UniversitätsKlinikum Heidelberg

The HIT facility, technology, clinical applications and research: novel approaches in particle therapy

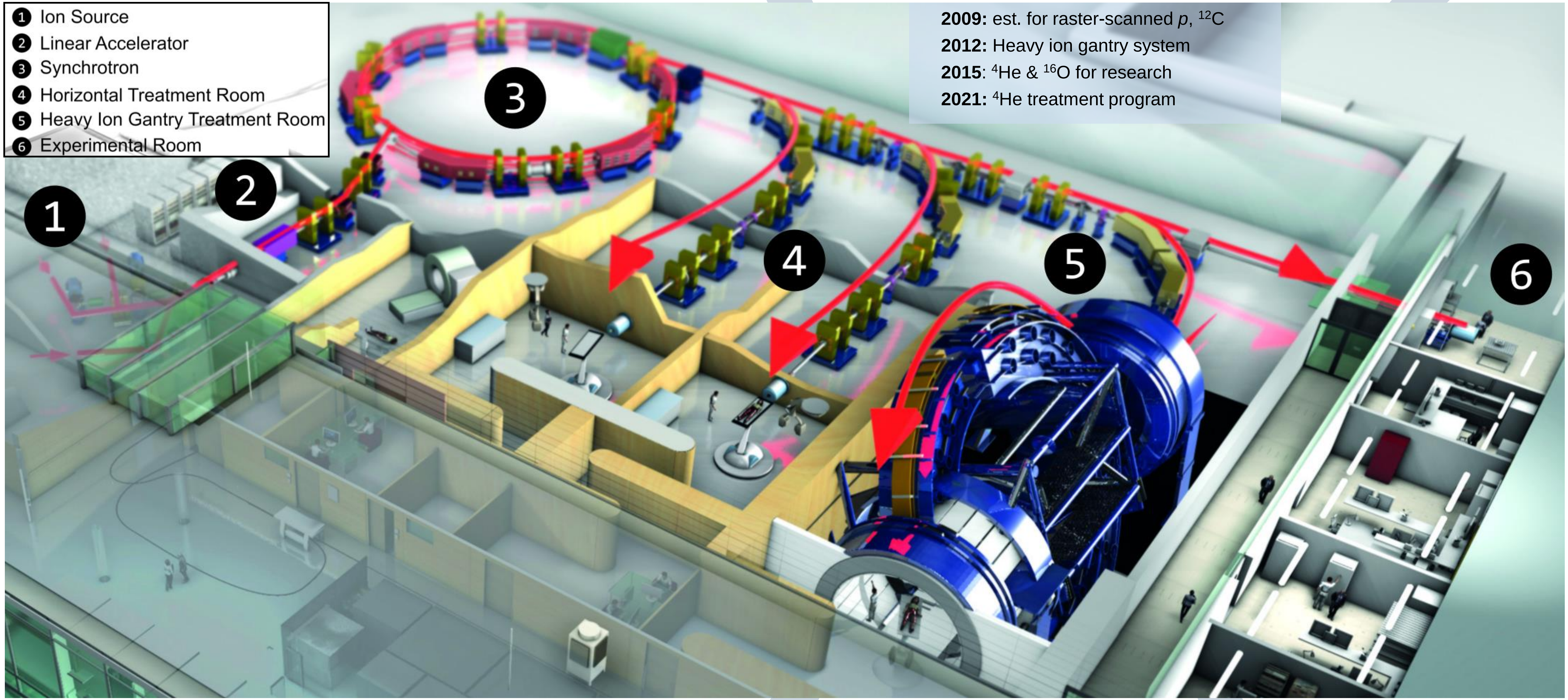
Prof. Dr. Andrea Mairani

Heidelberg Ion Beam Therapy Center (HIT)
Department of Radiation Oncology, University Clinic Heidelberg
German Cancer Research Center (DKFZ)
National Center for Tumor Diseases (NCT)
Centro Nazionale di Adroterapia Oncologica (CNAO)

Heidelberg Ion-Beam Therapy Center (HIT)

1. Ion Source
2. Linear Accelerator
3. Synchrotron
4. Horizontal Treatment Room
5. Heavy Ion Gantry Treatment Room
6. Experimental Room

