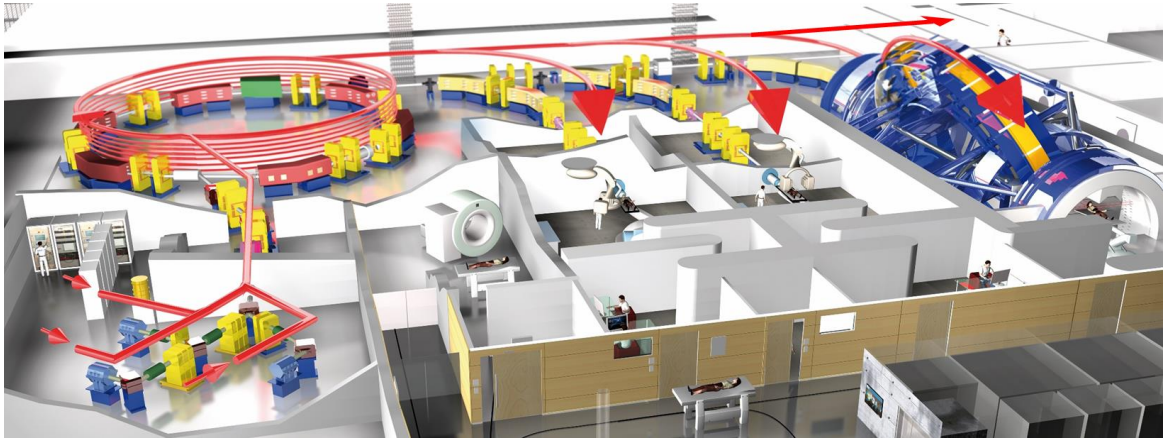
HEIDELBERG UNIVERSITY HOSPITAL

HIT Heidelberger Ionenstrahl-Therapiezentrum

# Clinical experience with hadron therapy at the Heidelberg Ion Beam therapy center since 2009





UK HD

# First treatment with C12 in Europe, December 1997 @ GSI

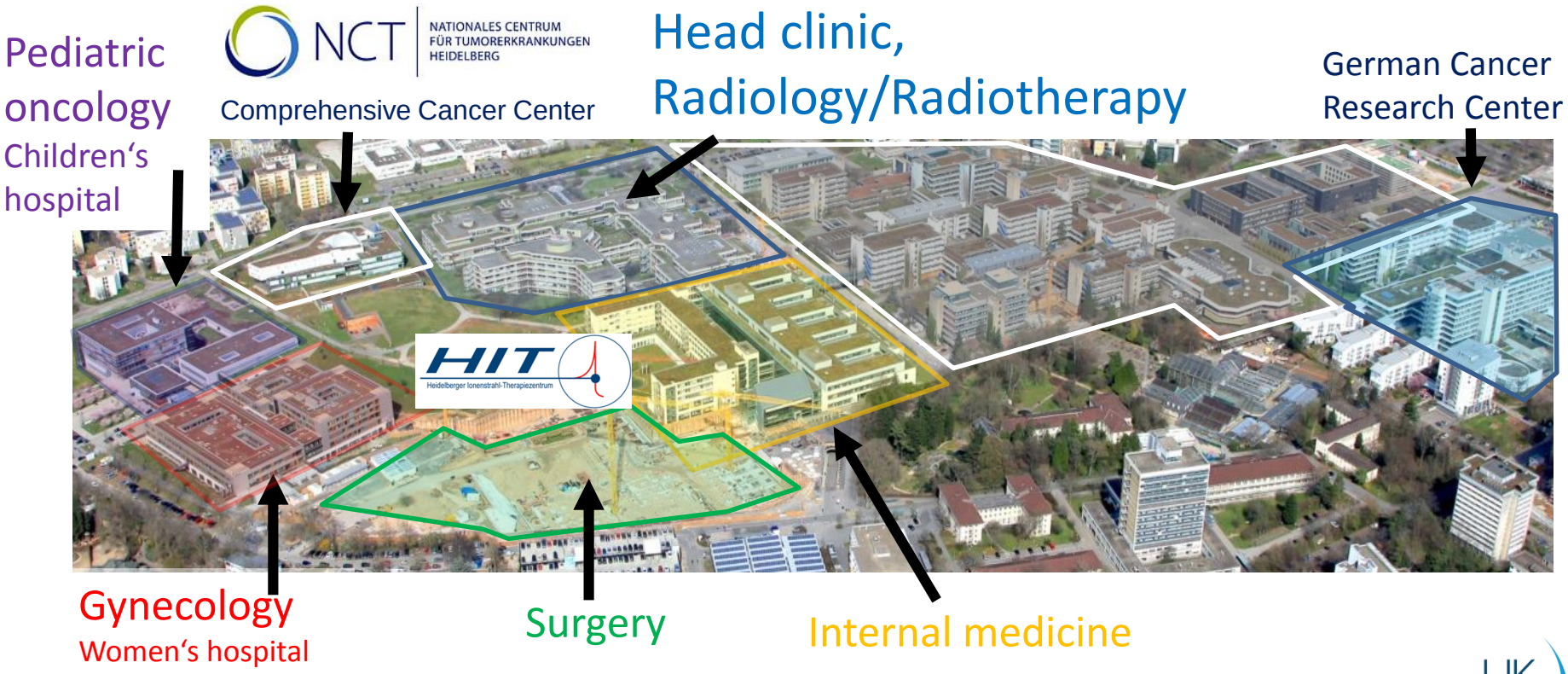
**n=440, 1998-2008**

# First treatment @ HIT in 2009

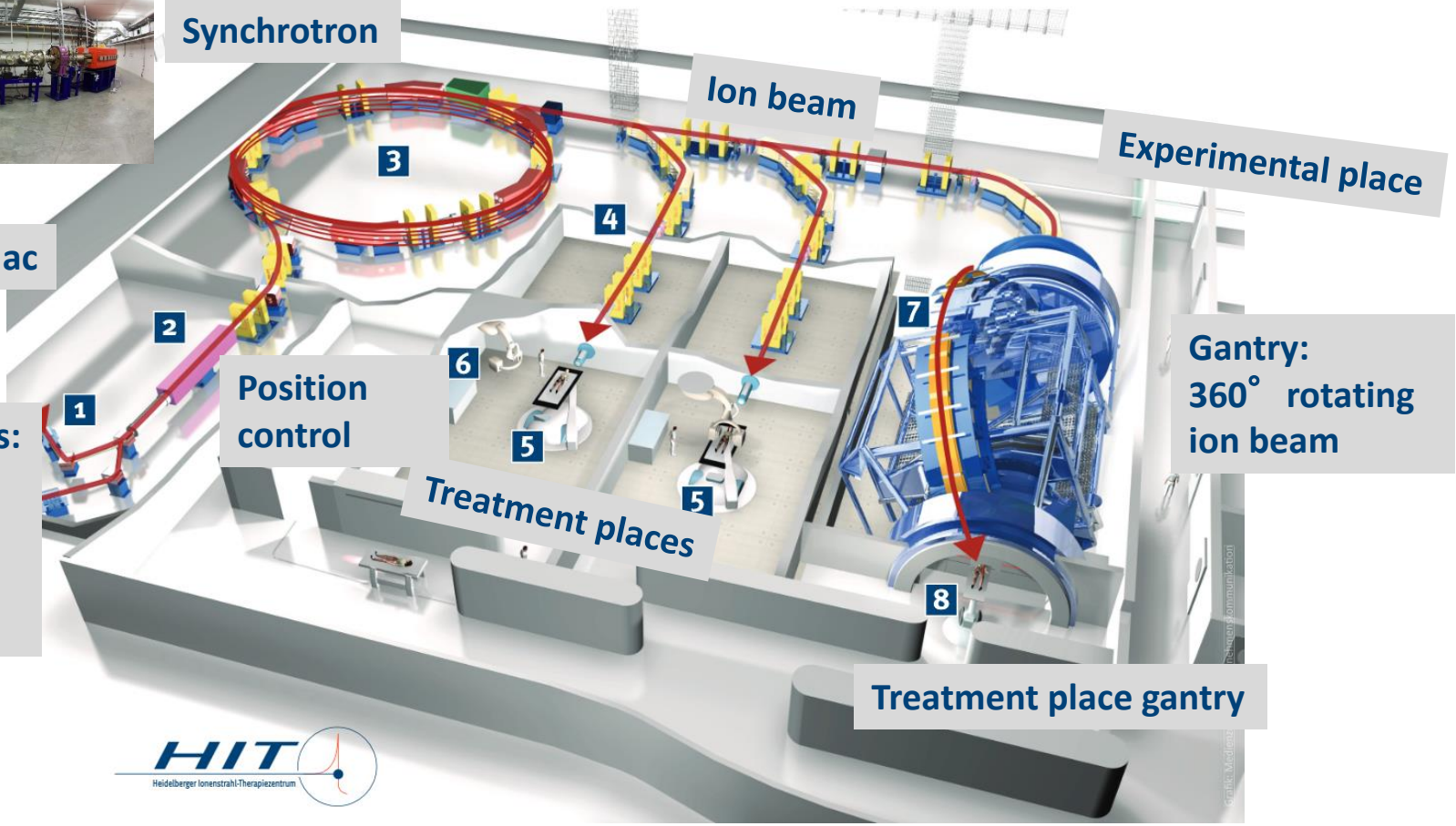
**CONSTRUCTION HIT : 2003-2009,**
**FIRST TREATMENT @ HIT IN 2009**

