



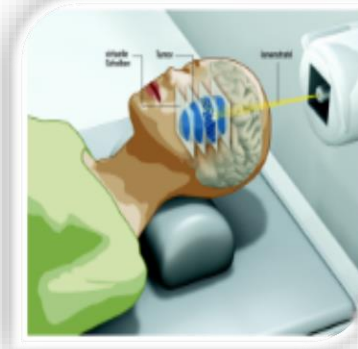
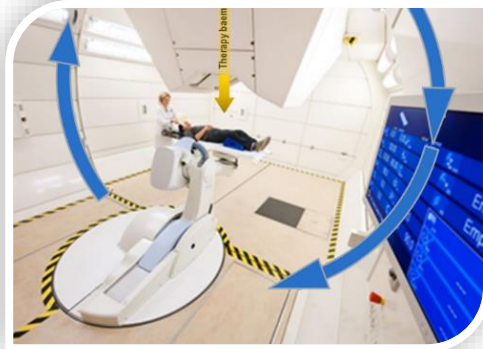
HEIDELBERG
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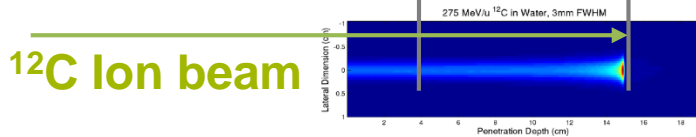
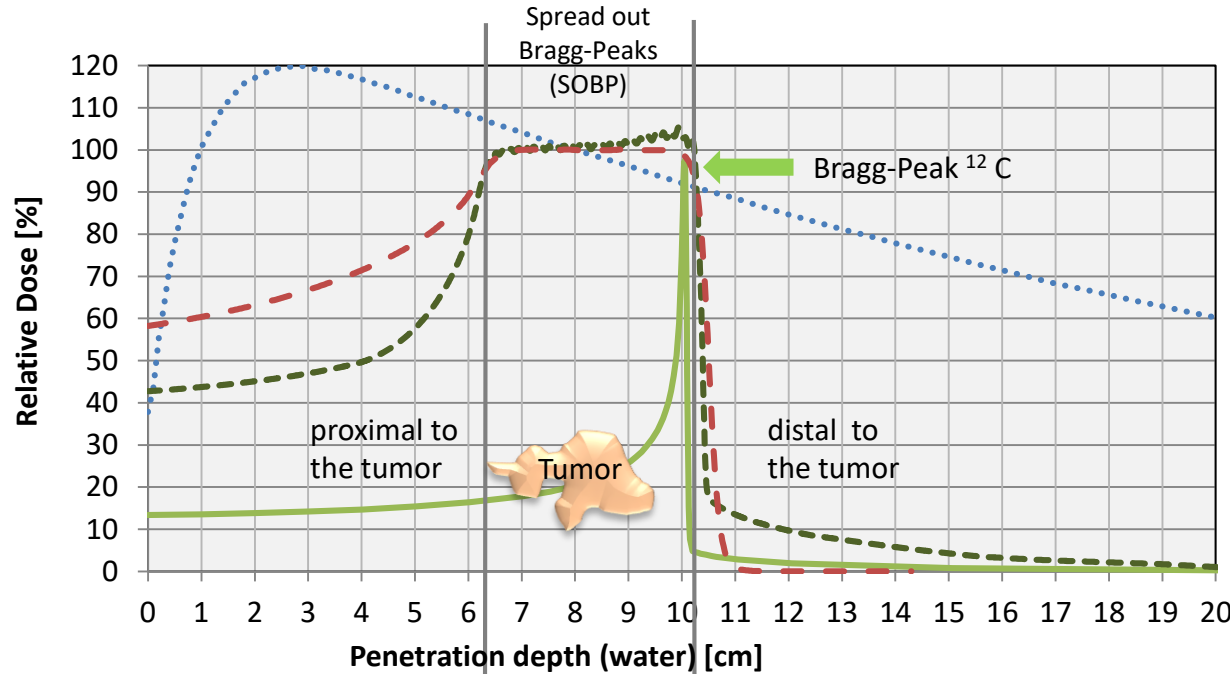
Ion-Beam Therapy at HIT: Options for Multi-Ion Treatment and Research

Riga-Workshop, 28.06.2023

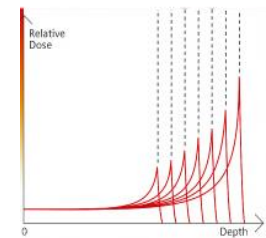
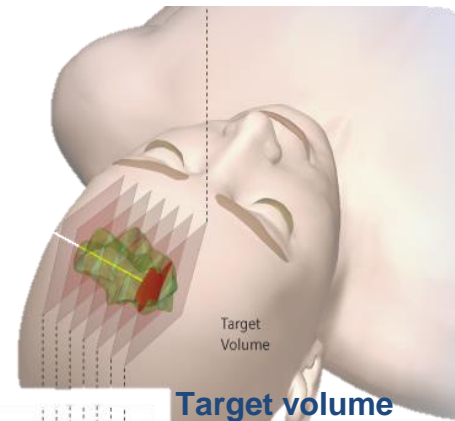
Thomas Haberer, CTO HIT



Rationale for charged particle therapy



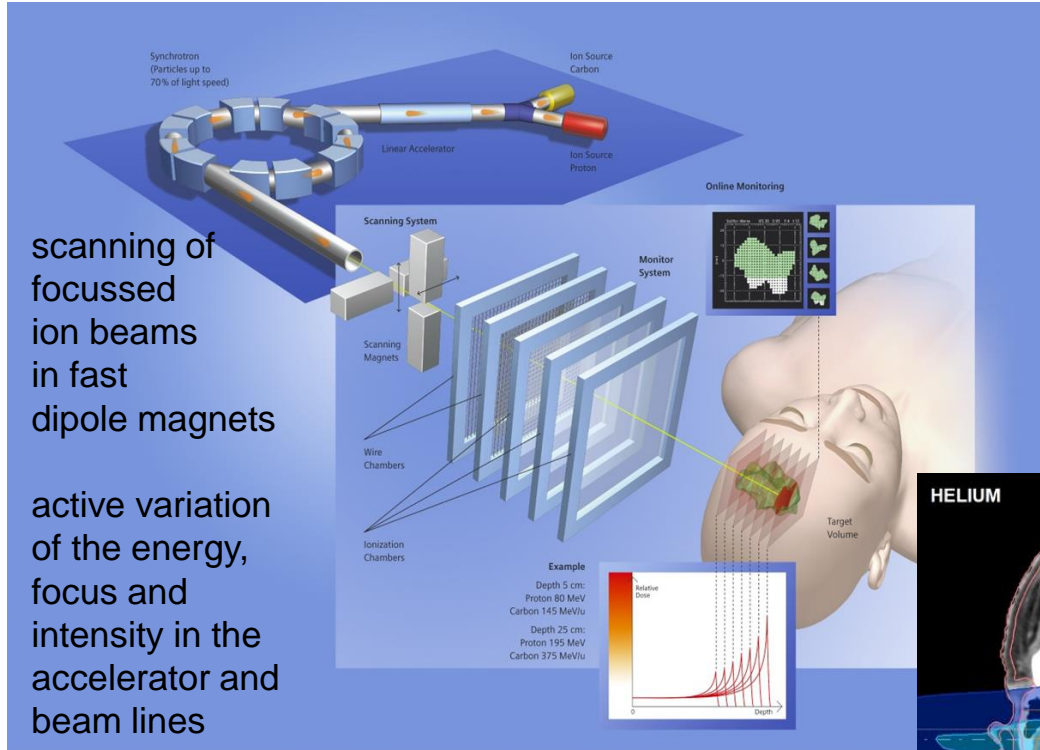
- Sparing of healthy tissue by
- reducing doses (due to steep dose gradient → lower NTCP)
 - reducing irradiated volume → lower risk of secondary cancer



Target volume coverage by active variation of

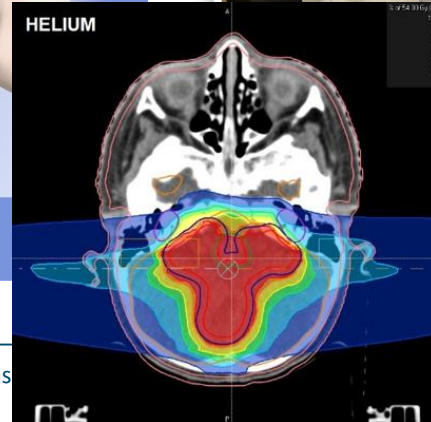
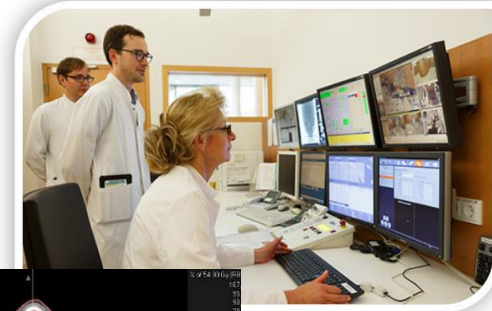
- * beam energy
- * focus
- * intensity

Rasterscanning Dose Delivery



scanning of focussed ion beams in fast dipole magnets

active variation of the energy, focus and intensity in the accelerator and beam lines

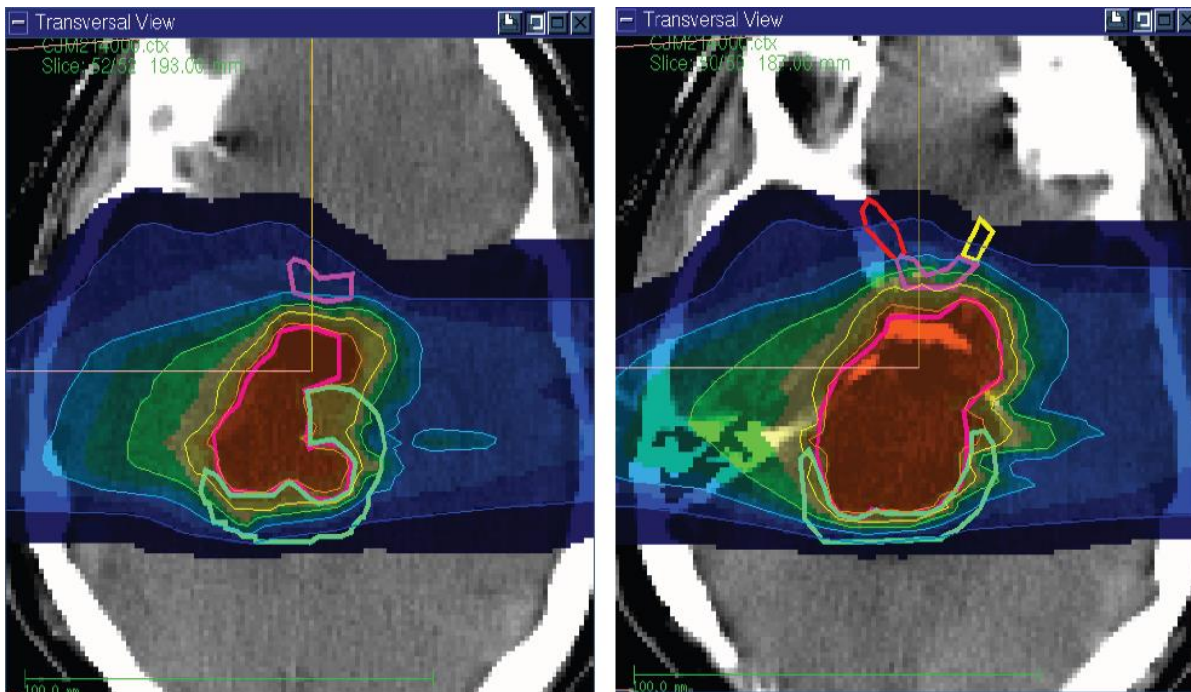


Haberer, HIT: Multi-Ion Treatment and Research Options

Haberer et al., NIM A, 1993



Dose Conformation via Rasterscanning e.g. Skull Base Chordomas



Excellent sparing of normal tissue and organs at risk

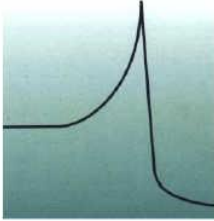
GSI, 1997 – 2008, 440 Patienten, C12



1stRx@GSI: 13.December 1997

Design Phase

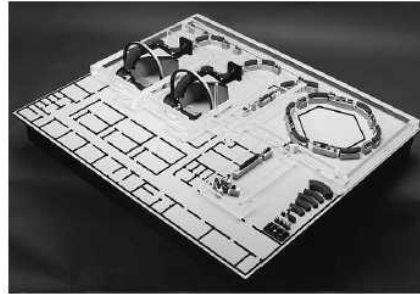
Proposal for a dedicated
ion beam facility for
cancer therapy



Proposal 1998

HICAT-the **Heavy Ion Cancer Therapy** accelerator
facility for the clinic in Heidelberg

Technical Description



Technical Design 2000

HICAT-**Heavy Ion Cancer Therapy** accelerator facility
(Die Schwerionen-Therapieanlage für das Klinikum Heidelberg)

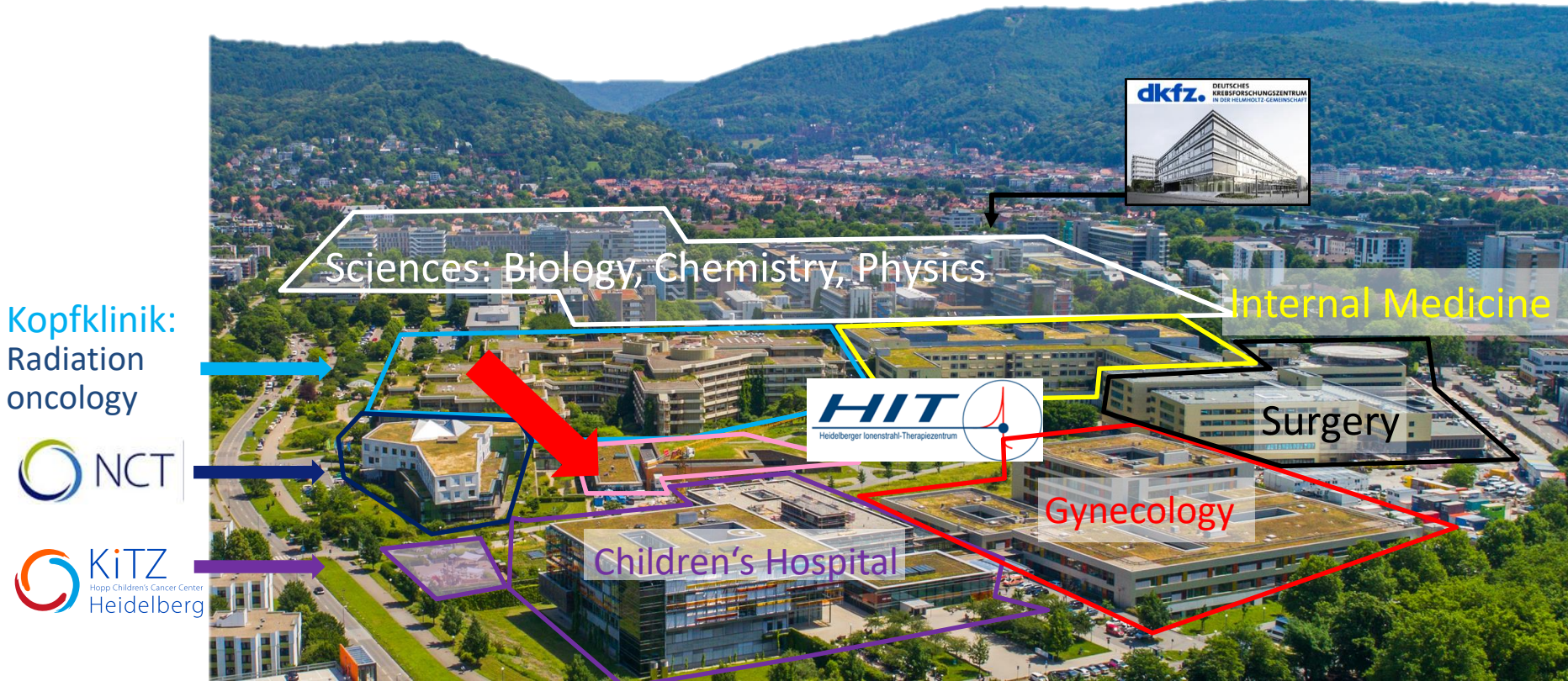
Machbarkeits-Studie



Feasibility Study 2000

Heidelberg - Campus Neuenheimer Feld

- ✓ Radiation-Oncology and HIT is integrated in the clinic ring
- ✓ Translational and academic research are in close neighbourhood