2009: est. for raster-scanned *p*, ^{12}C
2012: Heavy ion gantry system
2015: ^{4}He & ^{16}O for research
2021: ^{4}He treatment program



How to move forward ion beam therapy? Technology

- Fast Monte Carlo calculations for all beam modalities
- Decrease range uncertainties
- Change the beam modality: ^{4}He ion vs. proton beams (^{12}C vs. ^{16}O ions)
- Improve the delivery (set-up) technique: arc irradiation (high LET advantage)
- Multi-Ion Irradiation (also biological advantage)
- FLASH-like irradiation (also biological advantage)

How to move forward ion beam therapy?
Biology

- “Novel” biological model
- Arc irradiation with high LET advantage for hypoxic tumour
- FLASH-irradiation (and mini-beams): sparing normal tissue
- Combined treatments: DNA damage repair interface (DDRi) drugs + external ion beam therapy

A Fast Monte Carlo Engine for Particle Therapy

MonteRay

BioPT

Development and Benchmarking of a Monte Carlo Dose Engine for Proton Radiation Therapy

Peter Lysakovski[1,2], Alfredo Ferrari[1], Thomas Tessonnier[1], Judith Besuglow[1,2,3,4,5], Benedikt Kopp[1], Stewart Mein[1,3,4,5], Thomas Haberer[1], Jürgen Debus[1,5,6] and Andrea Mairani[1,7,3,8*]

MEDICAL PHYSICS
The International Journal of Medical Physics Research and Practice

RESEARCH ARTICLE | Open Access

Development and benchmarking of the first fast Monte Carlo engine for helium ion beam dose calculation: MonteRay

Peter Lysakovski, Judith Besuglow, Benedikt Kopp, Stewart Mein, Thomas Tessonnier, Alfredo Ferrari, Thomas Haberer, Jürgen Debus, Andrea Mairani

First published: 21 December 2022 | https://doi.org/10.1002/mp.16178

MEDICAL PHYSICS
The International Journal of Medical Physics Research and Practice

RESEARCH ARTICLE | Open Access

Development and validation of MonteRay, a fast Monte Carlo dose engine for carbon ion beam radiotherapy

Peter Lysakovski, Benedikt Kopp, Thomas Tessonnier, Stewart Mein, Alfredo Ferrari, Thomas Haberer, Jürgen Debus, Andrea Mairani

First published: 25 September 2023 | https://doi.org/10.1002/mp.16754

- MonteRay for proton, helium and carbon ion beams is capable of accurate dose calculations when evaluated against measurement and FLUKA simulations
- Speedups of 20-60x vs. FLUKA on same hardware
- Combinatorial Geometry has been implemented
- Handling different biological models
- Extension to IORT electrons and VHEE for FLASH radiotherapy recently done

Med Phys. 2024 Jun 8. doi: 10.1002/mp.17180. Online ahead of print.

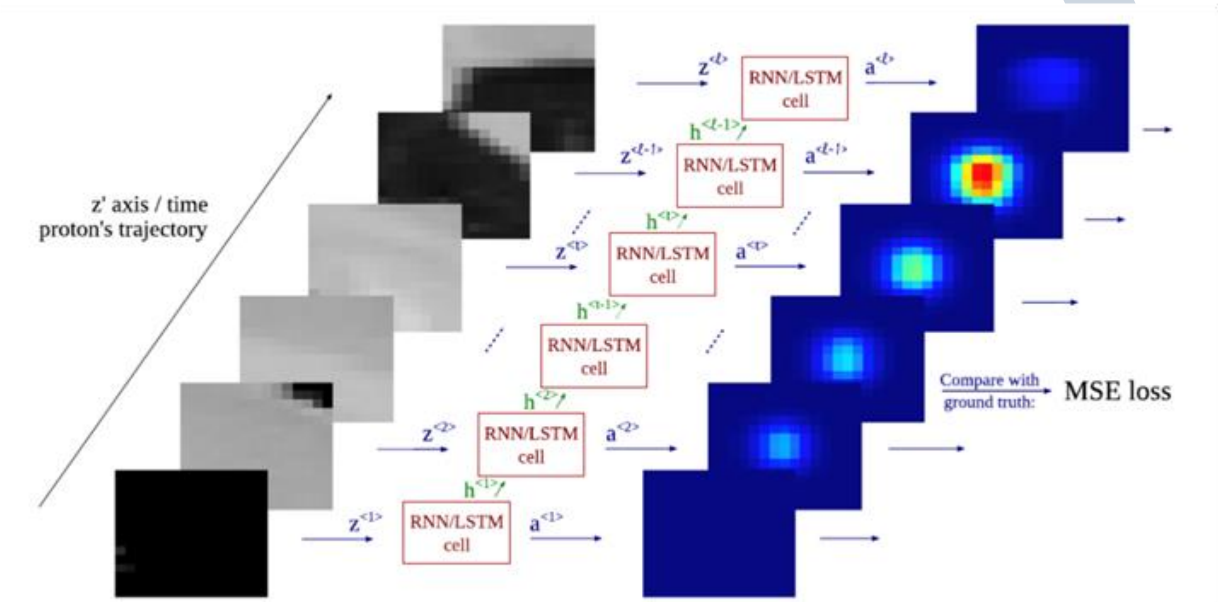
Development and verification of an electron Monte Carlo engine for applications in intraoperative radiation therapy