# Embedded in the clinical environment

- fully integrated into the clinical environment and workflow
- surrounded by academic research environment
- compact size requiring  60 m x 70 m ground surface

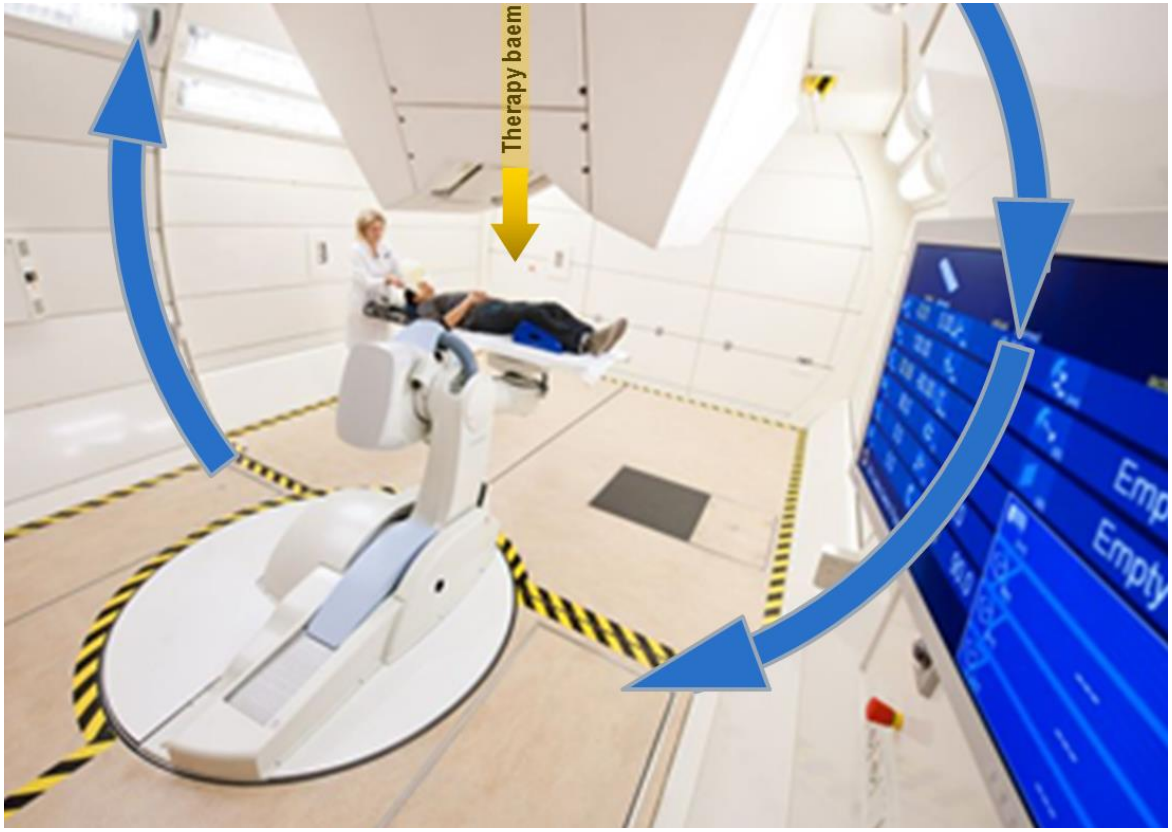


# Heidelberg Ion-Beam Therapy Center (HIT)



# Treatment place Gantry: Optimal irradiation angle

HIT is the world's first heavy ion treatment facility with a **360° rotating beam delivery** system (gantry)



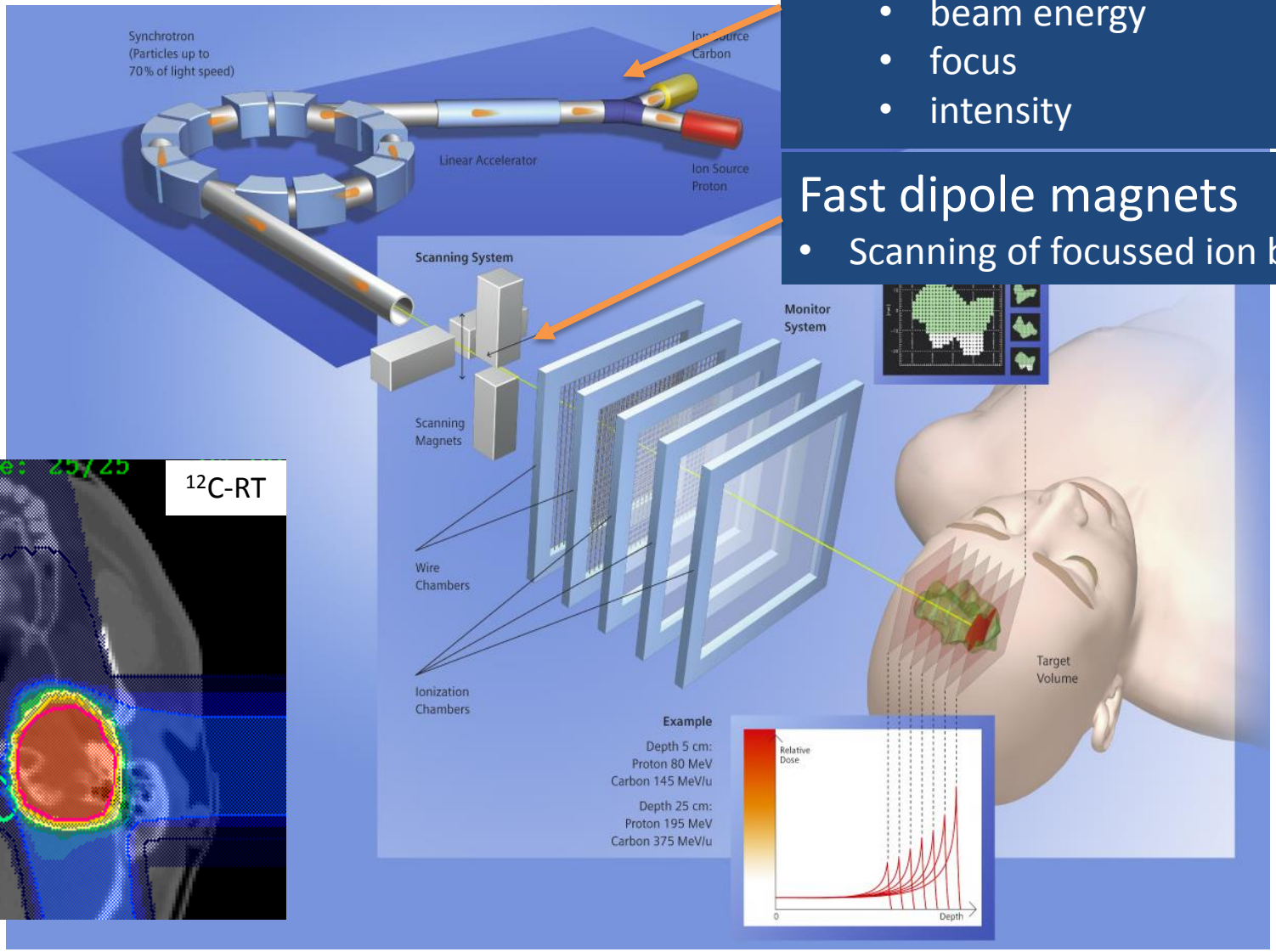

# Active Raster Scanning

## Accelerator and beam line

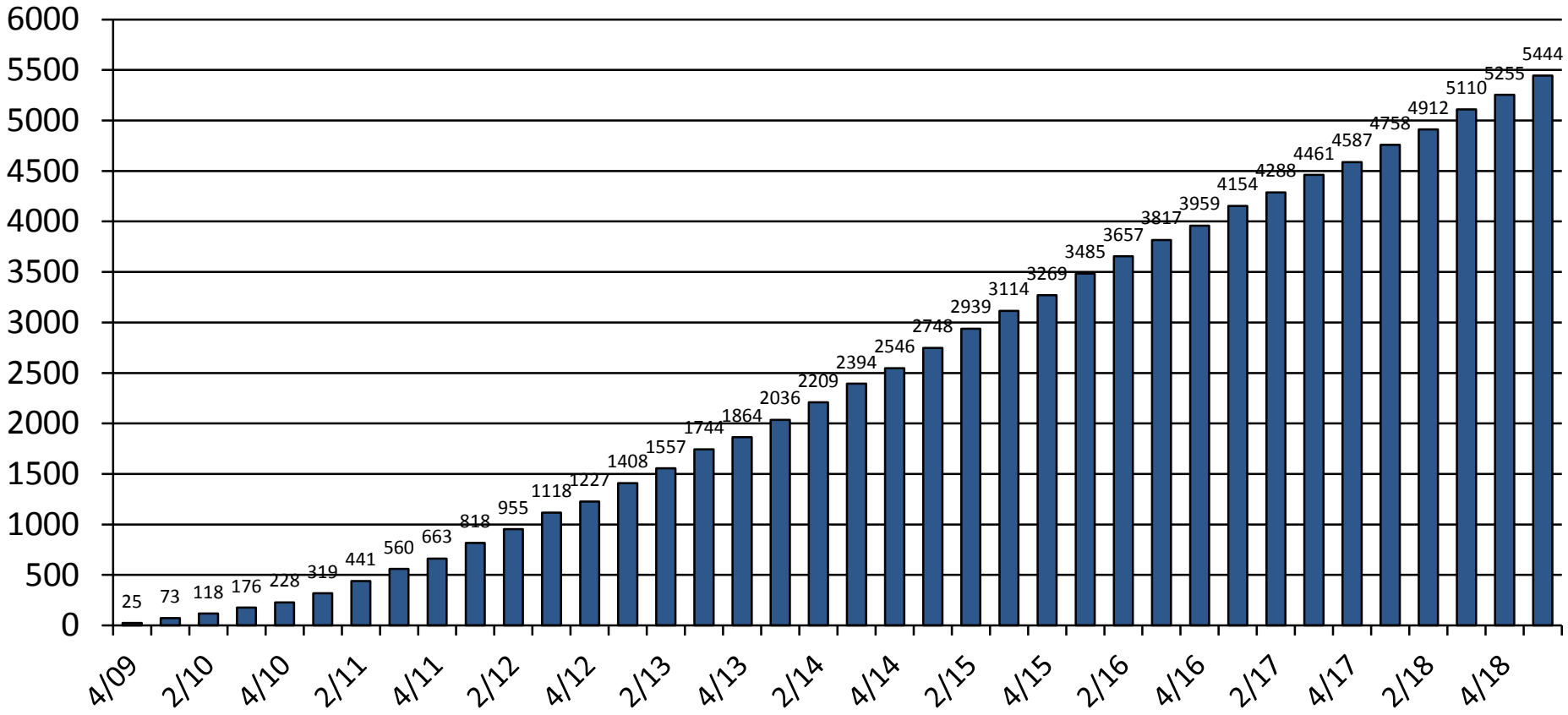
- Active variation of
  - beam energy
  - focus
  - intensity