Department Radiation Oncology



Radiotherapy Equipment

- 5 Linear accelerators (Elekta) at Kopfklinik
- 1 TomoTherapy
- 1 Ethos (Varian) at DKFZ
- 1 MR-Linac (MRIDian)
- 1 CyberKnife
- 1 Brachytherapy unit
- 1 Intraoperative radiotherapy (IOERT) unit
- Ion beam therapy at HIT with 3 treatment places

Structure of the Clinic

- ~4500 patients per year
- Ward with 62 beds for in-patients
- Out-patients at NCT
- 27 Tumor conferences
- 14 Specialized consultations



Diagnostic Equipment:

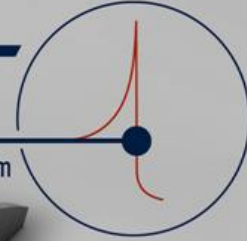
- 2 CT
- 2 MRI
- 1 PET /CT
- Sonography



Coverage of the complete spectrum of radiation therapy treatments
Expansion of therapy options through participation in clinical studies

HIT

Heidelberger Ionenstrahl-Therapiezentrum



Ion sources clinical:

- Proton
- Carbon
- Helium

Experimental-only:

- Oxygen

Synchrotron

experimental beam line

2 horizontal beam treatment rooms

1

In room CT



2

MR (shuttle)



3

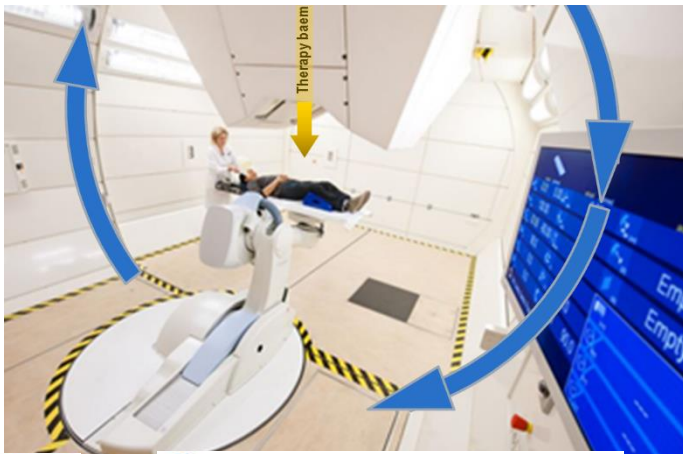
online MRT



Treatment room with ion-gantry:

- 360° rotatable
- 670 t weight

HIT-Accelerator, Beam Delivery and Gantry

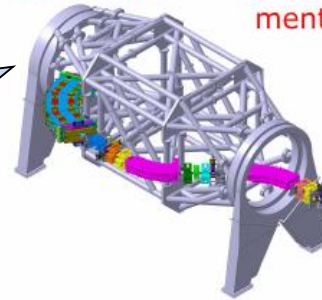


Ion Gantry

2 Horizontal treatment rooms

48 - 430 MeV/u Synchrotron

High energy beam transport

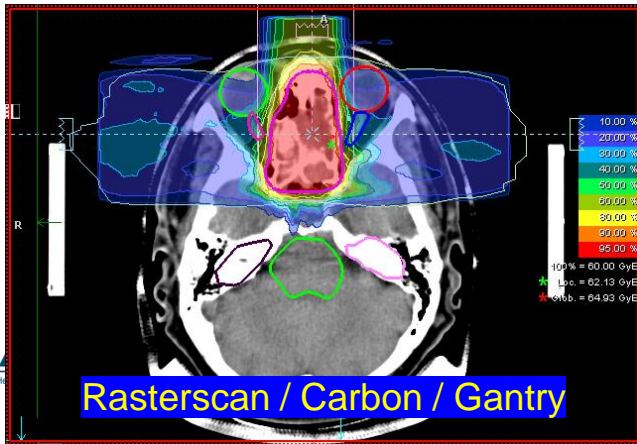
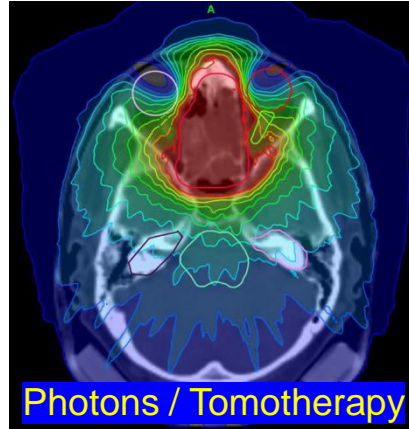


Experimental area

Scanning ion gantry:

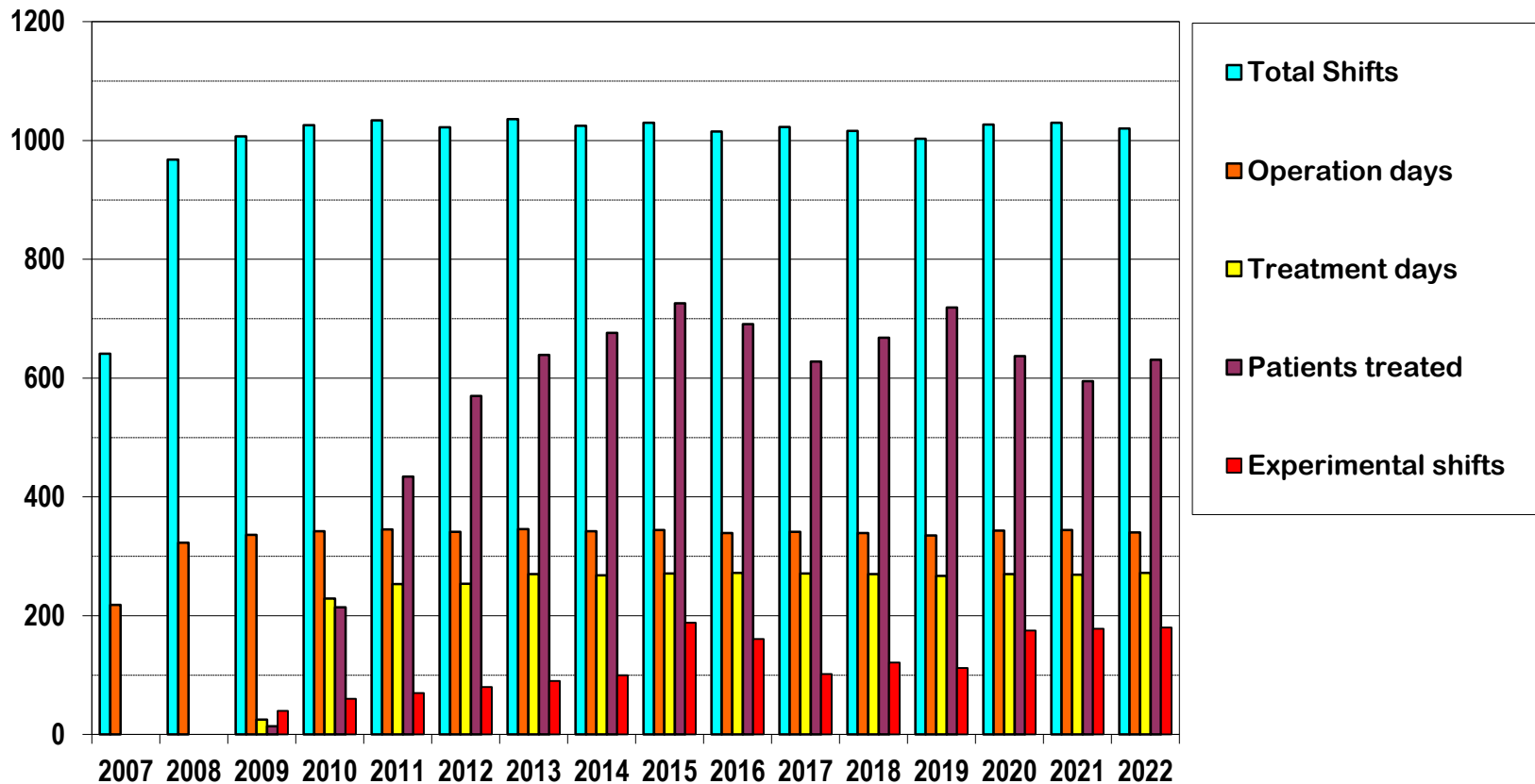
- isocentric barrel-type
- world-wide first ion gantry
- 2D beam scanning upstream to final bending, minimum divergence due to edge focussing
- $\pm 180^\circ$ rotation, $3^\circ / \text{second}$
- 13m diameter
25m length
600 to rotating
(145 to magnets)

Scanning Ion Gantry @ HIT



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

1st Rx: Oct 19th, 2012, oligo-astrocytoma



2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022
 8000+ patients treated 50 – 70 daily proton / carbon = 1 / 1 ~45% @ gantry
 28.6 million synchrotron cycles Year 370.000 gantry rotations availability > 97%
 39.000 hrs patient treatment 19.000 hrs research and development only 8 days lost since 2009

Clinical trials at HIT, recently finished

Over 7000 patients were treated with protons or carbon ions since 2009

| Area | Name | Entity | Phase | Beam modality | Status |
|-------------|------------|--------------------------------|-------|------------------------|-----------|
| Sarkoma | OSCAR | Osteosarkoma | II | Protons and C12 | submitted |
| CNS | CINDERELLA | Glioblastoma (recurrent) | II | C12 | analysis |
| | CLEOPATRA | Glioblastoma | II | Boost: Protons vs. C12 | analysis |
| Head & Neck | TPF-C_HIT | HNSCC of Larynx | II | C12 Boost | analysis |
| | COSMIC | Adenoid cystic carcinoma | II | C12 Boost | published |
| | ACCEPT | Adenoid cystic carcinoma | II | C12 Boost | published |
| Prostate | KOLOG | Prostate carcinoma (recurrent) | II | C12 | analysis |
| | PROLOG | Prostate carcinoma (recurrent) | II | Protons | analysis |
| | IPI | Prostate carcinoma | II | Protons vs. C12 | published |
| GI | PANDORA | rectal carcinoma (recurrent) | II | C12 | closed |



Clinical trials at HIT

| Area | Name | Entity | Phase | Beam modality | Status |
|---------------------------|-------------------|---|-------|------------------------|------------|
| Chordoma & Chondrosarcoma | ISAC | sacral chordoma | II | Protons vs. C12 | recruiting |
| | HIT Chordom | skull base chordoma | III | Protons vs. C12 | recruiting |
| | HIT Chondrosarkom | skull base chondrosarcoma | III | Protons vs. C12 | recruiting |
| | RETRO-ION | Sarcom of posterior abdominal wall | II | C12 | recruiting |
| CNS | MARCIE | Atypical meningioma | II | C12 Boost | recruiting |
| | GRIPS | Glioma (high-grade) | III | Protons vs. IMRT | recruiting |
| H&N | ACCO | Adenoid cystic carcinoma (H&N) | II | C12 vs. IMRT+C12 Boost | recruiting |
| | IMRT HIT-SNT | HNSCC of sinus | II | C12 Boost | recruiting |
| | CARE | Re-irradiation for recurrent or progressive locally advanced head and neck tumors | II | C12 | recruiting |
| Lung | INKA | Pancoast tumor of the lung | II | C12 | recruiting |
| GI | PROMETHEUS | Hepatocellular carcinoma | II | C12 | recruiting |
| | PACK | pankreas carcinoma | II | C12 | recruiting |
| Prostate | PAROS | Prostate carcinoma (recurrent) | III | IMRT vs. Protons | recruiting |



Salivary gland tumours / 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**



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

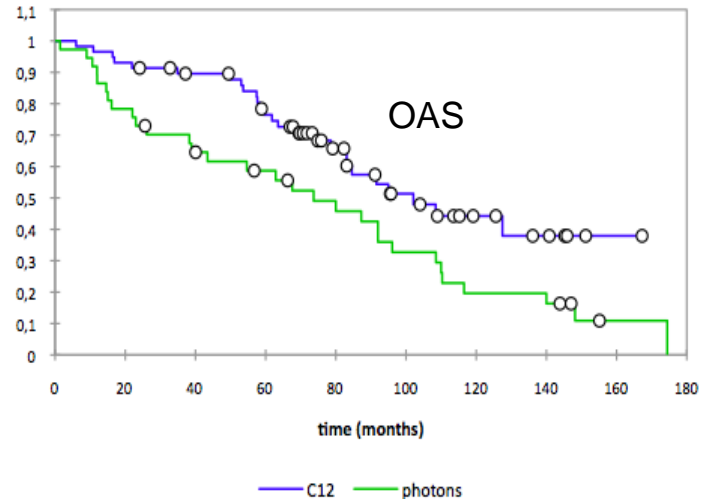
Alexandra D. Jensen MD, MSc , Anna V. Nikoghosyan MD, Melanie Poulakis DDS, Angelika Höss MSc, Thomas Haberer PhD, Oliver Jäkel PhD, Marc W Mürter MD, Daniela Schulz-Ertner MD, Peter E. Huber MD, PhD, Jürgen Debus MD, PhD

First published: 4 June 2015 [Full publication history](#)

DOI: 10.1002/cncr.29443 [View/save citation](#)

Cited by: 0 articles [Check for new citations](#)

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

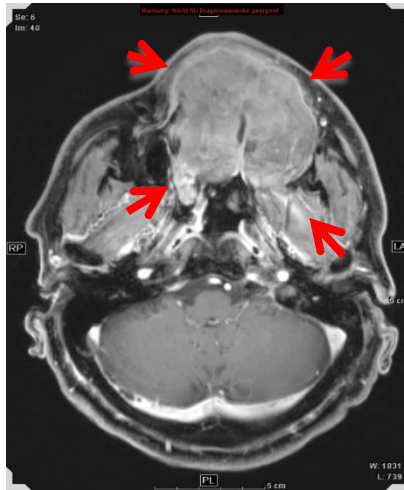


COSMIC-Trial

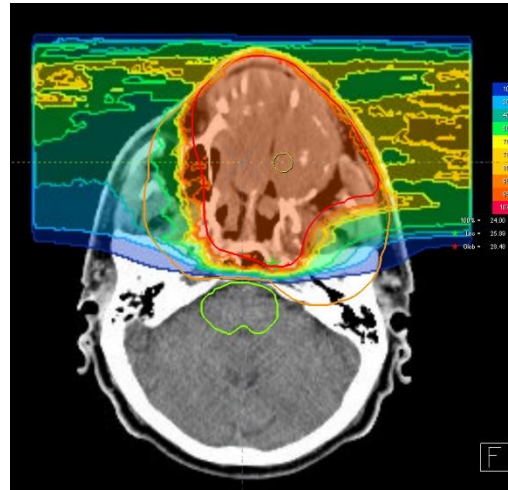
COmbined therapy of malignant **Salivary gland tuM**ors with **IMRT** and **Carbon ions**