Luisa Rank [1, 2], Peter Lysakovski [1], Gerald Major [3], Alfredo Ferrari [2], Thomas Tessonnier [1], Jürgen Debus [1, 4, 5], Andrea Mairani [1, 4, 5, 6, 7]

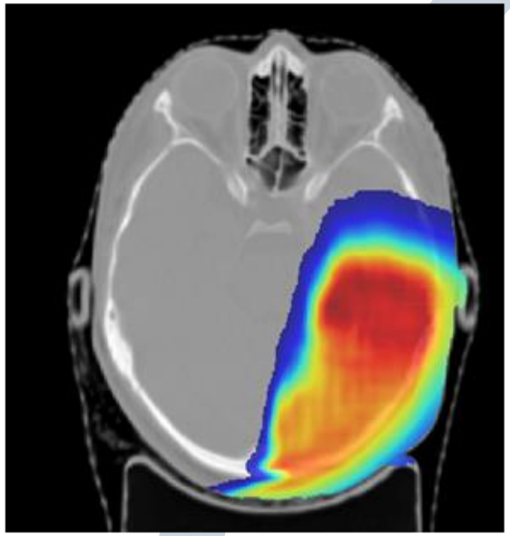
iba DOSIMETRY

Funded by:
Federal Ministry of Education and Research
Grant No. 13GW0436A

Artificial Neural Networks (ANNs) for particle dose calculation



ANN dose calculation:



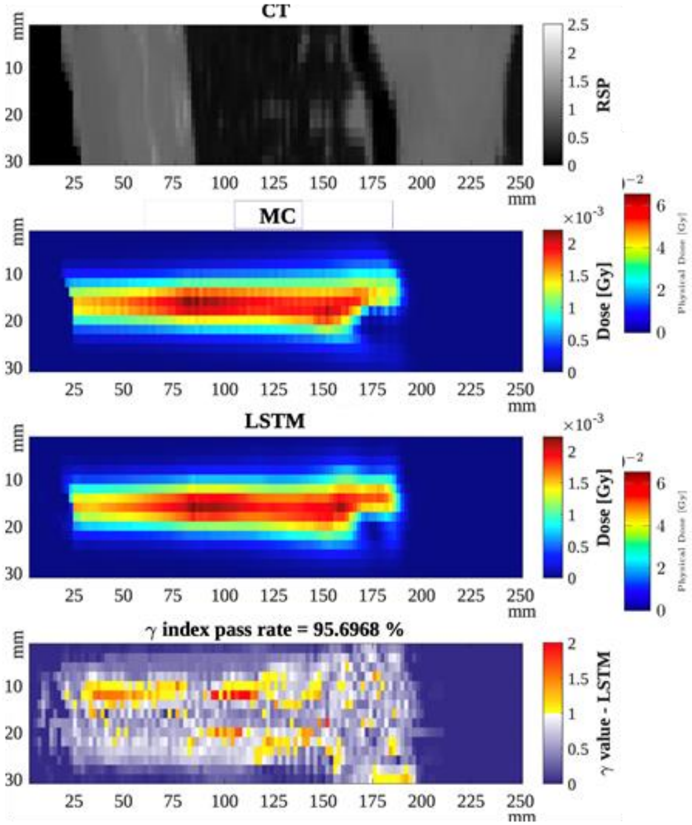
- **Question**: Can we estimate the delivered dose in a proton treatment plan using ANNs?
- **Motivations:**
  - Speed
  - Accuracy

