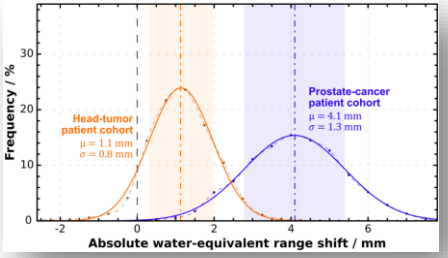
Validation of superior accuracy

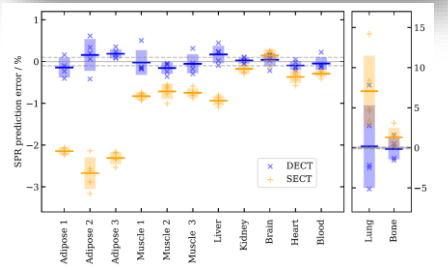
Proof of clinical relevance

Proof of benefit for patient variabilities

Prototype development



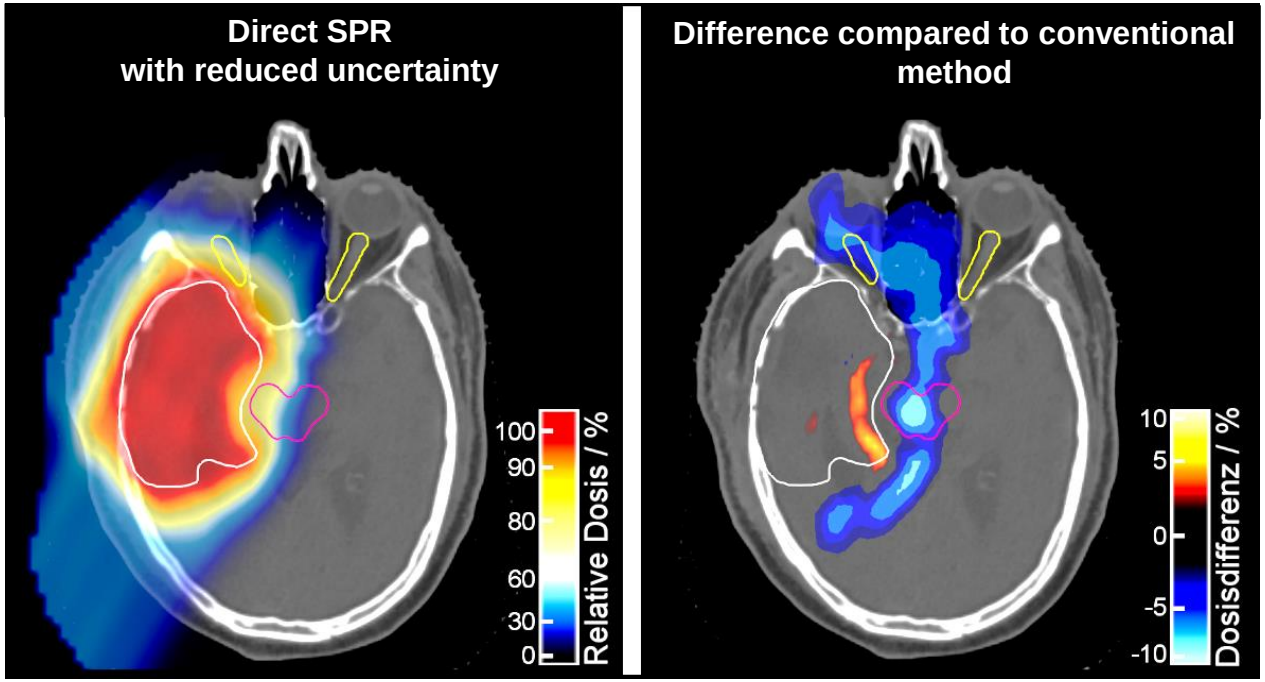




Dual-energy CT for accurate range prediction

Clinical implementation of DirectSPR in treatment planning in 2019

At the same time: **Reduction of safety margin by 35%**

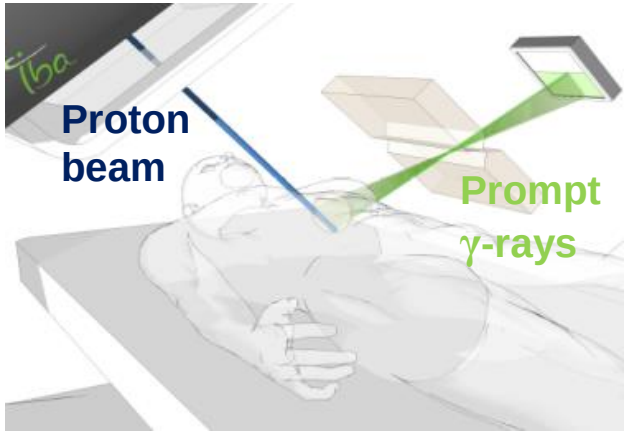


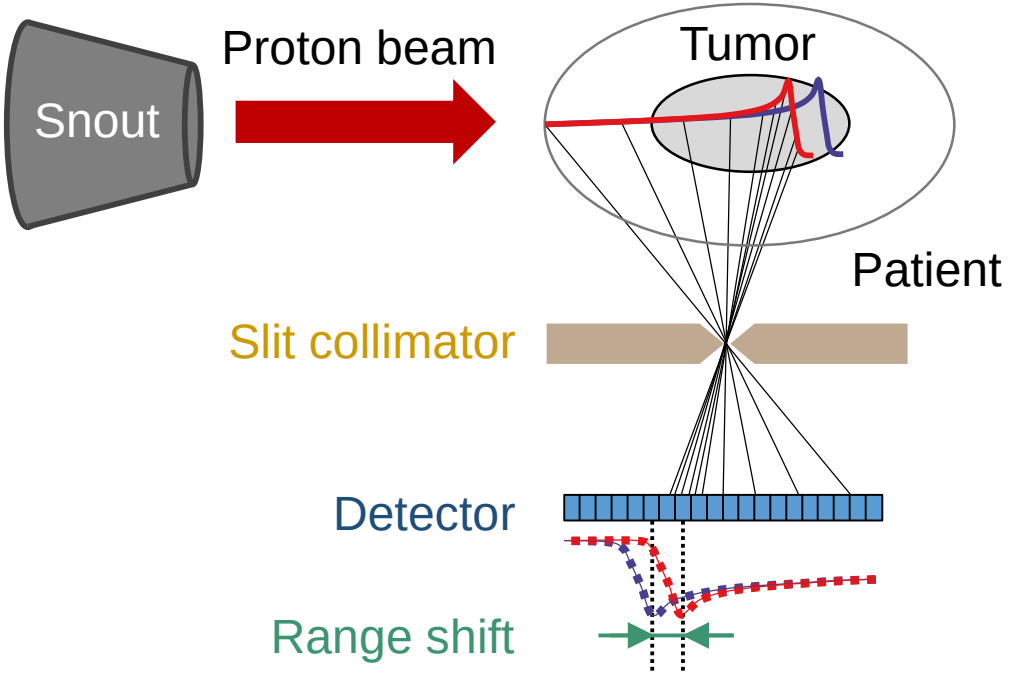
Wohlfahrt et al. IJROBP 2017
Möhler et al. PMB 2017
Wohlfahrt et al. Radiother Onccol 2017
Wohlfahrt et al. IJROBP 2018
Wohlfahrt et al. IJROBP 2019
Wohlfahrt & Richter BJR 2020
Peters et al. Radiother Oncol 2021
Berthold et al. IJROBP 2021
Peters et al. Radiother Oncol 2021
Richter & Wohlfahrt Springer 2022
Peters, Wohlfahrt, Richter, IOP 2024

→ Worldwide most accurate PT planning ☑

Prompt gamma based treatment verification

Goal: Online treatment verification system to detect deviations from planned delivery

