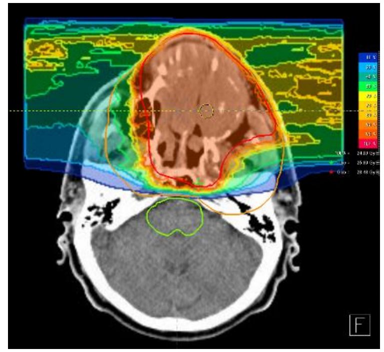
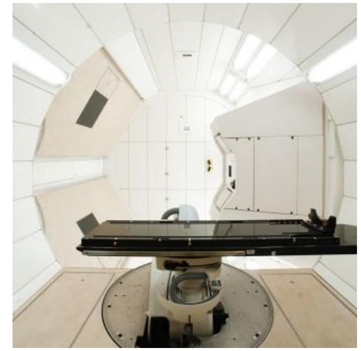
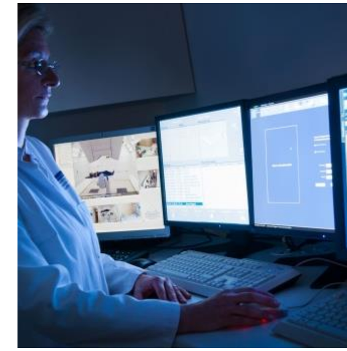
HEIDELBERG UNIVERSITY HOSPITAL

Heidelberger Ionenstrahl-Therapiezentrum







Introduction of Carbon ion beam therapy in Europe and clinical trials

Jürgen Debus

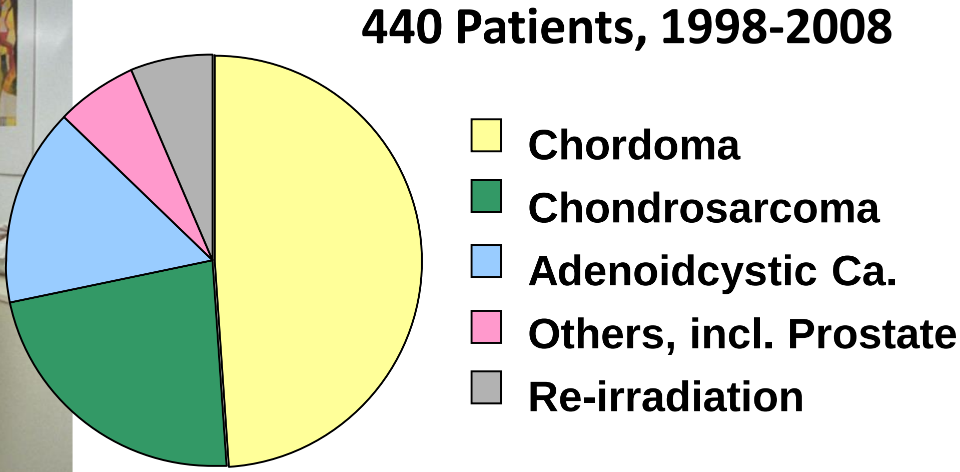
PTCOG 2019, Manchester UK

Faculty Disclosure

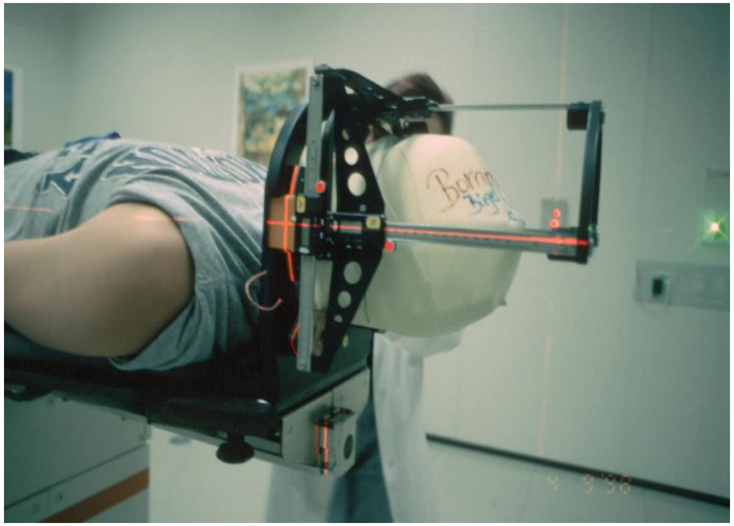
	No, nothing to disclose
X	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
Raysearch	x	X	x					
Accuray			X					
Elekta			X					
Siemens			X					
Merck Serono	X	X	X					

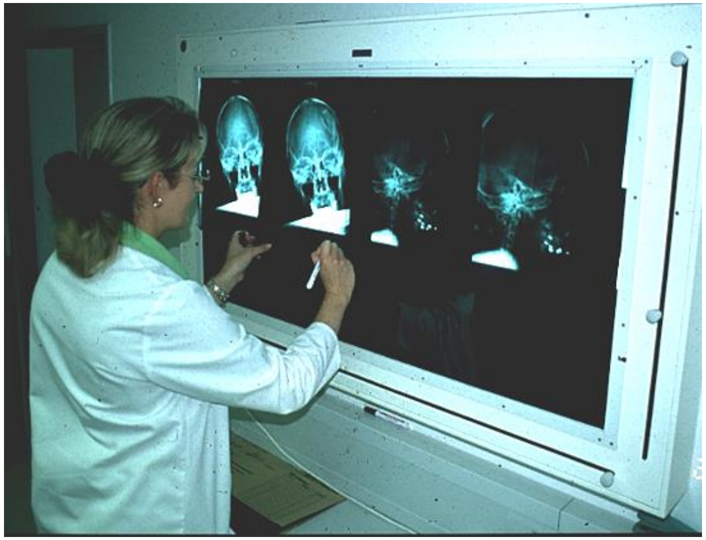
1980-1997 biolog. treatment planning
1993: first prototype of rasterscanner
1994: medical treatment room
1997: First patient treated with C-12 at GSI



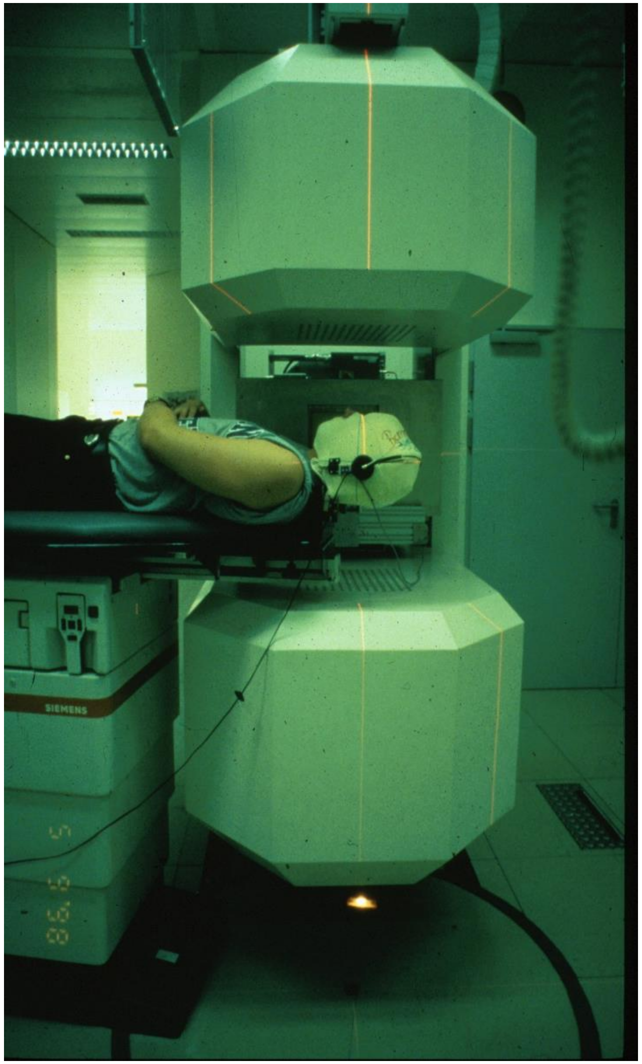
Patient Positioning In The Early Clinical Studies (1997-2008)



Stereotactic Setup

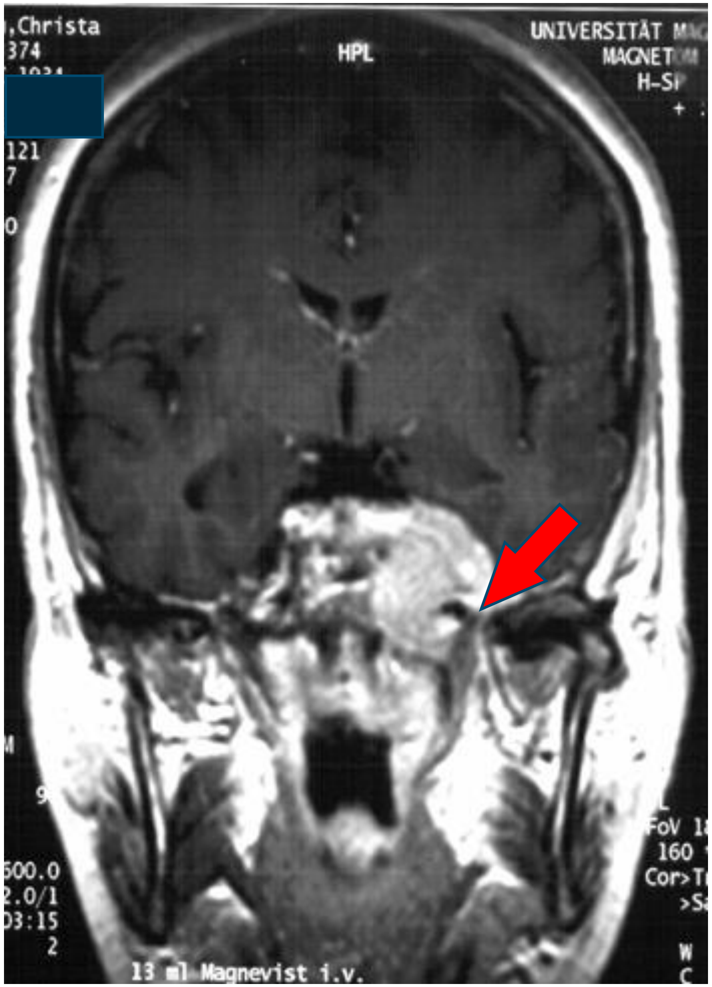


Daily IGRT



Online in-beam PET

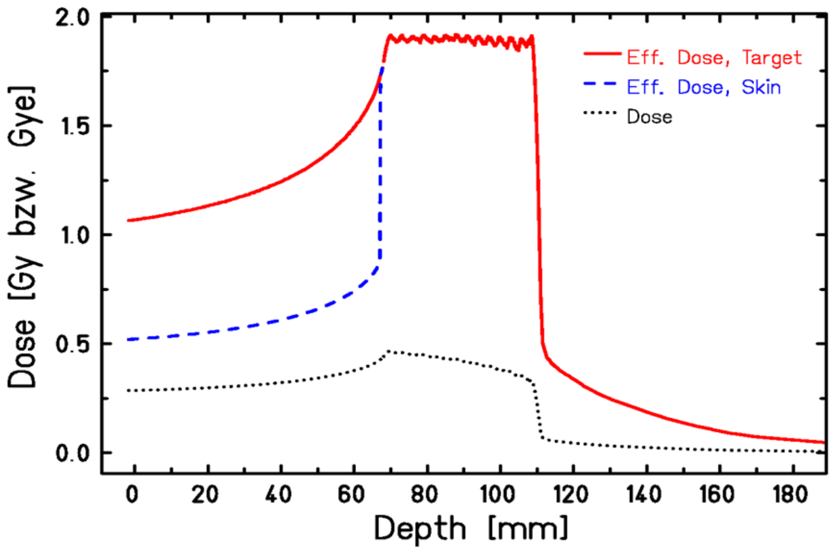
Early Clinical Response: Adenoidzystic Carcinoma:

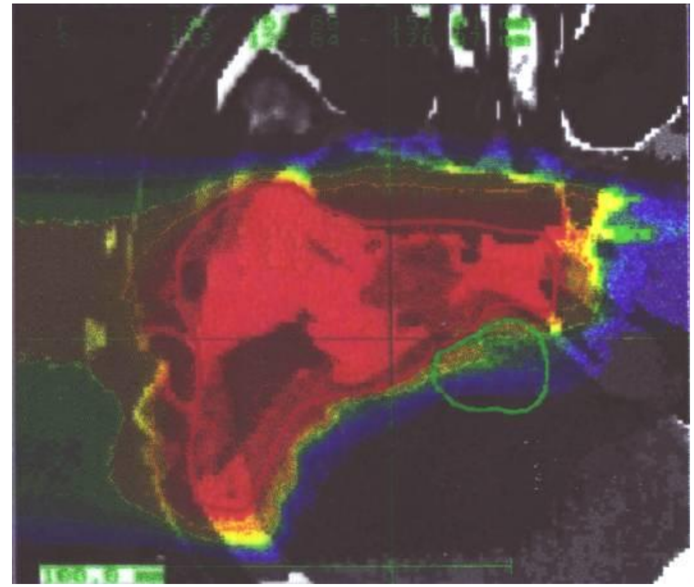


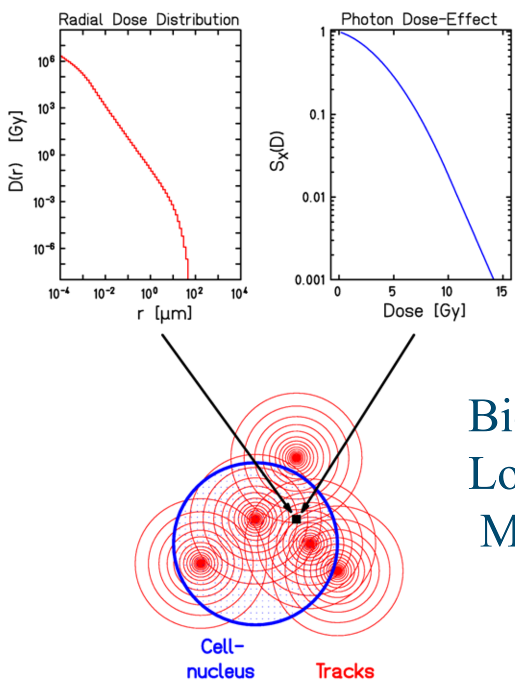
Before RT

6 Weeks after RT

Acceptable Skin Reaktion

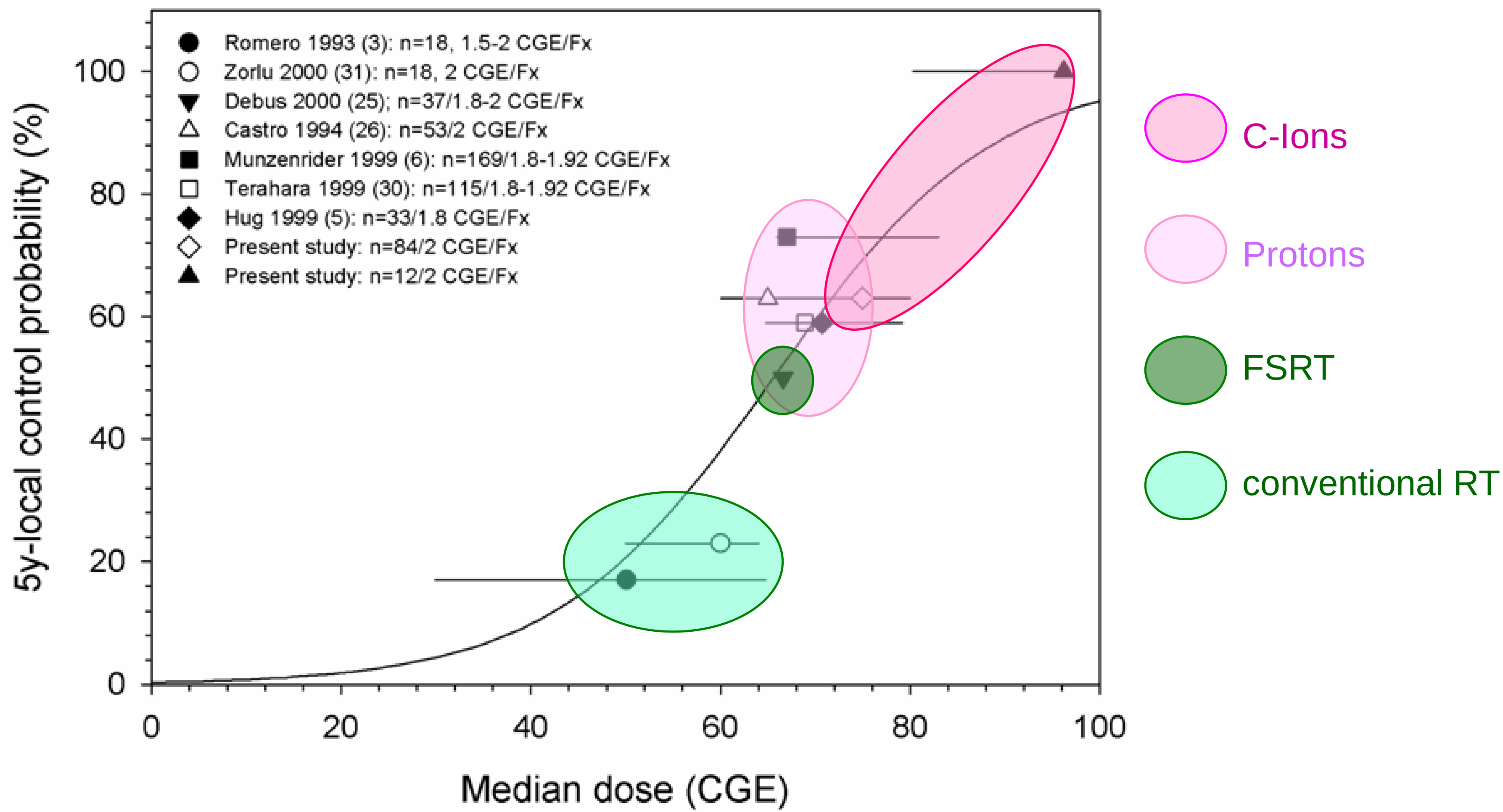






Biol.Wikungung:
Local Effect
Model :LEM

Radiotherapy of Skull Base Chordomas
Motivation: Dose Response Relationship



D. Schulz-Ertner, IJROBP 2007

1998: Project proposal for „HIT“

2000: Feasibilty study: HIT is feasible

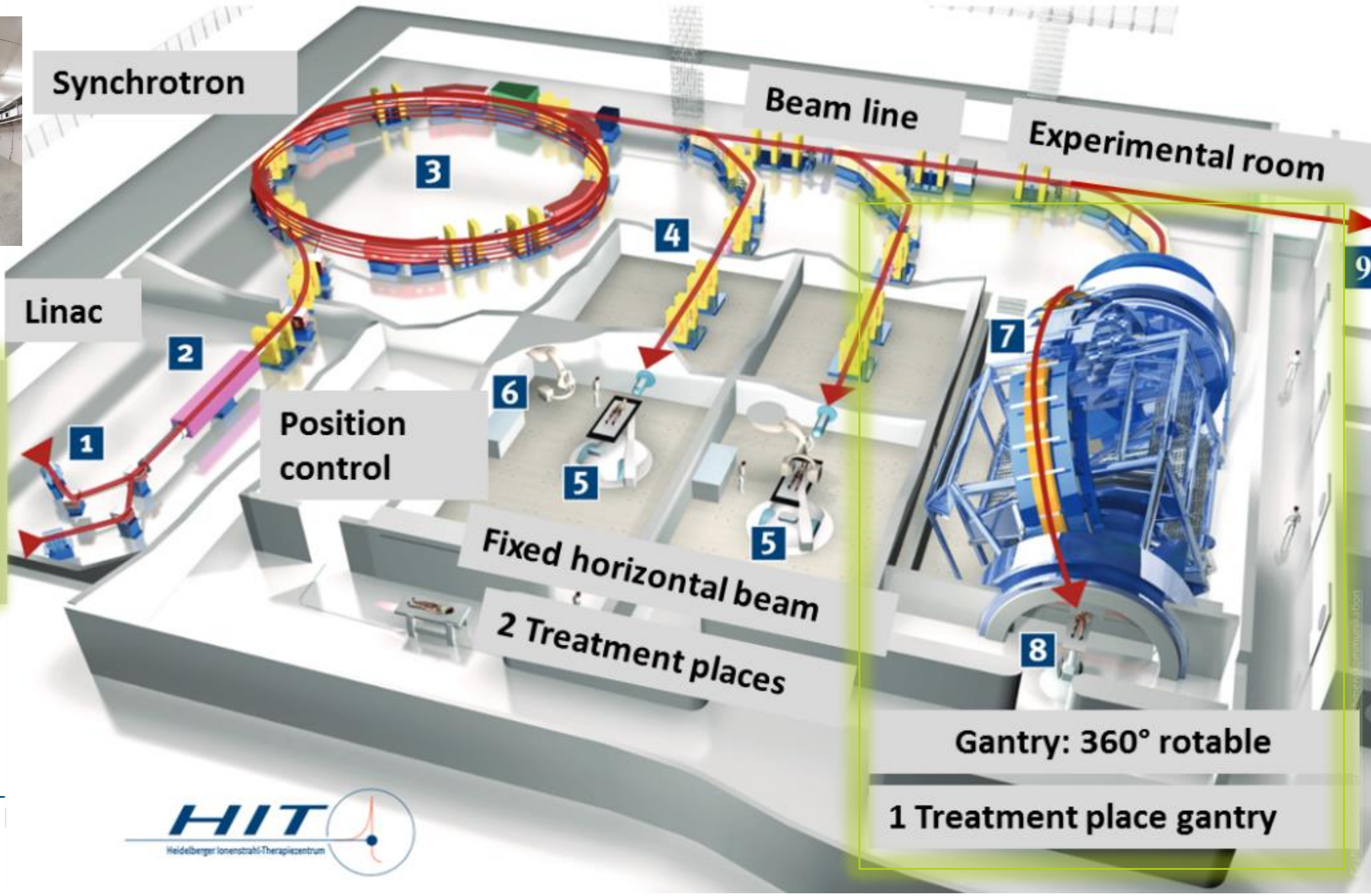
2001: Scientiffic board agrees, planning started

2004: Foundation stone ceremony

2009: first patient at HIT

Heidelberg Ion Therapy Center

- ✓ HIT is the world's first heavy ion treatment facility with a 360° **rotating beam delivery** system (gantry).
- ✓ HIT is Europe's first combined treatment facility using **protons and heavy ions** for radiation therapy.