Challenges:

- Many input/output parameters
- Informative data to train
- Heterogenities with distant correlations between inputs and the outputs

The "Pencil Beam Approach" to training the neural network

Results:



γ-index analysis ([1%, 3 mm])

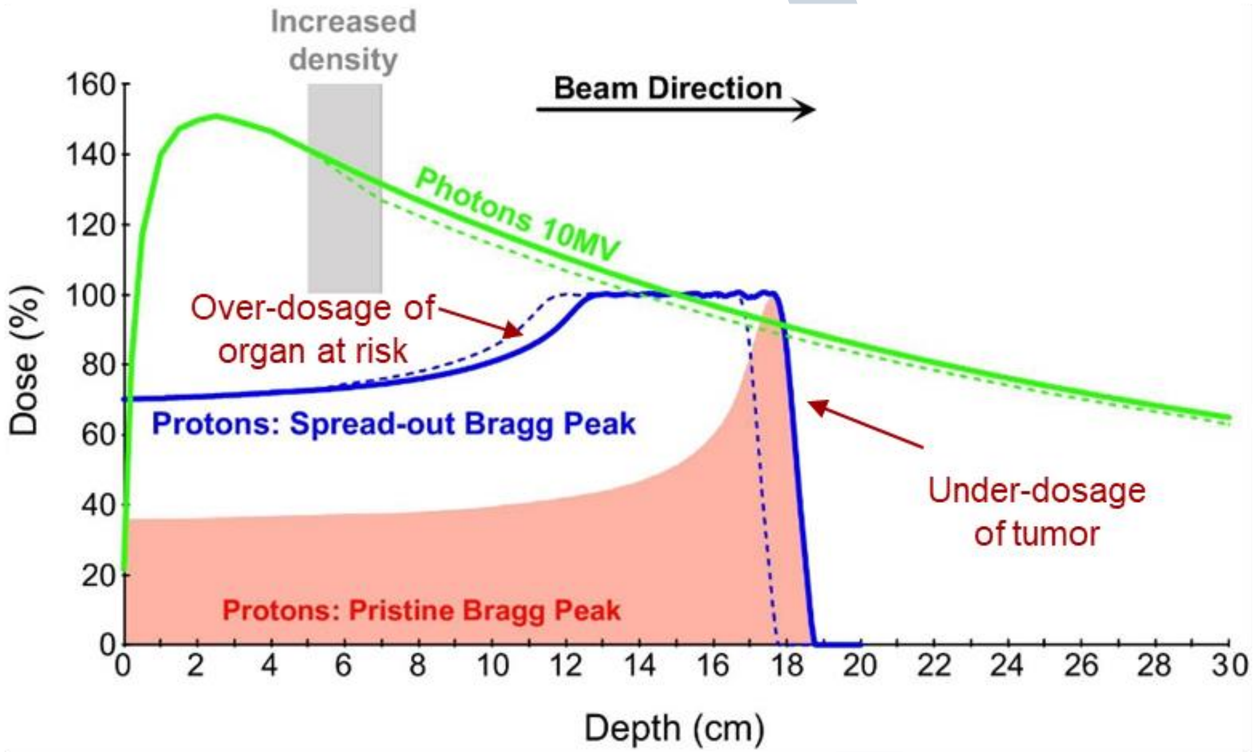
	mean (%)	std (%)	min (%)	max (%)
Patient 0	98.50	1.00	93.93	99.82
Patient 1	98.27	0.97	94.66	99.65
Patient 2	98.35	1.30	94.35	99.78
Patient 3	98.45	1.10	94.51	99.60
Patient 4	96.71	3.01	81.66	99.61
Patient 5	97.47	1.87	87.82	99.61

Energy (MeV)	mean (%)	std (%)	min (%)	max (%)
67.85	98.56	1.30	95.35	99.79
104.25[h]	97.74	1.48	92.57	99.74
134.68	94.51	2.99	85.37	99.02

Neishabouri et al. (2020). Long short-term memory networks for proton dose calculation in highly heterogeneous tissues. Medical Physics.