## Fast dipole magnets

- Scanning of focussed ion beams



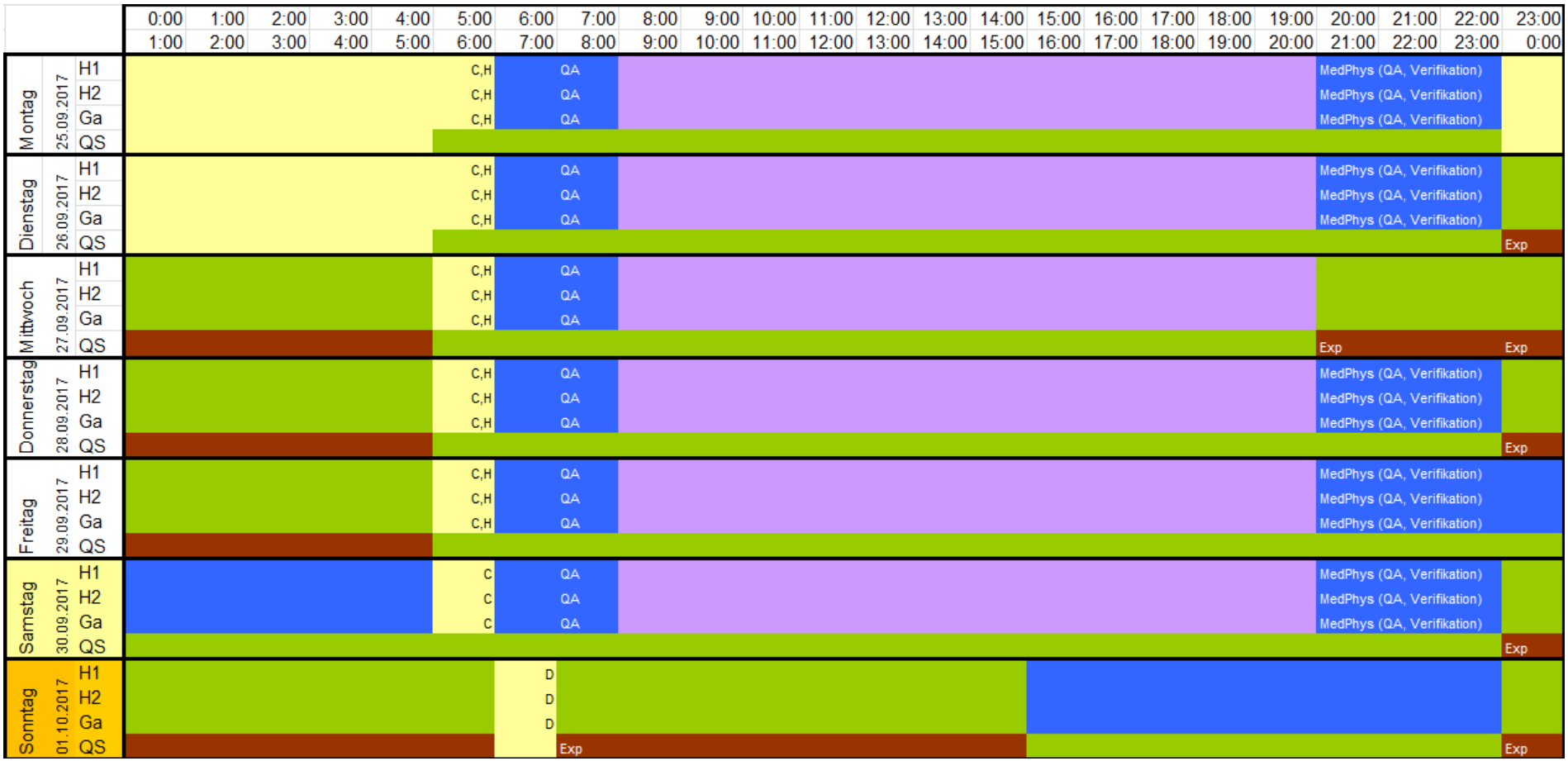
# Patients @ HIT




| 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | Q1 2019 |
|---|---|---|---|---|---|---|---|---|---|---|
| 14 | 214 | 435 | 570 | 637 | 676 | 723 | 690 | 628 | 668 | 189 |

# A week at the HIT – beam time plan

Experiments QA Patient Treatment QA



# Main tumor entities treated at the HIT

- Chordoma
  - Chondrosarcoma
    - Head & neck tumors/salivary gland tumors
      - Glioma
        - Meningioma, AKN
          - Pediatric tumors (e.g. CNS, Sarcoma, Craniopharyngeoma)
            - Prostate Cancer
              - Lung cancer (Pancoast-tumors)
                - Lymphoma in young patients

                - …

# Clinical trials @ HIT

- **IMRT HIT-SNT** (C12 boost RT; sinunasal tumors) completely recruited (36/36)
- **INKA** (neoadj. C12, inop. sulcus superior tumors) recruiting (11/20)
  - MARCIE (C12 boost RT; meningeomas Grad 2) recruiting (32/40)
  - PROMETHEUS (C12; HCC) recruiting (16/36)
  - CINDERELLA (C12 recurrent gliobastoma) f/u Phase (56/56 Phase 1)
- **COSMIC** (C12 boost RT; salivary gland tumors) published
  - KOLOG (hypofract. C12; recurrent prostate cancer) f/u Phase (40/40)
  - APROVE (H1; cervical and endometrial cancer) recruiting (18/25)
  - PROLOG (hypofract. H1; recurrent prostate cancer) f/u Phase (70/70)
  - CLEOPATRA (H1 vs. C12 boost RT; prim. gioblastoma) f/u Phase (97/97)
  - SB chordoma: H1 vs. C12 recruiting (126/319)
- **SB chondrosarcoma:** H1 vs. C12 recruiting (82/154)
- **ISAC** (C12/H1; sacral chordoma) recruiting (61/100)
- **OSCAR** (H1 + C12 boost; inoperable osteosarcoma) f/u Phase (20/20)
  - IPI (C12/H1; prostate carcinoma) f/u Phase (92/92)
  - PAROS (prostatic cavity) recruiting (1/897)

Just initiated:

Retro-Ion

In preparation:

- **ACCO**

CARE

Extrem-Ion

# Salivary gland tumors / Adenoid cystic carcinoma

C12 pilot project, patients treated before 2009, mainly T4 (R1/2 or inoperable)

- 58 patients treated with C12 at the GSI (18 GyE C12 + 54 Gy Photons)
- 37 patients treated with photons (66 Gy)
  - ➢ Significantly **higher LC in the C12 group**

3y-LC:
C12: 84 %
Photon IMRT: 56 %

Cancer

Original Article

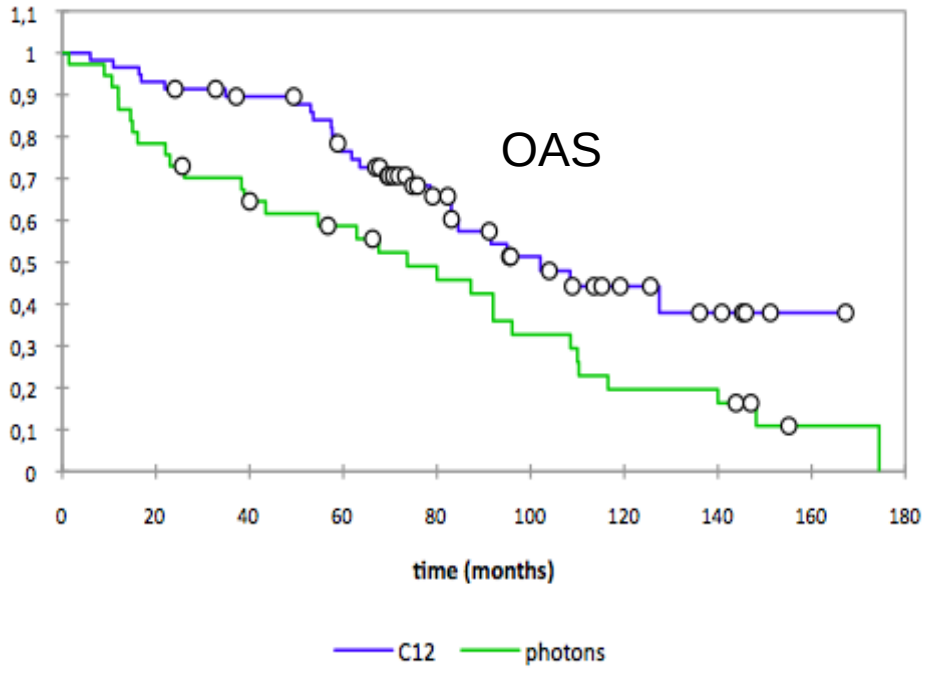
**Combined intensity-modulated radiotherapy plus raster-scanned carbon ion boost for advanced adenoid cystic carcinoma of the head and neck results in superior locoregional control and overall survival**