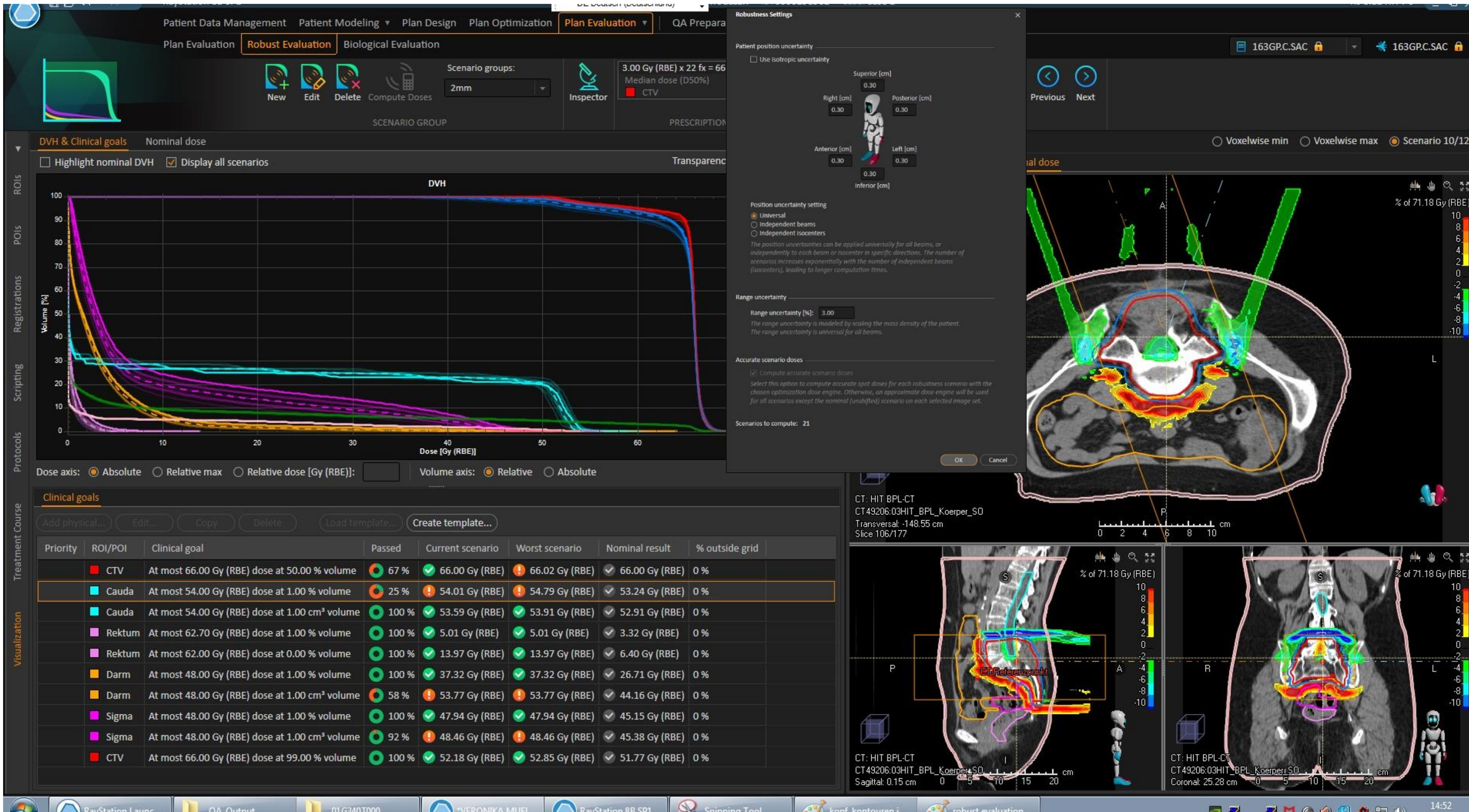


Indications currently treated at HIT and MIT

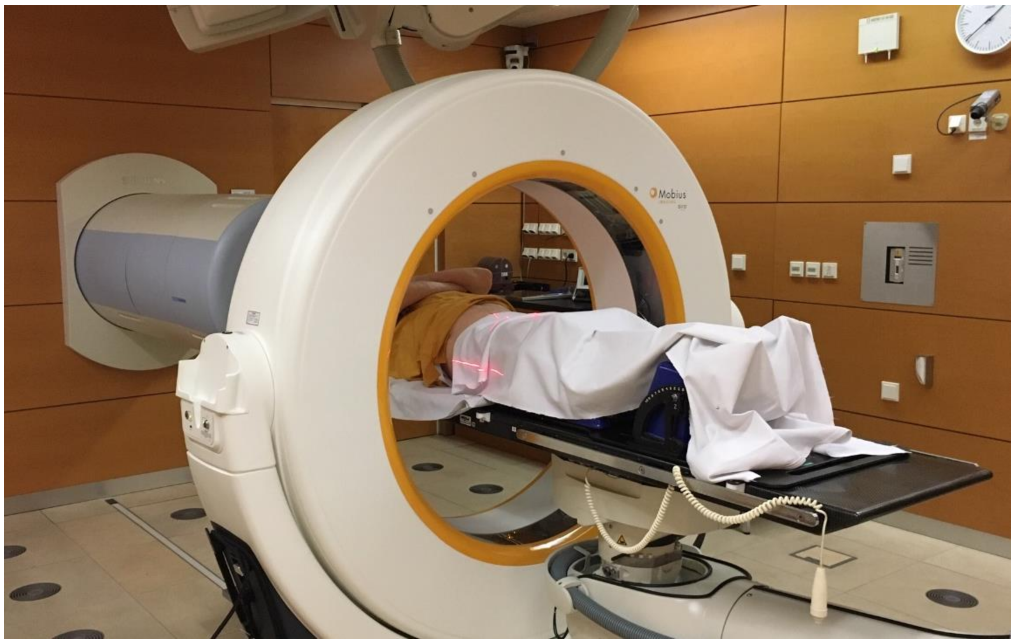
Indications	
Tumors in children and young adults	Ependymoma Retinoblastoma, Medulloblastoma, Glioma, Lymphoma, Sarcoma, Neuroblastoma, Teratoma Craniopharyngeoma
Chordoma and Chondrosarkoma of the skull base	
Cerebral Arterioveneuos Malformations (AVM) Mediastinal Lymphoma (protons)	

Within phase II clinical trials
Adenoid cystic carzcnoma (ACC)
Glioma Grad II/III in adults, **glioblastoma**
Paraspinal sarcoma and carcinoma, non-operable osteo- and chondrosarcoma of axis skeleton
Meningeoma of skull base - (> 15 ccm) and atypical forms, incompletely resected or sinus cavernosus involvement
Advanced **head and neck tumors** without distant metaastases
Hepatocellular carcinoma
Thoracic tumors: Lung carcinoma (NSCLC, inoperabel stage I-III), and pleural mesothelioma stage I-III, if pleuropneumonectomy is not possible
Locally advanced **gynecological malignoma**, previously treated with RT or not suitabefr brachytherapie.
Esophageal carcinoma not resectable
Soft tissue sarcoma/chordoma am Körperstamm (neo)-adjuvant and primary if inoperable and extremities after extremity conserving surgery
Locally advanced **pancreatic carcinoma** TxNxM0 with (neo-)adjuvant particle therapy or inoperability
Pituitary gland adenoma (inoperabel, not suitable for radiosurgery /SRS
Craniopharyngeoma
Akusticus neurinoma (inoperabel, not suitable for radiosurgery /SRS

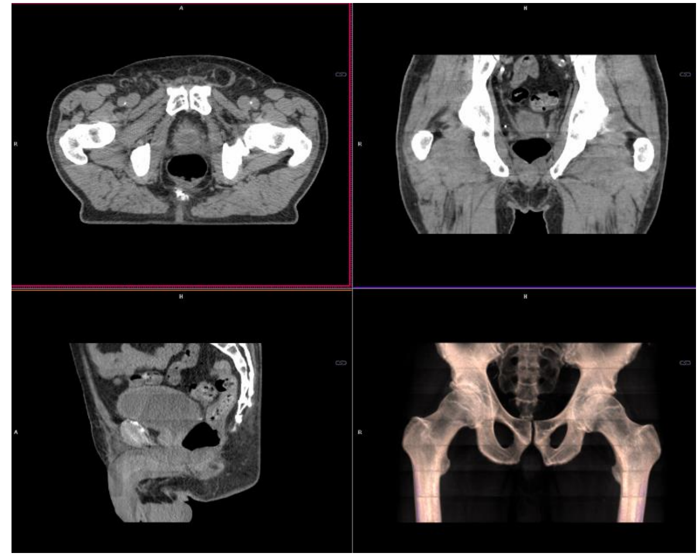
Evaluation Of Plan Robustness In Particle RT: Quantitate Dose Uncertainty Incl. RBE



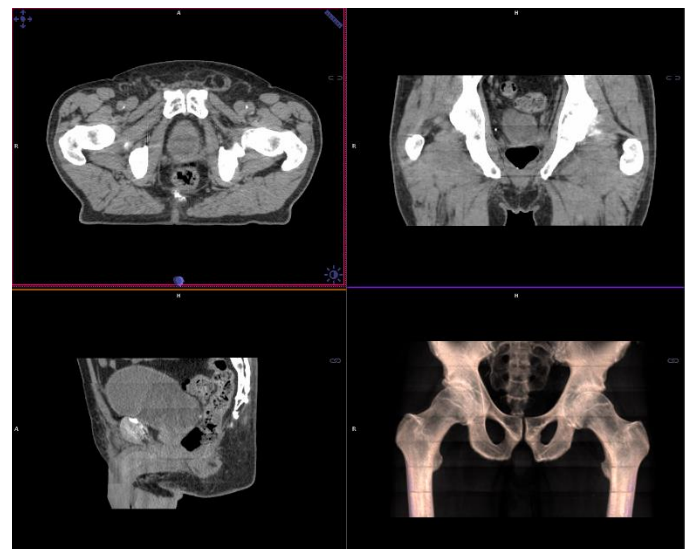
In Room Imaging For Particle RT



Carbon Ion Nozzle with Airo -CT

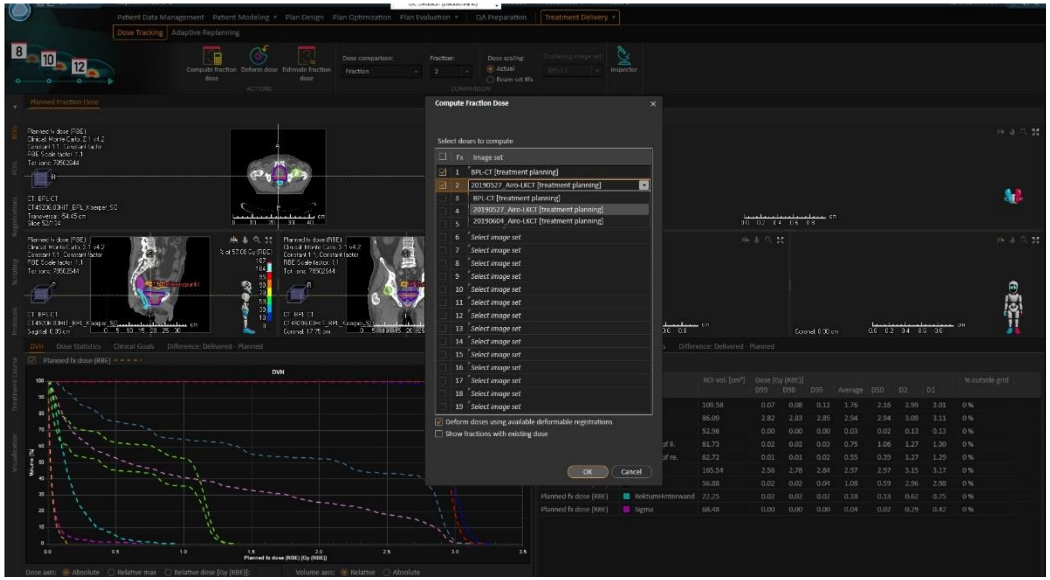


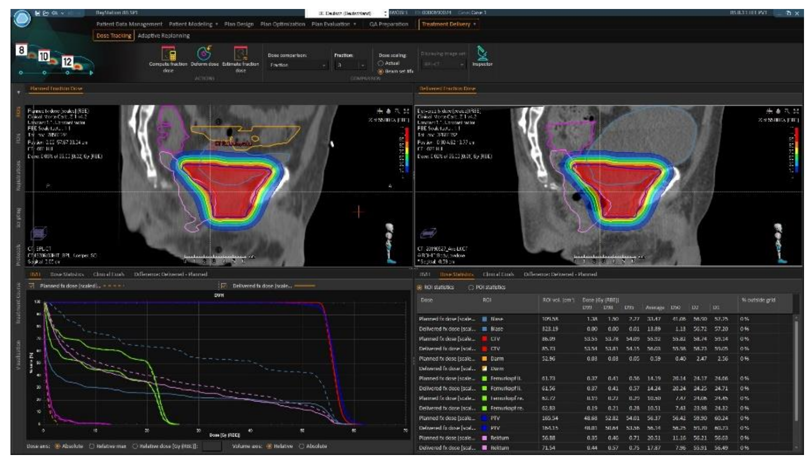
week 1



week 2

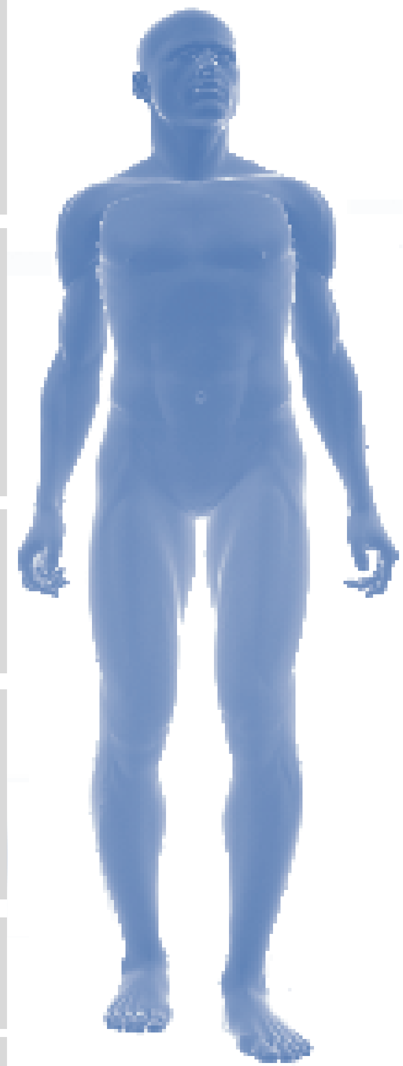
Dose Tracking In Prostate Cancer





Clinical trials

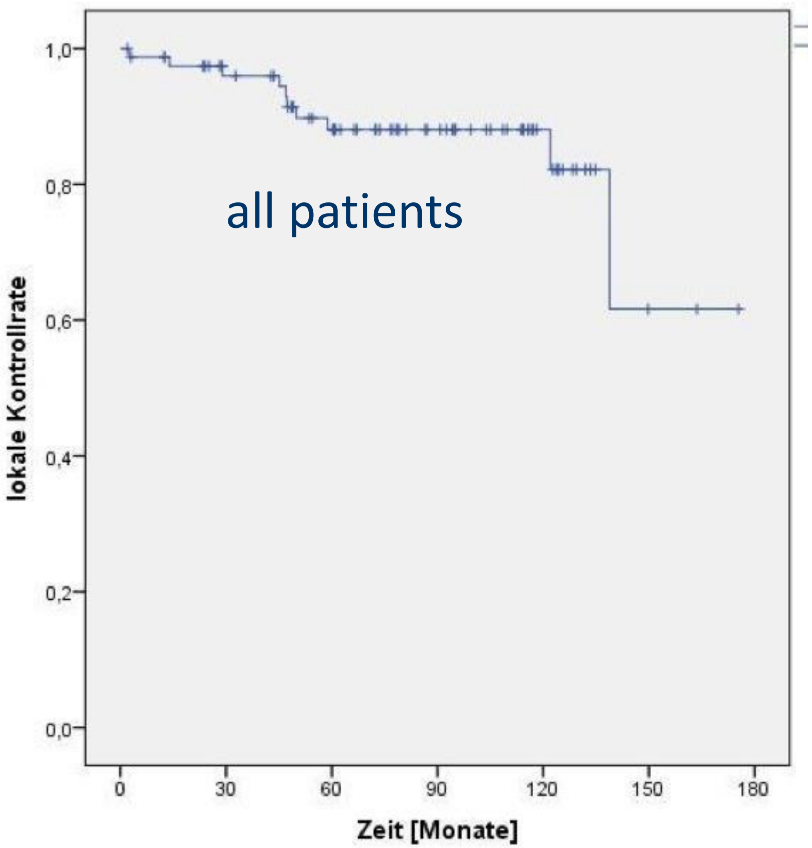
Chordoma & Sarkoma	Chordoma of the scull base: H1 vs. C12 recruiting ISAC (C12/H1 for sacral chordoma) recruiting SB chondrosarcomas: H1 vs. C12 recruiting **OSCAR** (H1 + C12 boost; inoperable osteosarkoma) recruiting
Head & Neck	**COSMIC** (C12 boost RT; salivary glands ACC) published **ACCO** (C12 only; salivary glands ACC) approved ACCEPT (C12 boost RT + Erbitux for ACC) recruiting TPF-C HIT (C12 boost RT; head&neck) closed IMRT HIT-SNT (C12 boost RT; sinu-nasal cancer) recruiting
Brain	CLEOPATRA (H1 vs. C12 boost RT; prim. glioblastoma) f/u phase CINDERELLA (C12 recurrent gliobastoma) f/u phase MARCIE (C12 boost RT, meningeomas grade 2) recruiting
Prostate	IPI (C12/H1 for prostate cancer) f/u phase PROLOG (hypofract. H1 for prostate cancer recurrence) f/u phase PAROS (hypofract H1 vs IMRT prostate-CA adjuvant/salvage KOLOG (hypofract. C12 for Prostate cancer recurrence) f/u phase
GI	PROMETHEUS (C12 for HCC) recruiting PANDORA (C12 for recurrent rectal carcinoma) recruiting
Lung	INKA (neoadj. C12 for inop. sulcus superior tumors NSCLC) recruiting

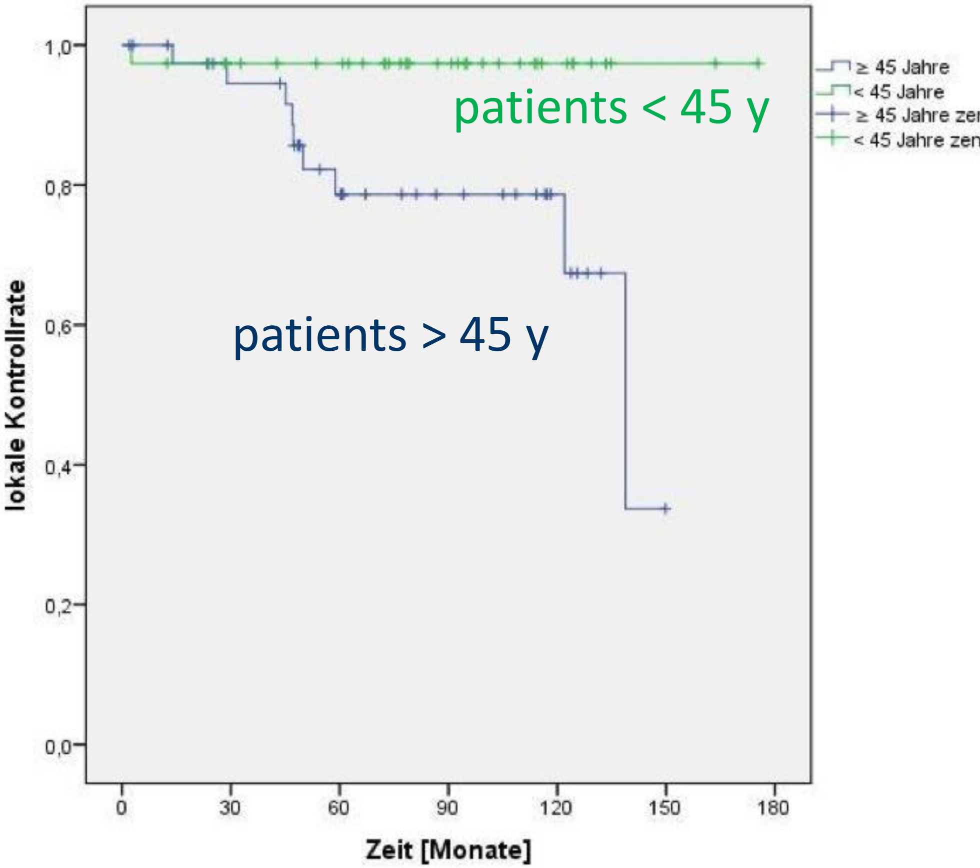


Carbon ions

Skull Base Chondrosarcoma
local control

- C-12 treatment 1997-2007 (GSI)
- act. 10 yrs LC 88 %
- act. 10 yrs LC (< 45 J): 98%