Dual-layer spectral CT imaging for particle therapy

Motivation: particle therapy and range uncertainties



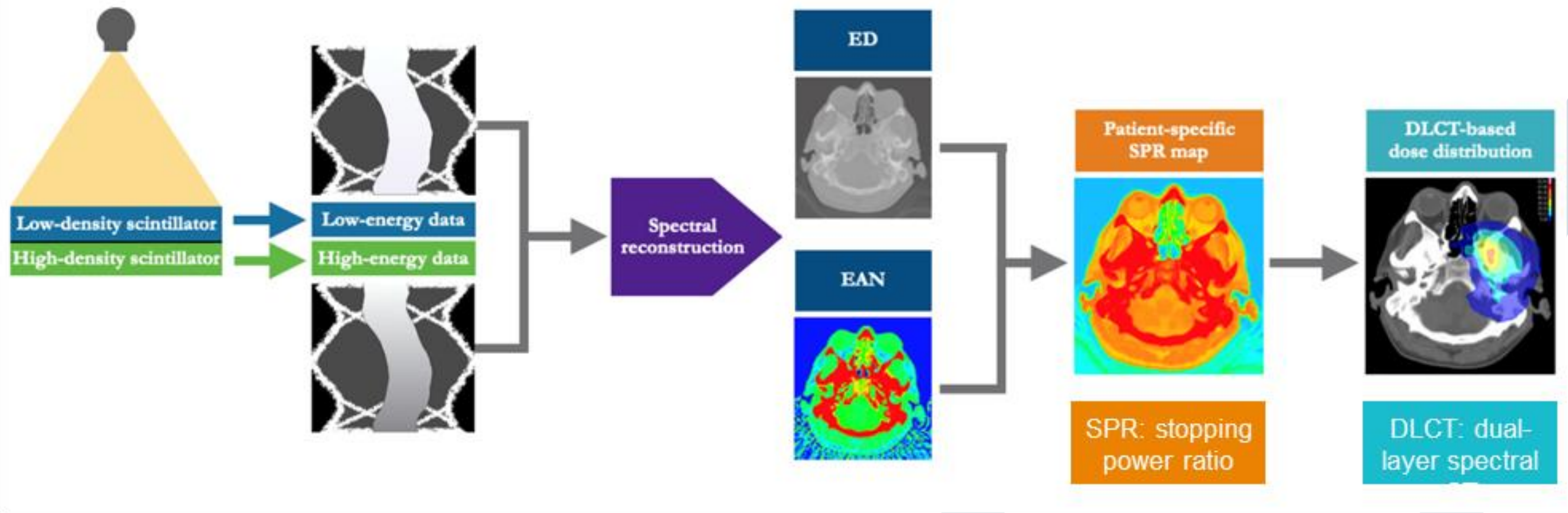
— calculated depth–dose curve
--- actual depth–dose curve

Adapted from: Engelsman M et al. (2013) Semin Radiat Oncol.
doi: 10.1016/j.semradonc.2012.11.003

Range uncertainties must be carefully accounted for
→ Accurate dose calculation is **crucial for treatment planning**

Dual-layer spectral CT imaging for particle therapy

The Workflow:



→ Pre-clinical evaluation of **patient-specific SPR** estimates with DLCT

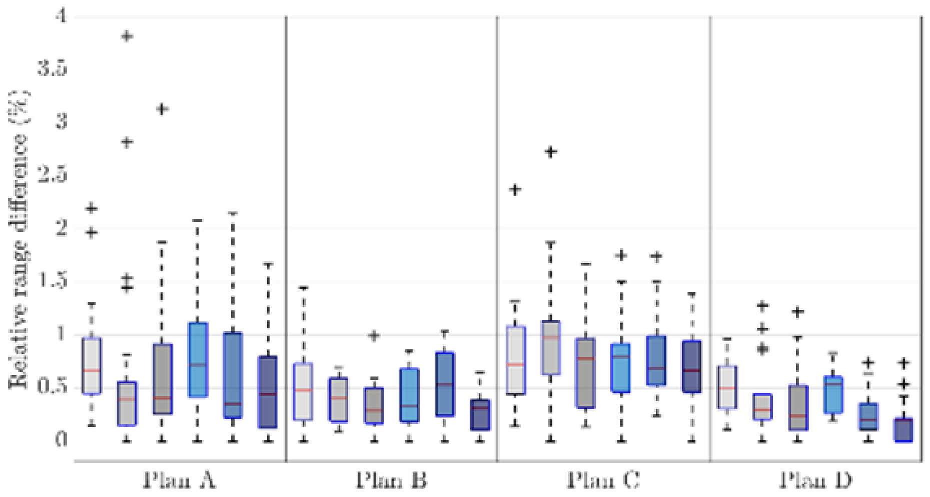
→ DLCT provides **improved particle range prediction** compared to conventional CT

→ **Reduced uncertainty caused by intra- and inter-patient tissue composition differences** during treatment planning

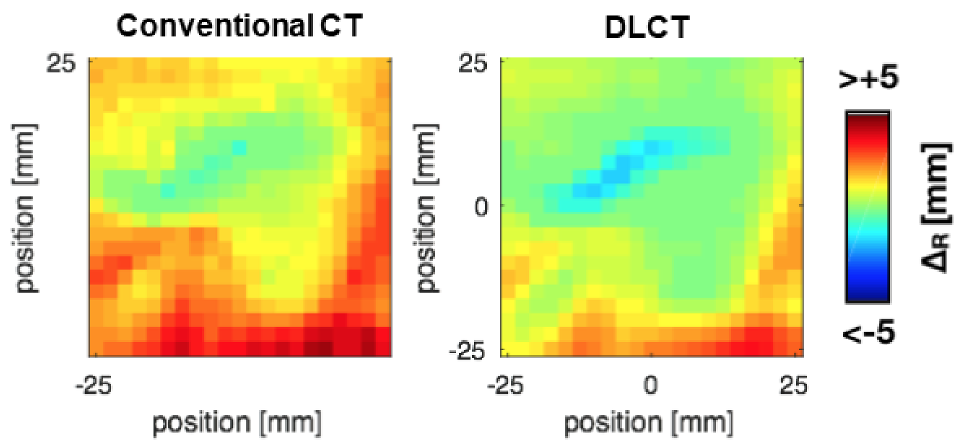
Longarino FK et al. (2021) J Appl Clin Med Phys. doi: 10.1002/acm2.13465

Dual-layer spectral CT imaging for particle therapy

Treatment planning study for brain tumors:



Dosimetry study in anthropomorphic head phantom:



- → Most advantageous in **highly heterogeneous structures**
- → DLCT-based SPR prediction may improve ion range calculation and eventually lead to **reduced range uncertainty margins**
- → **Further clinical investigations** using larger patient cohorts and examining other treatment regions are foreseen

Faller FK et al. (2020) Phys Med Biol. doi: 10.1088/1361-6560/ab735e
Longarino FK et al. (2021) J Appl Clin Med Phys. doi: 10.1002/acm2.13465

A successful story: **Helium ion therapy** from research to clinic

Physics in Medicine & Biology
IPEM Institute of Physics and Engineering in Medicine

CrossMark

OPEN ACCESS

RECEIVED
6 September 2021

REVISED
10 February 2022

ACCEPTED FOR PUBLICATION

TOPICAL REVIEW

Roadmap: helium ion therapy

Andrea Mairani[1,2,3,4], Stewart Mein[1,3,4,5], Eleanor Blakely[6], Jürgen Debus[1,3,4,5,7], Marco Durante[8,21], Alfredo Ferrari[1], Hermann Fuchs[9,10], Dietmar Georg[9,10], David R Grosshans[11], Fada Guan[11,19], Thomas Haberer[1], Semi Harrabi[1,4,5,7,20], Felix Horst[8], Taku Inaniwa[12,13], Christian P Karger[4,18], Radhe Mohan[11], Harald Paganetti[14,15], Katia Parodi[16], Paola Sala[17], Christoph Schuy[8], Thomas Tessonnier[1], Uwe Titt[11] and Ulrich Weber[8]