Alexandra D. Jensen MD, MSc, Anna V. Nikoghosyan MD, Melanie Poulakis DDS, Angelika Höss MSc, Thomas Haberer PhD, Oliver Jäkel PhD, Marc W Münter MD, Daniela Schulz-Ertner MD, Peter E. Huber MD, PhD, Jürgen Debus MD, PhD

**First published:** 4 June 2015 Full publication history

**DOI:** 10.1002/cncr.29443 View/save citation

**Cited by:** 0 articles Check for new citations

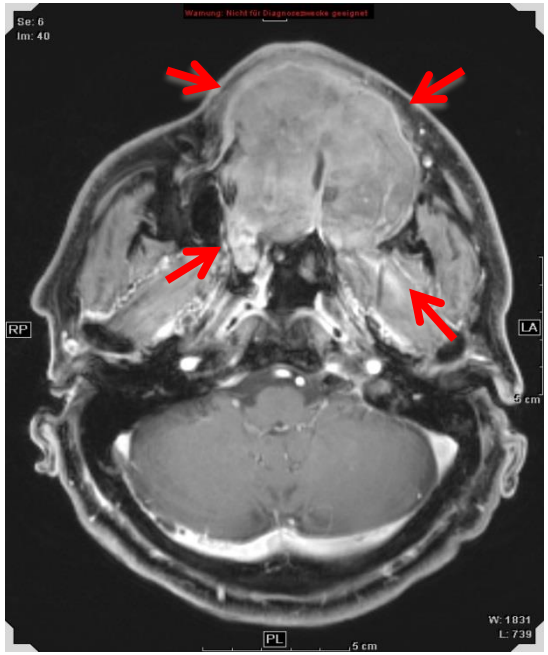


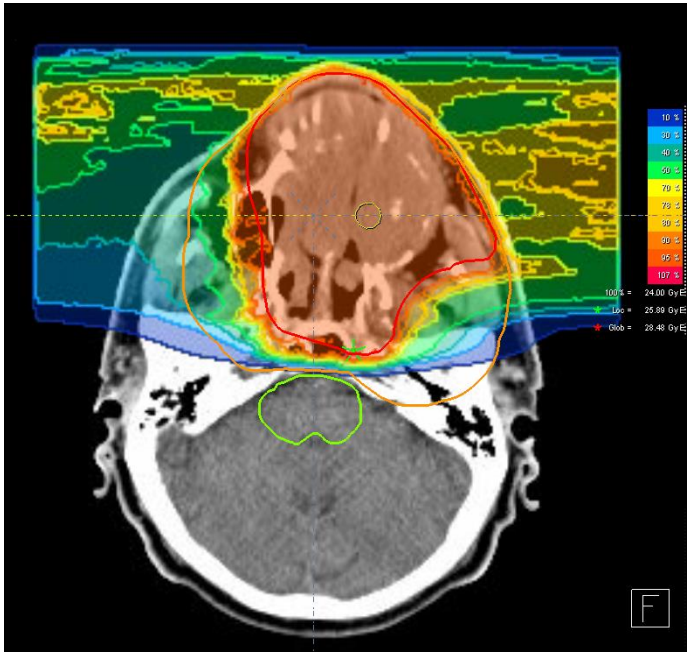
# COSMIC-Trial

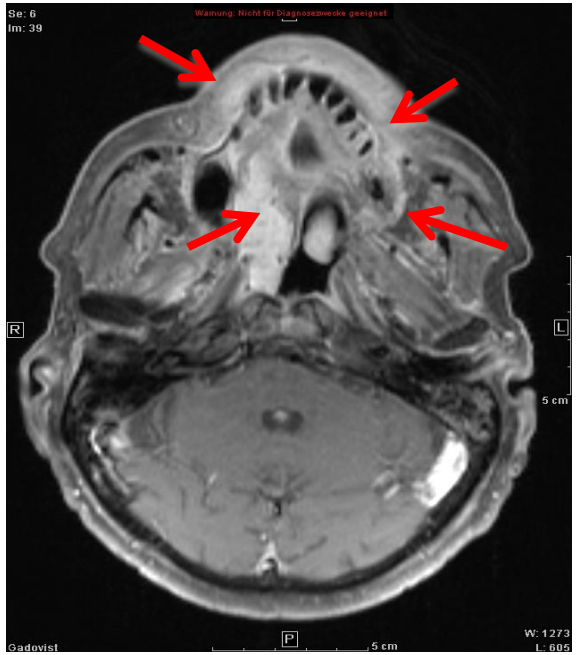
**CO**mbined therapy of malignant **S**alivary gland tu**M**ors with **I**MRT and **C**arbon ions

- Phase II feasibility study, dose escalation (**18GyE to 24 GyE** C12 boost)
  - 54 patients treated at HIT from 2010 to 2011, 89% ACC
  - No dose limiting acute toxicity
  - Late Toxicity > CTC°2 : < 5%

LC after 3 years: 82 %




Pre-treatment situation

Treatment planning
C-12 boost

6 weeks post RT

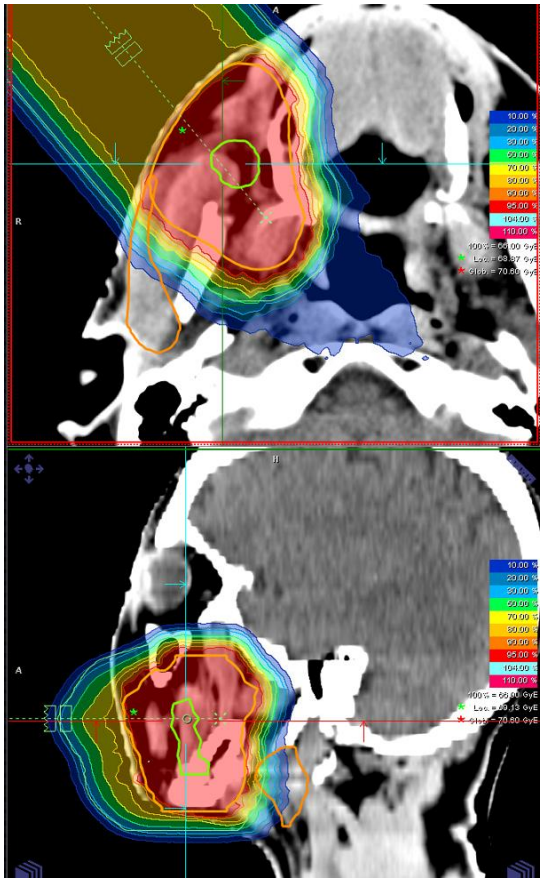
# Upcoming ACCO-Trial

**A**denoid **C**ystic carcinoma and **C**12 **O**nly

- In the COSMIC-Trial, local relapse was predominantly in field (79%)
- Can dose escalation in the target volume via C12-only treatment reduce local relapse rate?

**ACC of H&N**
Inoperabel / R1 / R2

| C12 + IMRT | C12 Only |
|---|---|
| BP: 8 x 3 GyE C12<br>PP: 25 x 2 Gy IMRT | BP: 5 x 3 GyE C12<br>PP: 17 x 3 GyE C12 |



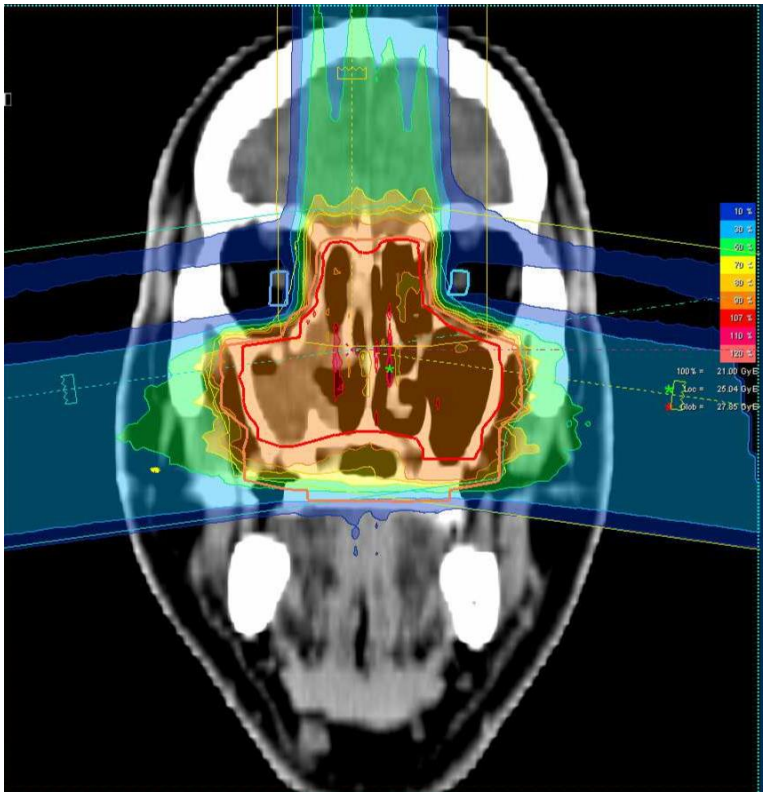
# IMRT-HIT-SNT-Trial

**Phase II trial**, initiated 2011

- **36 patients** with SCC/Adeno-CA of nasal cavity/paranasal sinus
- Background: IMRT reduced toxicity but did not enhance LC, often in-field relapse
- Last patient enrolled 08/2019