Uhl et al. Cancer, 2014

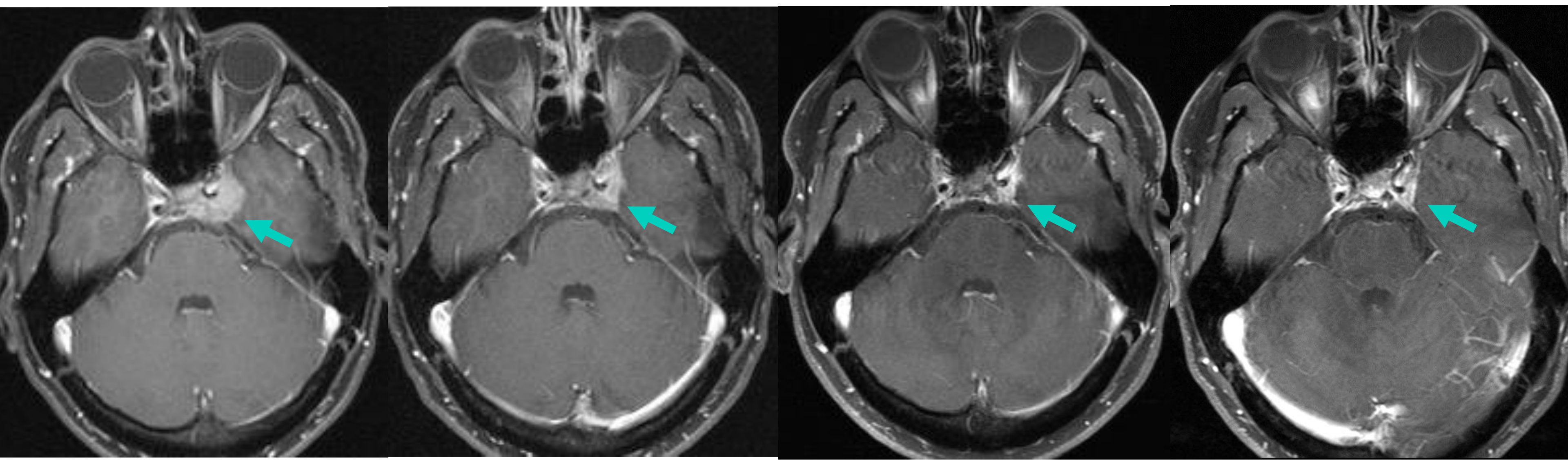
UK HD

Carbon ions

Chondrosarcoma

Symptoms at Diagnosis: Double vision

2005 | 2007 | 2011 | 2015

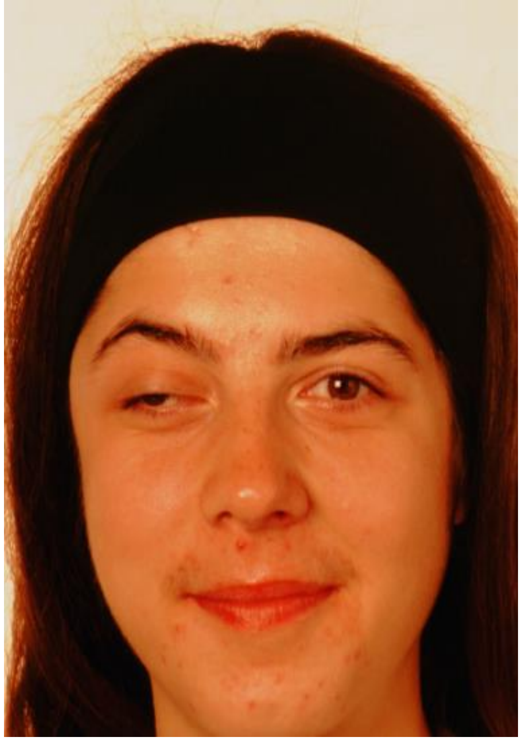


Before C-12 RT | Follow-up

Petroclival Chondrosarcoma

Reduction of neurological symptoms

18 year old patient



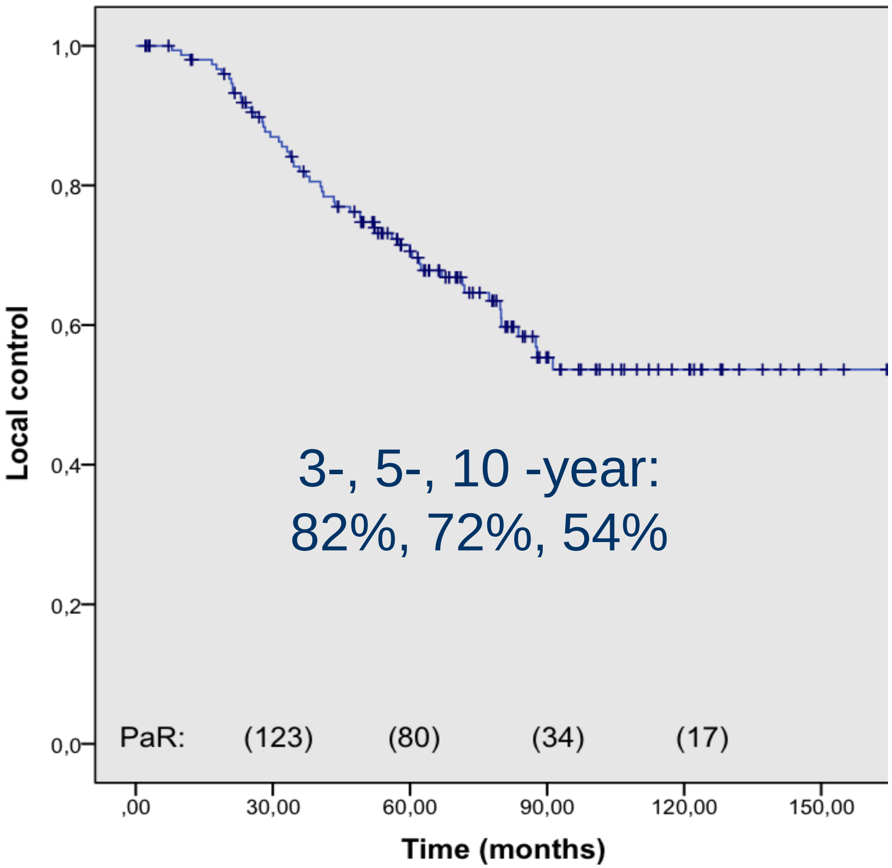
before RT

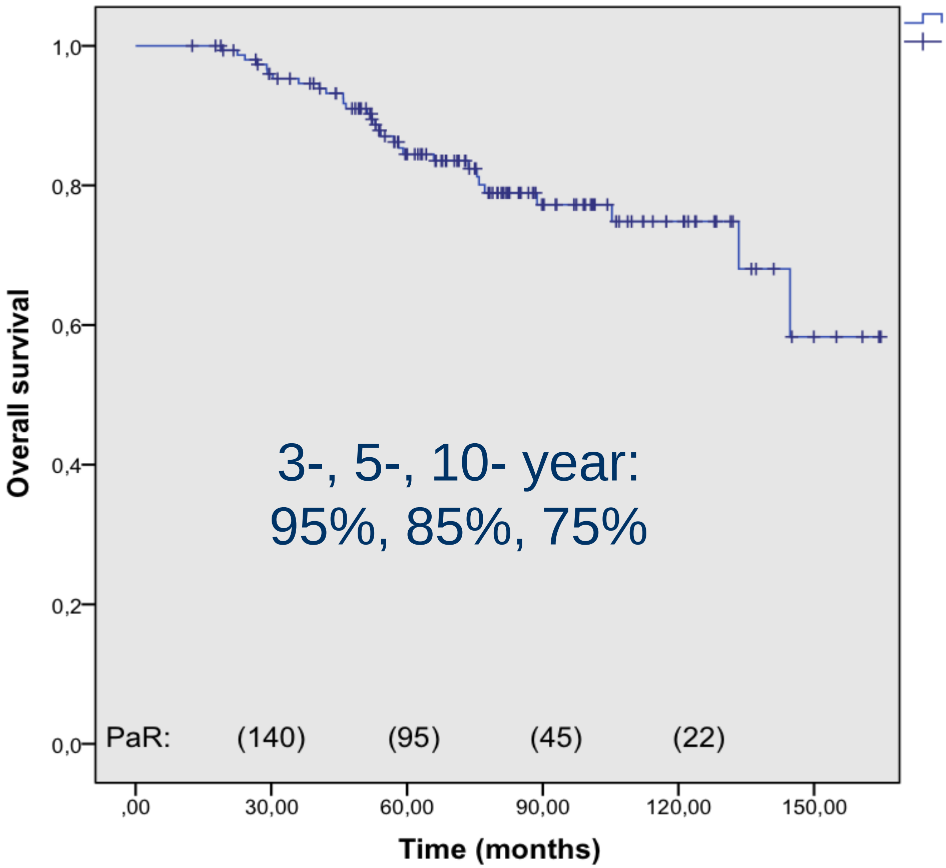
6 weeks after RT

12 / 27 patients show reduced symptoms

Skull Base Chordomas treated at GSI

Uhl M et al., Cancer 2014; 120(10): 1579–1585.





Carbon ions

HIT Trial for Skull Base Chondrosarcomas

Start: 2010
Recruitment 6/18: 77

SB Chondrosarcoma
n = 154

- 63 Gy(RBE) C12 (21 Fx)
- 70 Gy(RBE) Protons (35 Fx)

Original Article

Mattke et al., Cancer 2018

High Control Rates of Proton- and Carbon-Ion–Beam Treatment With Intensity-Modulated Active Raster Scanning in 101 Patients With Skull Base Chondrosarcoma at the Heidelberg Ion Beam Therapy Center

>> Carbon ion and protons were equally effective (LC and OS)

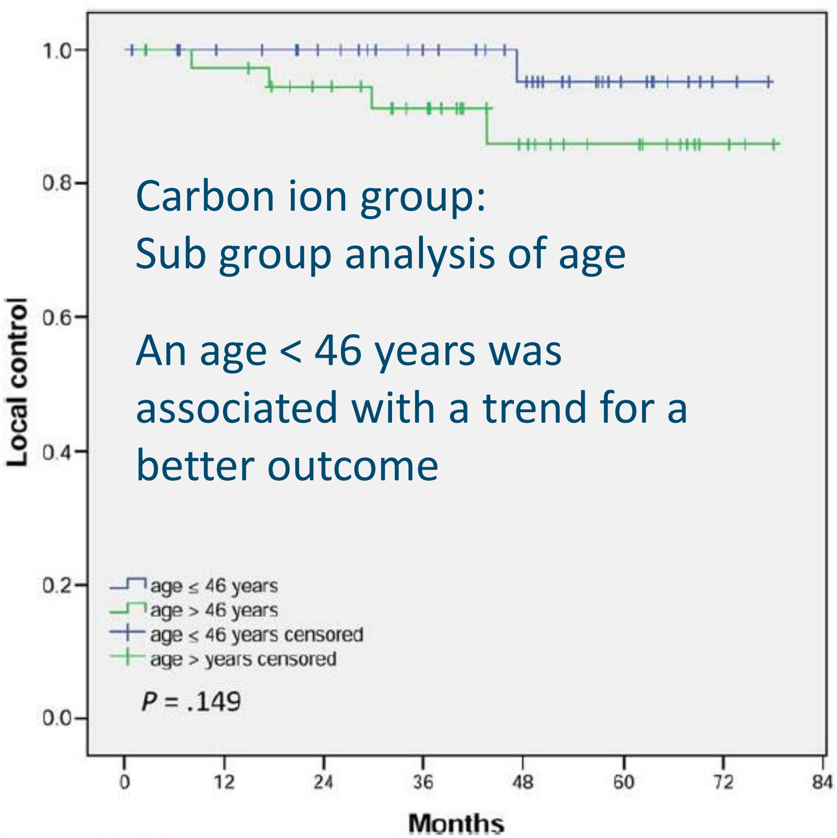


Figure 3. Subgroup analysis of age in the carbon-ion group.

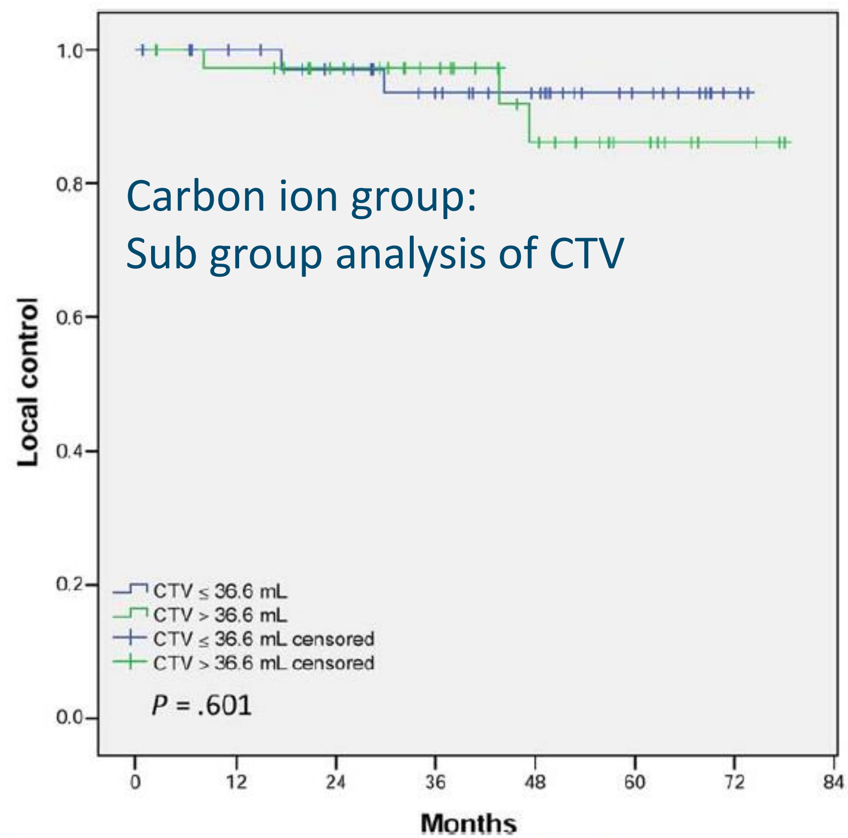


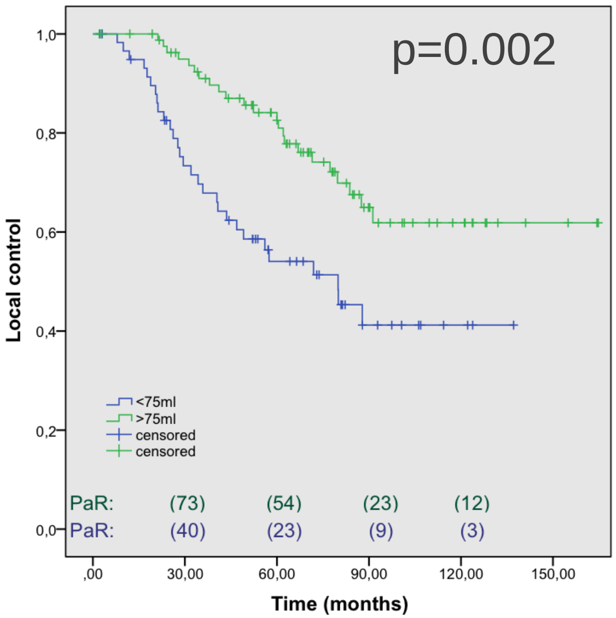
Figure 4. Subgroup analysis of the clinical target volume in the carbon-ion group.

Skull Base Chordomas treated at GSI

Uhl M et al., Cancer 2014; 120(10): 1579–1585.

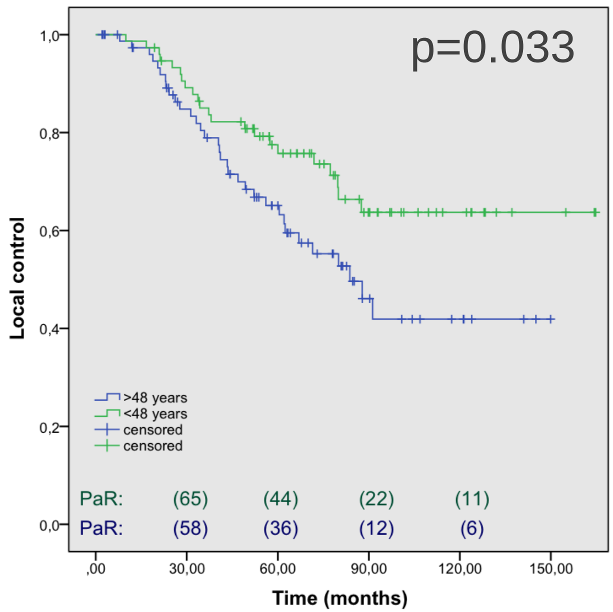
Prognostic factors

Boost Volume
<> 75 ml

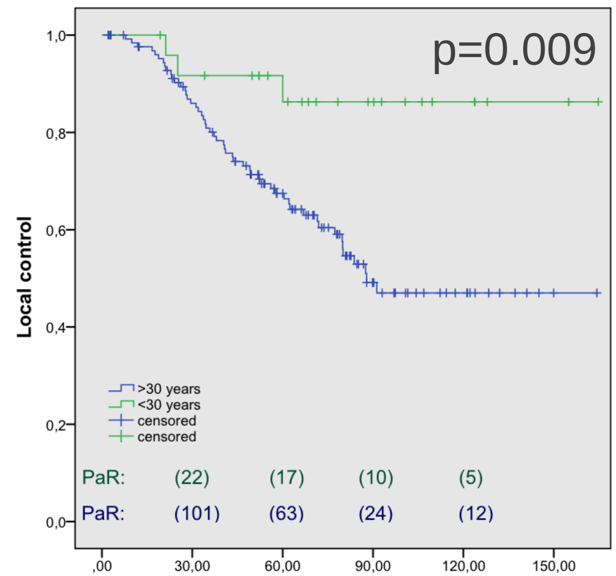


age

<> 48 y



<> 30 y



Carbon ions

HIT Trial for Skull Base Chordomas

prospective, randomized phase III trial

Hypothesis: 10% increase in LPFS by using carbon ions

Start: 2010
Recruitment 6/18: 105

SB Chordoma

n = 344

60-66 GyE C12 (20-22 Fx)

72-76 GyE Protons (36-38 Fx)

Nikoghosyan et al. BMC Cancer 2010. 10, 607

ISAC- Trial

Ion irradiation of SAcrococygeal Chordoma

Hypofractionated Protons- vs. C-12-RT

Pilot trial

Prospective randomized phase II trial

2-armed

100 Patients (50 per Arm)

Stratification CTV <1000ml>

Primary endpoint: Feasibillity/Toxicity (Incidence >=Grad 3-5)

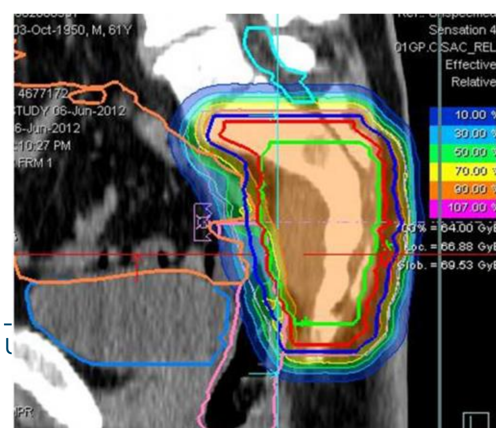
secondary endpoint : OS, LPFS, QoL

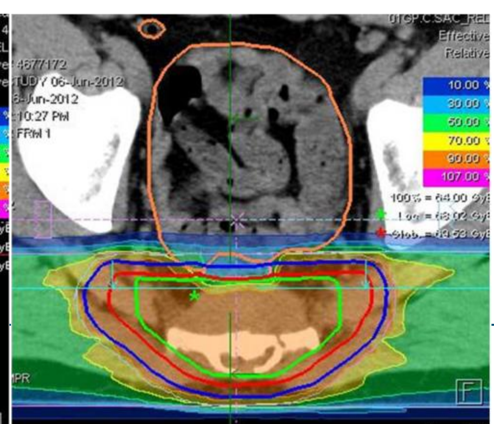
randomization

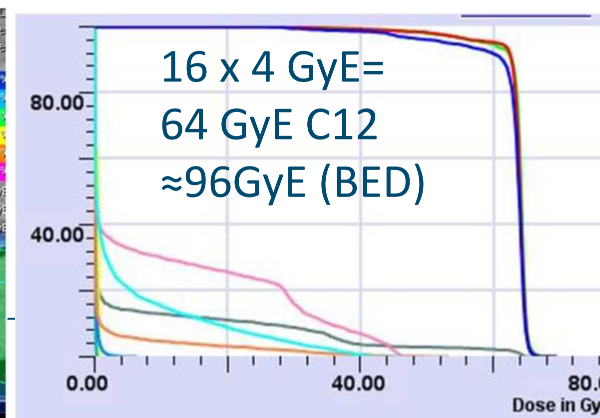
Arm A (proton therapy):
- Total dose to the PTV : 64 GyE a 4 GyE SD.
- **BED: 96Gy**

Arm B (carbon ion therapy):
- Total dose to the PTV : 64 GyE a 4 GyE SD.

BED: 96Gy







COSMIC Trial

Combined therapy of malignant **s**alivary gland tu**m**ors with **I**MRT and **c**arbon ions

- Phase II feasibility study
- 53 Patients
- median follow-up 42 months;

IMRT (Photons) alone vs IMRT (Photons) + Carbon ion boost

patient characteristics

- microscopically incomplete resections (R1, n = 20),
- gross residual disease (R2, n=17),
- inoperable disease (n=16)
- 89 % ACC,
- 57% had T4 tumors.

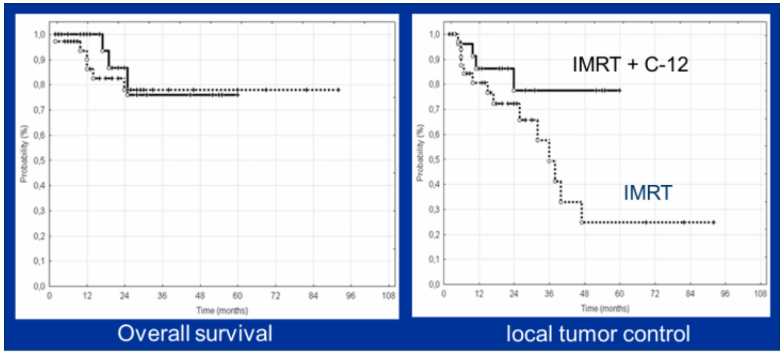
most common primary sites

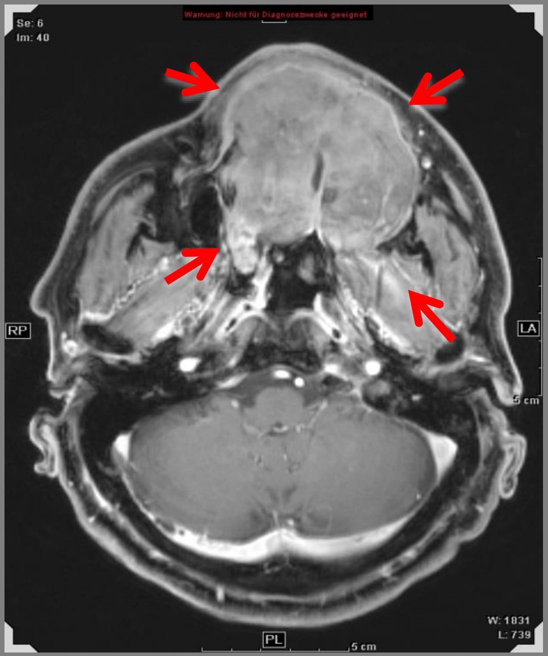
paranasal sinus (34%), submandibular gland, palate

Carbon ion (C-12) Boost and IMRT is highly effective in Salivary gland tumors

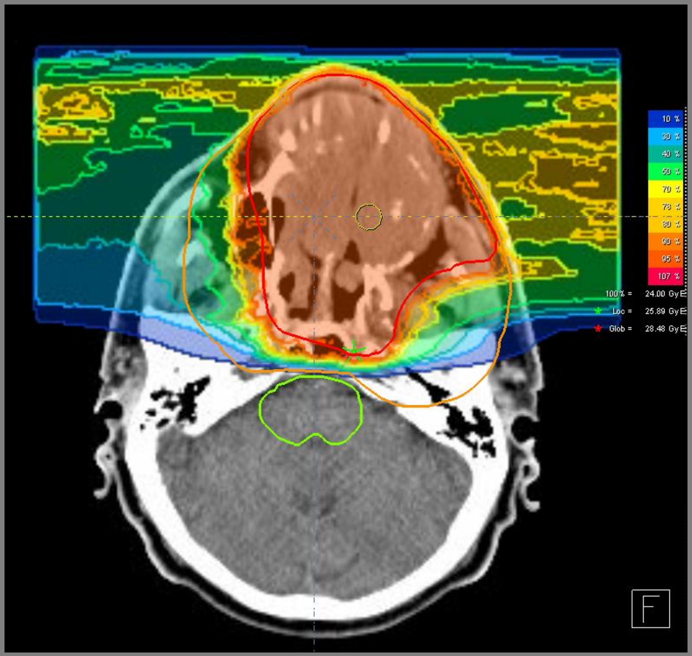
- No dose limitting acute toxicity
- Late Toxiciy > CTC grade 2 : < 5%