MEDICAL PHYSICS | WEBINAR | SPONSORED

Helium ion beam therapy

19 Aug 2022 Sponsored by *Physics in Medicine & Biology*

Available to watch now, the IOP Publishing journal, ***Physics in Medicine & Biology***, discusses the current state-of-the-art and future directions of helium ion therapy

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
ASTRO

Articles | Publish | Topics | Multimedia | CME ↗ | About | Contact

AUDIO

July 15, 2023

Red Journal Podcast July 15, 2023

0:00 / 0:00

Advances in Particle Therapy - Proton Track-end Counts and Helium Ion Treatment Planning

Networking and cooperation with other institutions

Physics in Medicine & Biology

CrossMark

OPEN ACCESS

RECEIVED
6 September 2021

REVISED
10 February 2022

ACCEPTED FOR PUBLICATION
8 April 2022

PUBLISHED
5 August 2022

TOPICAL REVIEW

Roadmap: helium ion therapy

Andrea Mairani[1,2,3,4], Stewart Mein[1,3,4,5], Eleanor Blakely[6], Jürgen Debus[1,3,4,5,7], Marco Durante[8,21], Alfredo Ferrari[1], Hermann Fuchs[9,10], Dietmar Georg[9,10], David R Grosshans[11], Fada Guan[11,19], Thomas Haberer[1], Semi Harrabi[1,4,5,7,20], Felix Horst[8], Taku Inaniwa[12,13], Christian P Karger[4,18], Radhe Mohan[11], Harald Paganetti[14,15], Katia Parodi[16], Paola Sala[17], Christoph Schuy[8], Thomas Tessonnier[1], Uwe Titt[11] and Ulrich Weber[8]

1 Heidelberg Ion-Beam Therapy Center (HIT), Department of Radiation Oncology, Heidelberg University Hospital, Heidelberg, Germany
2 National Centre of Oncological Hadrontherapy (CNAO), Medical Physics, Pavia, Italy
3 Division of Molecular and Translational Radiation Oncology, National Center for Tumor Diseases (NCT), Heidelberg University Hospital, 69120 Heidelberg, Germany
4 National Center for Radiation Research in Oncology (NCRO), Heidelberg Institute for Radiation Oncology (HIRO), Heidelberg, Germany
5 German Cancer Consortium (DKTK) Core-Center Heidelberg, German Cancer Research Center (DKFZ), Heidelberg, Germany
6 Biological Systems and Engineering Division, Lawrence Berkeley National Laboratory, Berkeley, CA, United States of America
7 Clinical Cooperation Unit Radiation Oncology, Heidelberg Institute of Radiation Oncology (HIRO), National Center for Radiation Oncology (NCRO), Heidelberg University and German Cancer Research Center (DKFZ), Heidelberg, Germany
8 GSI Helmholtzzentrum für Schwerionenforschung, D-64291 Darmstadt, Germany
9 Division of Medical Physics, Department of Radiation Oncology, Medical University of Vienna, Austria
10 MedAustron Ion Therapy Center, Wiener Neustadt, Austria
11 The University of Texas MD Anderson cancer Center, Houston, Texas, United States of America
12 Department of Accelerator and Medical Physics, Institute for Quantum Medical Science, QST, 4-9-1 Anagawa, Inage-ku, Chiba 263-8555, Japan
13 Medical Physics Laboratory, Division of Health Science, Graduate School of Medicine, Osaka University, 1-7 Yamadaoka, Suita, Osaka 565-0871, Japan
14 Department of Radiation Oncology, Massachusetts General Hospital, Boston, United States of America
15 Harvard Medical School, Boston, United States of America
16 Ludwig-Maximilians-Universität München, Department of Experimental Physics—Medical Physics, Munich, Germany
17 INFN Sezione di Milano, Via Celoria 16, Milano I-20133, Italy
18 Department of Medical Physics in Radiation Oncology, German Cancer Research Center (DKFZ), Heidelberg, Germany
19 Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, 06510, United States of America
20 National Center for Tumor Diseases (NCT), Heidelberg University Hospital, 69120 Heidelberg, Germany
21 Technische Universität Darmstadt, Institut für Physik Kondensierter Materie, Darmstadt, Germany