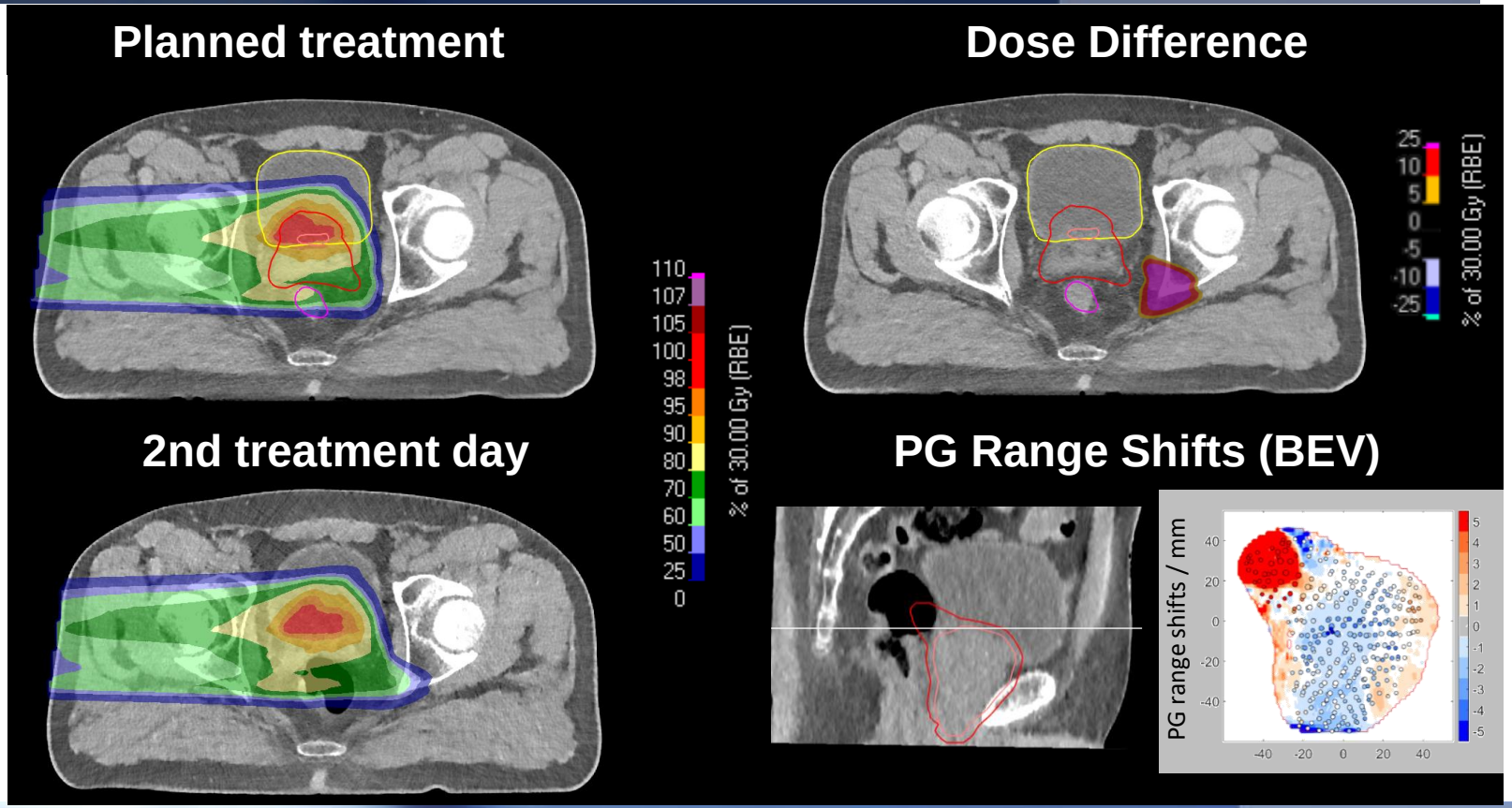




Benefits of PGI

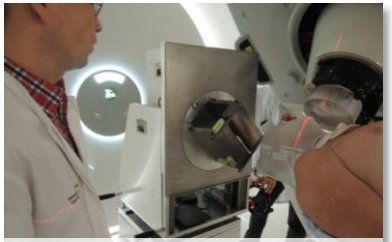
- ✓ No additional dose
- ✓ No treatment prolongation
- ✓ Safety net functionality