Schulz-Ertner, Cancer. 2005 Jul 15;104(2):338-44

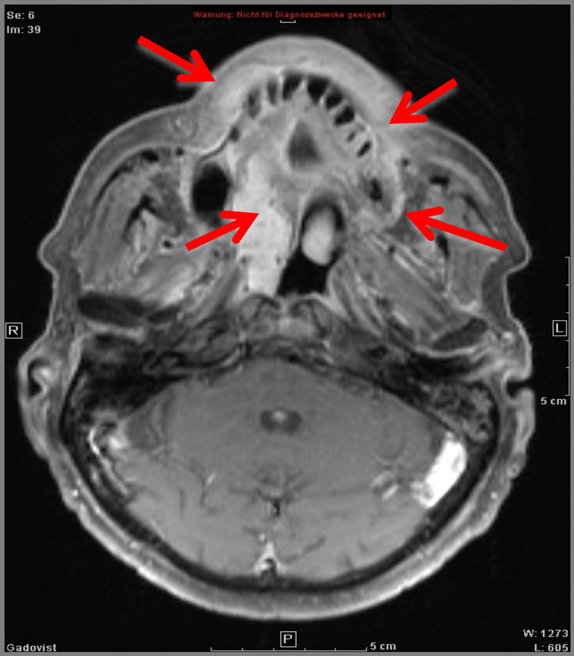




Pre-treatment situation



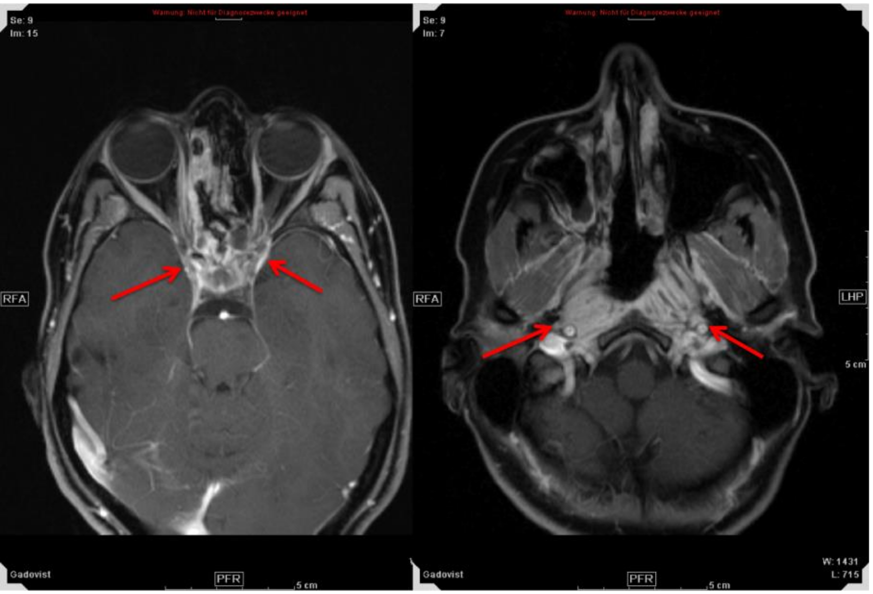
Treatment planning
C-12 boost



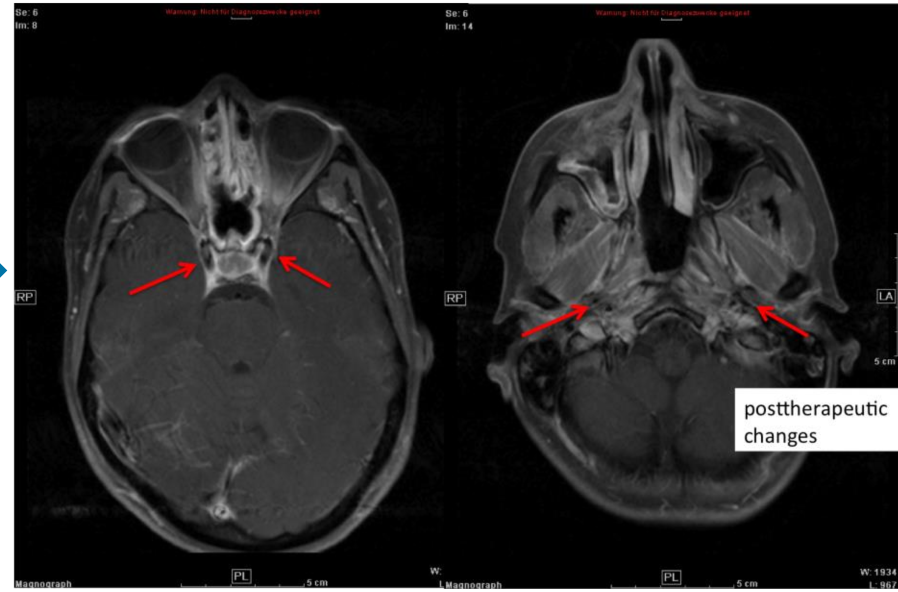
6 weeks post RT

ACC Initial treatment response and acute toxicity

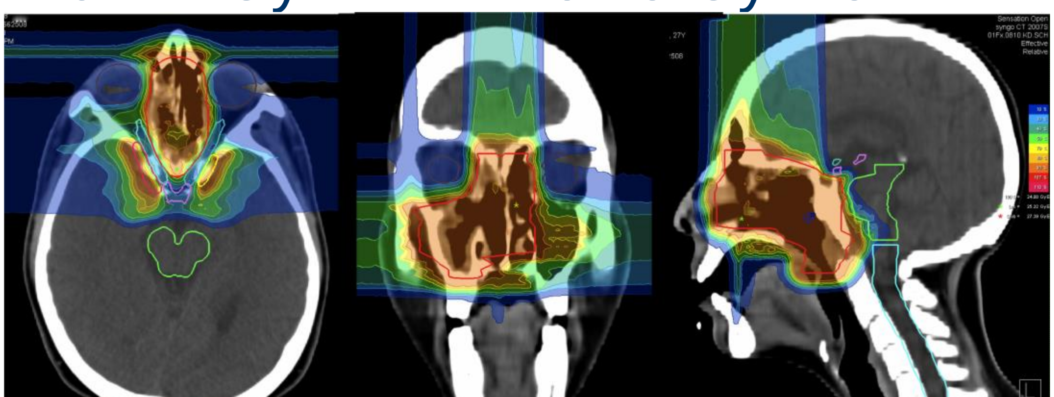
initial



Complete remission after 6 Months



25 x 2 Gy IMRT + 8x 3 GyE C-12

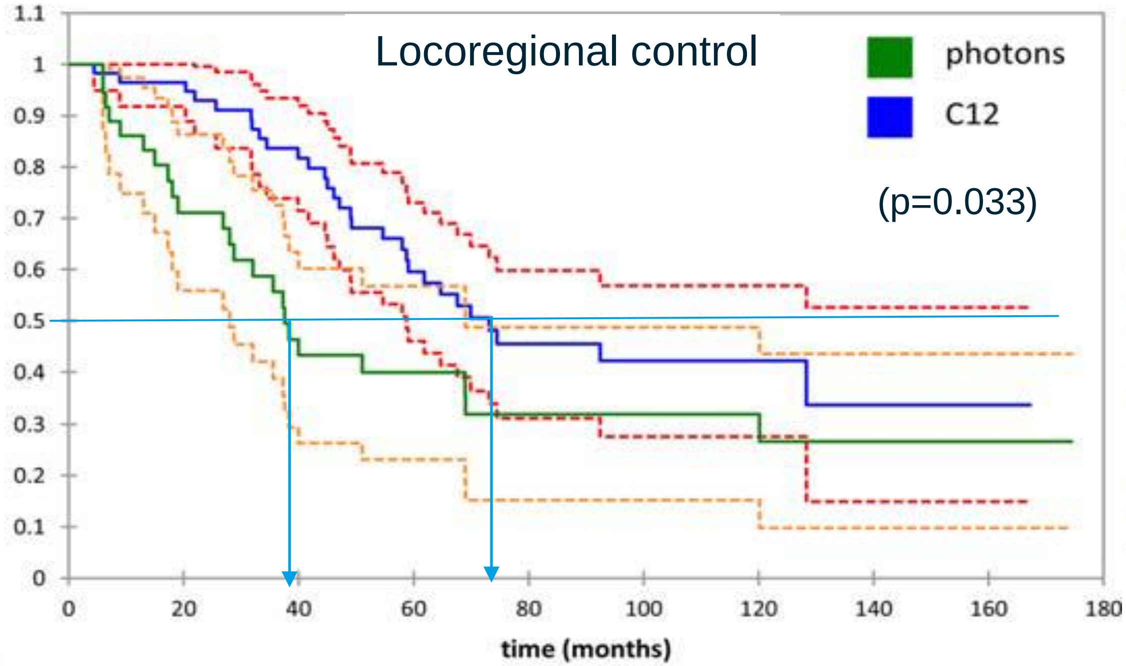


Acute toxicity remains low(< grade 4) in IMRT with carbon ion boost; also in R1-resected patients and patients undergoing re-irradiation. R2-resected patients showed high rates of treatment response

Jensen et al. Radiat Oncol, 2011

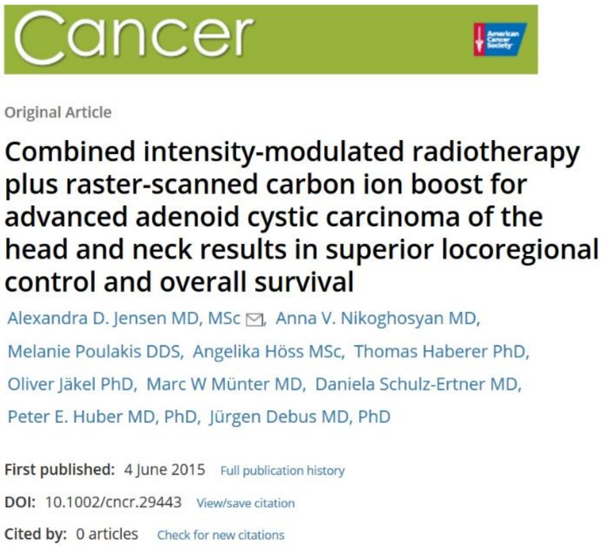
COSMIC- trial : long term results

Better local tumor control by C-12 irradiation leads to better long-term survival of locally advanced adenoid cystic carcinoma



numbers at risk:

C12:	58	55	43	28	17	11	8	5	2
photons:	37	24	15	12	9	7	7	5	2



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

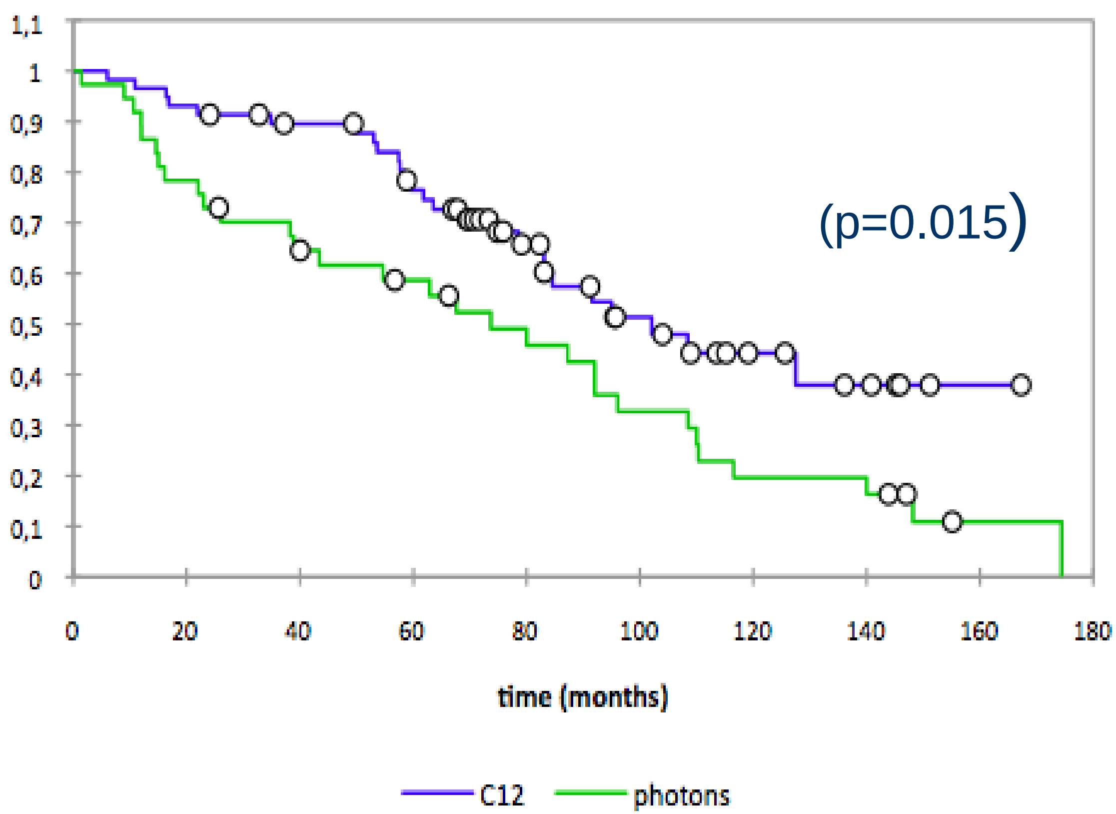
First published: 4 June 2015 Full publication history
DOI: 10.1002/cncr.29443 View/save citation
Cited by: 0 articles Check for new citations

Jensen et al. 2015, Cancer

COSMIC- trial : long term results

Better local tumor control by C-12 irradiation leads to better long-term survival of locally advanced adenoid cystic carcinoma

Overall Survival



Cancer

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First published: 4 June 2015 Full publication history

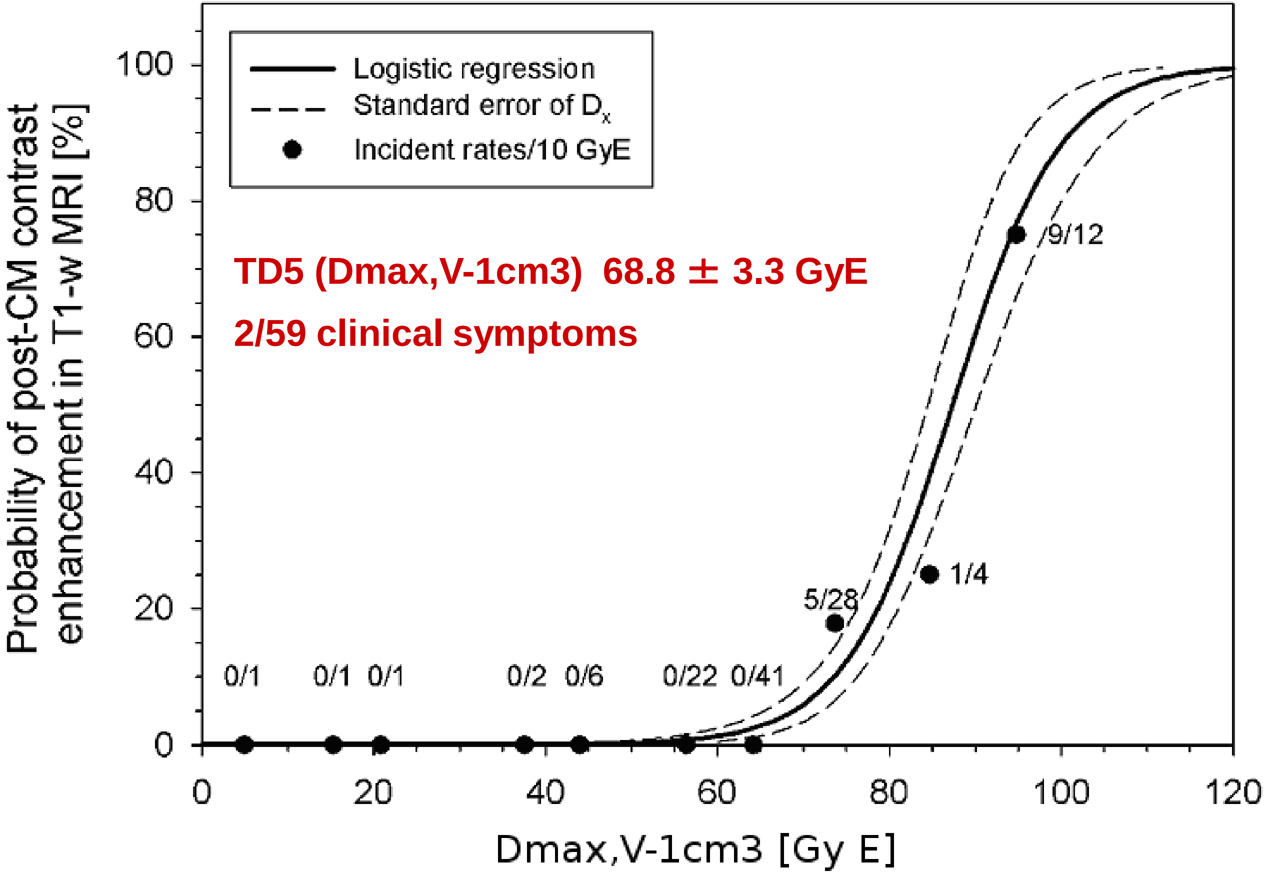
DOI: 10.1002/cncr.29443 View/save citation

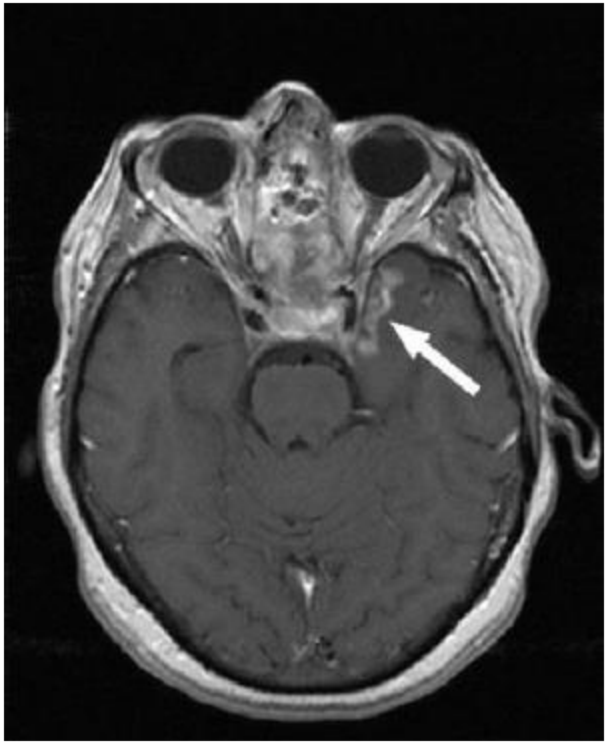
Jensen et al. 2015, Cancer

Late toxicity after carbon ion RT:

dose response for contrast enhancement in the temporal lobes

n= 59, 2002-2003, Folow-up 2,5 years



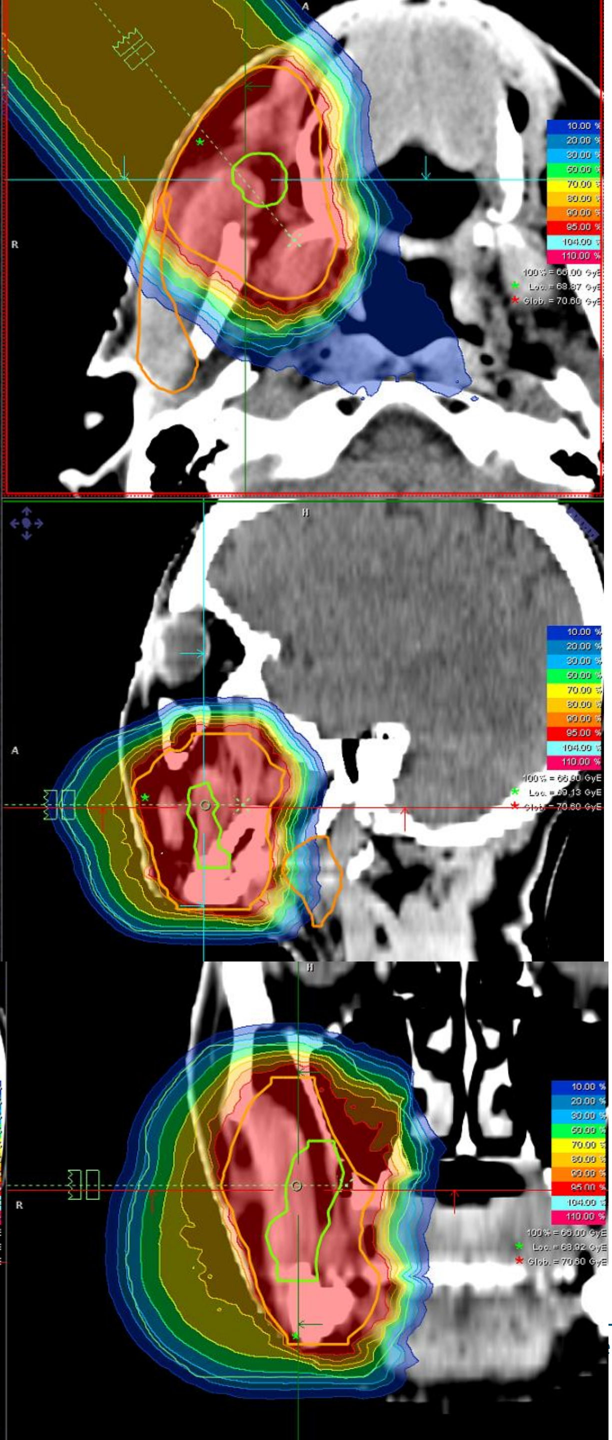


Schlampp et al., Int J Radiat Oncol Biol Phys, (2011) 80: 815ff

ACC Study Comparison

Locoregional Control

		3 yrs	4 yrs	5 yrs
IMRT	Jensen, 2015	56 %	43 %	40 %
IMRT + C12	Jensen, 2015	84 %	70 %	60 %
C12	Ikawa, 2017	89 %	82 %	69 %
C12	Mizoe, 2004	75 %	65 %	60 %



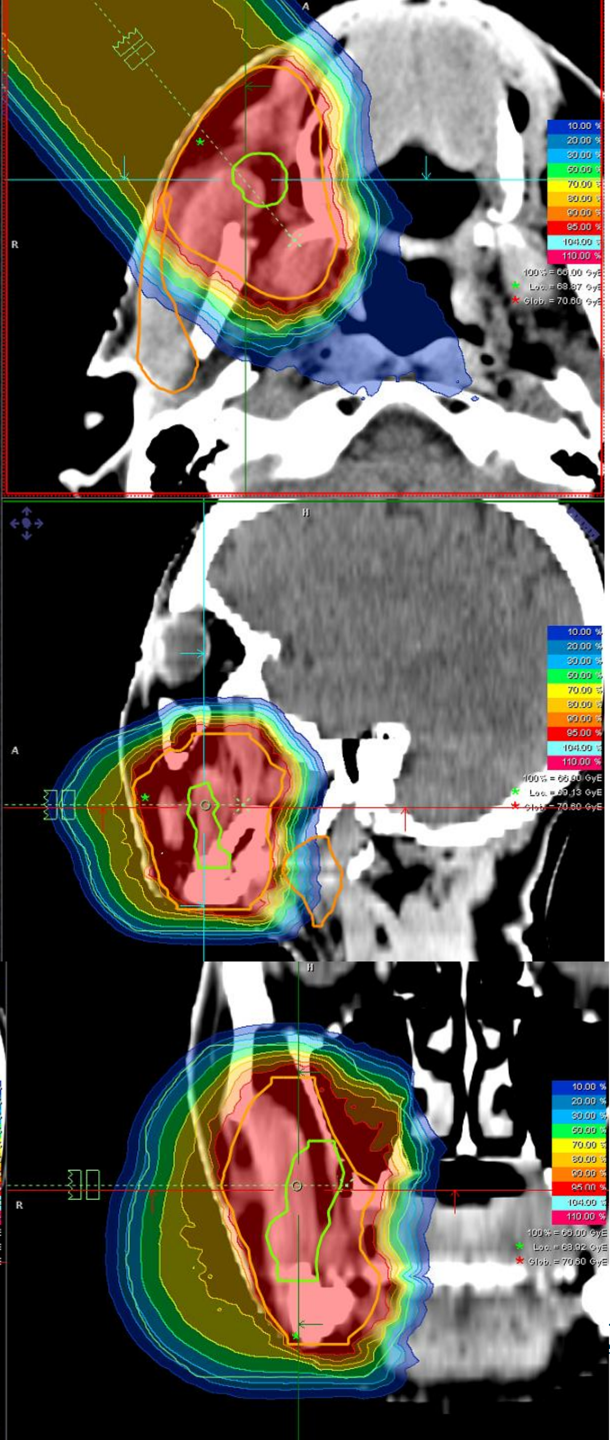
ACCO trial

Adenoid Cystic carcinoma Carbon Only

- Prospektive, randomized two armed Phase II trial
- 175 patients in 4 years
- ACC inoperabel and/or R1/R2 resected and/or (Pn+) and/or pT3/pT4