- 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%

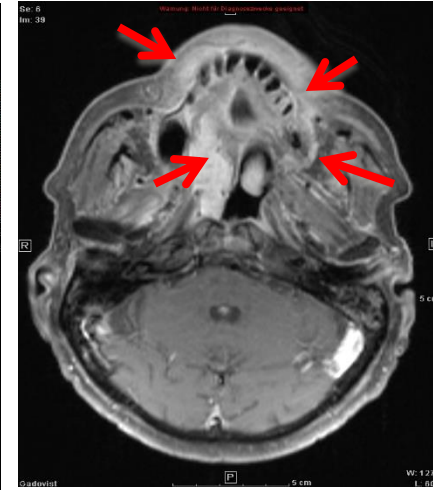
LC after 3 years: 82 %



Pre-treatment situation



Treatment planning
C-12 boost



6 weeks post RT

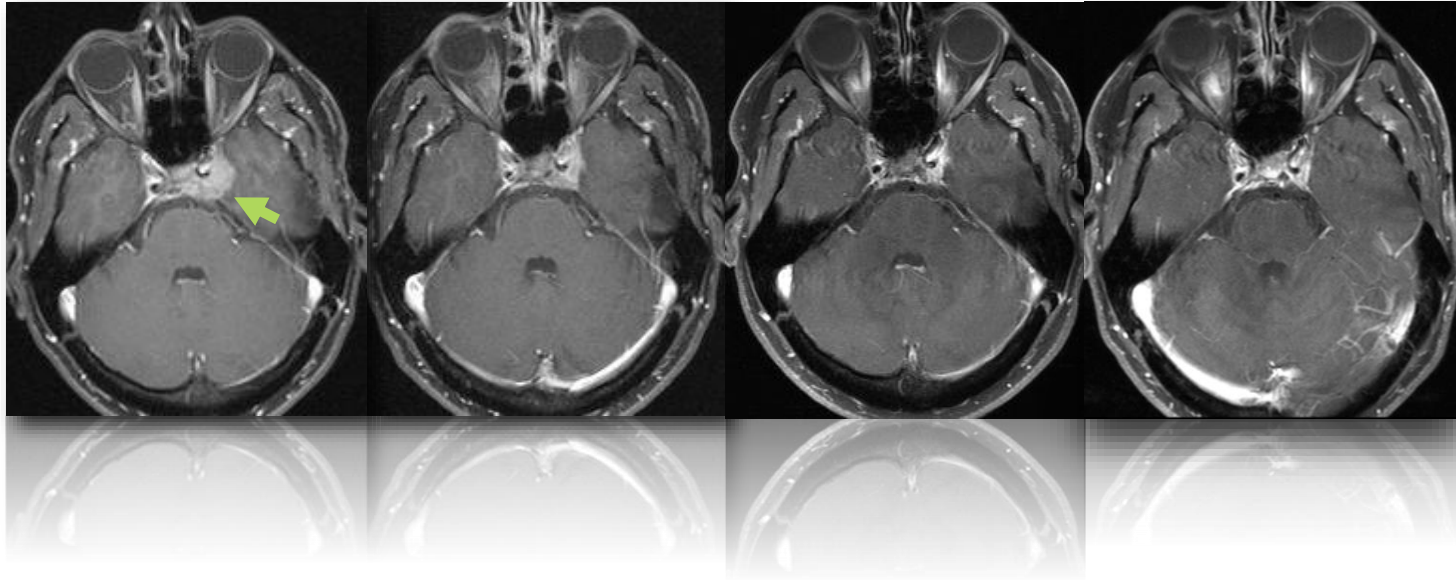
Skull Base Chondrosarcoma Long-term Follow-up

2005

2007

2011

2015



Skull Base Chondrosarcoma

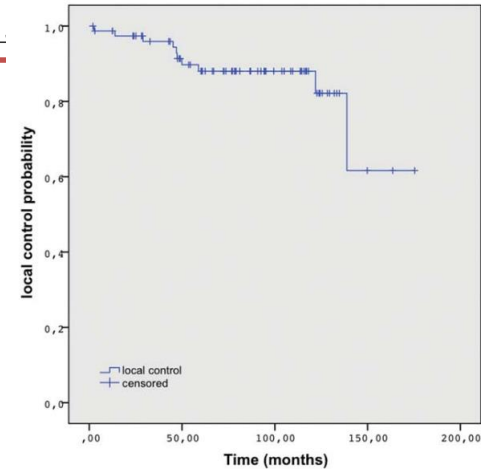
- Rare bone tumors, 5-12 % are localized at the skull base
- **Resection is often incomplete due to localisation**
- G1-G2 tumors are relatively radioresistant, rarely metastatic disease
- Symptoms: cranial nerve deficits (most commonly double vision)

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 M¹, Mattke M, Weizel 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%

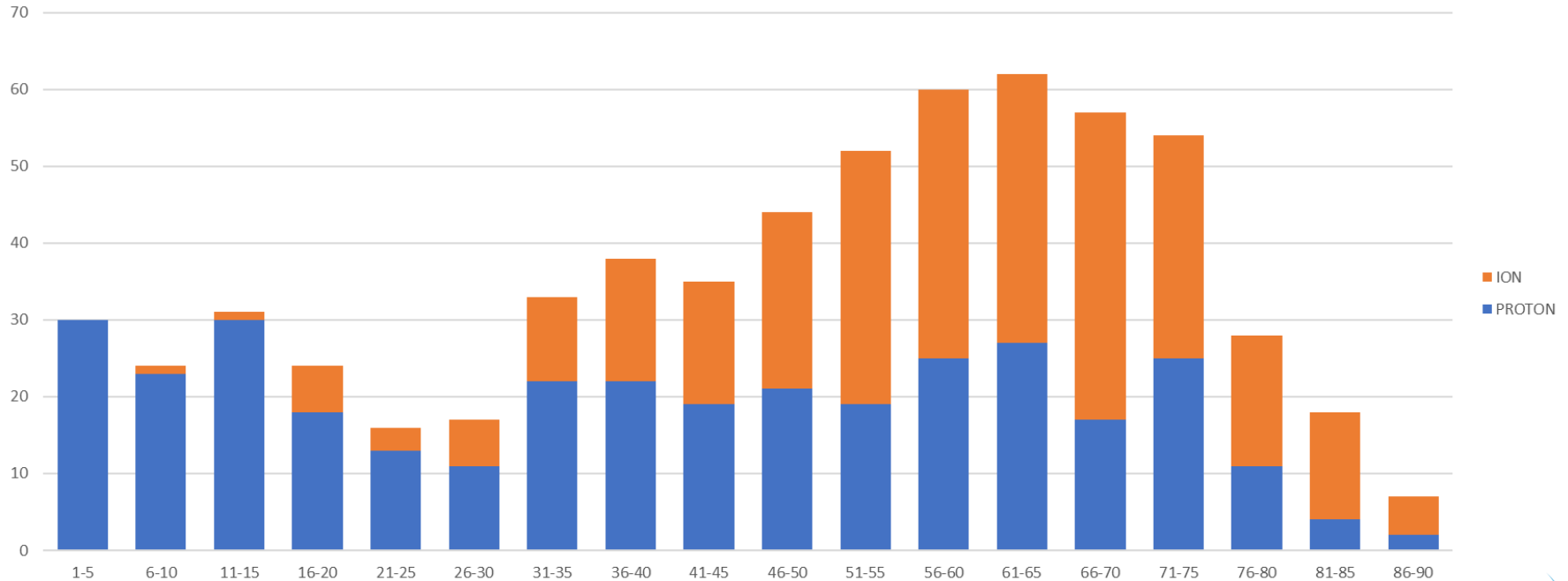


HIT's Weekly Schedule

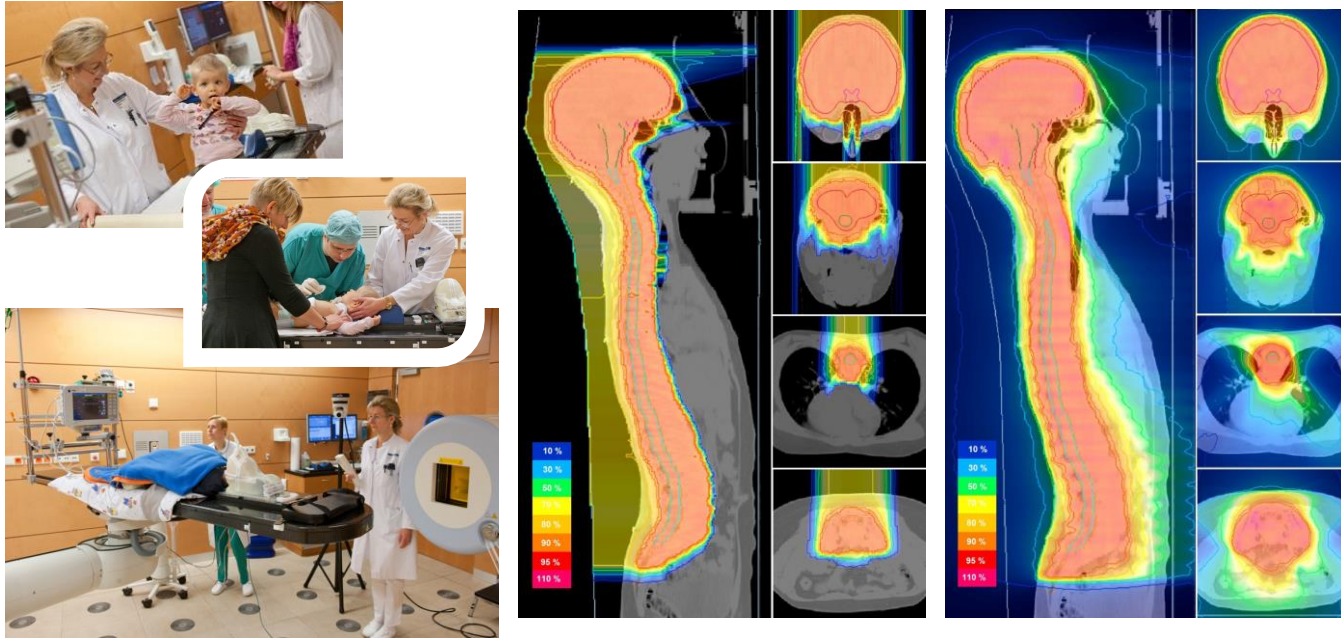
| | | Experiments | | | | | QA | | Patient Treatment | | | | | | | | | | QA | | | | | | | | |
|------------|------------|-------------|------|------|------|------|------|------|-------------------|------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------------|----------------------------|-------|-------|-------|-------|-------|------|-----|
| | | 0:00 | 1:00 | 2:00 | 3:00 | 4:00 | 5:00 | 6:00 | 7:00 | 8:00 | 9:00 | 10:00 | 11:00 | 12:00 | 13:00 | 14:00 | 15:00 | 16:00 | 17:00 | 18:00 | 19:00 | 20:00 | 21:00 | 22:00 | 23:00 | 0:00 | |
| | | 1:00 | 2:00 | 3:00 | 4:00 | 5:00 | 6:00 | 7:00 | 8:00 | 9:00 | 10:00 | 11:00 | 12:00 | 13:00 | 14:00 | 15:00 | 16:00 | 17:00 | 18:00 | 19:00 | 20:00 | 21:00 | 22:00 | 23:00 | 0:00 | | |
| Montag | 25.09.2017 | H1 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | |
| | H2 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | Ga | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dienstag | 26.09.2017 | H1 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | |
| | H2 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | Ga | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | Exp |
| Mittwoch | 27.09.2017 | H1 | | | | | | C,H | QA | | | | | | | | | | | | | | | | | | |
| | H2 | | | | | | C,H | QA | | | | | | | | | | | | | | | | | | | |
| | Ga | | | | | | C,H | QA | | | | | | | | | | | | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | Exp |
| Donnerstag | 28.09.2017 | H1 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | |
| | H2 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | Ga | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | Exp |
| Freitag | 29.09.2017 | H1 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | |
| | H2 | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | Ga | | | | | | C,H | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Samstag | 30.09.2017 | H1 | | | | | | C | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | |
| | H2 | | | | | | C | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | Ga | | | | | | C | QA | | | | | | | | | | | MedPhys (QA, Verifikation) | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | Exp |
| Sonntag | 01.10.2017 | H1 | | | | | | D | | | | | | | | | | | | | | | | | | | |
| | H2 | | | | | | D | | | | | | | | | | | | | | | | | | | | |
| | Ga | | | | | | D | | | | | | | | | | | | | | | | | | | | |
| | QS | | | | | | | | | | | | | | | | | | | | | | | | | | Exp |

Carbon ions and Protons: Age distribution

Children > Protonen



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

Radiation Dose-Response Relationship for Risk of Coronary Heart Disease in Survivors of Hodgkin Lymphoma

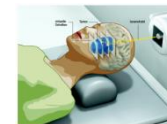
Frederika A. van Nimwegen, Michael Schaapveld, David J. Cutter, Cécile P.M. Janus, Augustinus D.G. Kroel, Michael Hauptmann, Karen Kooijman, Judith Roessink, Richard van der Maazen, Sarah C. Darby, Berthe M.P. Aleman and Flora E. van Leeuwen[†]

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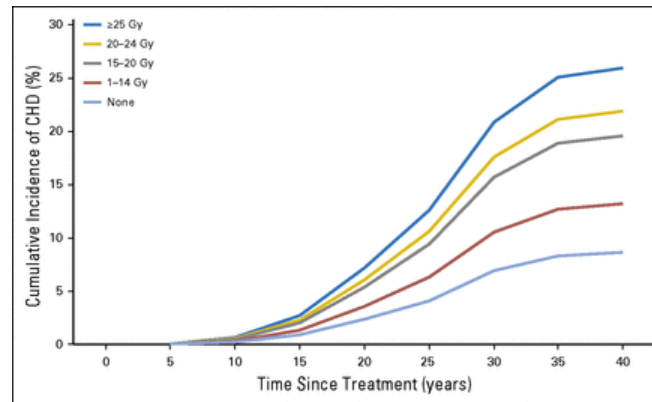
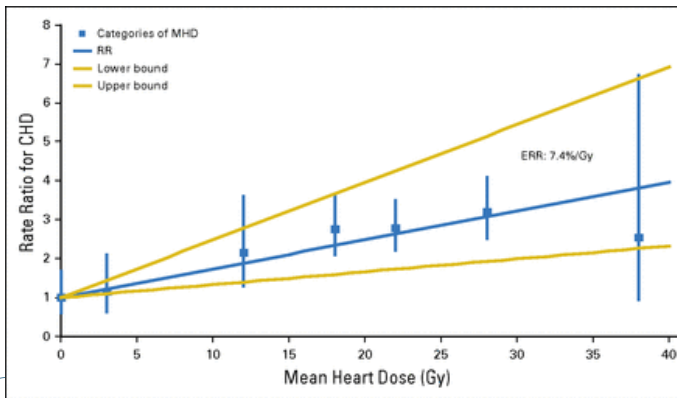
Published online before print
November 16, 2015; doi:10.1200/JCO.2015.32.4144
JCO January 06, 2016; vol. 34, no. 3; 232-243