Prompt gamma based treatment verification



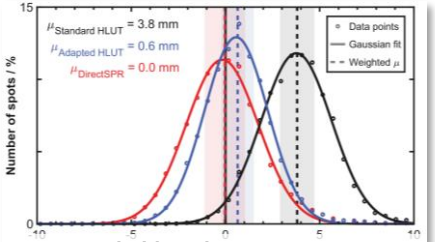
Prompt gamma based treatment verification

2014 — **First in-human application**



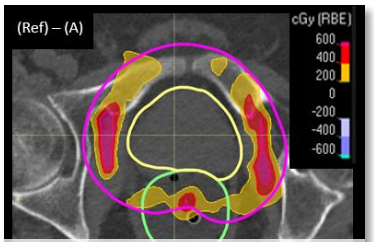
Richter et al. Radiother Oncol 2016

2018 — **In-human validation of DECT-based range prediction**



Berthold et al. IJROBP 2021

2022 — **Margin reduction potential quantified**

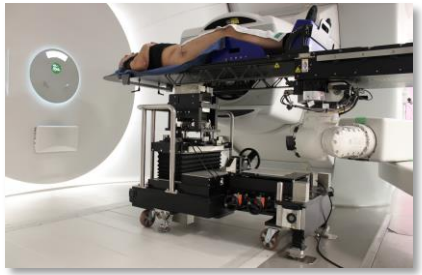


Bertschi et al. phiRO 2023

2025 — **1st interventional study: Trigger of adaption**

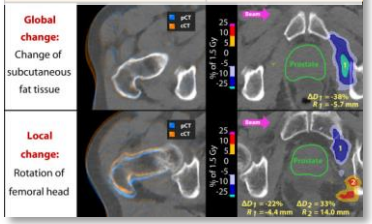
2014 — **1st generation prototype @ OncoRay**

2015–2020 — **2nd generation positioning system**



2020–2023 — **Detectability of anatomical changes**

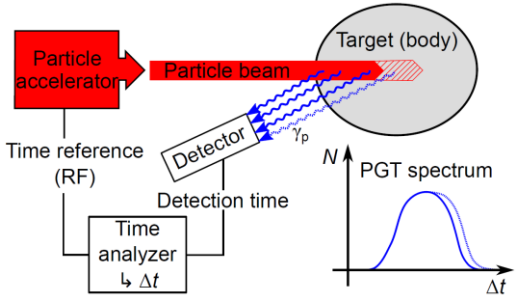
Pietsch et al. Med Phys 2022;
Berthold et al. IJROBP 2023



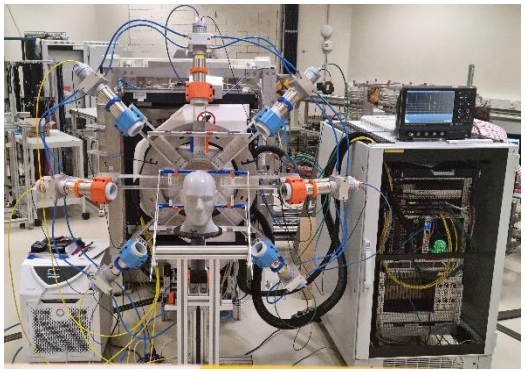
2025 — **1st interventional study: Trigger of adaption**