	Experimental arm: **Carbon only**		Control arm: bimodal RT (IMRT + Carbon)	
	CTV_GP	**CTV_BP**	**CTV_GP**	**CTV_BP**
Einzeldosis	3 Gy(RBE)	3 Gy(RBE)	2 Gy	3 Gy(RBE)
Gesamtdosis	51 Gy(RBE)	15 Gy(RBE)	50 Gy	24 Gy (RBE)
BED2Gy*	61 Gy	18 Gy	50 Gy	29 Gy
	22 FX in 4 weeks 5-6 FX per week		33 FX in ca. 6 weeks	

- Primäry endpoint: loco-regional control (5 years)



(approved)

ACCO trial

Adenoid Cystic carcinoma Carbon Only

- Prospective, randomised phase II trial
- 175 Patienten in 4 years
- ACC inoperabel and/or • R1/R2 resected and/or • (Pn+) and/or • pT3/pT4

	carbon ions only		photons + carbon ions	
	CTV_GP	CTV_BP	CTV_GP	CTV_BP
single dose	3 Gy(RBE)	3 Gy(RBE)	2 Gy	3 Gy(RBE)
total dose	51 Gy(RBE)	15 Gy(RBE)	50 Gy	24 Gy (RBE)
BED2Gy*	61 Gy	18 Gy	50 Gy	29 Gy
	22 FX in 4 weeks 5-6 FX per week		33 FX in ~ 6 weeks	

- Primary endpoint: loco-regional control (5 years)

Akbaba et al., Cancer 2018

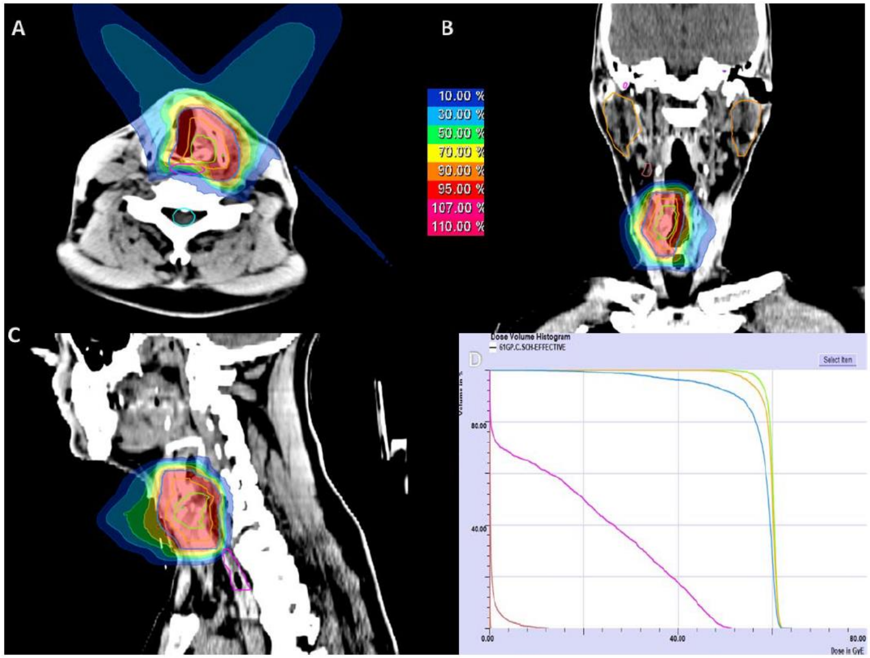
cancers

MDPI

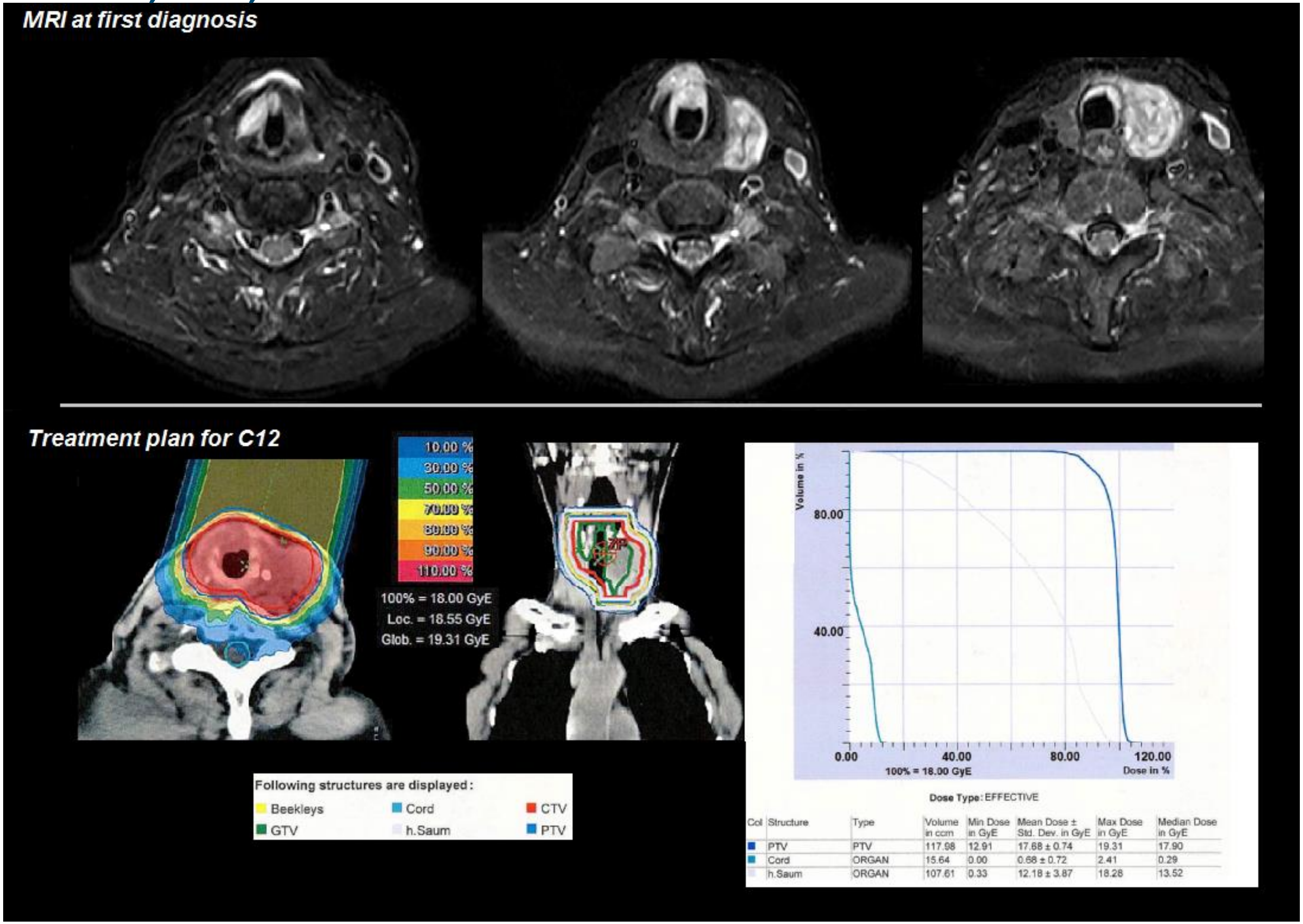
Article

Accelerated Hypofractionated Active Raster-Scanned Carbon Ion Radiotherapy (CIRT) for Laryngeal Malignancies: Feasibility and Safety

Sati Akbaba [1,2,3], Kristin Lang [1,2,3], Thomas Held [1,2,3], Olcay Cem Bulut [4], Matthias Mattke [1,2,3], Matthias Uhl [1,2,3], Alexandra Jensen [5], Peter Plinkert [4], Stefan Rieken [1,2,3], Klaus Herfarth [1,2,3], Juergen Debus [1,2,3] and Sebastian Adeberg [1,2,3,*]

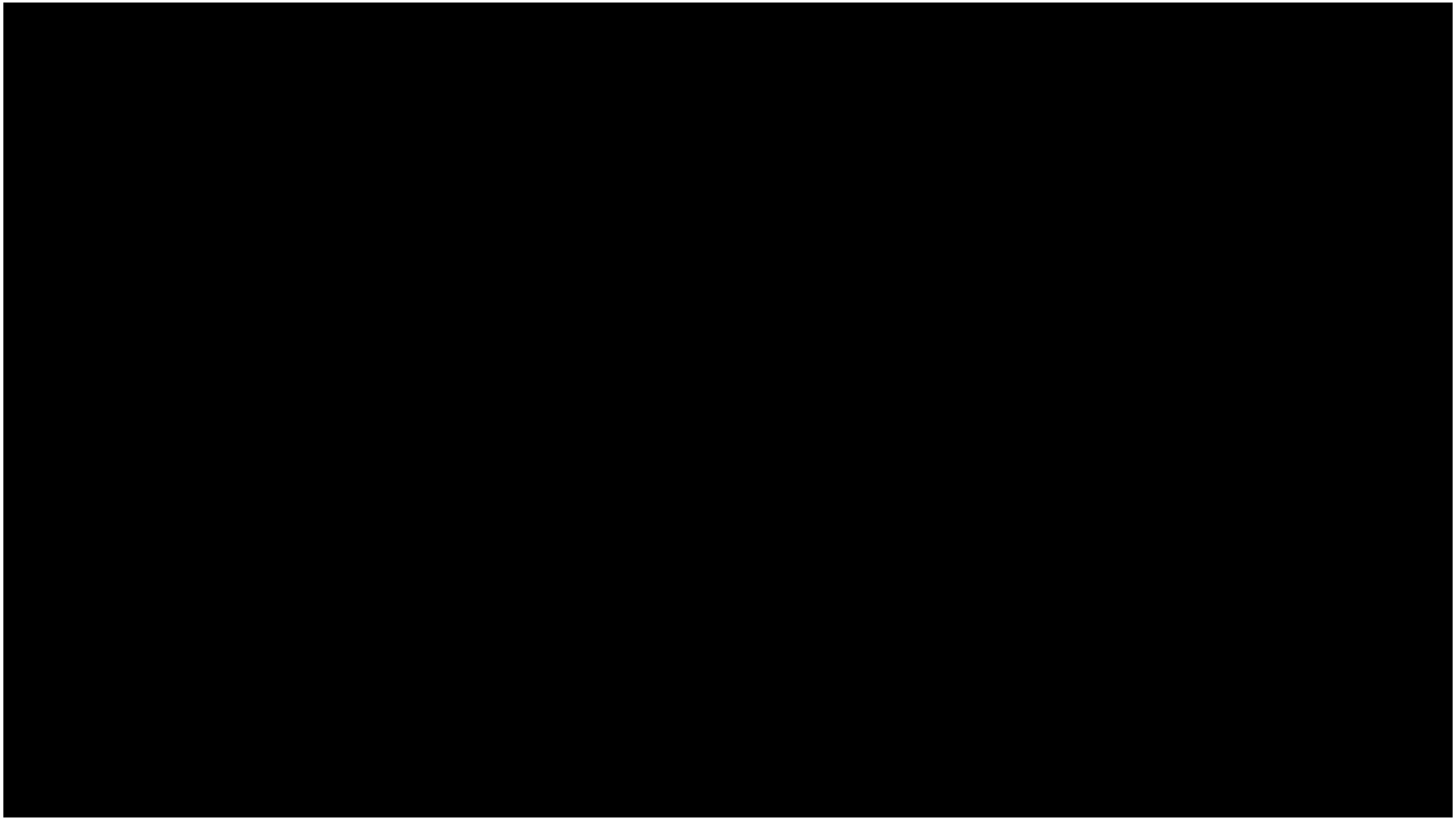


ACC, T4, definitive carbon ion RT 2016

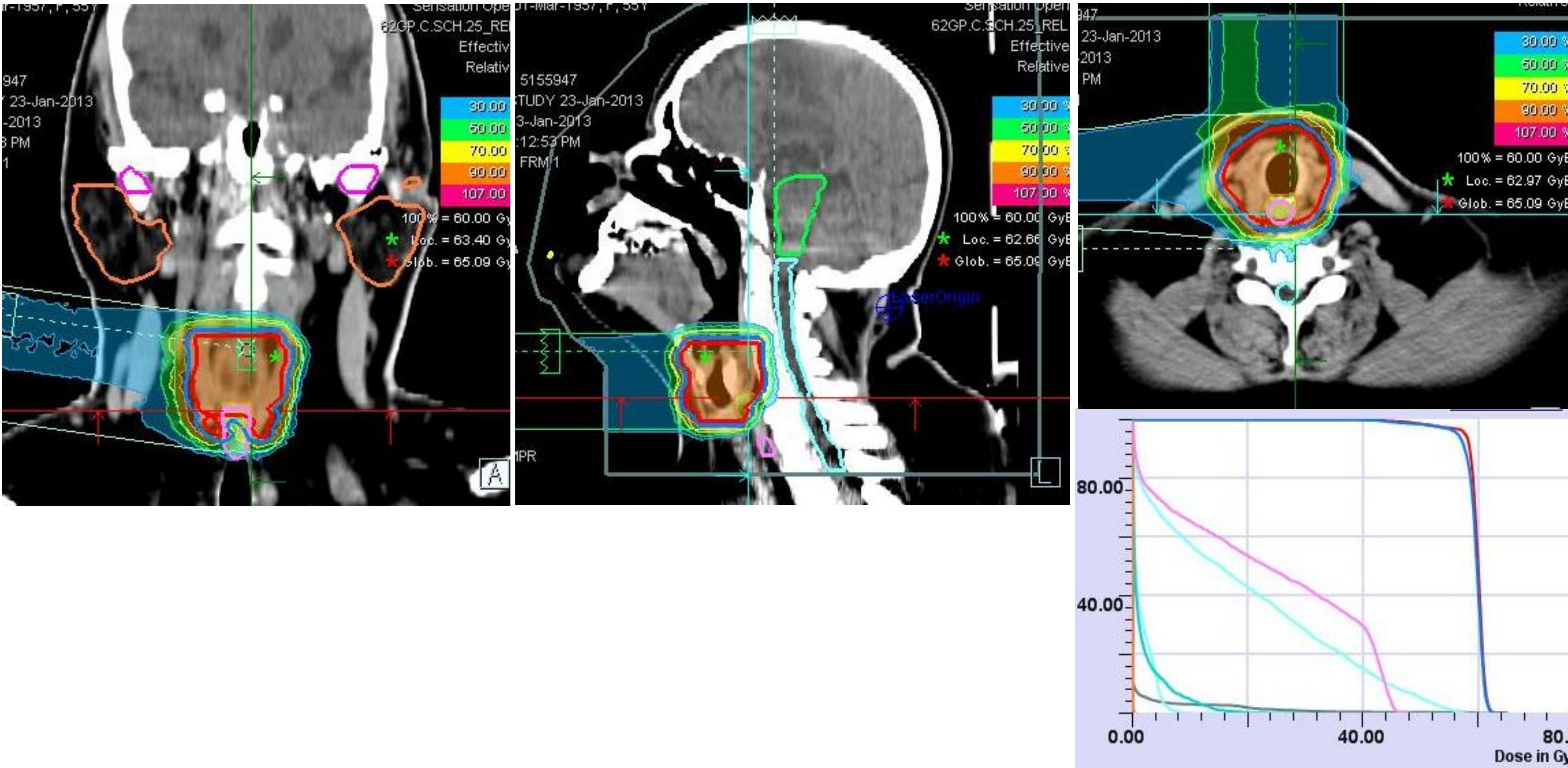


Col	Structure	Type	Volume in ccm	Min Dose in GyE	Mean Dose ± Std. Dev. in GyE	Max Dose in GyE	Median Dose in GyE
	PTV	PTV	117.98	12.91	17.68 ± 0.74	19.31	17.90
	Cord	ORGAN	15.64	0.00	0.68 ± 0.72	2.41	0.29
	h.Saum	ORGAN	107.61	0.33	12.18 ± 3.87	18.28	13.52

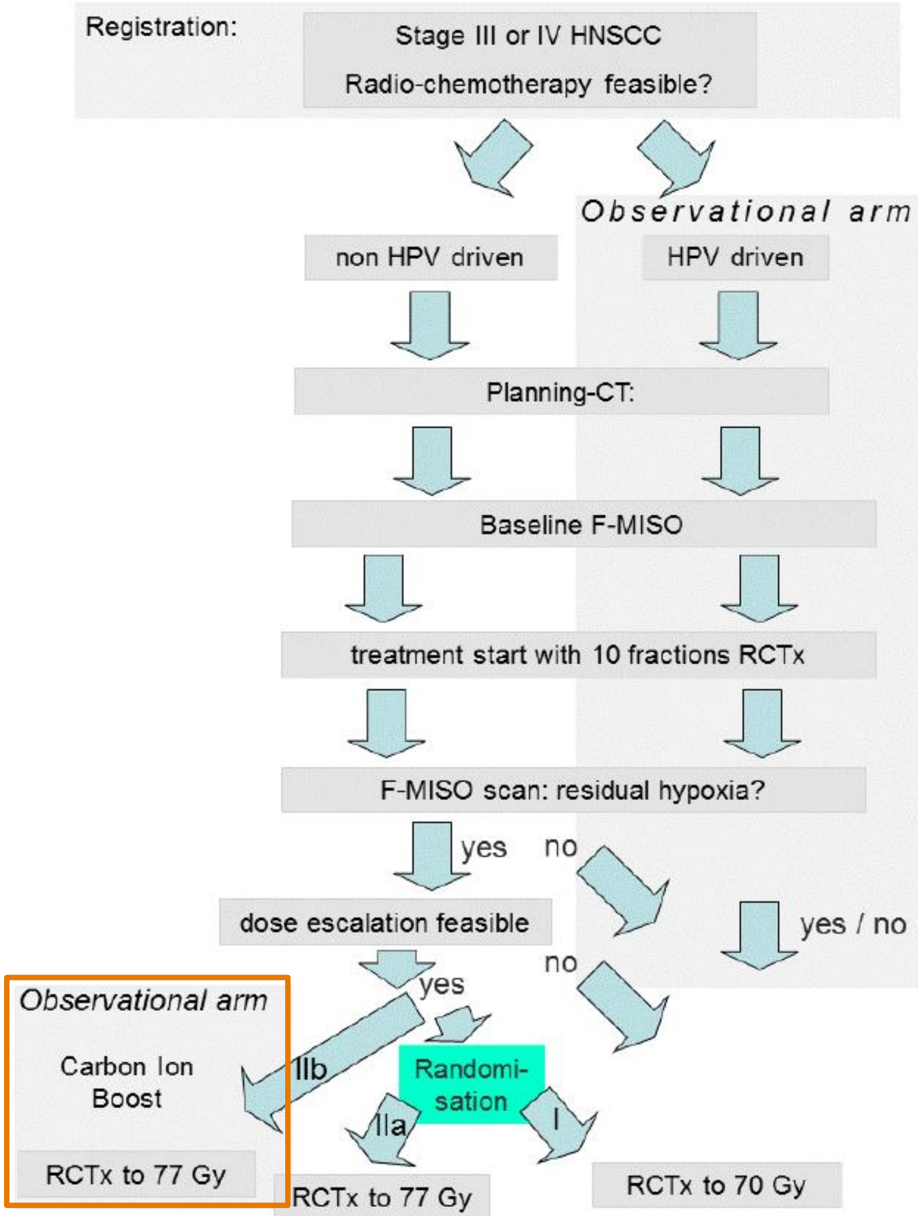
ACC, T4, definitive carbon ion RT 2016



Chondrosarcoma (G1) of the larynx:
organ preserving radiotherapy with 60 GyE C-12



Individualized radiation dose prescription in HNSCC based on F-MISO-PET Hypoxia-Imaging



INDIRA-MISO Trial

Secondary Aims of the Trial:

- LC , OS and tox of dose-escalation compared to standard therapy
- QoL during and after treatment
- evaluate FMISO uptake kinetics before treatment and after ten fractions of treatment in comparison to outcome
- investigate the association of pre-therapeutic FMISO-uptake and FMISO-uptake during radiochemotherapy to site of subsequent failure
- compare the uptake characteristics of primary tumors and recurrent tumors.
- **assess of different radiation qualities (photons, protons, carbon) in the treatment of hypoxic tumors**.