Abstract: Free
Full Text
PDF



Deterministic Late Effects

- ◆ additional relative risk for CHD: **7,4% / 1 Gy MHD**
- ◆ younger patients face higher risks





UNIVERSITÄTS
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HEIDELBERG



Haber

ch Op

Carbon, isocentre



z = 0

Helium, isocentre



z = 0

Proton, isocentre



z = 0

Carbon, 205mm H2O



z = 205

Helium, 205mm H2O



z = 205

Proton, 205mm H2O

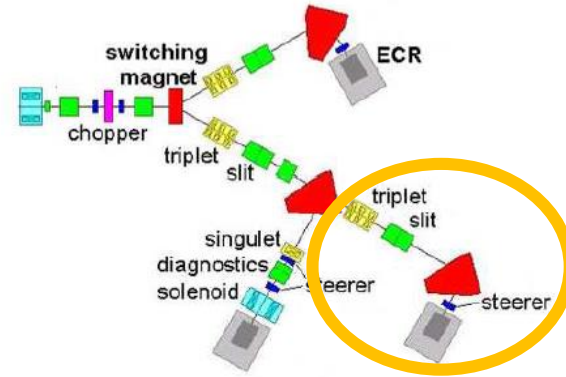
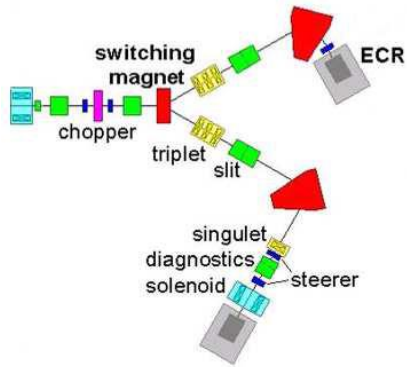


z = 205

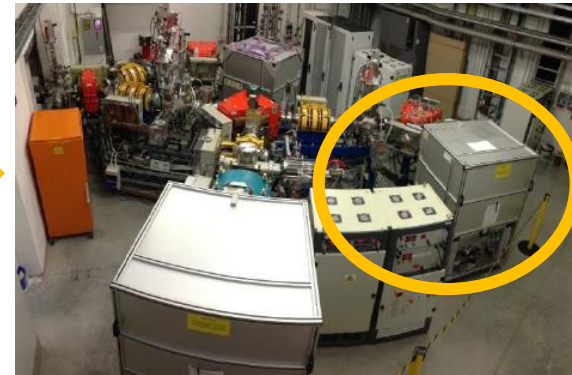
water column 205 mm



Helium-Ionsource Integration



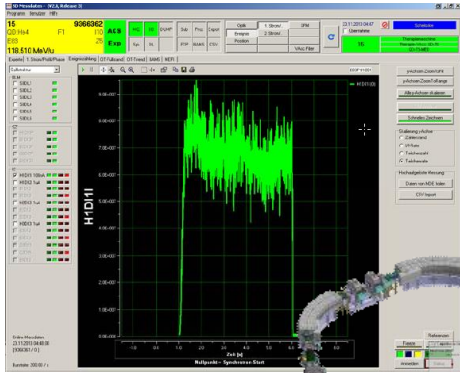
Helium
Ion source



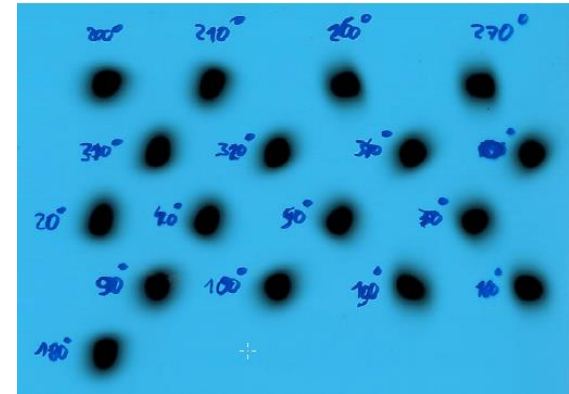
Accelerator- and Beamline-Tuning

4 isocenters 255 energies each,
4 spot sizes, 10 intensities
and 18 gantry angles:

367.200 combinations

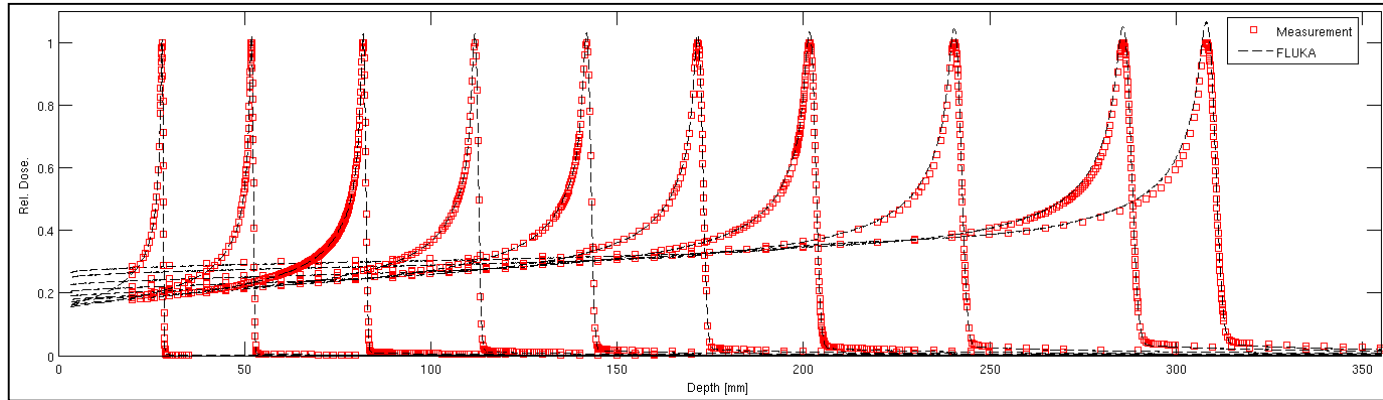


early extraction of
Helium into a
horizontal treatment
room



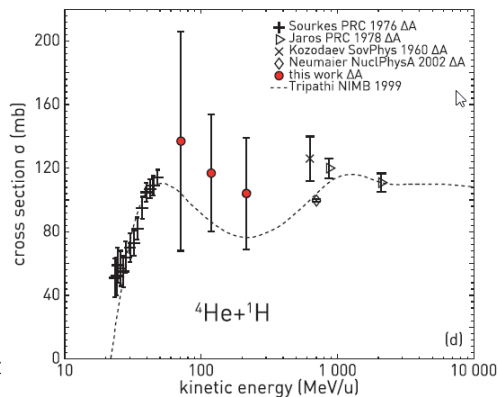
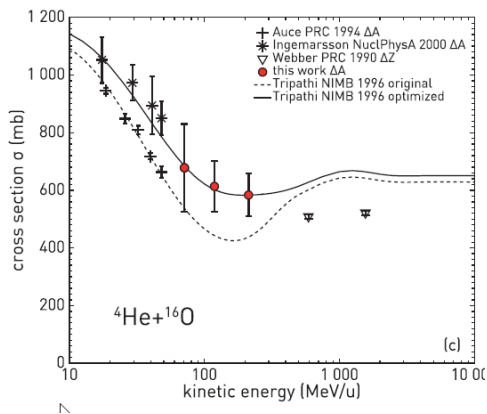
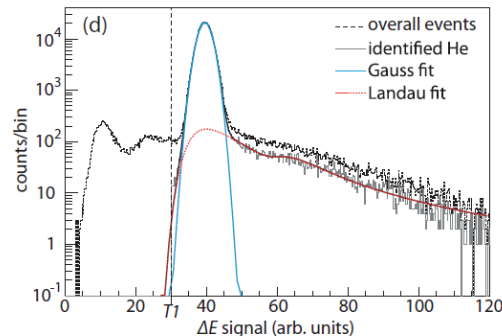
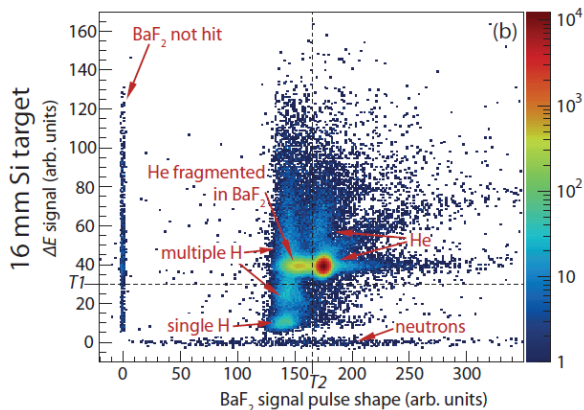
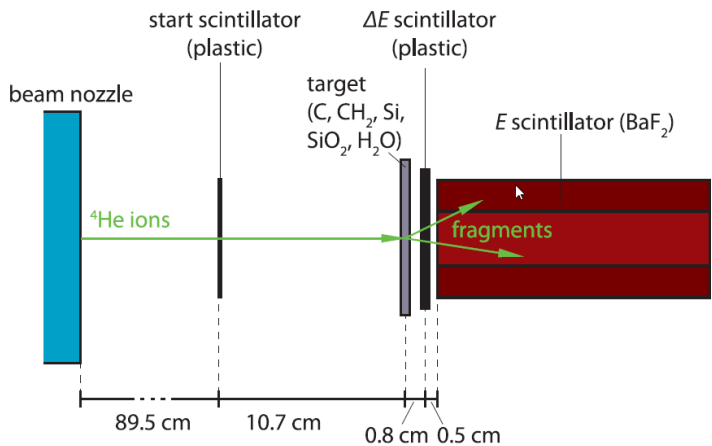
Helium beam spots at
gantry, all angles

Helium Depth-dose distributions: data vs MC



- Overall **good agreement** between simulations and measurements
- Range differences **< 0.10 mm**
- Dose differences **from 0.5 to 6%** in the high dose region
- Average dose-weighted dose-difference **from 0.4 to 2.5%**
 - **Good results** of the **FLUKA** models
 - Room for **improvements**, reaction cross section measurements see next slide

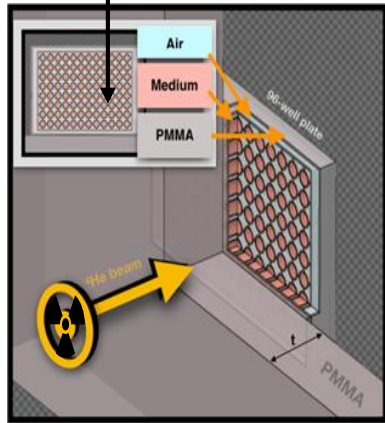
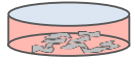
Helium Fragmentation in Water Measurements@HIT



Horst et al., PhysRevC99

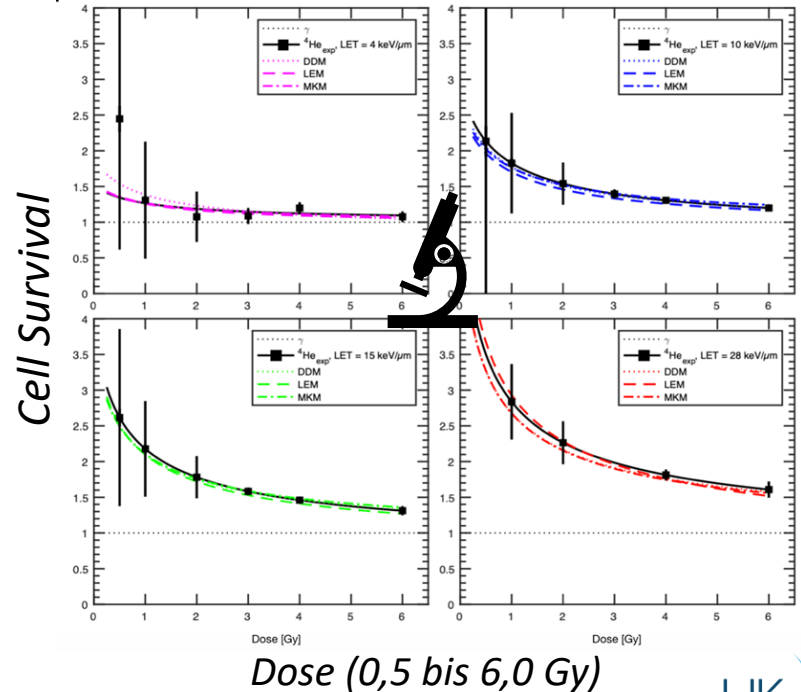
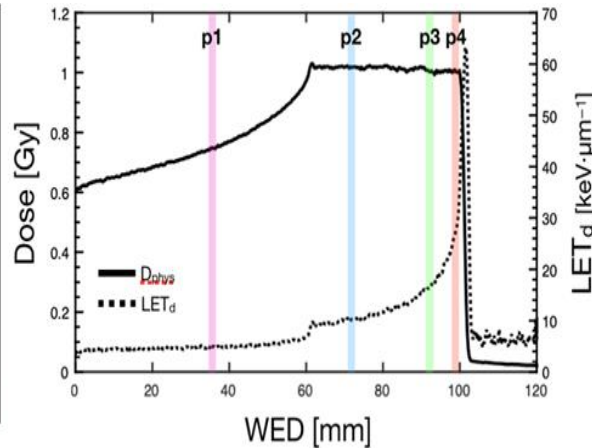
Radiobiological Studies / *in-vitro* Validation of Treatment Planning Outcome for 3 Models

cultivated cells



Irradiation
He-Ions

Depth in water (p1-p4)



Biophysical modeling and experimental validation of relative biological effectiveness (RBE) for ^4He ion beam therapy

Stewart Mein, Ivana Dokic, Carmen Klein, Thomas Tessonier, Till Tobias Böhlen, Guiseppa Magro, Julia Bauer, Alfredo Ferrari, Katia Parodi, Thomas Haberer, Jürgen Debus, Amir Abdollahi & Andrea Mairani