Next-generation PG treatment verification

Prompt Gamma-Ray Timing

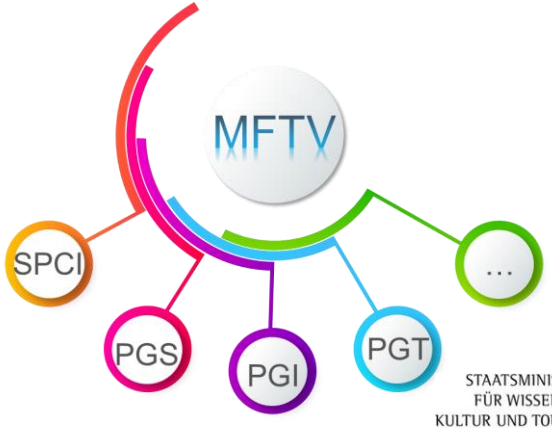


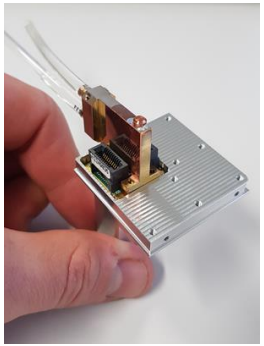
- Status: Realistic pre-clinical experiments



Multi-Feature Treatment Verification

- Use of all Prompt Gamma information (spatial, temporal, spectroscopic)
- Development of novel detector and analysis concept
- Status: First proof-of-principle prototype





STAATSMINISTERIUM FÜR WISSENSCHAFT KULTUR UND TOURISMUS

Freistaat SACHSEN

Golnik *et al.* PMB 2014; Hueso-Gonzalez et al. PMB 2015; Werner et al. PMB 2019; Pausch *et al.* NIMA 2020

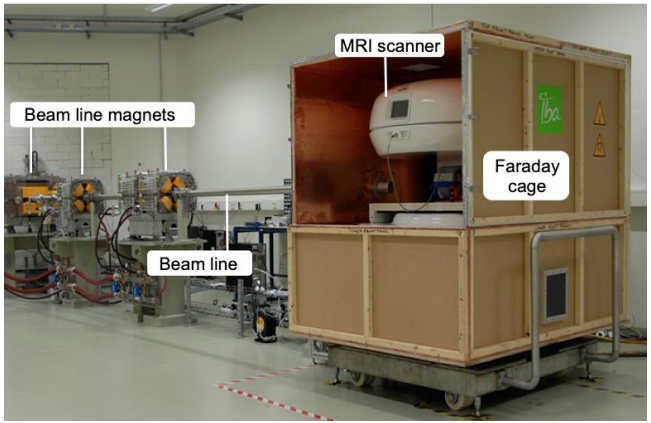
MR-integrated Proton Therapy

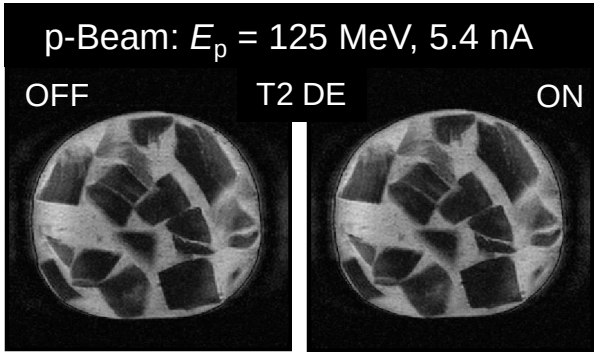
Main goal:

Increase the targeting precision through high soft-tissue contrast real-time MR image guidance