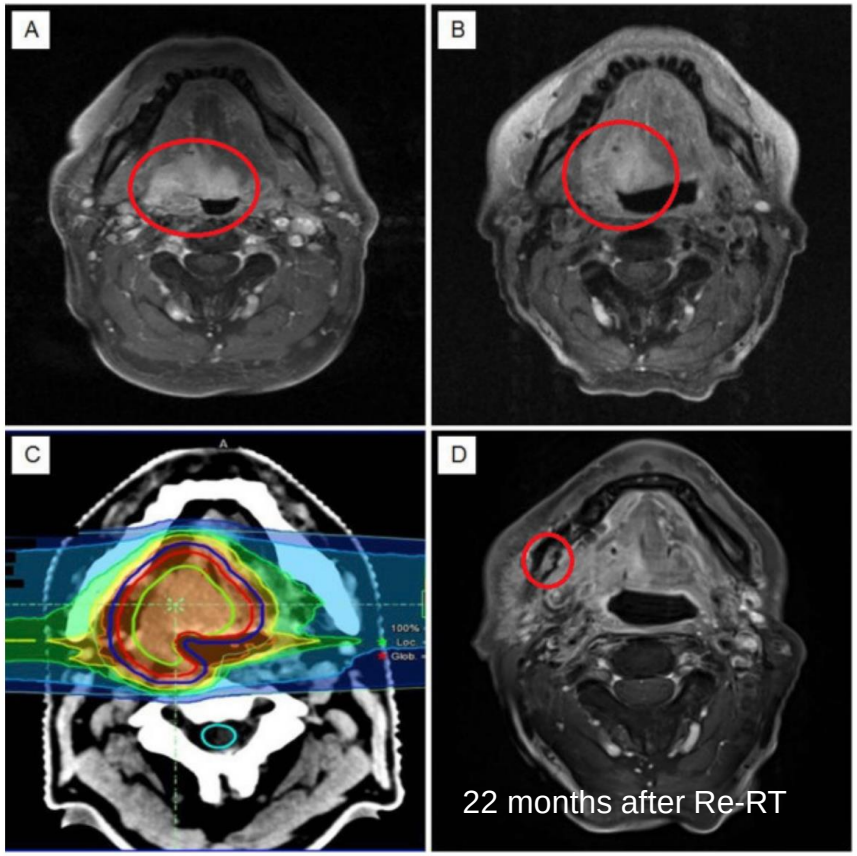
**IMRT + C12-boost**

- IMRT: PT + locoregional LN stations
- C12: PT
- Dose: **IMRT: 50 Gy in 25 fx**
  **C12: 24 GyE in 8 fx**



# Re-Radiotherapy in the head & neck region

- **229 patients** with recurrent HNC received **C12 Re-RT** between 2010 and 2017
- **51 GyE in 17 x 3 GyE**




- Median local PFS: 24,2 months
- Unexpected late toxicity ≥°3: 11,3 %
- Compared to 30% - 40% after photon Re-RT
  *(Takiar et al., Int J Radiat Oncol Biol Phys, 95 (2016))*

Int J Radiat Oncol Biol Phys. 2019 Jul 23. pii: S0360-3016(19)33504-7. doi: 10.1016/j.ijrobp.2019.07.021. [Epub ahead of print]

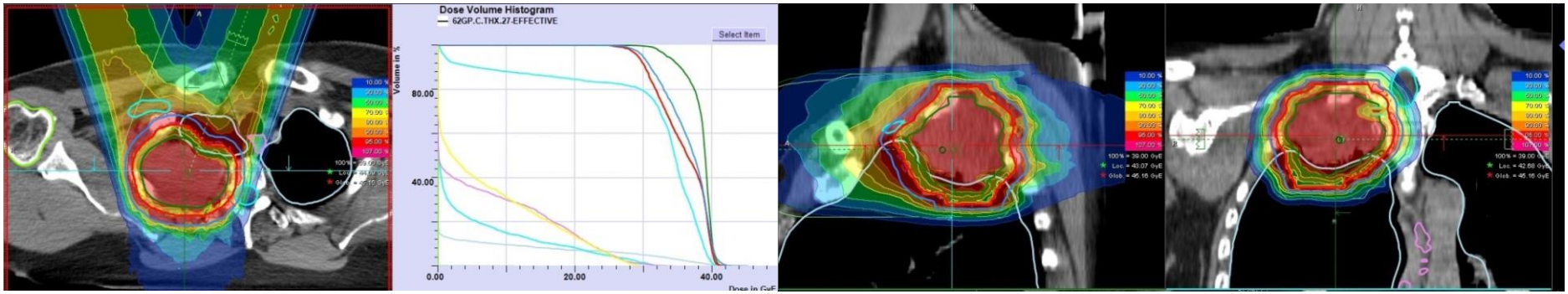
**Carbon Ion Reirradiation for Recurrent Head and Neck Cancer: A Single-Institutional Experience.**

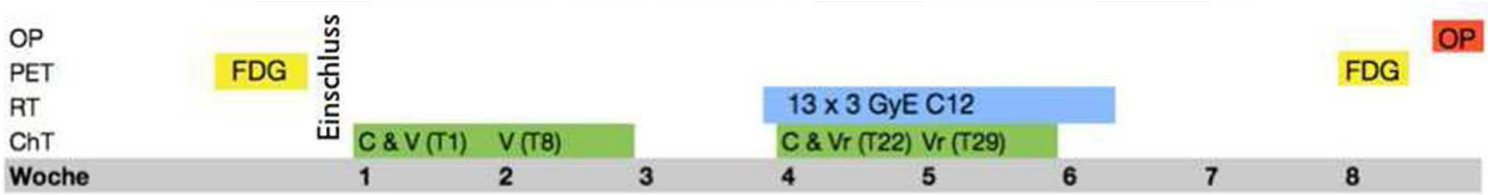
Held T[1], Windisch P[1], Akbaba S[1], Lang K[1], El Shafie R[1], Bernhardt D[1], Plinkert P[2], Kargus S[3], Rieken S[4], Herfarth K[4], Debus J[4], Adeberg S[5].

# INKA-Trial

**Prospective pilot-study** to determine the safety and feasibility of C12 RT in patients with Pancoast-tumors within a trimodal treatment concept

- 11/15 patients recruited
- Excellent metabolic & histopathological response
- No ≥ CTC°3 toxicity