Radiation Oncology, 14, Article number: 123 (2019) | Cite this article

seminar,

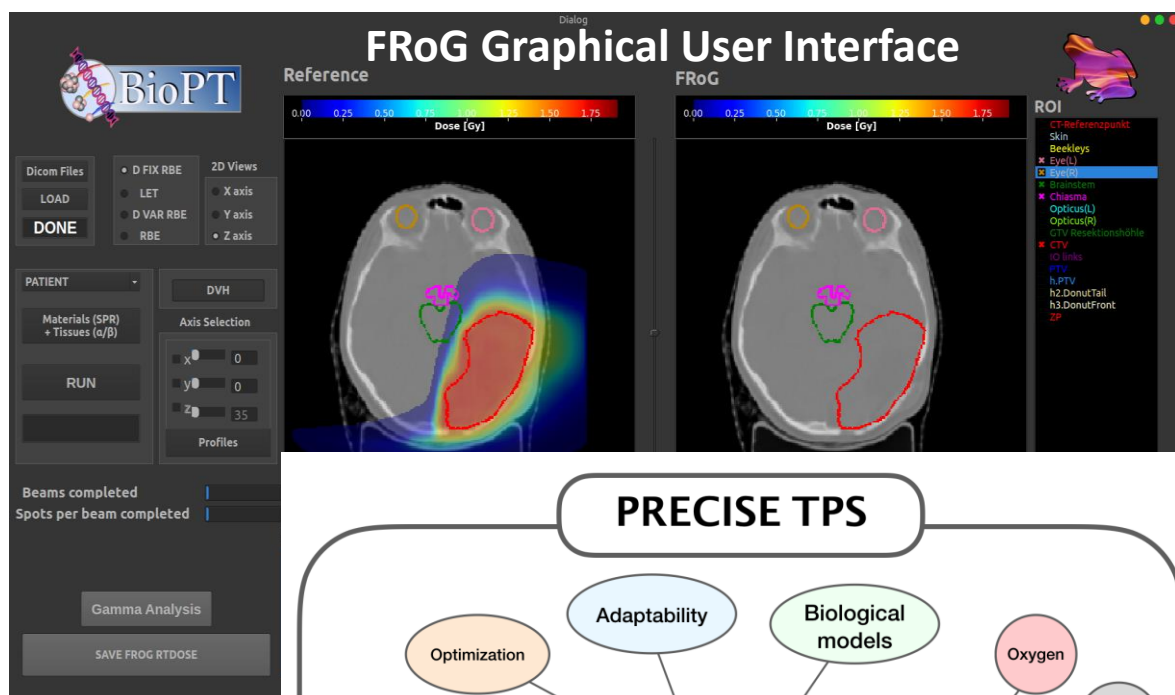




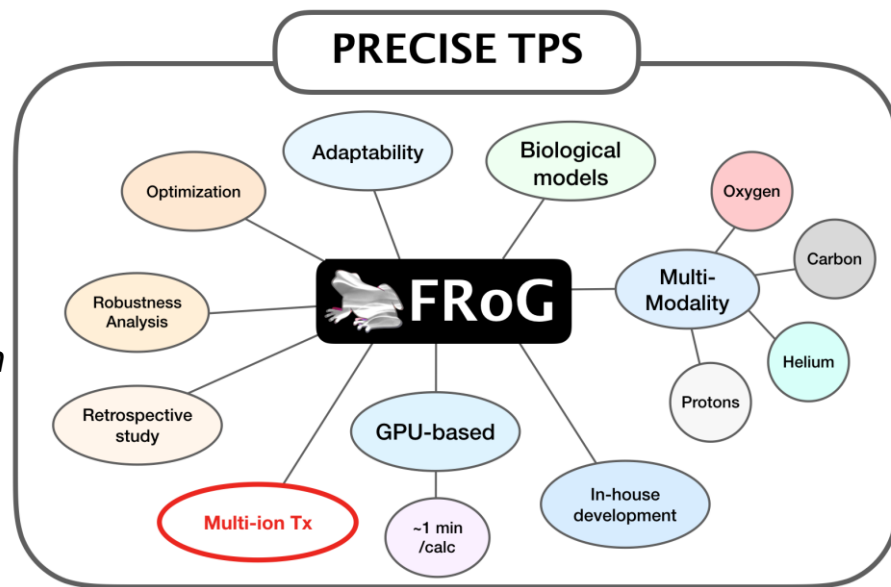
GPU-based Modelling

- QA routines
- Plan robustness analysis
- Automatic cohort analysis
- Dose* Volume Histogram (DVH) analysis
- Multi-tissue radio-sensitivity (α/β) assignment
- Gamma analysis
- Multi biological models
- Scoring: LET_d , D_{RBE} , $RBE...$

Andrea Mairani et al., HIT
S. Mein et al. 2018 Sci Rep.;
K. Choi et al. 2018 Cancers 10, 395;
S. Mein 2019 Phys. Med. 64, 123.



*PaRticle thERapy using
 single and Combined Ion
 optimization StratEGies*



Recent Literature (*BioPT*): ^4He RBE modeling

Data-driven RBE parameterization for helium ion beams

A Mairani^{1,2}, G Magro^{1,3,4}, I Dokic^{2,5,6,7}, S M Valli⁸, T Tessonnier^{7,8}, R Galm^{2,5,6,7}, M Ciocca¹, K Parodi^{2,3,4}, A Ferrari⁹, O Jäkel^{2,6}, T Haberer², P Pedroni¹ and T T Böhlen¹⁰

¹ Medical Physics Unit, CNAO Foundation, Via Strada Campeggi 10, I-27100 Pavia, Italy

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⁵ German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany

⁶ Center for Helium Ion Therapy (HIRO), D-69120 Heidelberg, Germany

⁷ German Cancer Research Center (DKFZ), Im Neuenheimer Feld 400, D-69120 Heidelberg, Germany

⁸ Ludwig-Maximilians-Universität München, D-85748 Garching b. Munich, Germany

⁹ European Organization for Nuclear Research (CERN), CH-1211 Geneva, Switzerland

¹⁰ Medical Physics Unit, CNAO Foundation, Via Strada Campeggi 10, I-27100 Pavia, Italy

Biologically optimized helium ion plans: calculation approach and its *in vitro* validation

A Mairani^{1,2}, I Dokic^{2,3,4,5}, G Magro¹, T Tessonnier^{5,6}, F Kamp⁷, D J Carlson⁸, M Ciocca¹, F Cerutti⁹, P R Sala¹⁰, A Ferrari⁹, T T Böhlen¹¹, O Jäkel^{2,4}, K Parodi^{2,5,6}, J Debus^{2,5}, A Abdollahi^{2,3,4,5} and T Haberer²

¹ Medical Physics Unit, CNAO Foundation, Via Strada Campeggi 53, I-27100 Pavia, Italy

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³ German Cancer Consortium (DKTK), Translational Radiation Oncology, National Center for Tumor Diseases (NCT), Heidelberg Institute of Radiation Oncology (HIRO), D-69120 Heidelberg, Germany

⁴ German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany

⁵ Department of Radiation Oncology, Heidelberg University Hospital, Im Neuenheimer Feld 400, D-69120 Heidelberg, Germany

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⁷ Department of Radiation Oncology, Ludwig-Maximilians-Universität München, Marchioninistr. 15, D-81377 Munich, Germany

⁸ Dept. of Therapeutic Radiology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA

Optimizing the modified microdosimetric kinetic model input parameters and ^4He ion beam therapy applications

A Mairani^{1,2}, G Magro¹, T Tessonnier³, S Molinelli¹, A Ferrari⁶, K Parodi^{2,3,4}, and T Haberer²

¹ CNAO Foundation, Via Strada Campeggi 10, I-27100 Pavia, Italy

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³ Department of Radiation Oncology, Heidelberg University Hospital, Im Neuenheimer Feld 400, D-69120 Heidelberg, Germany

⁴ Institut für Medizinische Physik und Klinische Strahlentherapie, Universität München, Am Coulombwall 1, D-85748 Garching b. Munich, Germany

⁵ Medical Physics Unit, CNAO Foundation, Via Strada Campeggi 10, I-27100 Pavia, Italy

⁶ European Organization for Nuclear Research (CERN), CH-1211 Geneva, Switzerland

⁷ Department of Radiation Oncology, Ludwig-Maximilians-Universität München, Marchioninistr. 15, D-81377 Munich, Germany

⁸ Dept. of Therapeutic Radiology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA

⁹ Department of Radiation Oncology, Ludwig-Maximilians-Universität München, Marchioninistr. 15, D-81377 Munich, Germany

¹⁰ Department of Radiation Oncology, Ludwig-Maximilians-Universität München, Marchioninistr. 15, D-81377 Munich, Germany

¹¹ Medical Physics Unit, CNAO Foundation, Via Strada Campeggi 10, I-27100 Pavia, Italy

Mein et al. *Radiation Oncology* (2019) 14:123
<https://doi.org/10.1186/s13014-019-1295-z>

Radiation Oncology

RESEARCH

Open Access



Biophysical modeling and experimental validation of relative biological effectiveness (RBE) for ^4He ion beam therapy

Stewart Mein^{1,2,3,4,5}, Ivana Dokic^{1,2,3,4}, Carmen Klein^{1,2,3,4}, Thomas Tessonnier^{2,6}, Till Tobias Böhlen⁷, Giuseppe Magro⁸, Julia Bauer², Alfredo Ferrari⁹, Katia Parodi^{2,10}, Thomas Haberer², Jürgen Debus^{1,2,3,4,5}, Amir Abdollahi^{1,2,3,4} and Andrea Mairani^{2,8*}

Abstract

Background: Helium (^4He) ion beam therapy provides favorable biophysical characteristics compared to currently administered particle therapies, i.e., reduced lateral scattering and enhanced biological damage to deep-seated tumors like heavier ions, while simultaneously lessened particle fragmentation in distal healthy tissues as observed with lighter protons. Despite these biophysical advantages, raster-scanning ^4He ion therapy remains poorly explored e.g., clinical translational is hampered by the lack of reliable and robust estimation of physical and radiobiological uncertainties. Therefore, prior to the upcoming ^4He ion therapy program at the Heidelberg Ion-beam Therapy Center (HIT), we aimed to characterize the biophysical phenomena of ^4He ion beams and various aspects of the associated models for clinical integration.

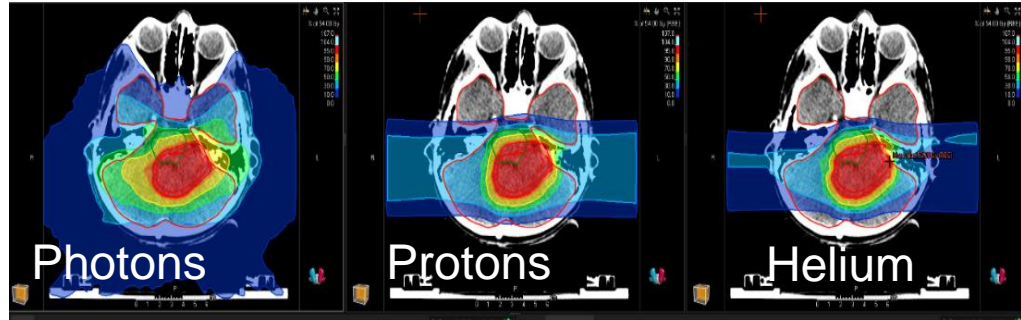
Methods: Characterization of biological effect for ^4He ion beams was performed in both homogenous and patient-like treatment scenarios using innovative models for estimation of relative biological effectiveness (RBE) in cells and



In-silico Studies - RayStation - Helium-Module

Analysed entities so far:

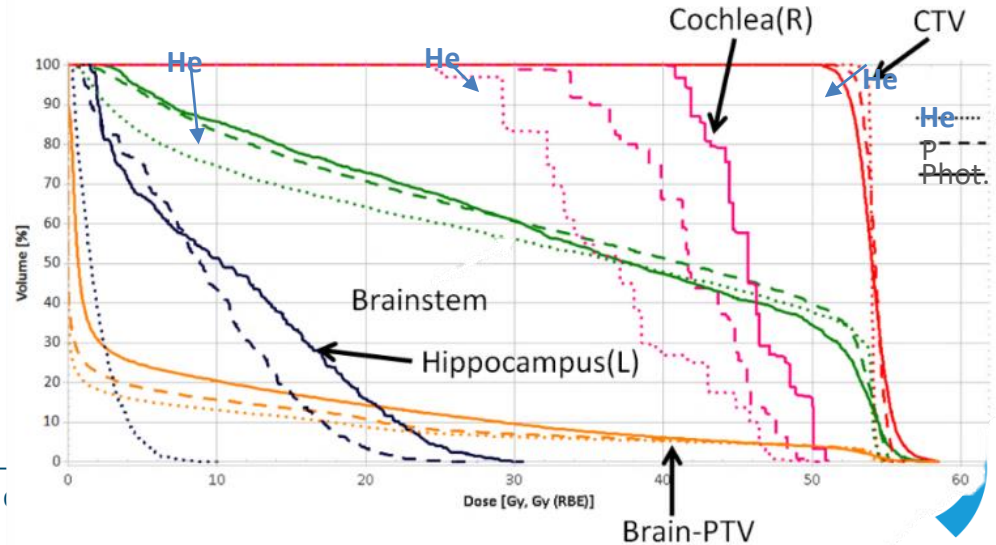
- Meningioma
- Low-grade Glioma
- **Ependymoma**
- Head-and-neck
- Prostate



Normal tissue complication probability (NTCP)

Superior sparing of brainstem and Cochlea

Coverage of clinical target volume (CTV) best for Helium

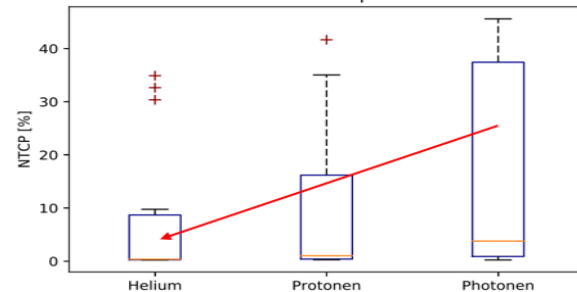
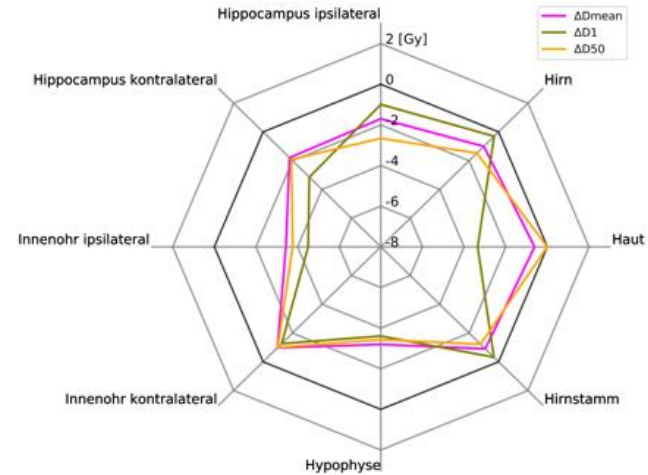


Clinical Rationale Helium

- Low-grade glioma: dosereduction up to 5 Gy(RBE)
- Superior organ-at-risk sparing: f.e. pituitary gland and inner ear