2015: Strategic decision: Development of MR integrated PT am OncoRay

1. Step: 1st MRiPT proof-of-principle prototype - 0,22 T MRI at fixed horizontal beamline

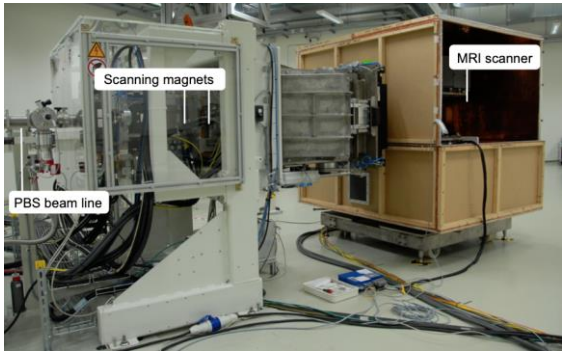




Dresdner Fleischwurst

MR-integrated Proton Therapy

2. Step: 0,22 T MRI at the horizontal PBS beamline



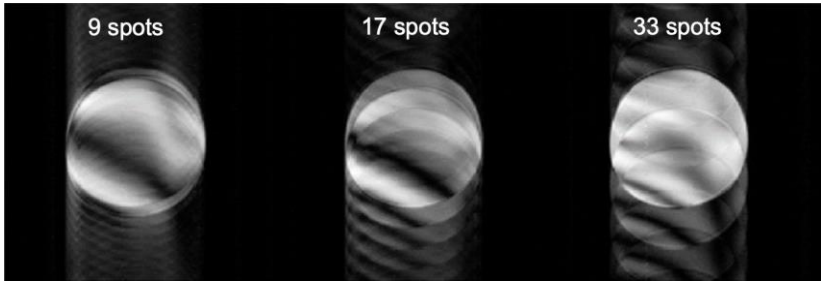
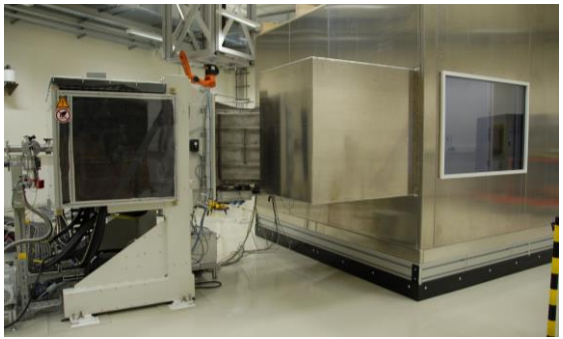
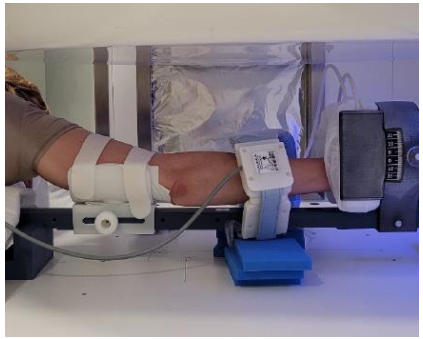