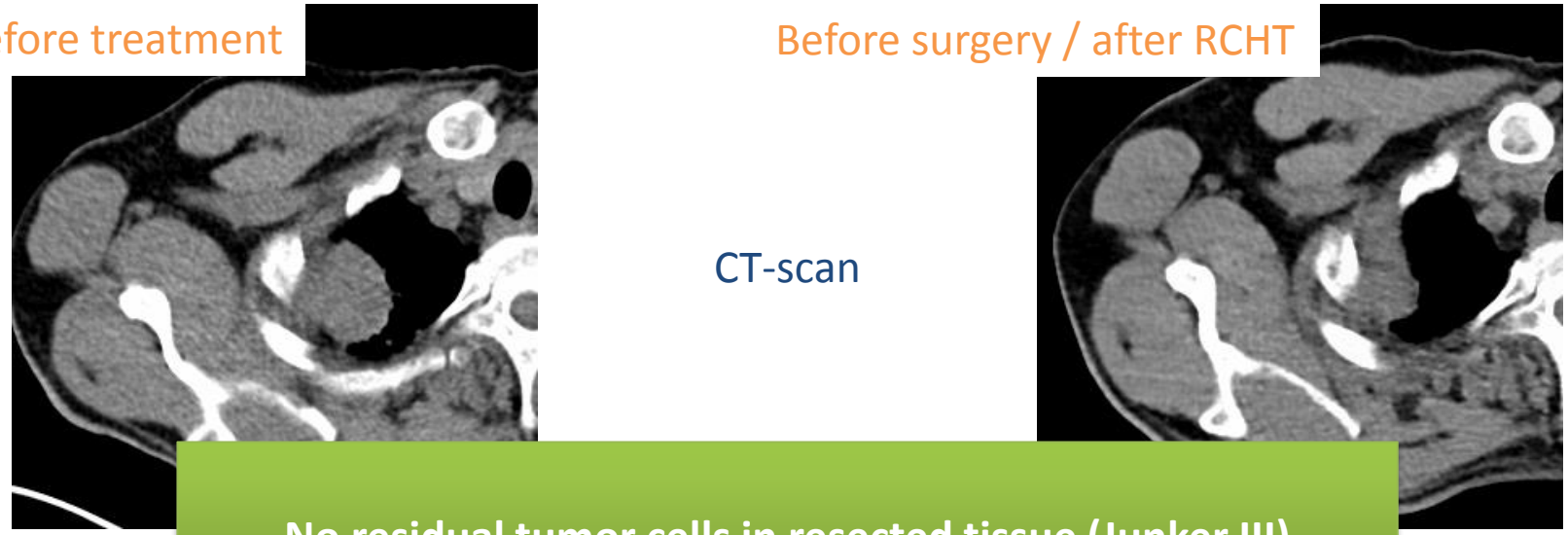


# INKA-Trial

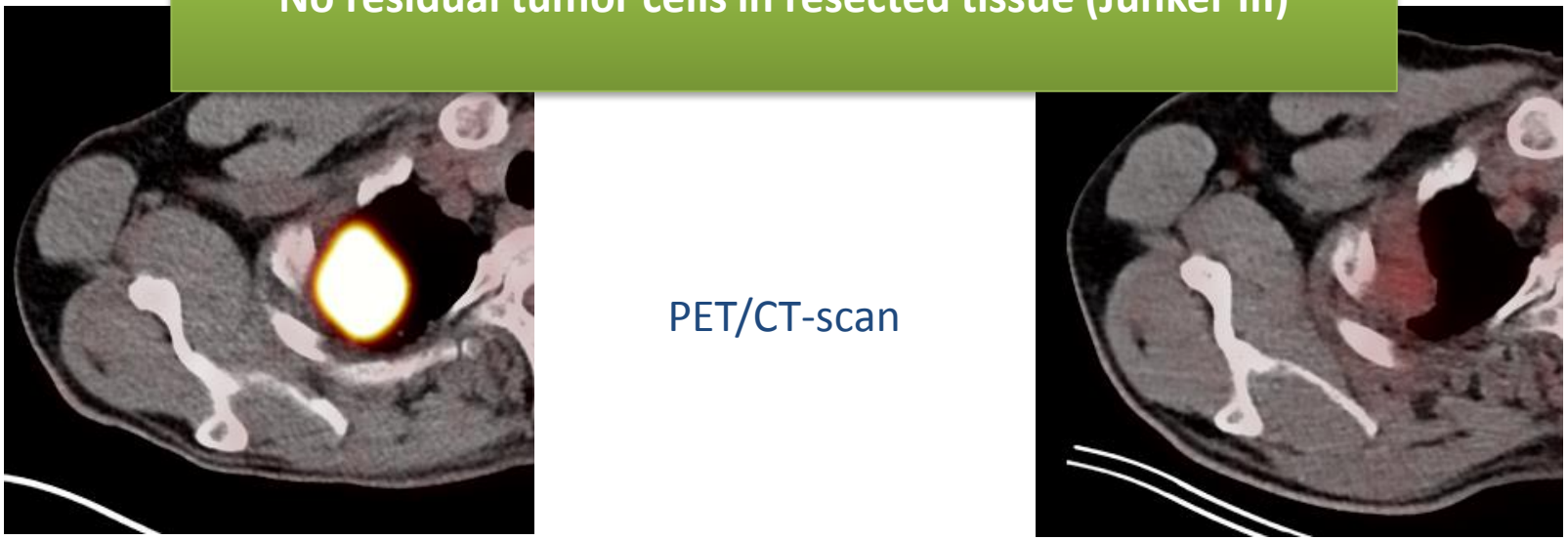
Before treatment

Before surgery / after RCHT



CT-scan

**No residual tumor cells in resected tissue (Junker III)**



PET/CT-scan

# Skull base Chondrosarcoma

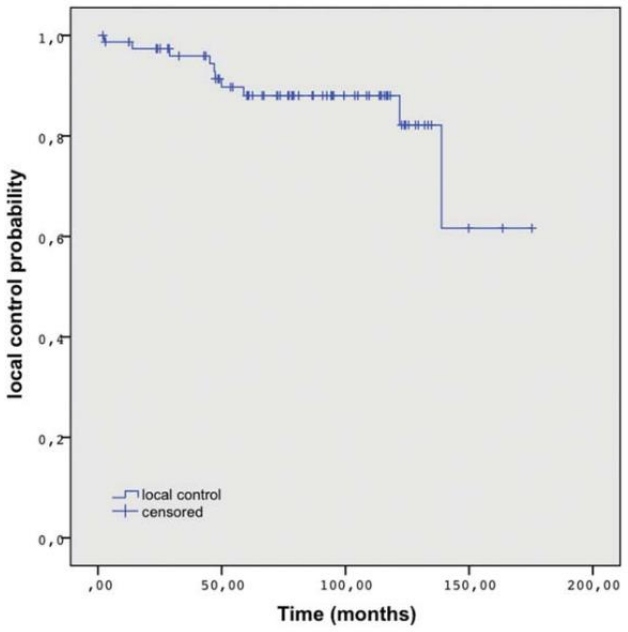
- Rare bone tumors, 5-12 % are localized at the skull base
- **Resection is often incomplete due to localisation**
- G1-G2 tumors are relatively radioresistent, rarely metastatic disease
- Symptoms: cranial nerve deficits (most commonly double vision)

Cancer. 2014 May 15;120(10):1579-85. doi: 10.1002/cncr.28606. Epub 2014 Feb 5.

**High control rate in patients with chondrosarcoma of the skull base after carbon ion therapy: first report of long-term results.**

Uhl M[1], Mattke M, Welzel T, Oelmann J, Habl G, Jensen AD, Ellerbrock M, Haberer T, Herfarth KK, Debus

- 79 pat. after biopsy/ incomplete resection (R2)
- Median follow-up 91 months
- C12 treatment @ GSI 60 GyE in 3 GyE/fx
- 10 yrs LC: 88 %
- 10 yrs LC (<45 J): 98%



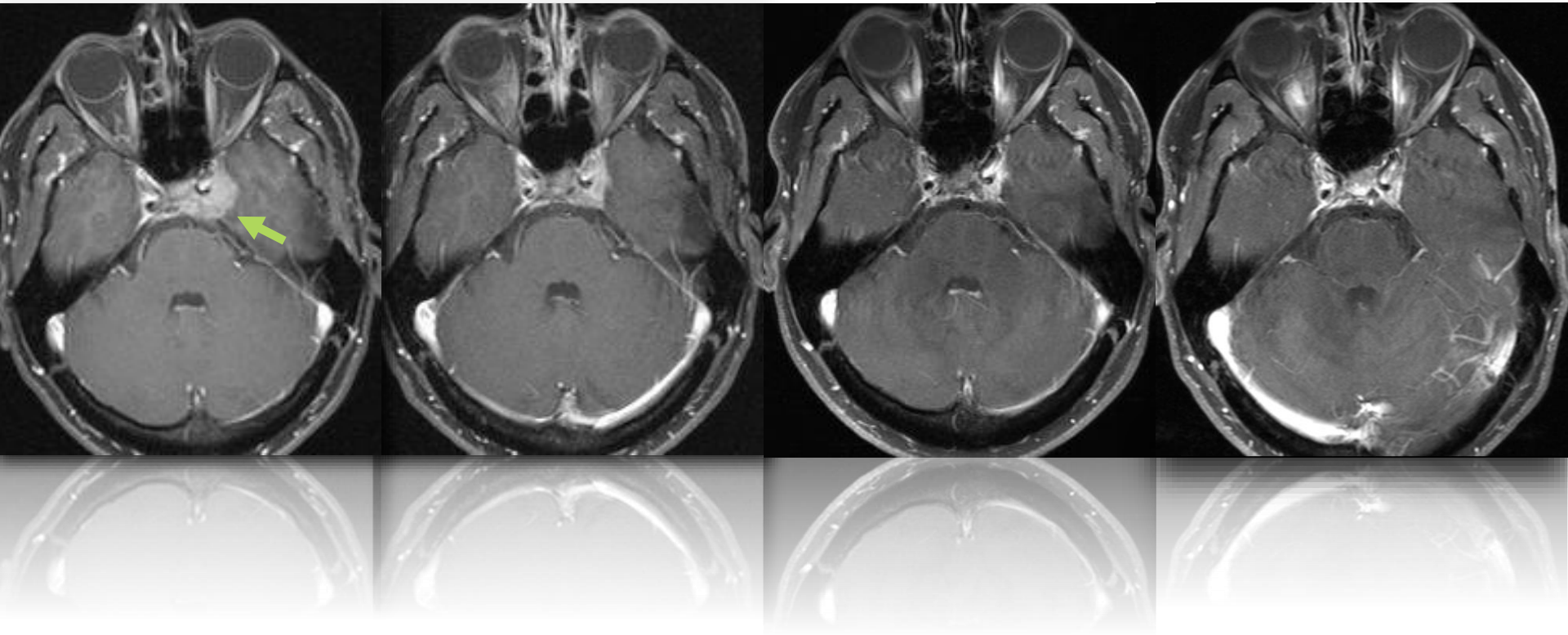
# 18y old patient with petroclival chondrosarcoma