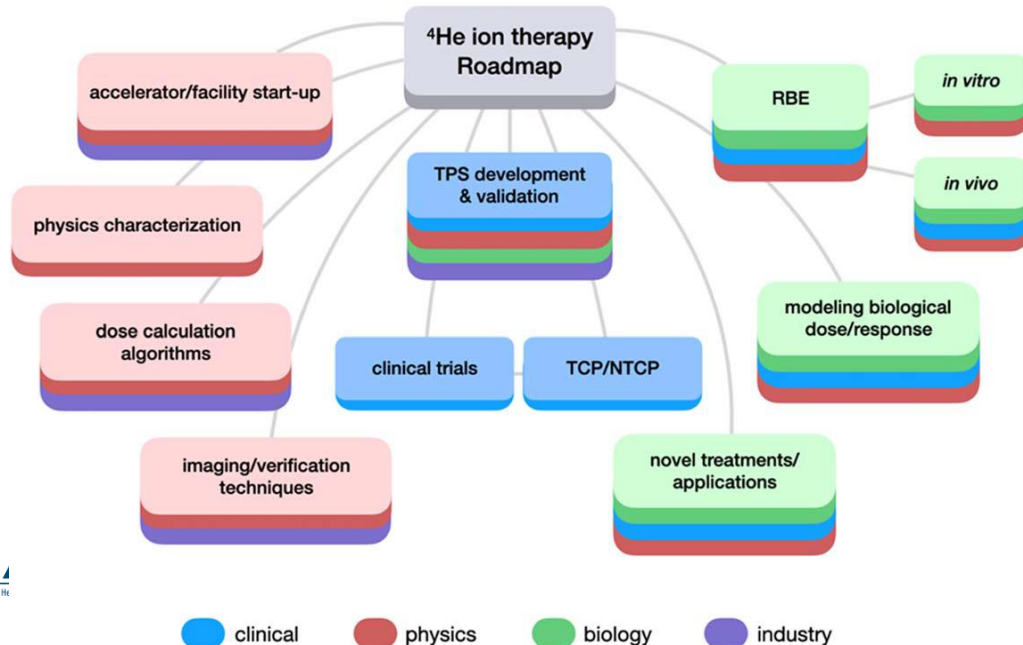
| Risikoorgan | | Helium | Protonen | Photonen | He vs Pr |
|----------------------|-------------------|--------|----------|----------|-------------------|
| | | | | | Differenz absolut |
| Hypophyse | D _{mean} | 14 ± 4 | 18 ± 4 | 27 ± 4 | -3,2 ± 0,6* |
| | D ₁ | 24 ± 5 | 28 ± 5 | 32 ± 5 | -3,6 ± 0,8* |
| | D ₅₀ | 14 ± 4 | 17 ± 4 | 27 ± 4 | -3,4 ± 0,8* |
| | ID | 7 ± 2 | 8 ± 2 | 12 ± 2 | -1,5 ± 0,4* |
| Innenohr ipsilateral | D _{mean} | 13 ± 4 | 16 ± 4 | 22 ± 4 | -3,4 ± 0,6* |
| | D ₁ | 23 ± 5 | 27 ± 4 | 32 ± 4 | -5 ± 1* |
| | D ₅₀ | 12 ± 4 | 16 ± 4 | 22 ± 4 | -3,8 ± 0,7* |
| | ID | 16 ± 5 | 21 ± 5 | 29 ± 5 | -4,6 ± 0,9* |

Notiz: D_{mean}, D₁ und D₅₀ in Gy, ID in Gy · cm³. * bedeutet statistisch signifikant mit p-Wert < 0,05. Die Tabelle zeigt die sich ergebenden Mittelwerte mit den Standardfehlern des Mittelwerts (n = 15).



Roadmap: helium ion therapy

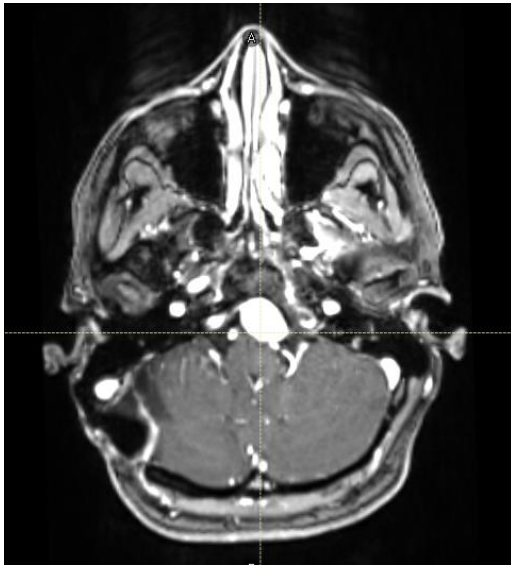
Andrea Mairani^{1,2,3,4}, Stewart Mein^{1,3,4,5}, Eleanor Blakely⁶ , Jürgen Debus^{1,3,4,5,7}, Marco Durante^{8,21} 
 Alfredo Ferrari¹, Hermann Fuchs^{9,10} , Dietmar Georg^{9,10} , David R Grosshans¹¹, Fada Guan^{11,19} ,
 Thomas Haberer¹, Semi Harrabi^{1,4,5,7,20}, Felix Horst⁸, Taku Inaniwa^{12,13}, Christian P Karger^{4,18} ,
 Radhe Mohan¹¹ , Harald Paganetti^{14,15} , Katia Parodi¹⁶ , Paola Sala¹⁷ , Christoph Schuy⁸,
 Thomas Tessonnier¹, Uwe Titt¹¹ and Ulrich Weber⁸



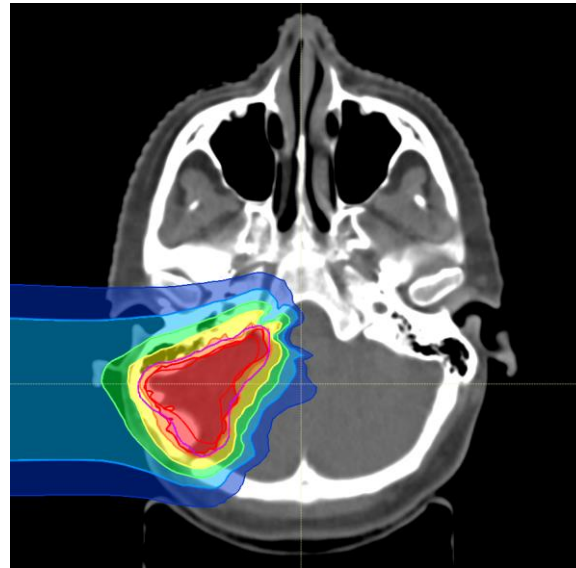
1. Carante, M.P., et al., *Biological effectiveness of He-3 and He-4 ion beams for cancer hadrontherapy: a study based on the BIANCA biophysical model*. Phys Med Biol, 2021. 66(19).
2. Hintz, L., et al., *Relative biological effectiveness of single and split helium ion doses in the rat spinal cord increases strongly with linear energy transfer*. Radiother Oncol, 2022. 170: p. 224-230.
3. Kopp, B., et al., *Development and Validation of Single Field Multi-Ion Particle Therapy Treatments*. Int J Radiat Oncol Biol Phys, 2020. 106(1): p. 194-205.
4. Kopp, B., et al., *Rapid effective dose calculation for raster-scanning (4)He ion therapy with the modified microdosimetric kinetic model (mMKM)*. Phys Med, 2021. 81: p. 273-284.
5. Longarino, F.K., et al., *Dual-layer spectral CT for proton, helium, and carbon ion beam therapy planning of brain tumors*. J Appl Clin Med Phys, 2022. 23(1): p. e13465.
6. Mairani, A., et al., *Data-driven RBE parameterization for helium ion beams*. Phys Med Biol, 2016. 61(2): p. 888-905.
7. Mairani, A., et al., *Optimizing the modified microdosimetric kinetic model input parameters for proton and (4)He ion beam therapy application*. Phys Med Biol, 2017. 62(11): p. N244-n256.
8. Mairani, A., et al., *Roadmap: helium ion therapy*. Phys Med Biol, 2022. 67(15).
9. Mein, S., et al., *Fast robust dose calculation on GPU for high-precision (1)H, (4)He, (12)C and (16)O ion therapy: the FRoG platform*. Sci Rep, 2018. 8(1): p. 14829.
10. Mein, S., et al., *Biophysical modeling and experimental validation of relative biological effectiveness (RBE) for (4)He ion beam therapy*. Radiat Oncol, 2019. 14(1): p. 123.
11. Mein, S., et al., *Dosimetric validation of Monte Carlo and analytical dose engines with raster-scanning (1)H, (4)He, (12)C, and (16)O ion-beams using an anthropomorphic phantom*. Phys Med, 2019. 64: p. 123-131.
12. Mein, S., et al., *Spot-scanning hadron arc (SHArc) therapy: A proof of concept using single- and multi-ion strategies with helium, carbon, oxygen, and neon ions*. Med Phys, 2022. 49(9): p. 6082-6097.
13. Mein, S., et al., *Spot-Scanning Hadron Arc (SHArc) Therapy: A Study With Light and Heavy Ions*. Adv Radiat Oncol, 2021. 6(3): p. 100661.
14. Mein, S., et al., *Biological Dose Optimization for Particle Arc Therapy Using Helium and Carbon Ions*. Int J Radiat Oncol Biol Phys, 2022. 114(2): p. 334-348.
15. Tessonnier, T., et al., *Experimental dosimetric comparison of (1)H, (4)He, (12)C and (16)O scanned ion beams*. Phys Med Biol, 2017. 62(10): p. 3958-3982.
16. Tessonnier, T., et al., *Proton and helium ion radiotherapy for meningioma tumors: a Monte Carlo-based treatment planning comparison*. Radiat Oncol, 2018. 13(1): p. 2.
17. Tessonnier, T., et al., *FLASH Dose Rate Helium Ion Beams: First In Vitro Investigations*. Int J Radiat Oncol Biol Phys, 2021. 111(4): p. 1011-1022.

First Rx using Rasterscanned He-Ions

female patient 30 yrs
recurrent anaplastic
soft-tissue sarcoma, 2021



pretreated in 2015
60 Gy(RBE) Carbon

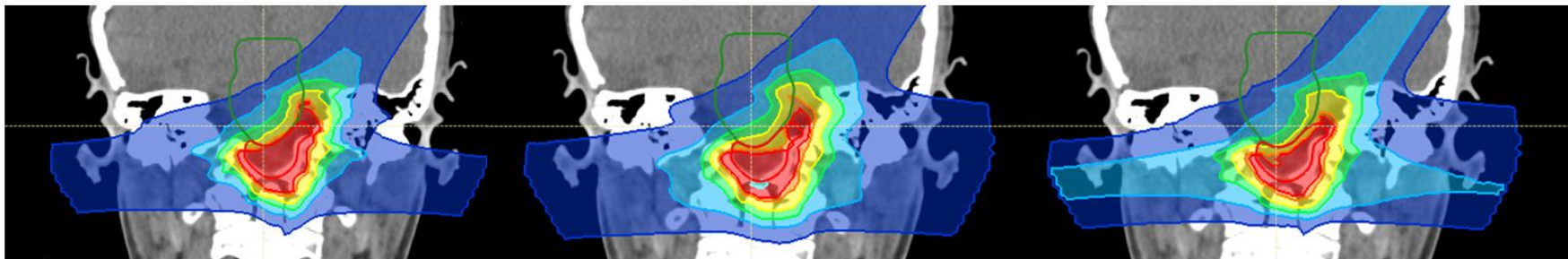


First Rx using Rasterscanned He-Ions

Helium (mMKM)

Protons (RBE =1,1)

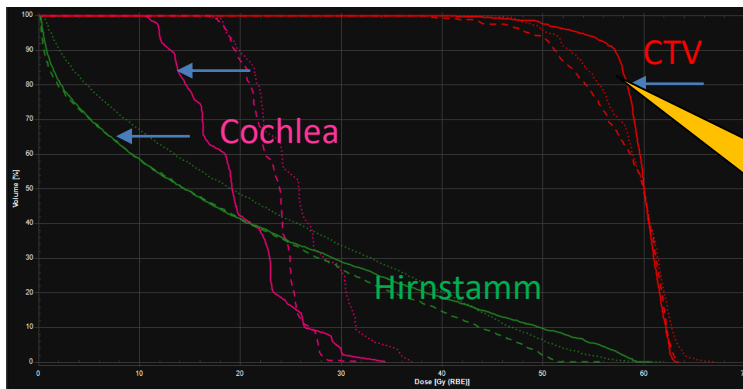
Carbon (LEM I)



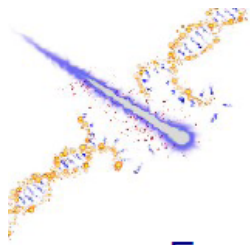
Helium ———

Protons ······

Carbon - - - -

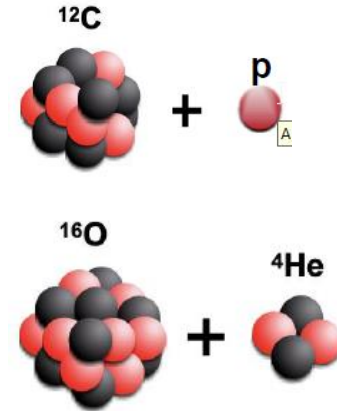
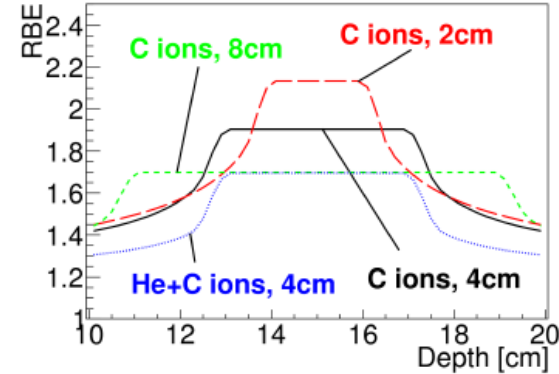
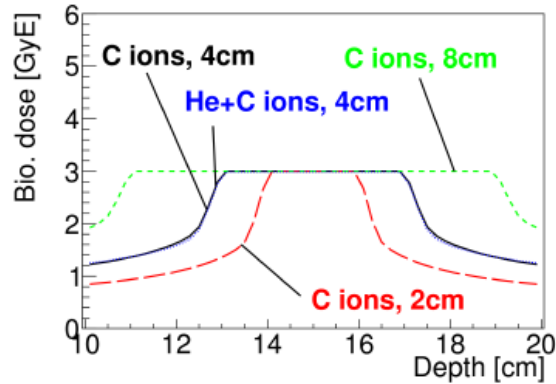
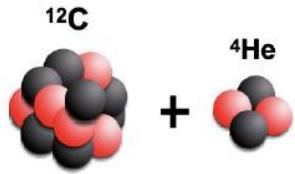


HIT, July 20th, 2021:
First patient treatment
with rasterscanned
Helium beams
Full remission after 1yr



Dual ion fields

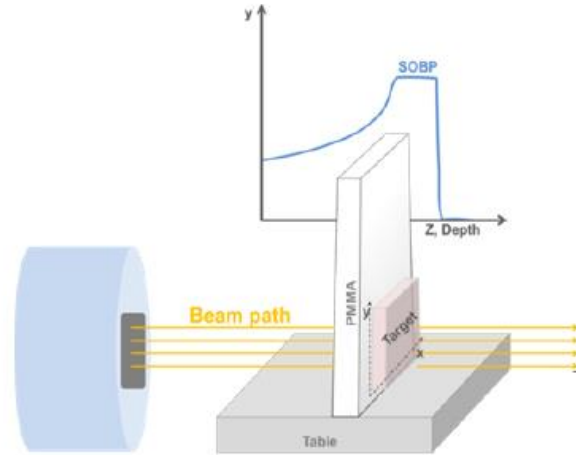
Example: He+C fields with const. RBE in PTV to have a constant radiation quality as a function of field size



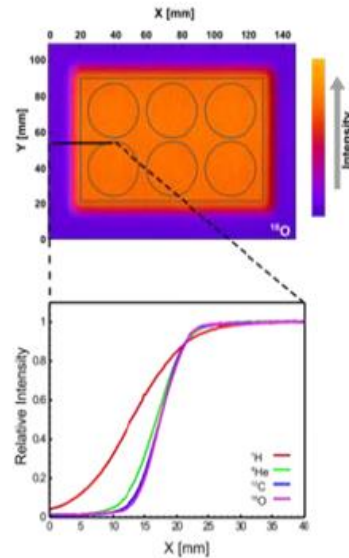
- + Reduces risk for possible relative misestimations as a function of field size (and also field depth)
- Dilutes (the probably advantageous) high-LET component of C ions.
- + However for treatments with higher-LET ions, such as oxygen, the mixture with lower-Z ions could additionally help to reduce the fragmentation tail.