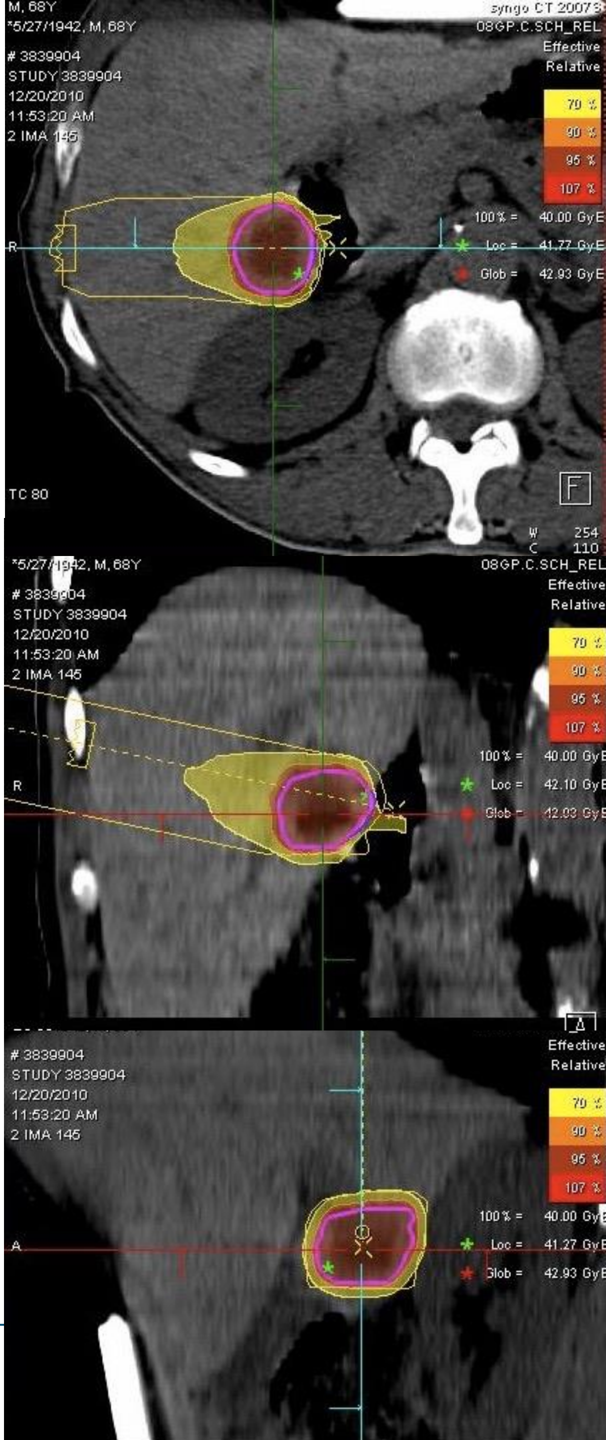
UK HD

Neo-Adiuvant Trials

PROMETHEUS Trial

Inoperable Liver Cancer

- Monocentric
- Dose escalation trial
- 4 x 10-14 Gy(RBE(NIRS)) C12
- 4 x 7.1 -10.5 Gy (RBI(GSI)) C12
- Safety & Response
- Start 5/11



Combs et al., BMC Cancer 2011

Physics Contribution

Mapping of RBE-Weighted Doses Between HIMAC– and LEM–Based Treatment Planning Systems for Carbon Ion Therapy

International Journal of Radiation Oncology biology • physics

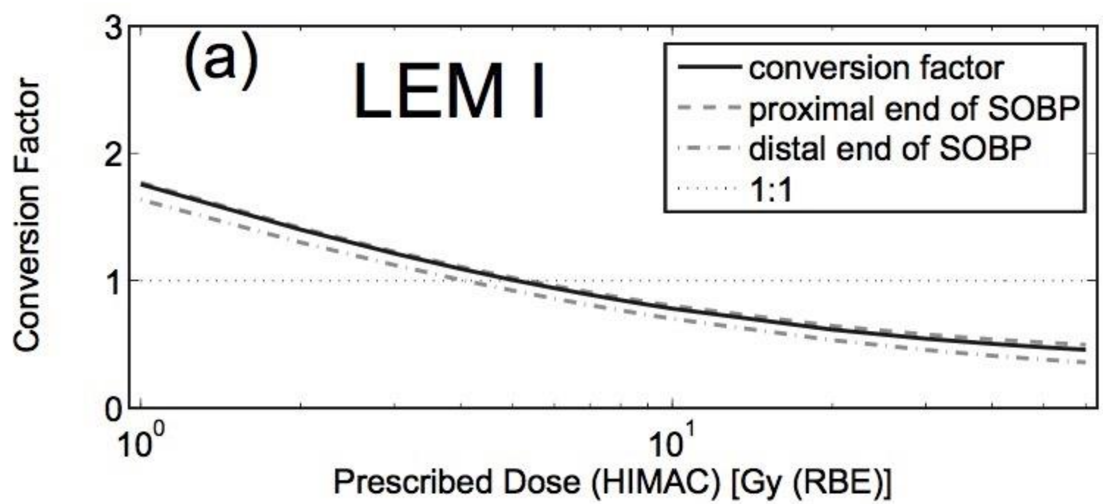
Volume 84 • Number 3 • 2012

Olaf Steinsträter, Ph.D.,* Rebecca Grün, M.Sc.,*,†,‡ Uwe Scholz, M.Sc.,*,§ Thomas Friedrich, Ph.D.,* Marco Durante, Ph.D.,*,§ and Michael Scholz, Ph.D.*

Table 1 Comparison of median and EUD calculated for LEM estimated RBE-weighted dose distributions in dependence of prescribed HIMAC RBE-weighted doses, d_{presc}^{HIMAC}, for 60-mm SOBPs (depth according to Fig. 1b) and both RBE tables (LEM I/LEM IV)

Prescribed RBE-weighted dose HIMAC, Gy (RBE)	RBE-weighted dose LEM, Gy (RBE)			
	LEM IV		LEM I	
	Median	EUD	Median	EUD
1	1.65	1.73	1.76	1.74
2	2.65	2.76	2.80	2.78
3	3.46	3.59	3.64	3.61
4	4.17	4.31	4.37	4.33
5	4.81	4.97	5.03	4.98
6	5.41	5.58	5.64	5.58
7	5.98	6.15	6.22	6.15
8	6.52	6.70	6.77	6.69
9	7.04	7.23	7.30	7.20
10	7.54	7.73	7.81	7.70
20	12.08	12.26	12.32	11.92
30	16.14	16.31	16.33	15.30
40	20.07	20.15	20.14	18.18
50	23.95	23.95	23.82	20.81
60	28.06	27.97	27.44	23.30

Abbreviations: EUD = equivalent uniform dose; HIMAC = Heavy-Ion Medical Accelerator facility, National Institute of Radiological Science, Japan; LEM = Local Effect Model (versions I and IV); RBE = Relative Biological Effectiveness; SOBP = spread-out Bragg peak.



Neo-Adiuvant Trials

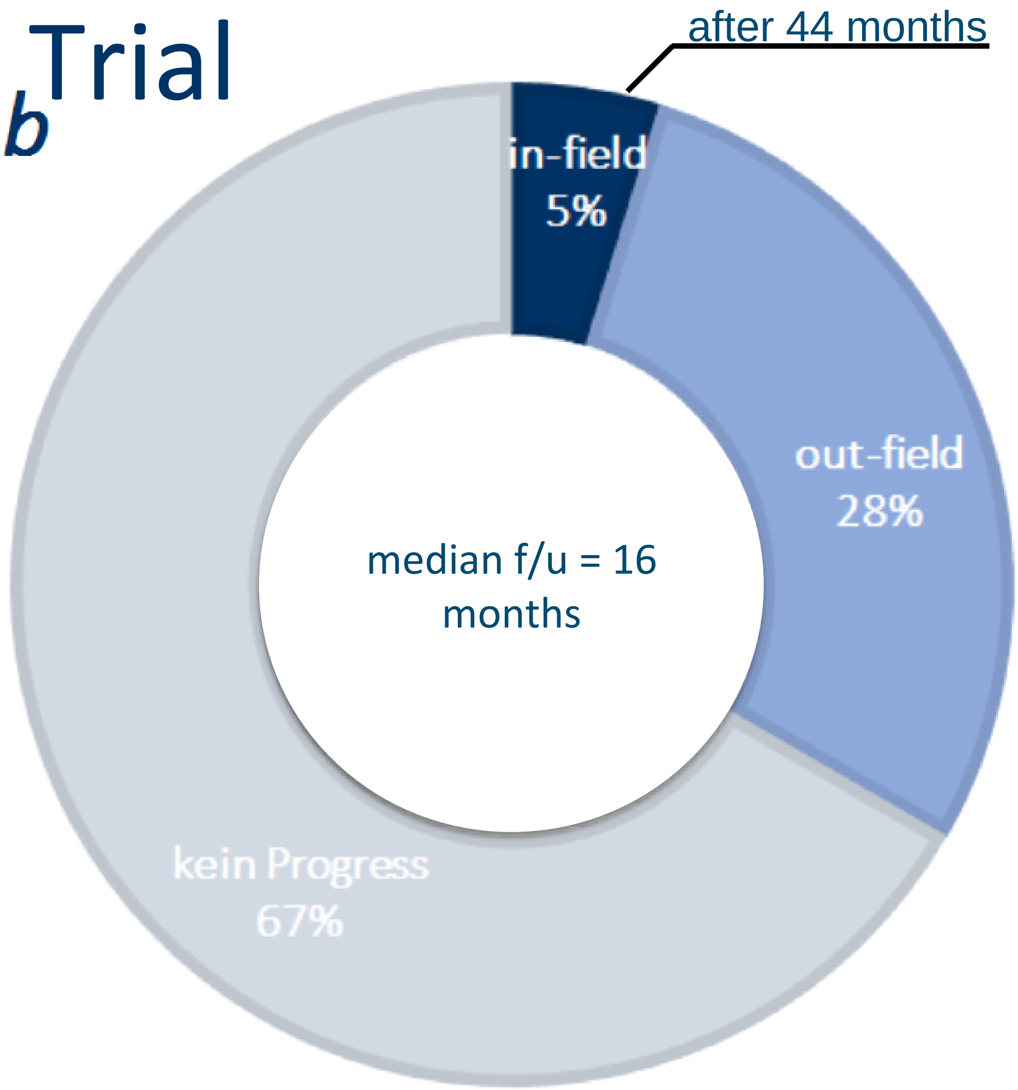
PROMETHEUS$_b$ Trial

Preliminary Results

21 Patients

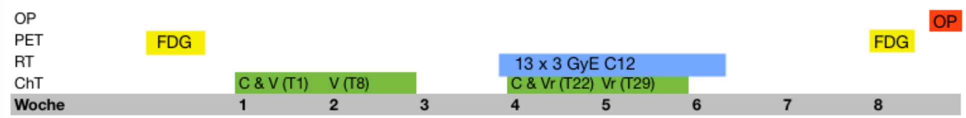
Recurrences
- 1/3 liver progression
- 2 patients with distant metastases

Toxicity
- few low grade toxicity NW (fatigue, diarrhea)

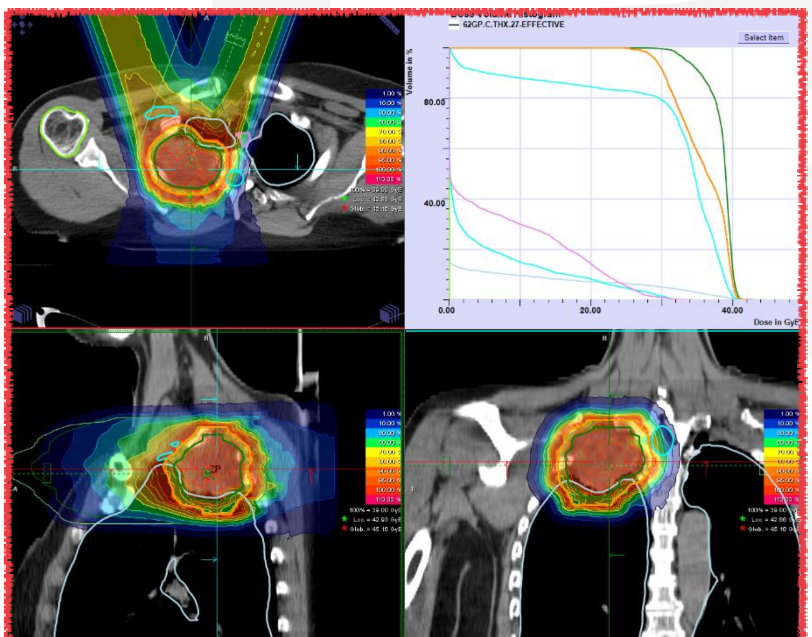


Neo-Adiuvant Trials: INKA trial

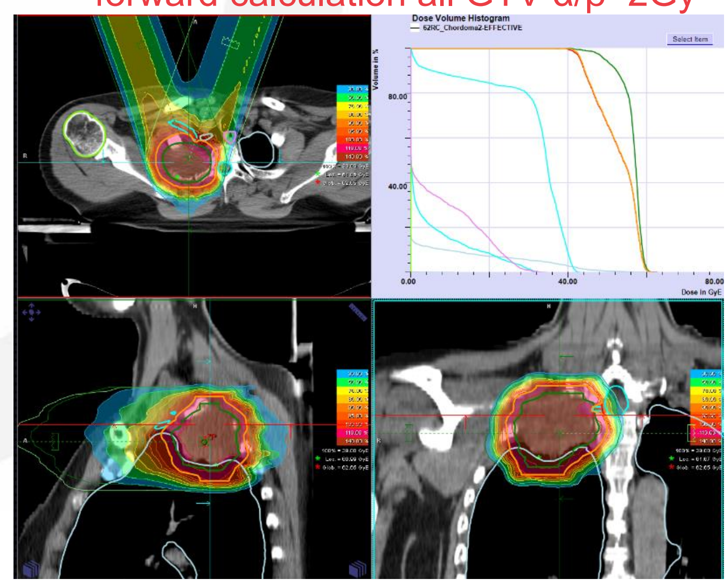
- Sulcus superior tumor
- trimodal treatment
- RT: 13 x 3 GyE C12
- Biolog. dose using GTV α/β=10Gy



C = Cisplatin 80 mg/m2 KOF
V = Vinorelbin 25 mg/m2 KOF
Vr = Vinorelbin (reduziert) 15 mg/m2 KOF



forward calculation all GTV α/β=2Gy



Neo-Adiuvant Trials

INKA trial

OP								OP
PET	FDG							FDG
RT				13 x 3 GyE C12				
ChT		C & V (T1)	V (T8)		C & Vr (T22)	Vr (T29)		
Woche		1	2	3	4	5	6	7 / 8

- Sulcus superior tumor
- trimodal treatment
- RT: 13 x 3 GyE C12
- Biolog. dose using GTV α/β=10Gy

C = Cisplatin 80 mg/m2 KOF
V = Vinorelbin 25 mg/m2 KOF
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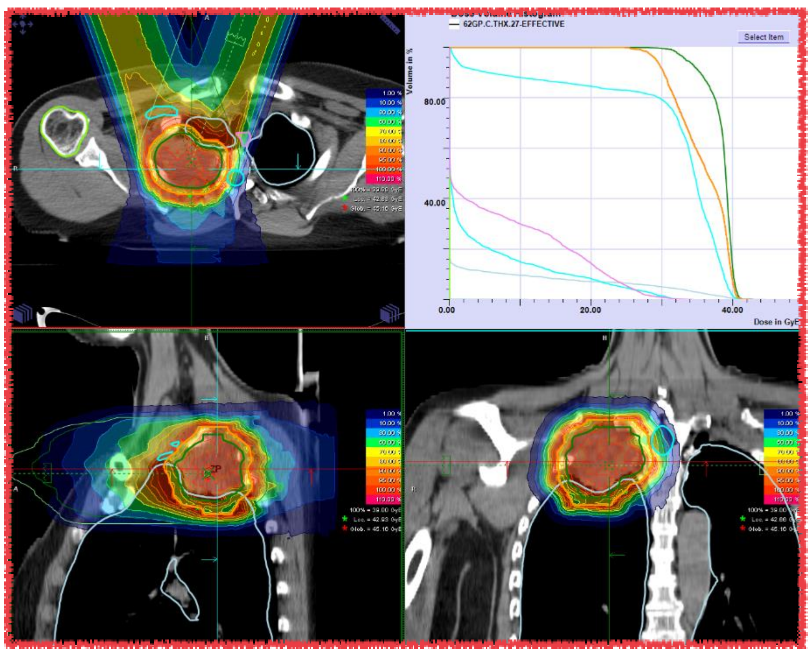
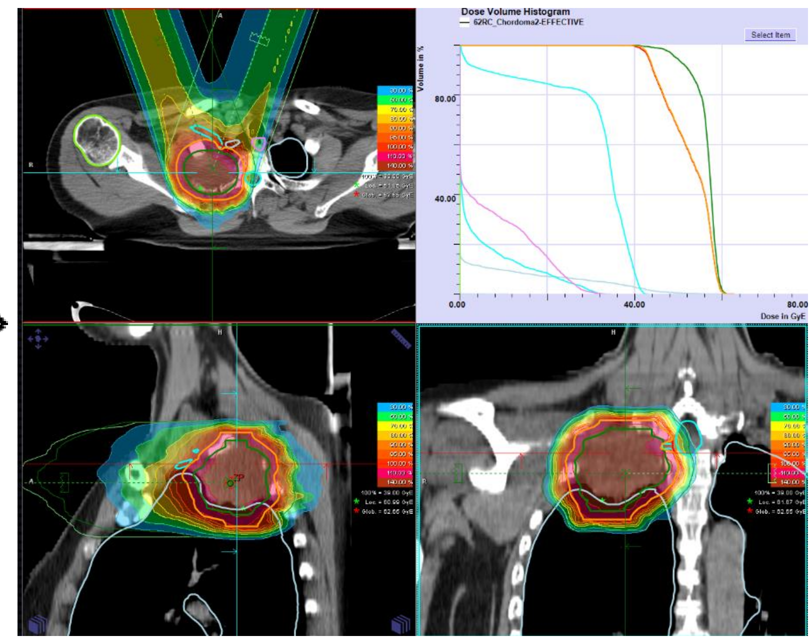
forward calculation all GTV α/β=2Gy





Clinical trial: OSCAR

HIT Heidelberger Ionenstrahl-Therapiezentrum · Dietmar Hopp Stiftung · NCT

OSteosarcoma – CArbon Ion Radiotherapy: Phase I/II therapy trial

Safety and efficacy of heavy ion radiotherapy in patients with inoperable osteosarcoma

Endpoints: LC, DFS, PFS, OS and the role of FDG-PET in response monitoring

Neoadjuvant Chemotherapy according to standard protocols (e.g. *EURAMOS1*)	**Proton / Carbon Ion-radiotherapy (HIT)** (54 GyE + 18 GyE C-12),	Adjuvant Chemotherapy (e.g. *EURAMOS1*, *HR1* (MAP))
Week 1 to 10	**Week 11 to 17**	**Week 18 to 36**

FDG-PET, optional

Inclusion of patients at least 3 weeks before HIT

Required Diagnostics <u>before</u> HIT:
- ✓ FDG-PET
- ✓ CT/MRT
- ✓ Tc99 bone scintigram
- ✓ Blood tests

Week 7-10

Required Diagnostics <u>after</u> HIT:
- ✓ FDG-PET **Week 17 and 36**
- ✓ CT/MRI and Tc99 bone scintigram **Week 23 and 36**
- ✓ Blood tests week 17, 23, 36

Follow-up Diagnostics 6, 12, 24, 36, 48 and 60 months after HIT

Clinical trial: OSCAR

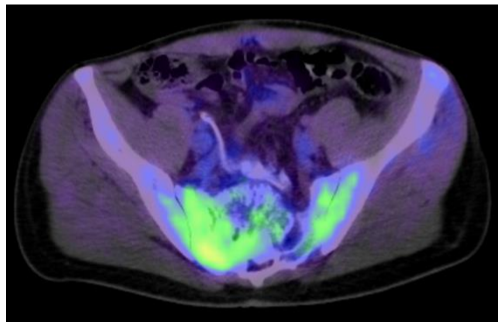
OSteosarcoma – CArbon Ion Radiotherapy: Phase I/II therapy trial

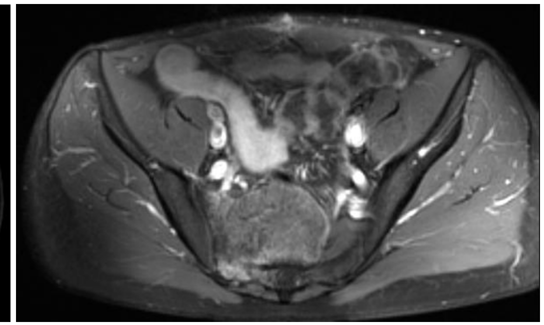
Safety and efficacy of heavy ion radiotherapy in patients with inoperable osteosarcoma

Endpoints: LC, DFS, PFS, OS and the role of FDG-PET in response monitoring

Male patient, 28 years

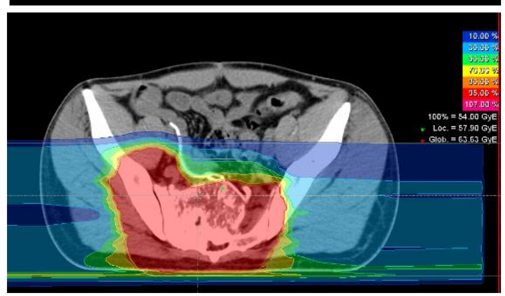
FDG PET prior to RT

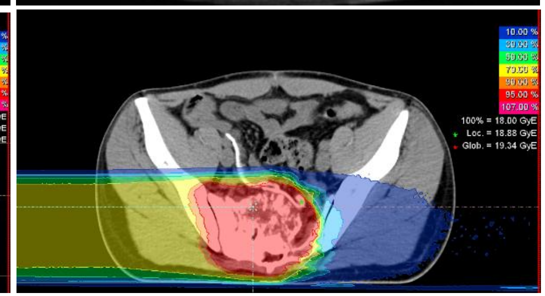




MRI prior to RT

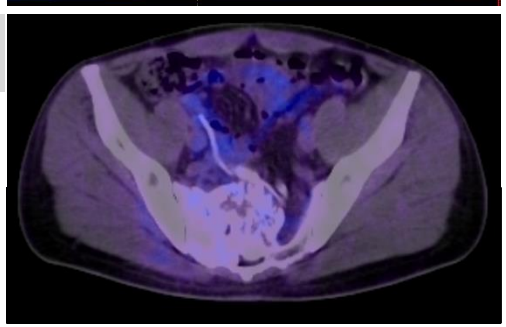
Basic proton plan





carbon ion boost plan

Follow up



MRI **7 years** after radiotherapy (2019)

FDG PET, **8 months** after radiotherapy complete remission

✓ Research platform

HIT

operates 24/7

08:00 - 22:00 h Patient treatment

22:00 – 08:00 h Research and QA

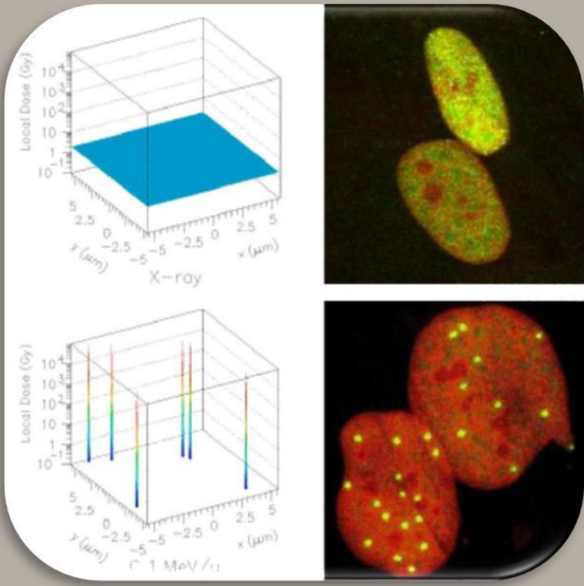
Exerimental beamline

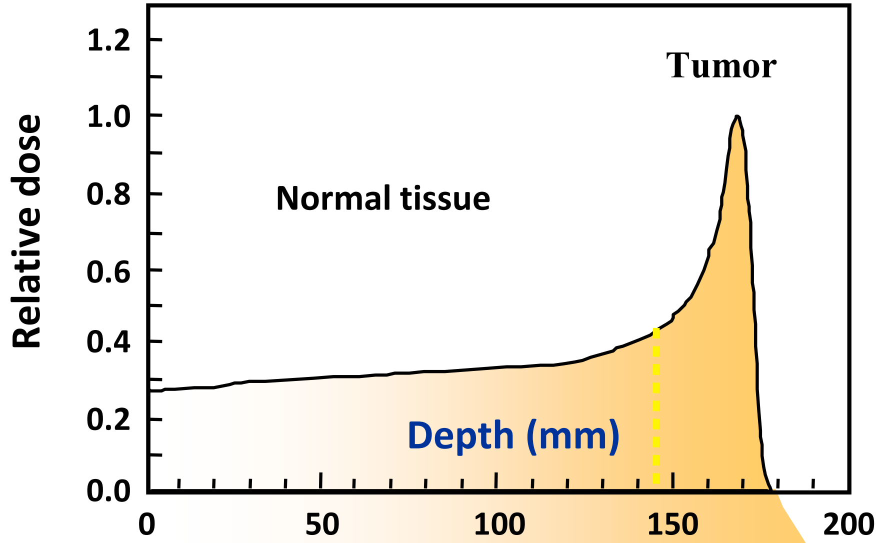
Staff

A team of more than 70 experts comprising:

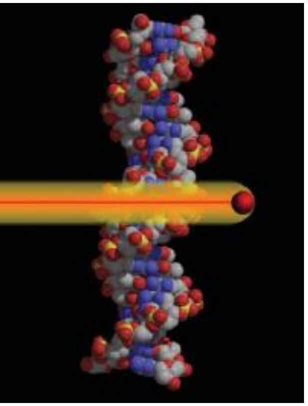
- Medical doctors
- Nurses,
- Medical radiology assistants
- Physicists
- Engineers
- Technicians

Animal facility and labs





Durante & Loeffler, *Nature Rev Clin Oncol* 2010



Energy	high	low
LET	low	high
Dose	low	high
RBE	≈ 1	> 1
OER	≈ 3	< 3
Cell-cycle dependence	high	low
Fractionation dependence	high	low
Angiogenesis	Increased	Decreased
Cell migration	Increased	Decreased

Potential advantages

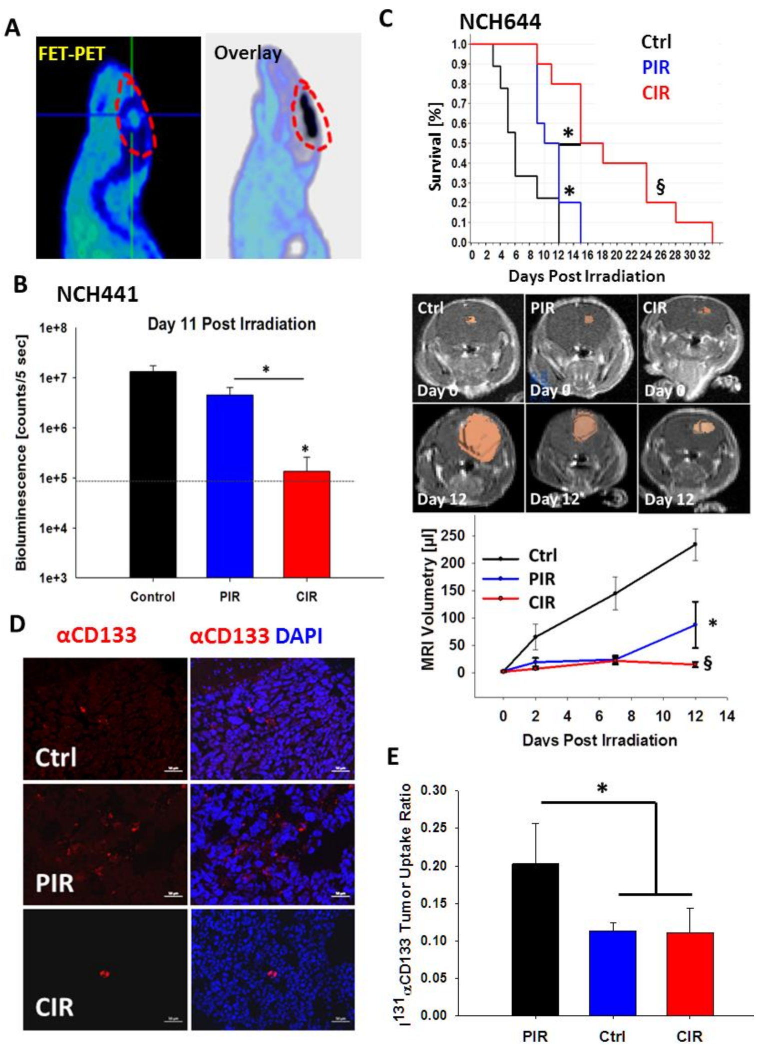
- High tumor dose, normal tissue sparing
- Effective for radio-resistant tumors
- Effective against hypoxic tumor cells
- Increased lethality in the target because cells in radio-resistant (S) phase are sensitized
- Fractionation spares normal tissue more than tumor
- Reduced angiogenesis and metastasis

Carbon irradiation overcomes glioma radioresistance by eradicating stem cells and forming an antiangiogenic and immunopermissive niche

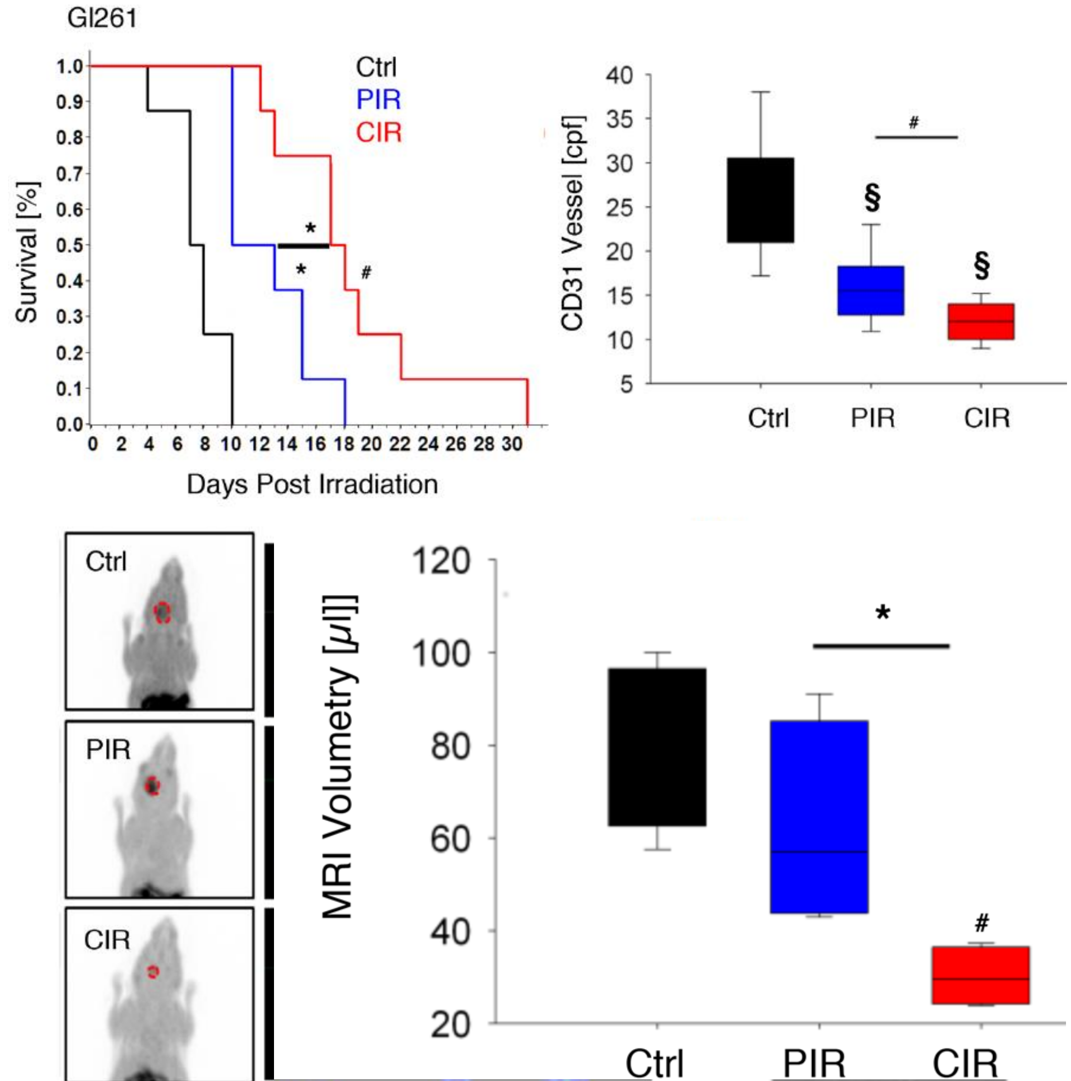
NCT Biological Dose Prescription (BioDose) P

Chiblak et al. JCI Insight. 2019

PDX GliomaStemCell model NCH644



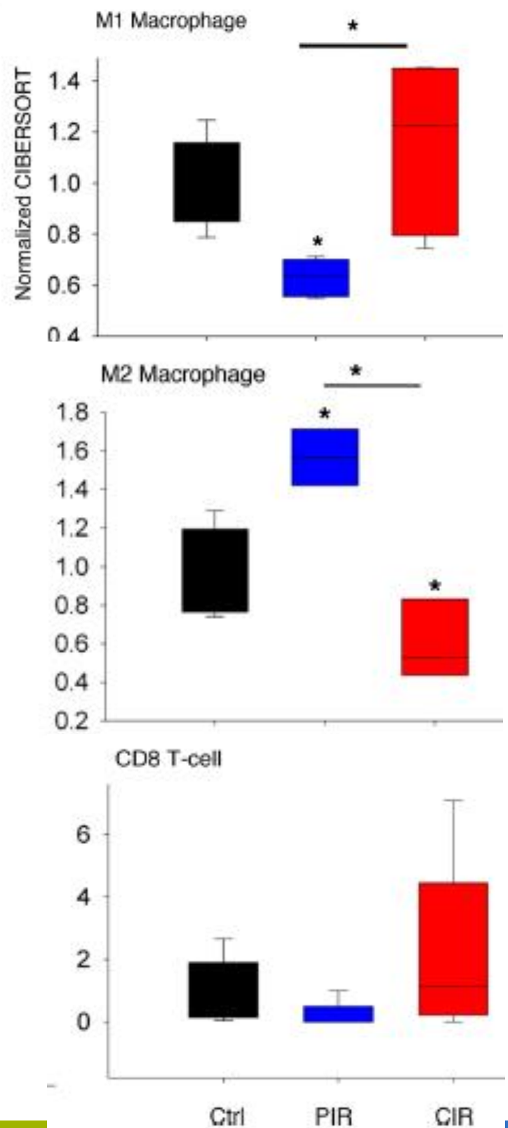
Beneficial effect of CIR in syngeneic, orthotopic murine GL261 glioma model

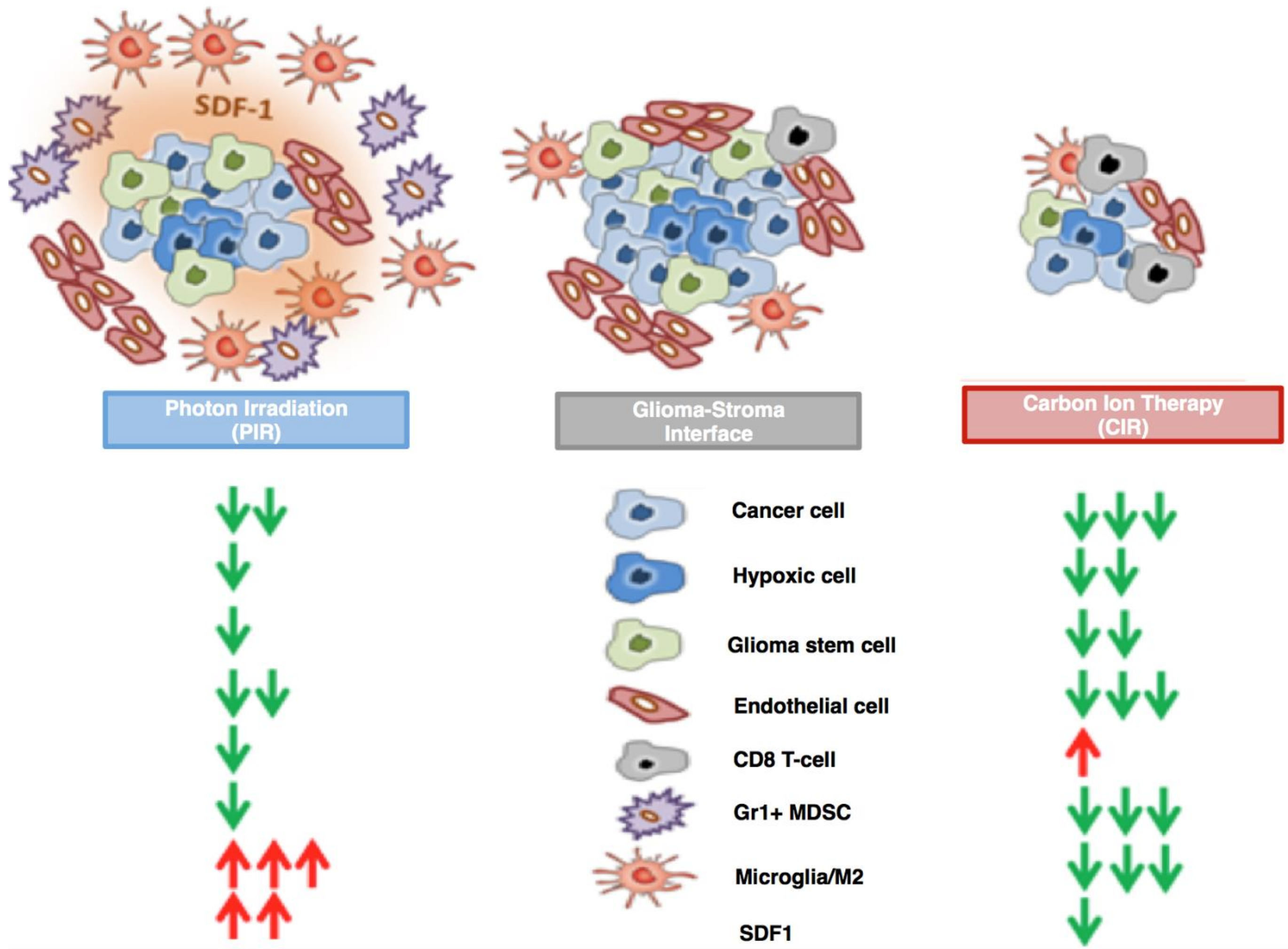


Highlight project: Carbon irradiation overcomes glioma radioresistance by eradicating stem cells and forming an antiangiogenic and immunopermissive niche

NCT Biological Dose Prescription (BioDose)

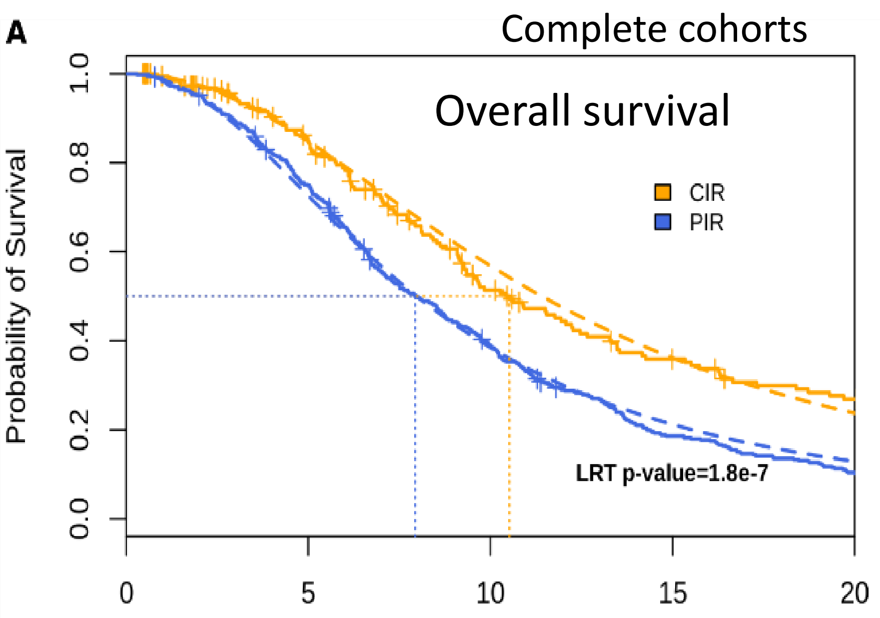
S. Chiblak et al. JCI Insight. 2019



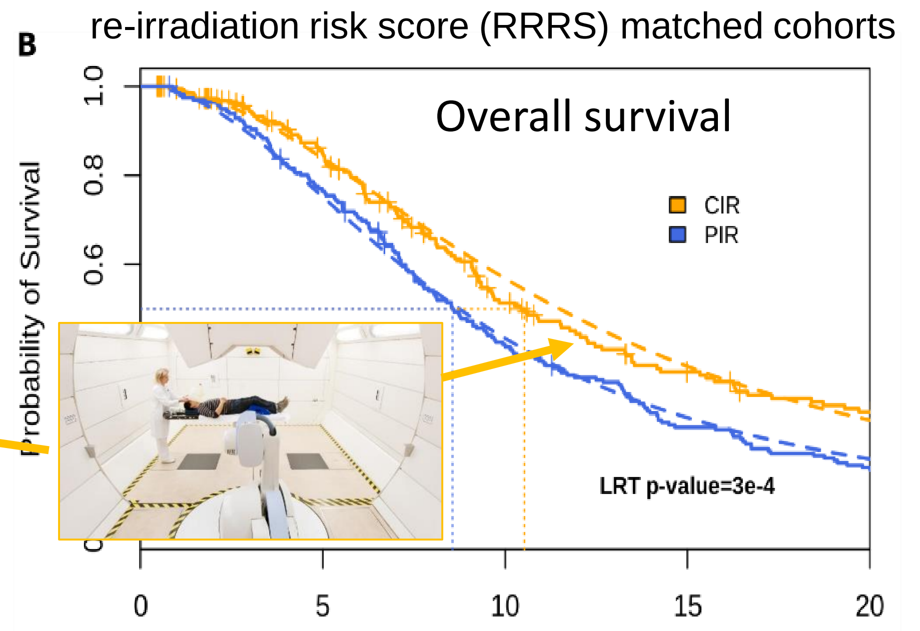


Carbon irradiation (CIR) is superior to photon irradiation (PIR) in patients with **recurrent** high-grade glioma

NCT Biological Dose Prescription (BioDose) *Knoll, M. et al. 2019, J Clin Oncol suppl*



No. at risk	0	5	10	15	20
CIR	197	142	77	49	35
PIR	476	353	180	84	47



No. at risk	0	5	10	15	20
CIR	197	142	77	49	35
PIR	197	149	80	44	27

In DKTK-ROG multicenter cohort n:**565** rHGG patients (grade III: 63, IV: 479) underwent RiP between 1997-2016 with a median dose of 36 Gy in 14 fractions

Dashed line: loglogistic parame-tric survival regression fit.
Solid lines: Kaplan-Meier curves .

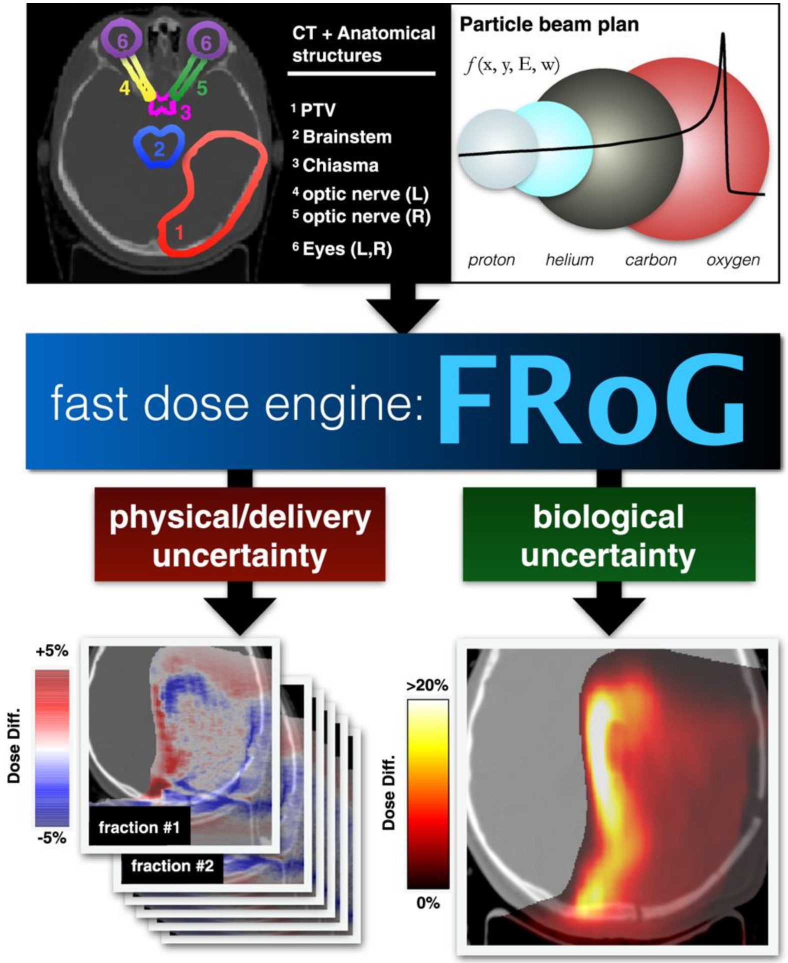
197 patients with rHGG (grade III: 71, IV: 126) received RiCi between Nov 2009 and Feb 2018 at **HIT** with a median dose of 42GyRBE in 14 fractions

Median follow up: 34.2 months for RiCi
7.1 months for RiP (DKTK)

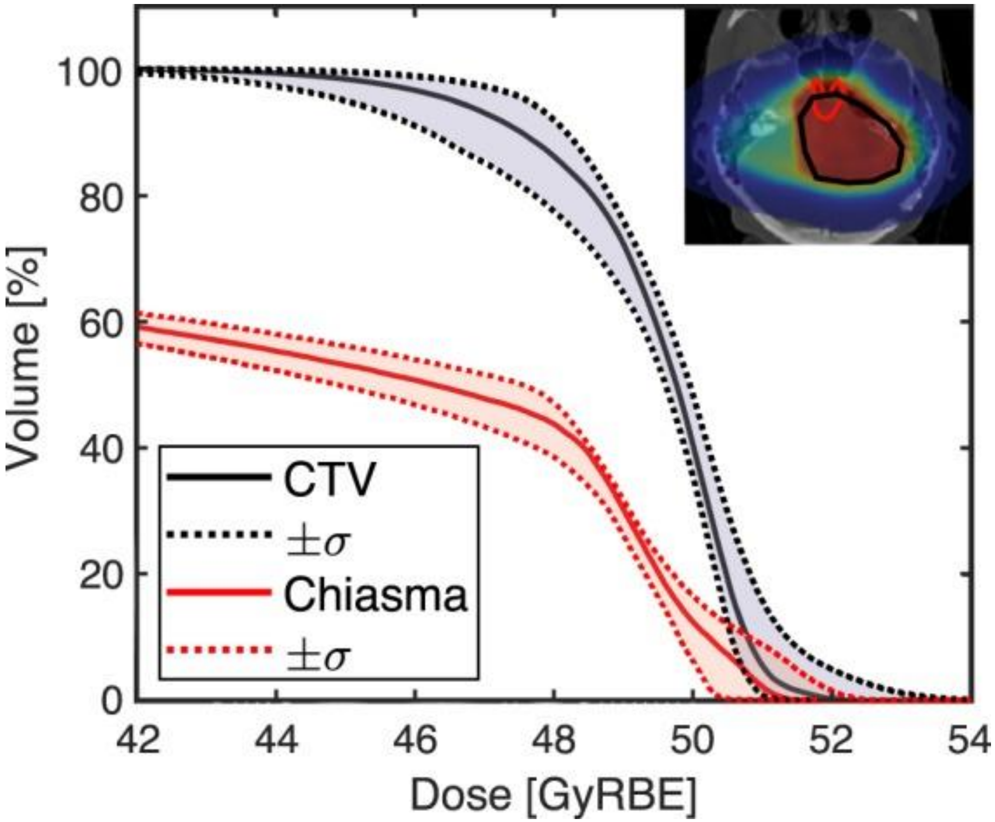
Development of FRoG Fast Recalculation on GPU