before RT

6 weeks after RT

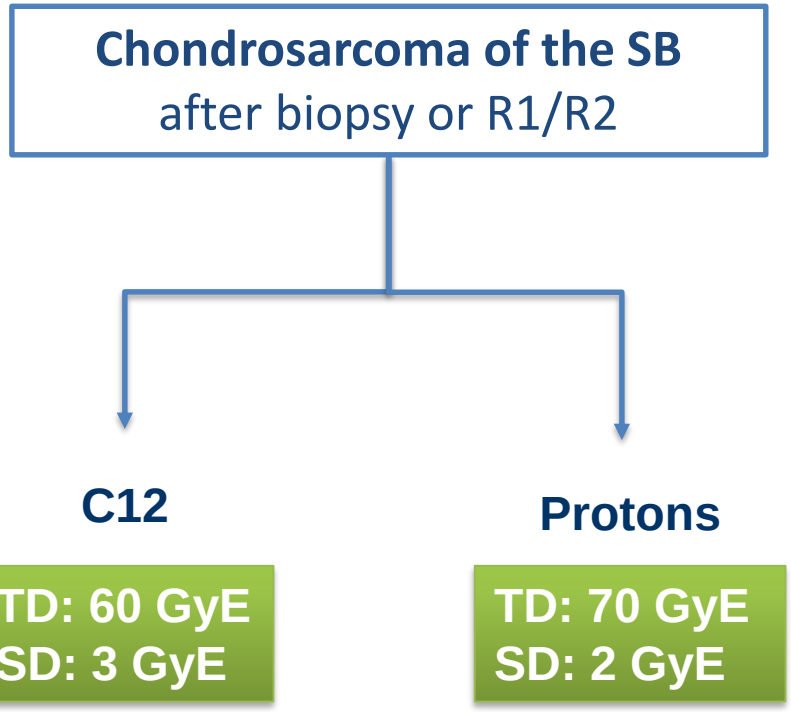
# Skull base Chondrosarcoma

2005 2007 2011 2015



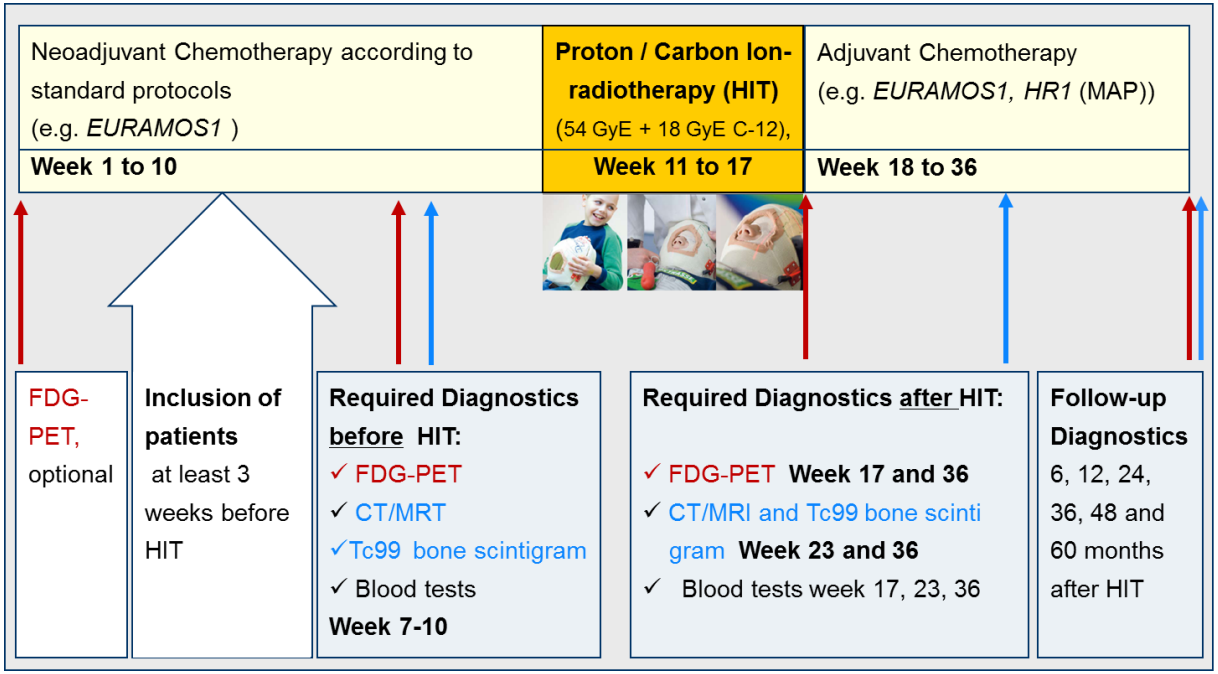
# HIT Trial for SB chondrosarcoma

- Prospective **randomized phase III trial**
- Non inferior trial: 5y-LPFS by using C12 equal to H+ with less toxicity?
- Started in 2010, in 08/2019: **82/154 recruited**

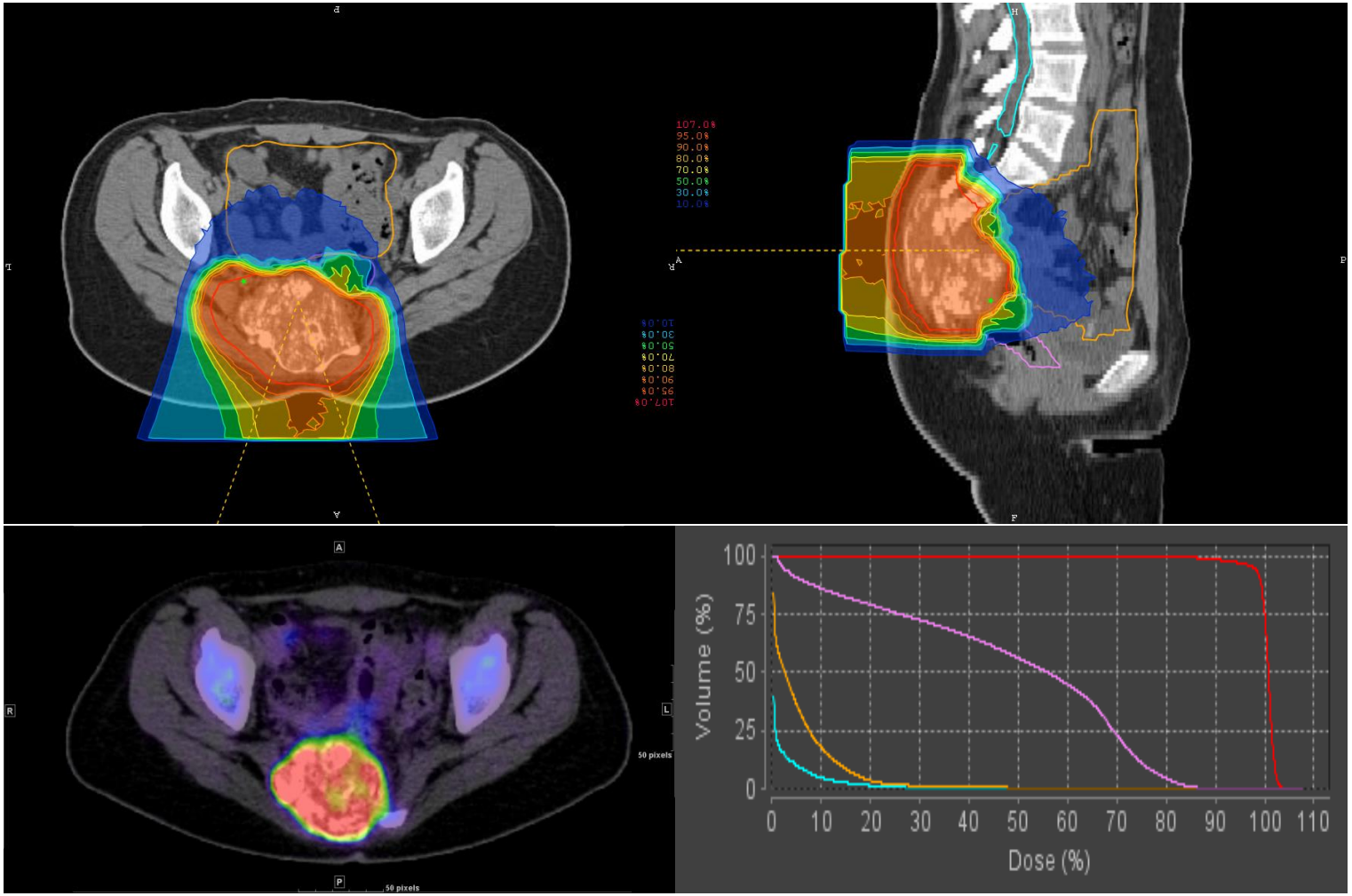


# OSCAR – Osteosarcoma trial

- **OS**teosarcoma – **CA**rbon Ion **R**adiotherapy
- **Phase I/II therapy trial** to determine the safety and efficacy of combined ion RT in patients (>6y) with inoperable osteosarcoma
- Secondary endpoints: local control disease-free and progression-free survival, Overall survival, role of **FDG-PET** in response monitoring
- **20/20 patients recruited**, data is being analysed