Different irradiation modalities at HIT (1H, 4He, 12C, 16O)

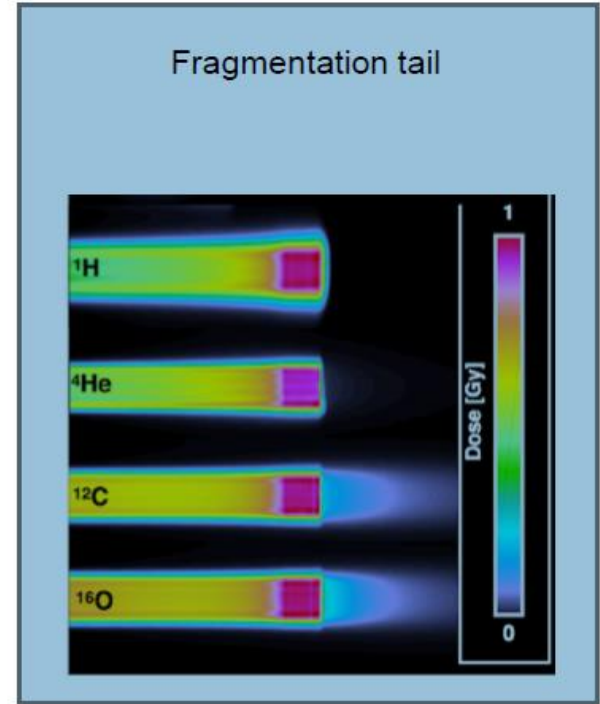
Experimental setup



Lateral scattering



Fragmentation tail



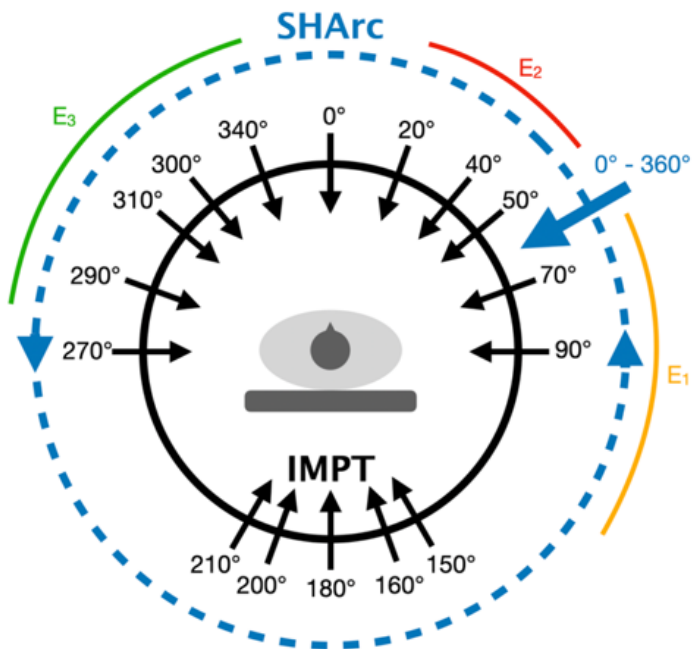
SF30 RBEs:

| | |
|-----------------|-----|
| ^1H | 1.1 |
| ^4He | 1.7 |
| ^{12}C | 2.7 |
| ^{16}O | 3.5 |

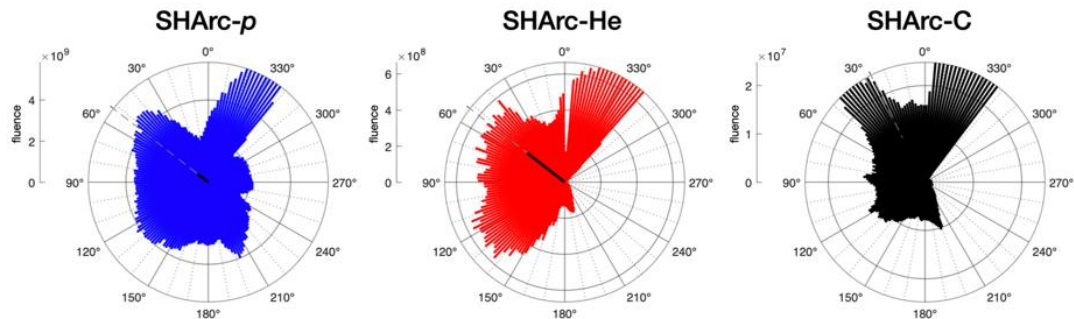
Dokic et al. 2021



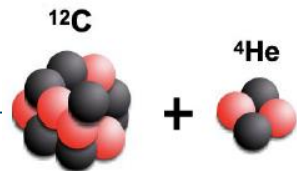
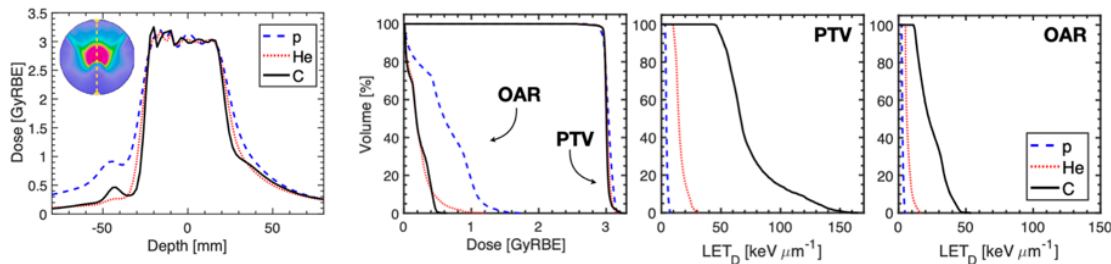
Spot-scanning Hadron Arc (SHArc) Therapy Study



angular fluence maps



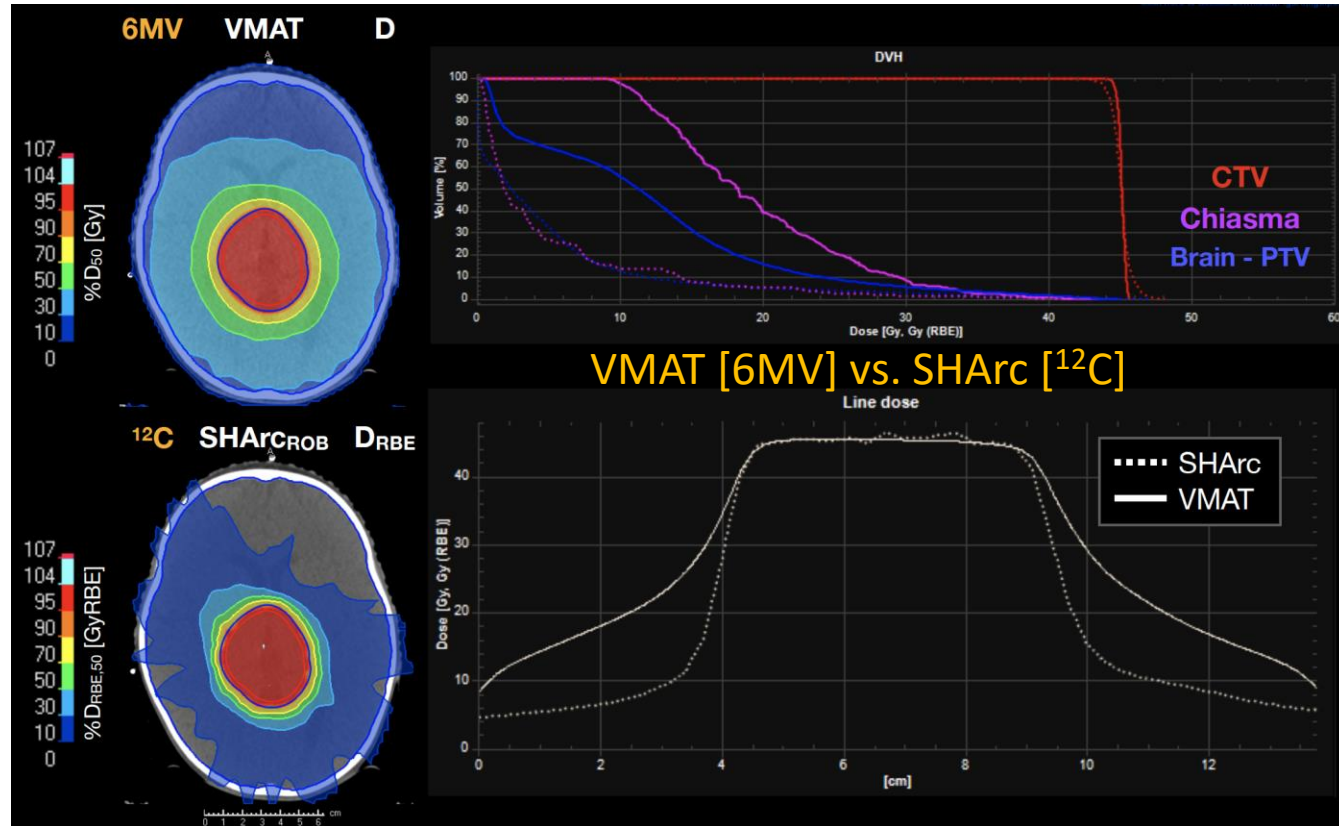
Depth-dose, D_VH, LET_VH



Spot-scanning Hadron Arc (SHArc) Therapy Study

SHArc

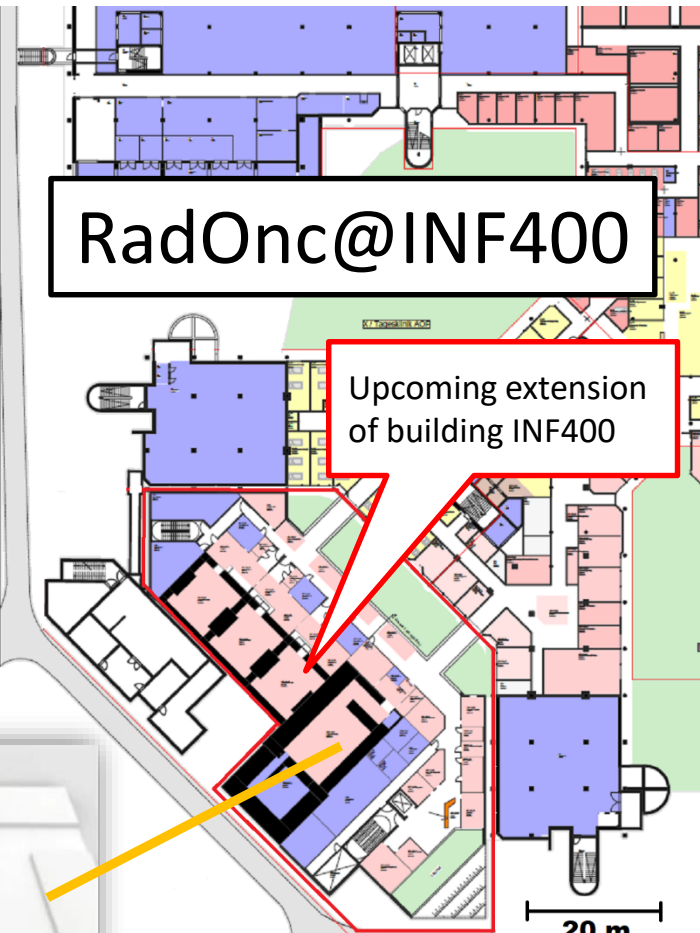
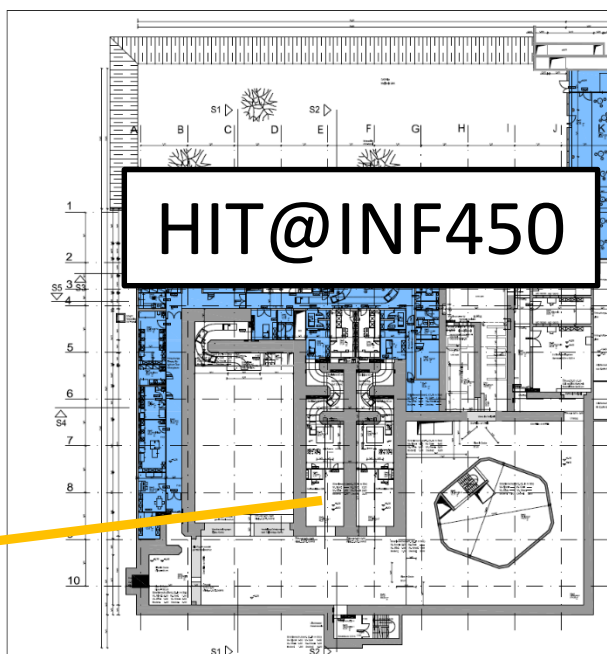
- Outperforms VMAT
- Robust plans
- Normal tissue and organs at risk sparing
- LET-VH can be tailored to the oxygenation status of the target
- Longer irradiation times
- Technical challenges ahead



New Modalities



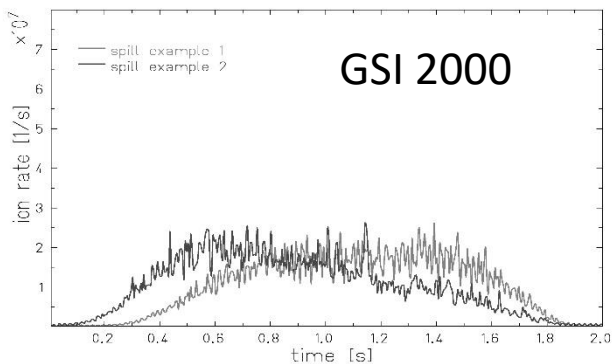
Chair with CT



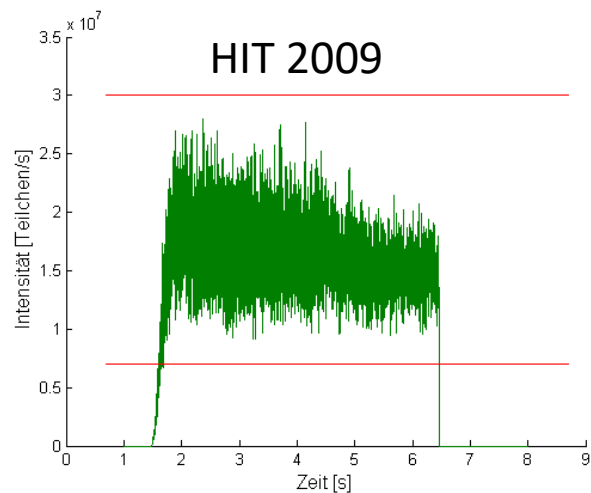
Single-room Proton system

Synchrotron Slow Extraction Optimization

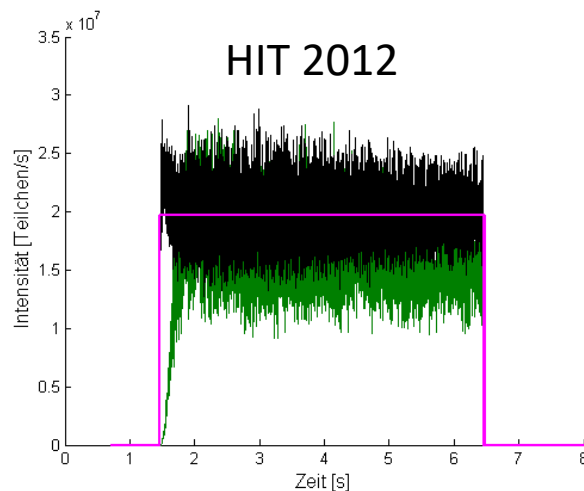
HIT 2022



GSI 2000



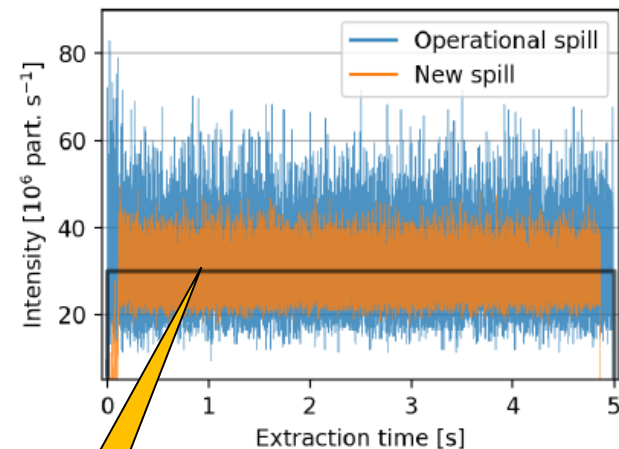
HIT 2009



HIT 2012

Ph.D.
Christian Schömers

Smoothest
extraction
ever!