Image deterioration when imaging during PBS beam delivery
→ Shielding required

3. Step: 2nd generation prototype 0,33 T MRI at the horizontal PBS beamline



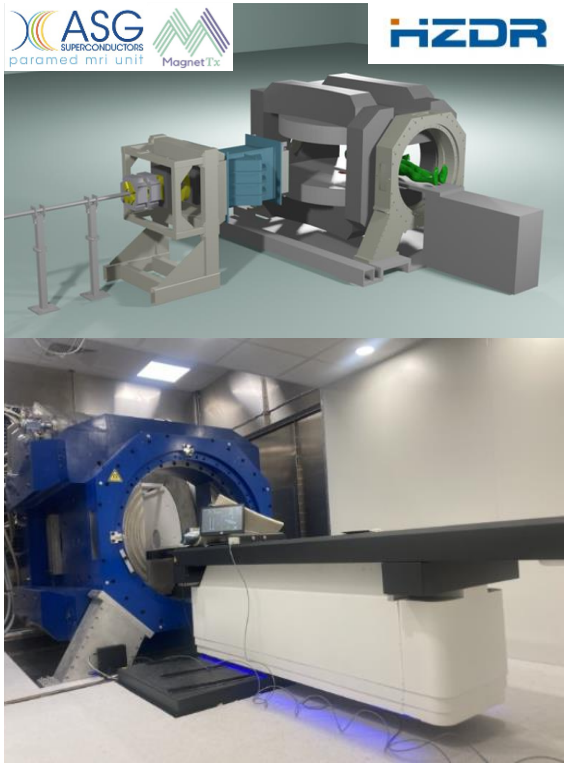


Goal:
First-in-human application for static tumors

Gantz *et al.* PMB 2018; Gantz et al. PMB 2020; Gebauer *et al.* Med Phys 2023

MR-integrated Proton Therapy

4. Step: 3rd generation 0.5 T whole-body MRI (mounted on rotatable gantry)



Goal: Real-time imaging during irradiation

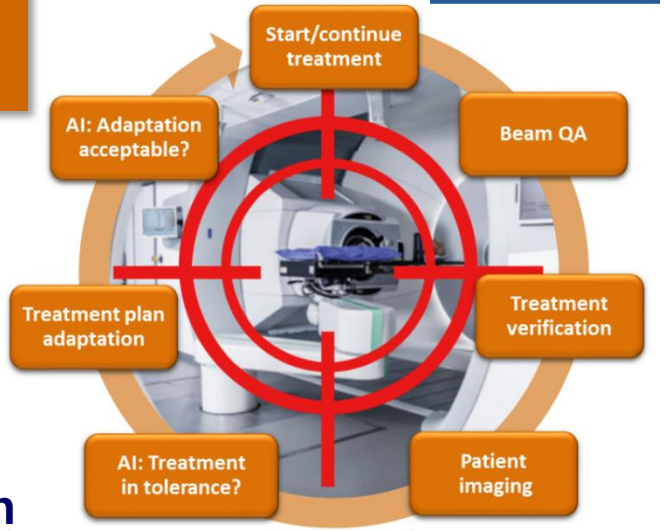
Outlook: Online-adaptive proton therapy

Next generation online-adaptive particle therapy:
online imaging & verification, online adaptation, minimal safety margin

Improve accuracy & adaptation capability towards physical limit

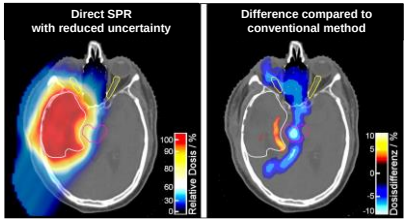
Benefit of superior dose distribution + **Benefit of online adaption capability** = **Best possible RT: Maximized clinical benefit**

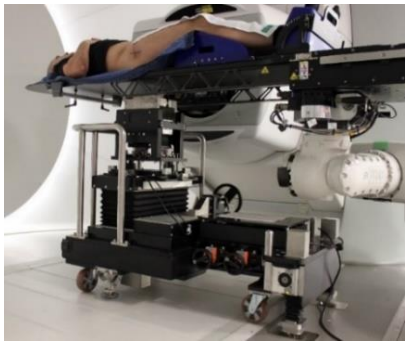
- **Why:** To react on anatomical changes during the course of treatment.
  To shrink uncertainty margins.
- **How:** Detect → React → Check
  AI supported closed feedback loop between imaging, adaption and verification



Summary

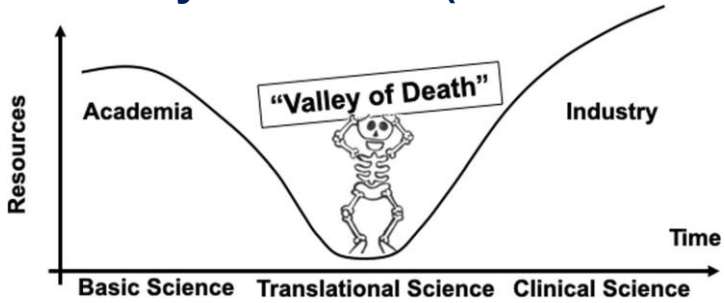
- 10 years ago particle therapy could not take full advantage of the superior physical dose distribution
- OncoRay contributed with several translational projects which are now used in (routine) clinical application:
  - **Direct DECT-based treatment planning**
  - **Prompt-Gamma treatment verification**
  - **On the way: MR integrated proton therapy**
- **Next step, missing to reach optimal treatment:**
  Realization of near-realtime online adaptive PT





Key factors for sucessful clinical translation

- **Choice a stepwise approach – Accept to not be perfect in the first place**
- **Have a long breath – “Valley of death” (includes funding!)**



Seyhan. Transl Med Commun 2019

- **Foster a team effort:**
  - Collaboration with industry
  - Interdisciplinary (do not stay in the niche of domain ”experts”)
- **Active support from clinical leaders!**

Ready for take off!

Destination: KUT

Thank you!