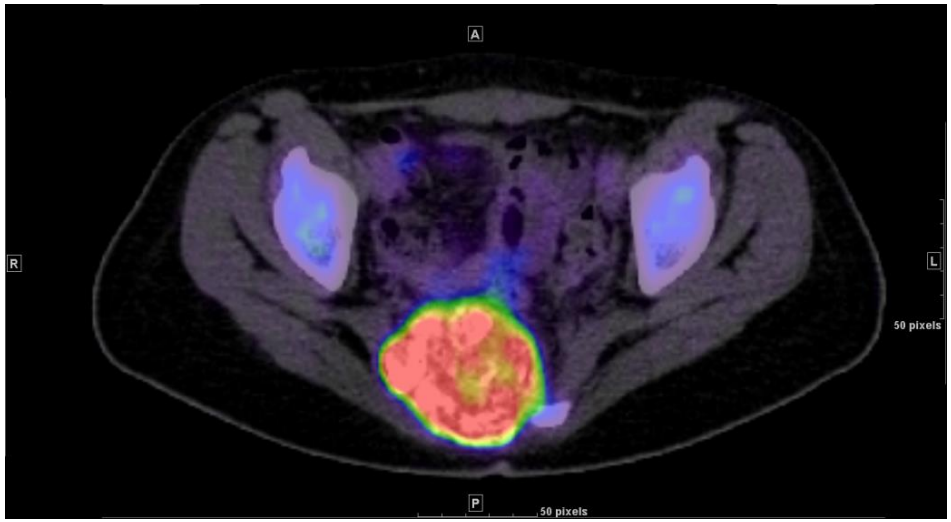


# 17 y/o female patient with osteosarcoma

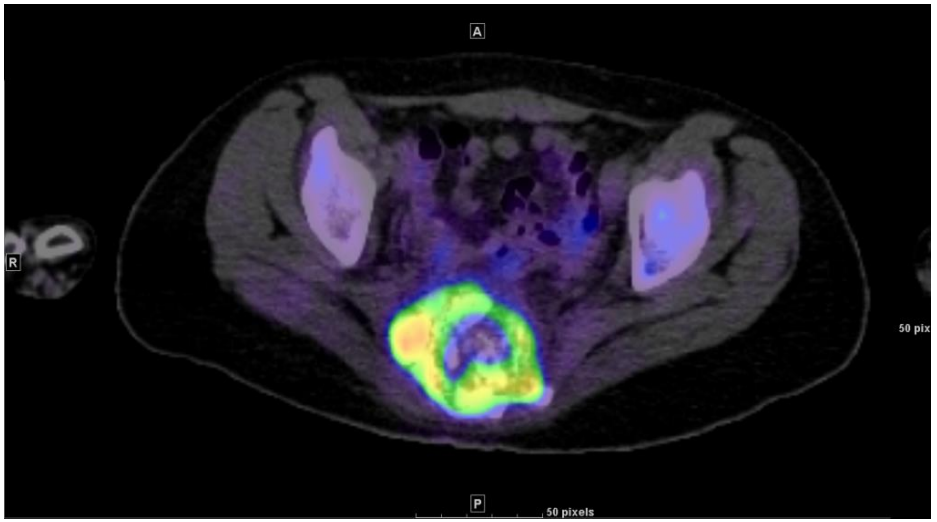


# 17 y/o female patient with osteosarcoma

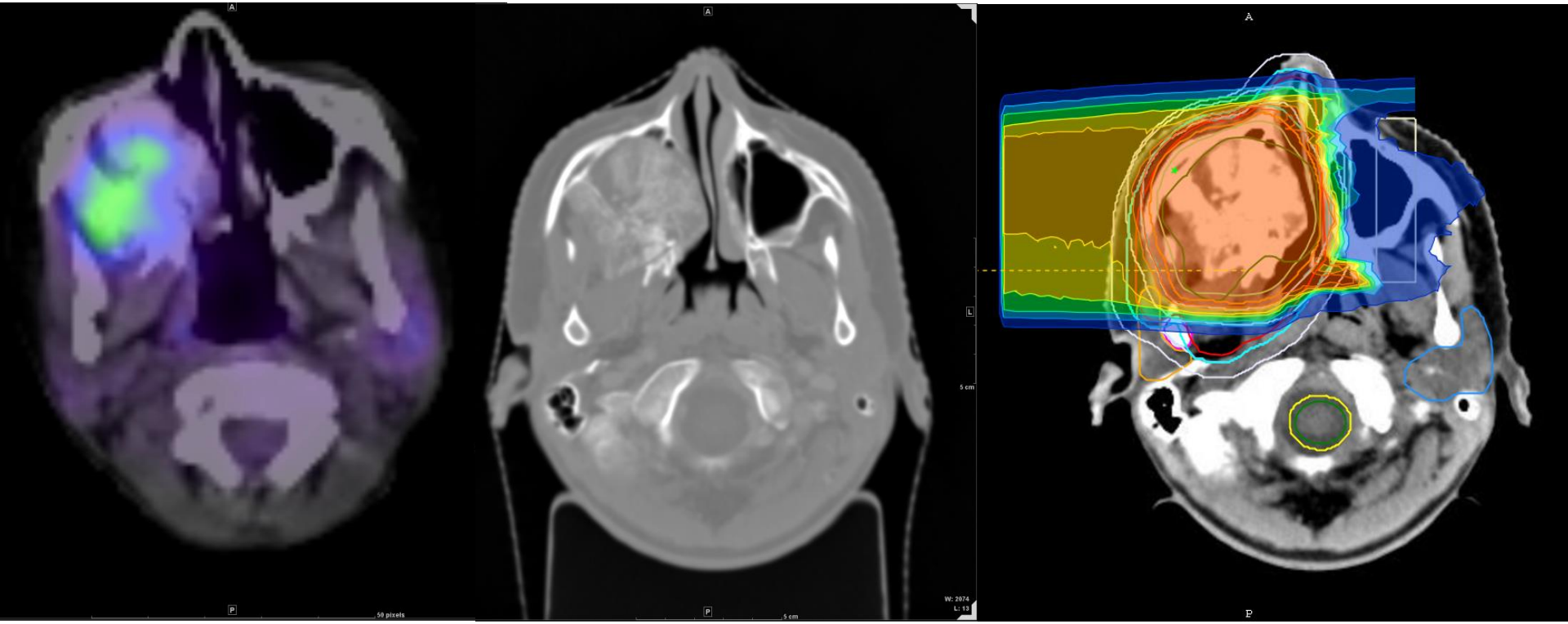
FDG PET before treatment



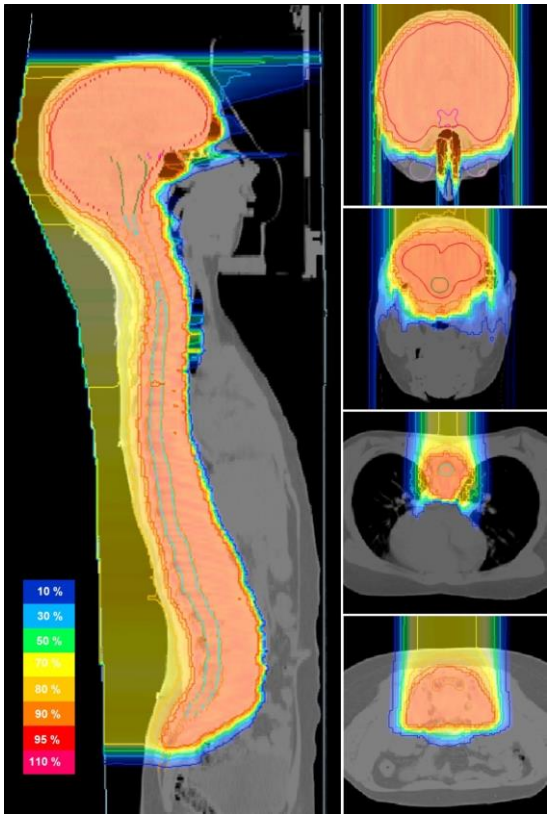

FDG PET at first follow up, 2 months after radiotherapy



# 13 y/o male patient with osteosarcoma

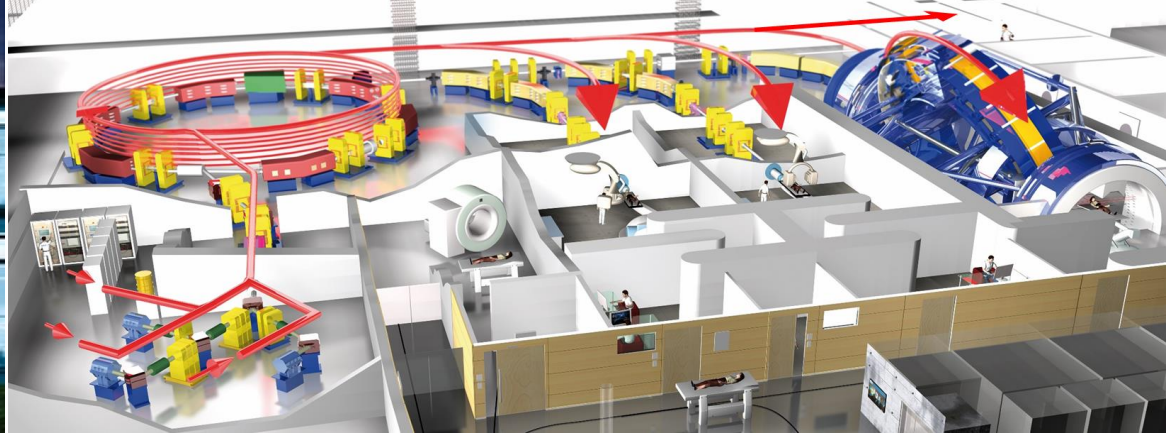


# Pediatric and young patients





- Reduced integral dose to non target regions
- Dose escalation at the target volume
- Reduced risk of secondary malignancies / late side effects



HIRO
Heidelberger Institut
für Radioonkologie

# Thank you very much!

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