Master-Thesis
Christopher Cortéz

ent and Research Options, HIT Seminar,



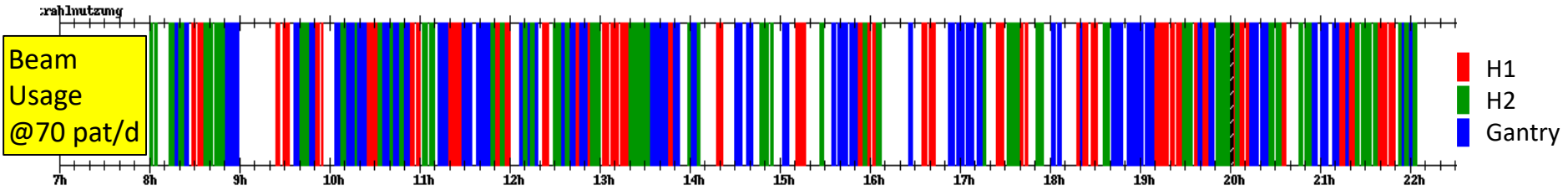
Nuclear Instruments and Methods in
Physics Research Section A:
Accelerators, Spectrometers, Detectors
and Associated Equipment
Volume 1040, 1 October 2022, 167137



Optimization of the spill quality for the
hadron therapy at the Heidelberg Ion-
Beam Therapy Centre

E.C. Cortés García, E. Feldmeier, M. Galonska, C. Schömers, M. Hun, S. Brons,
R. Cee, S. Scheloske, A. Peters, Th. Haberer

Ongoing Upgrades

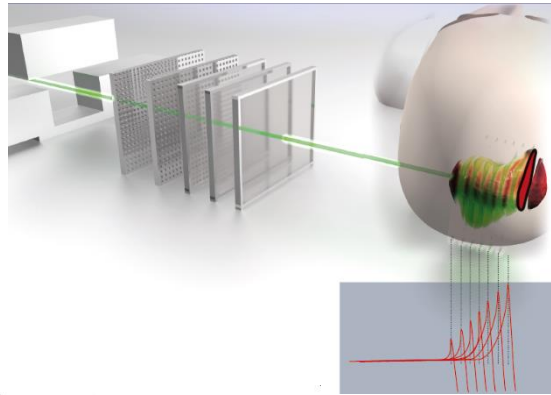


Enable multi-energy extraction:

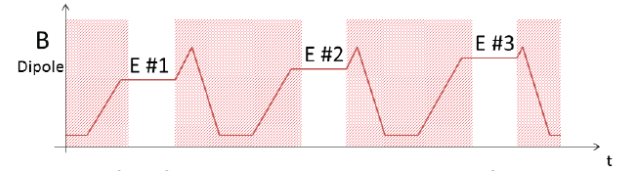
New Accelerator Control System

Irradiation time reduction ~ 40%

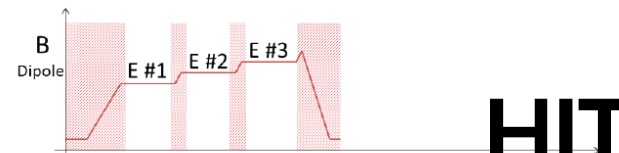
Energy saving ~ 15%



one extraction per synchrotron-cycle



multiple extractions per synchrotron-cycle



Intensity upgrade:

New RFQ c
Transmissi

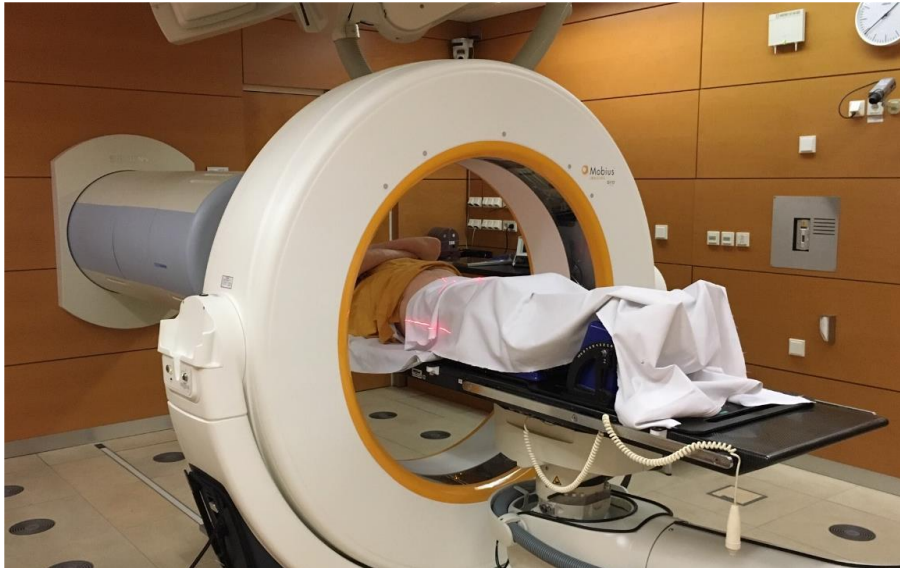


C. Schoemers et al.
"Reacceleration of ion beams
for particle therapy."
Proc. of IPAC2014, Dresden.



In-room Imaging / See what you treat!

HIT – H1 sliding CT



6.5 mm margin (peel) represents a volume comparable with the target!

Volumetric information defines patient set-up
Reduction of margins
Plan of the day
Fast replanning

Combining proton/ion beams with MRI

Motivation :

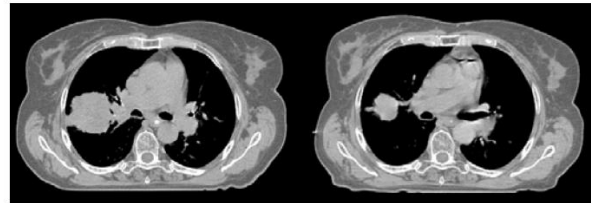
- “Seeing what you treat” → Online diagnostics would be favorable
- CT is almost standard today, but MRI causes no further radiation dose (especially important in pediatric treatments!)
- Tumor shrinkage during therapy – avoidance of errors in adapted dose allocation
- MR-Linac Systems (photons) are currently being introduced in radiotherapy



Lung Tumor shrinkage during p-therapy

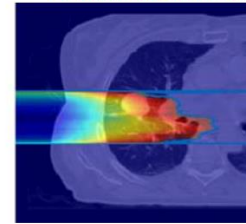
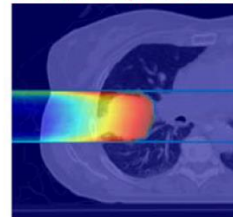
Initial Planning CT
GTV 115 cc

5 weeks later
GTV 39 cc



Beam stops at distal edge

Beam overshoot



MR guided Ion beam Therapy: ARTEMIS Project

Adaptive RadioThERapie mit MR gesteuerten IonenStrahlen

Aims

- Capture anatomical changes & changes in the tumor to allow for
- offline, online or weekly customization,
- >> providing optimal protection of the OAR

Within ARTEMIS a **demonstrator system** consisting of several components will be developed , which enables MR-guided irradiation with ions and protons.



ARTEMIS Vision:

- Turn the patient, not the beam
- Plan & adapt based on MRI

funded by:



Bundesministerium
für Bildung
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SIEMENS
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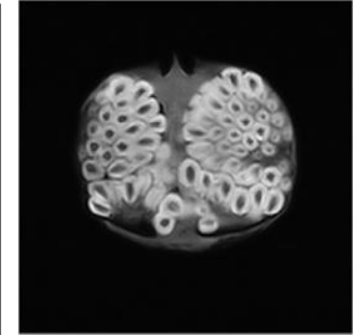
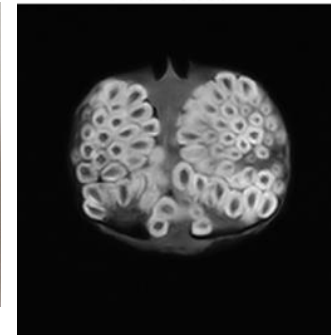
Heidelberger Ionenstrahl-Therapiezentrum

The „on-line“ MRT at HIT



Baseline

c irradiation



Sequence: 3D GRE (0.4 x 0.4 x 2.5)mm³
Irradiation: 10 x 10 cm raster grid ,
1 cm distances

Increasing Demand For Radiotherapy In Europe / Germany

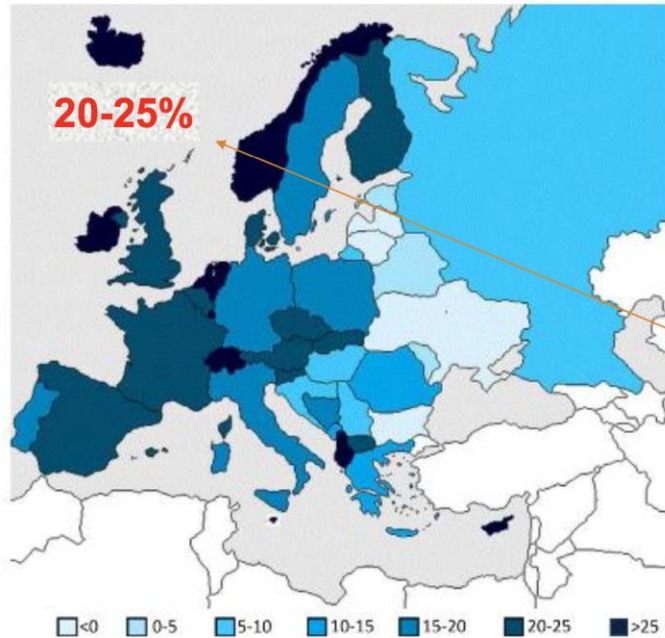


Fig. 1. Increase in new cancer patients that would require radiotherapy by 2025 by country (%).

ESTRO-HERO Analysis

How many new cancer patients in Europe will require radiotherapy by 2025? An ESTRO-HERO analysis



Josep M. Borras^{A,*}, Yolande Lievens^B, Michael Barton^C, Julieta Corral^D, Jacques Ferlay^E, Freddie Bray^F, Cai Grau^G

^AUniversity of Barcelona, IDIBELL, Barcelona, Spain; ^BRadiation Oncology Department, Ghent University Hospital, Ghent, Belgium; ^CCCORE Ingham Institute for Applied Medical Research, University of South Wales, Australia; ^DCatalan Cancer Strategy, Department of Health, Generalitat de Catalunya, Barcelona, Spain; ^ESection of Cancer Surveillance, International Agency for Research on Cancer (IARC), Lyon, France; and ^FDepartment of Oncology, Aarhus University Hospital, Aarhus, Denmark

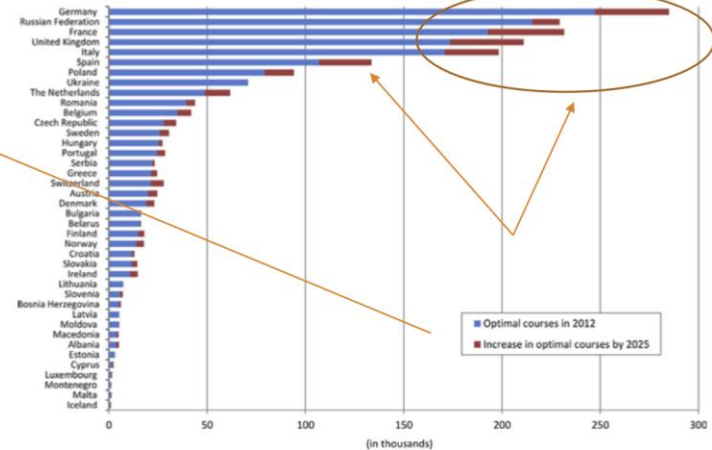



Fig. 2. Optimal number of courses of radiotherapy in 2012 and estimated absolute increase in optimal number of courses by 2025.

What will radiation oncology look like in 2050? A look at a changing professional landscape in Europe and beyond

Michael Baumann^{1,2,3} , Nadja Ebert^{1,2}, Ina Kurth¹, Carol Bacchus¹ and Jens Overgaard⁴

7. Conclusions

First of all, we firmly believe that radiation oncology will be at least as important in 2050 as it is today. A

and Hanahan, 2012). Radiotherapy has an impressive track record that demonstrates its curative potential in a wide variety of cancers. Given its unique features, radiotherapy will very likely remain a key component in the multidisciplinary, anticancer treatment arsenal of the future.

primary cancer care.

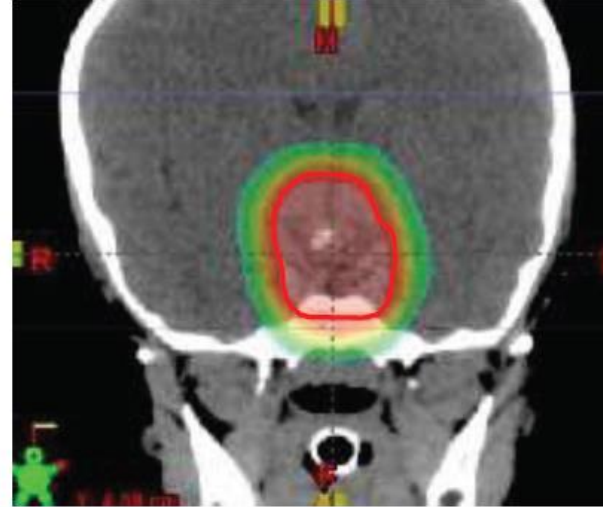
Another advance has come from the increased use of particle and proton irradiation (see Box 1) because of the higher precision of these techniques and because of other radiobiological considerations (Dutz *et al.*, 2019a; Dutz *et al.*, 2019b; Lühr *et al.*, 2018). Numerous new facilities that offer these treatment techniques

Progress

Photons 1980



Particles 2020



- Ion beam therapy is extremely precise
- Challenged by costs
- Image guidance and motion mitigation need to be improved
- Huge potential is evident

Thank You!