NCT Biological Dose Prescription (BioDose)

- **Integrating Physical Dose and RBE - Uncertainity by Modelling Spatial- and Time-Resolved Quantitative Imaging Data**

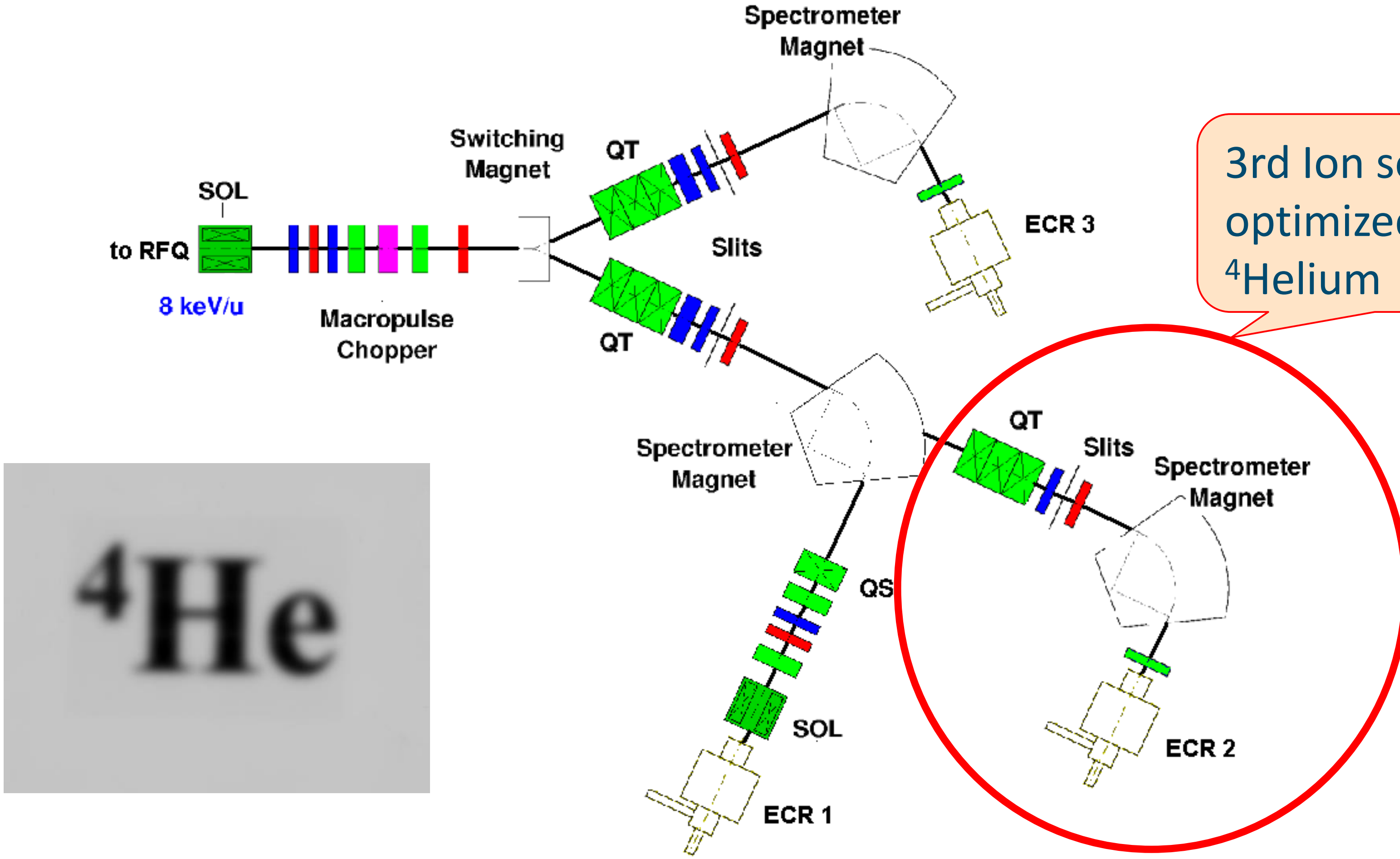


- enables comparative analysis of different models for estimation of physical and biological effective dose in 3D within minutes and in excellent agreement with Monte Carlo simulation.



Mein et al. Sci Rep. 2018,

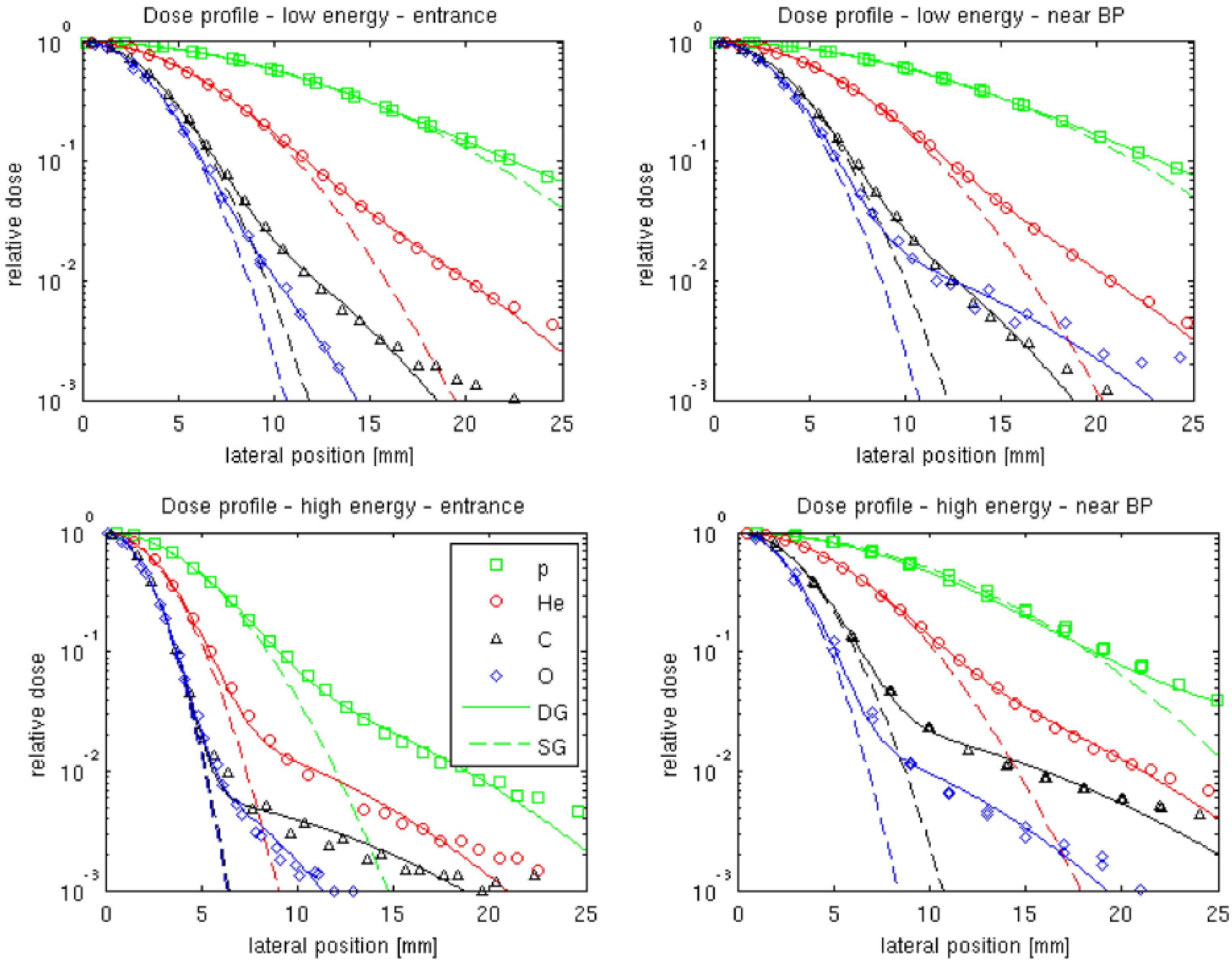
Next step: clinical helium-beams at HIT



3rd Ion source was optimized for ^{4}Helium

T. Haberer, **A. Mairani**, J. Debus, PTCOG 57, Cincinnati, 25/05/2018

Rationale for 4He-beam therapy: scattering



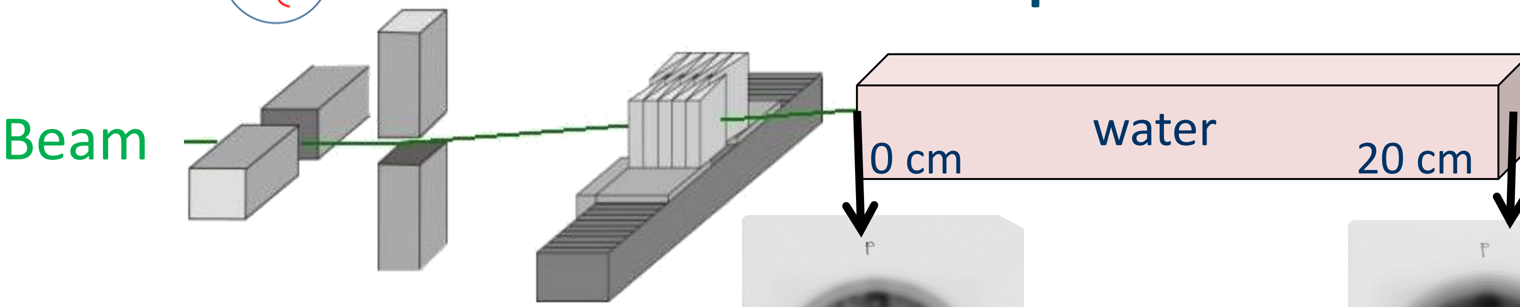
P
He
C
O

——— solid double Gaussian (DG) fits

- - - -dashed simple Gaussian (SG) fits.

T. Tessonnier , A. Mairani, et al. Physics in Medicine Biology, 2016, 62(10):3958-3982

Precision and penetration depth

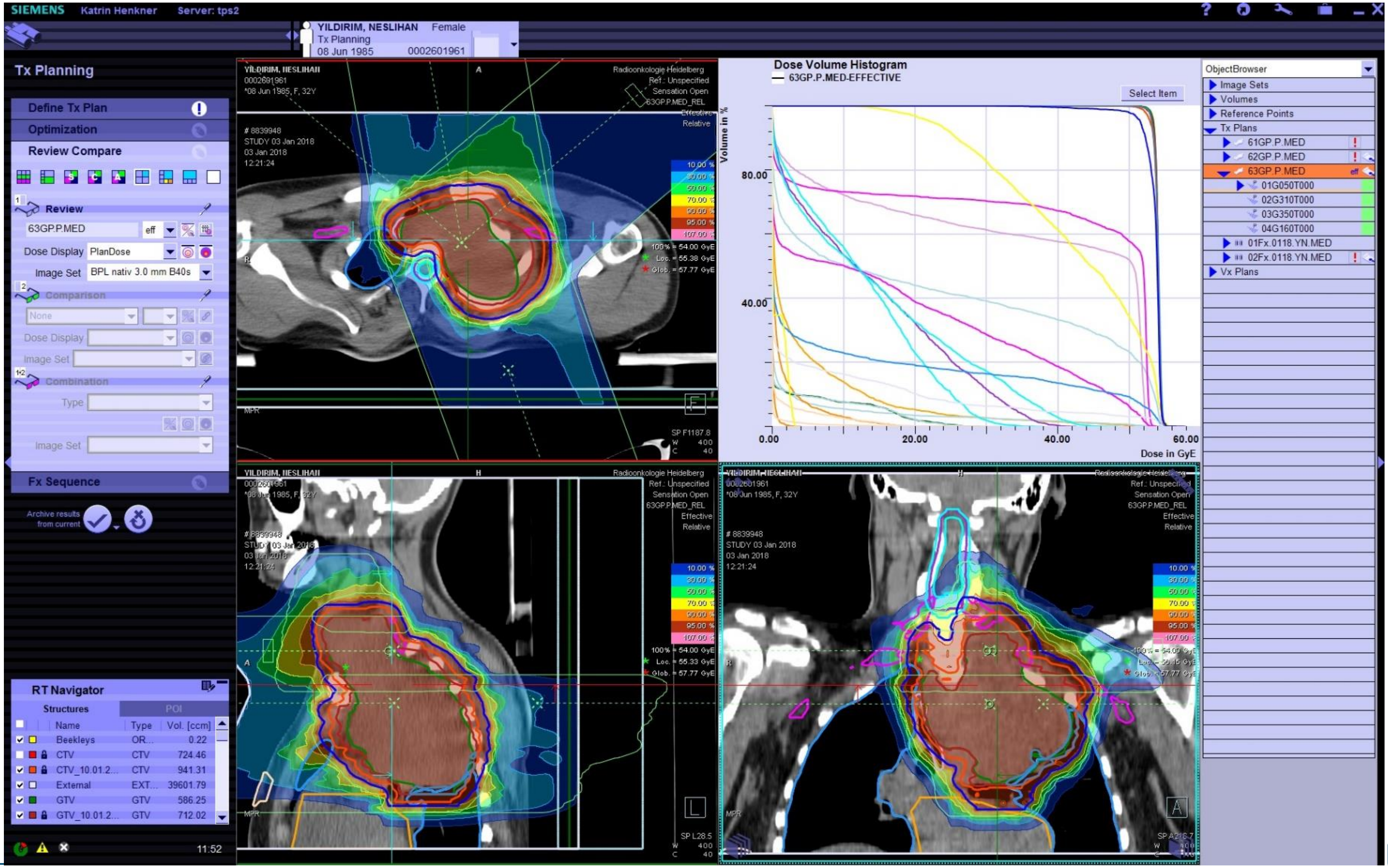


Protons
175 MeV

Helium ions
175 MeV/u

Carbon ions
330 MeV/u

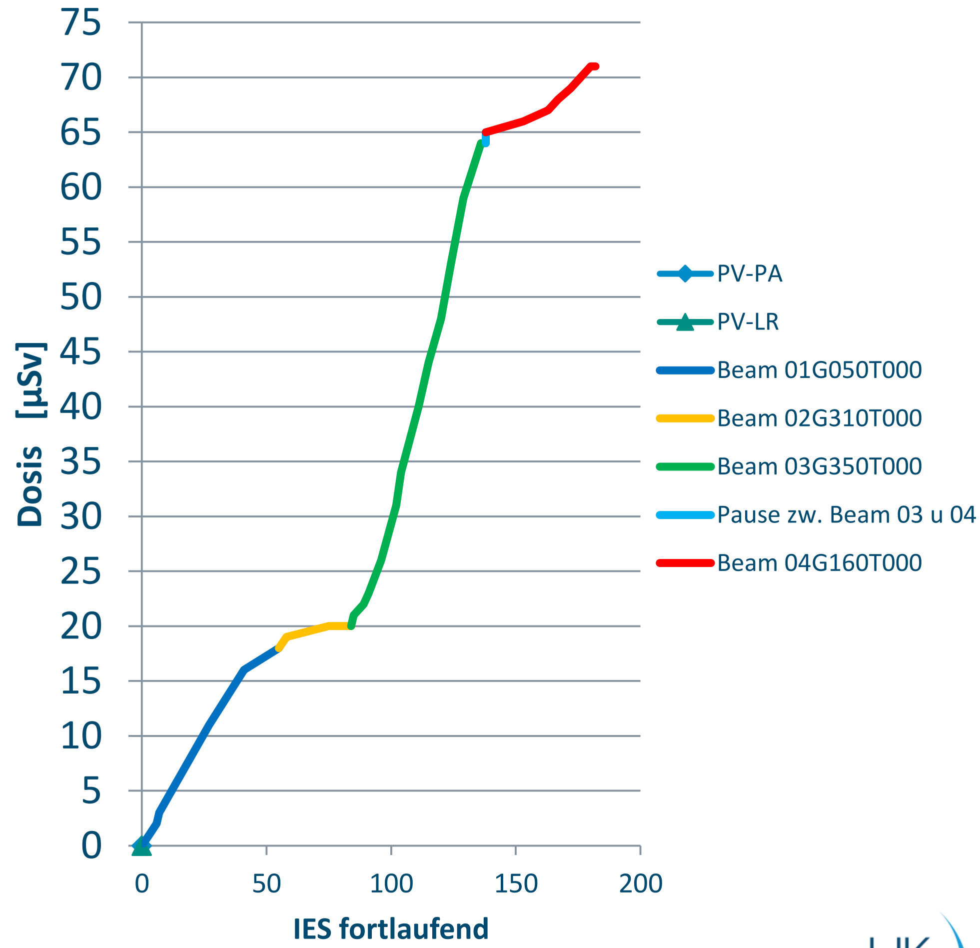
Pregant patient at HIT: Proton RT scanning beam



Measured doses (belly)

- Patient was irradiated from 4 directions
- Doses accumulated to total dose show significant differences
- dose optimization can only be don on a highly individual basis

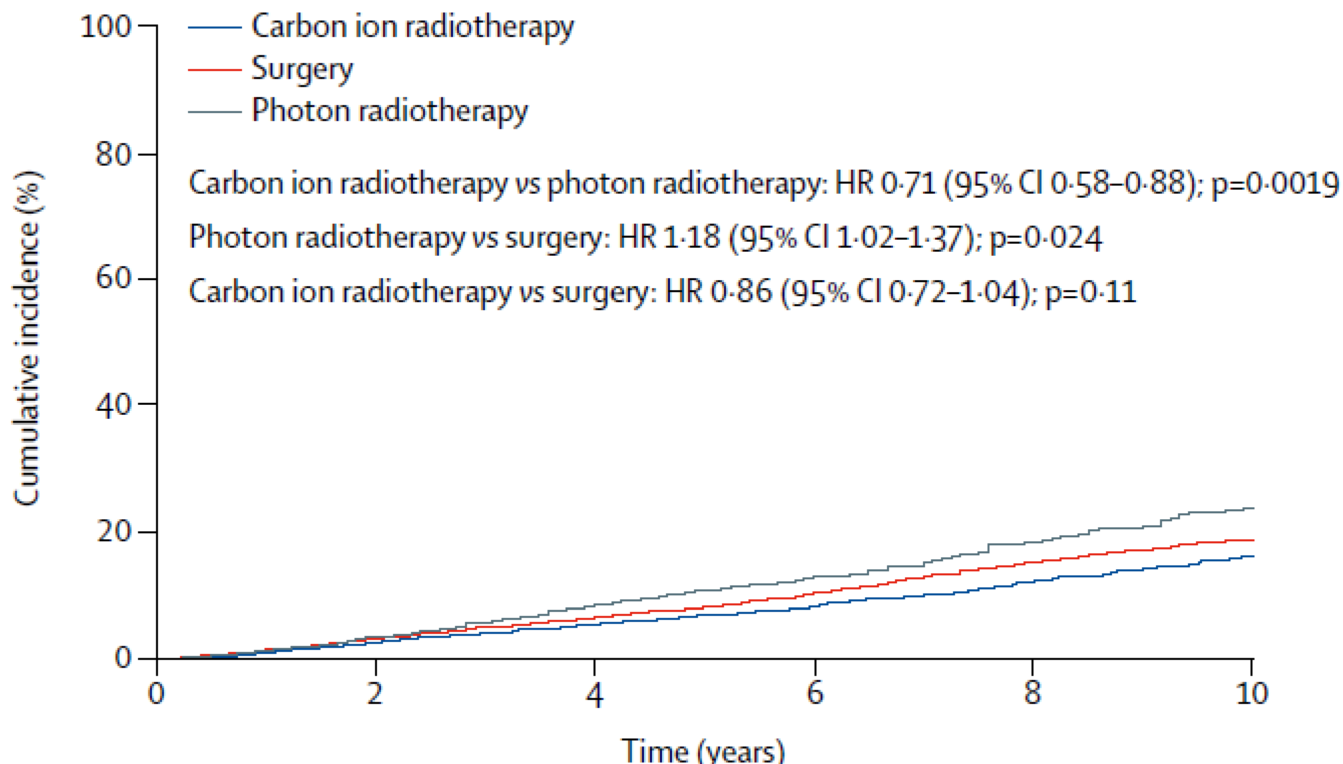
contribution of the treatment fields and X-ray on dose to the fetus



Risk of subsequent primary cancers after carbon ion radiotherapy, photon radiotherapy, or surgery for localised prostate cancer: a propensity score-weighted, retrospective, cohort study

Osama Mohamad, Takahiro Tabuchi, Yuki Nitta, Akihiro Nomoto, Akira Sato, Goro Kasuya, Hirokazu Makishima, Hak Choy, Shigeru Yamada, Toshitaka Morishima, Hiroshi Tsuji, Isao Miyashiro, Tadashi Kamada**

Mohamed et al. Lancet Oncol. 2019



Number at risk (number censored)	0	2	4	6	8	10
Carbon ion radiotherapy	1455 (0)	1402 (7)	1317 (24)	1069 (216)	712 (512)	413 (764)
Surgery	5948 (0)	5702 (6)	5325 (82)	2978 (2147)	1541 (3393)	1389 (3404)
Photon radiotherapy	1983 (0)	1900 (0)	1727 (34)	782 (863)	241 (1357)	193 (1367)

Conclusion

- Phase II data with C-12 warrant further investigations
- Since 2009 over 18 clinical studies on ion therapy started
- Challenge: state of the art IGRT and ART compared to photons
- Clinical application of He ions in the near future
- Research platforms are now available , providing p, He, C, and O ions in experimental beam lines
- The mechanism of high LET is beyond cell kill the modulation of the microenvironment
- Various research projects ranging from physics to biology: open to researchers from different fields

The European Network for Light ion Hadron Therapy

ENLIGHT

A multidisciplinary platform aimed at a coordinated effort towards ion beam research in Europe

HOME | SCIENCE | ADVISORY COMMITTEE | MEETINGS | PROJECTS | MEDIA | HIGHLIGHTS | EVENTS | JOB OPPORTUNITIES

The ENLIGHT network was established in 2002 to coordinate European efforts in hadrontherapy, and today has more than 700 participants from 25 European countries. A major achievement of ENLIGHT has been the blending of traditionally separate communities so that clinicians, physicists, biologists and engineers with experience and interest in particle therapy are working together.

TWITTER

HIGHLIGHTS

ULICE – Union of Light Ion Centres in Europe

ENVISION – European NoVel Imaging Systems for ION therapy

ENTERVISION – European training network in digital medical imaging for radiotherapy

PARTNER – Particle Training Network for European Radiotherapy

Particle Therapy Co-Operative Group

An organisation for those interested in proton, light ion and heavy charged particle radiotherapy

58TH ANNUAL CONFERENCE OF THE PARTICLE THERAPY CO-OPERATIVE GROUP

The premier scientific meeting in the field of particle therapy showcasing cutting edge science, NHS oncology and clinical practice in action.

10-15 June, 2019 Manchester, UK

NCT

Thank You !!!

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HOSPITAL

HEIDELBERG
FACULTY OF
MEDICINE

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NATIONALES CENTRUM
FÜR TUMORERKRANKUNGEN
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Universitätsklinikum Heidelberg
Thoraxklinik-Heidelberg
Deutsche Krebshilfe

HIRO
Heidelberg Institute
for **Radiation Oncology**

National Center for
Radiation Research in
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supported by:
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Heidelberg University Hospital
Heidelberg Ion-Beam Therapy Center (HIT)
Medical Faculty Heidelberg

dkfz.
GERMAN
CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

HIT
Heidelberger Ionenstrahl-Therapiezentrum