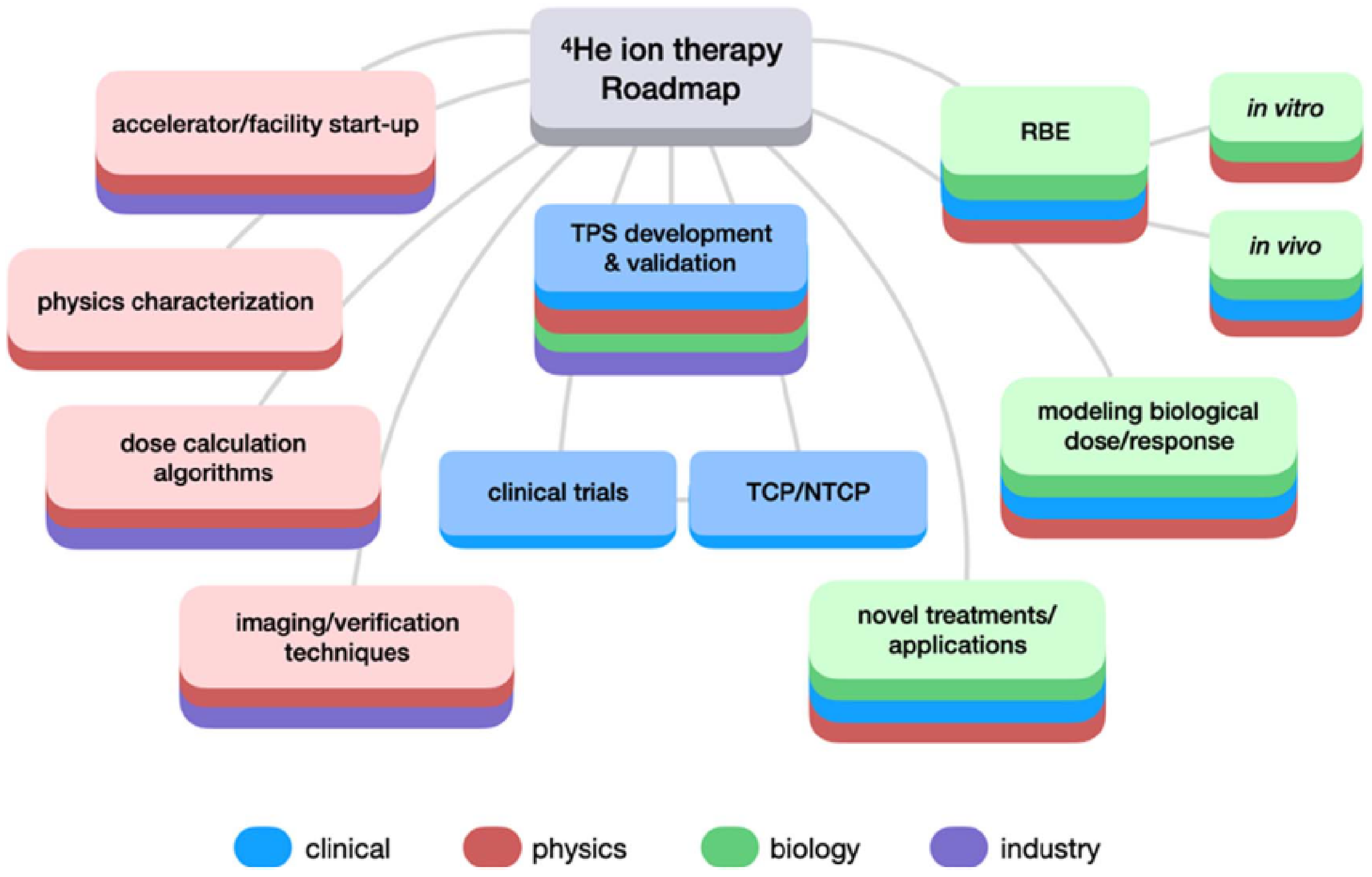
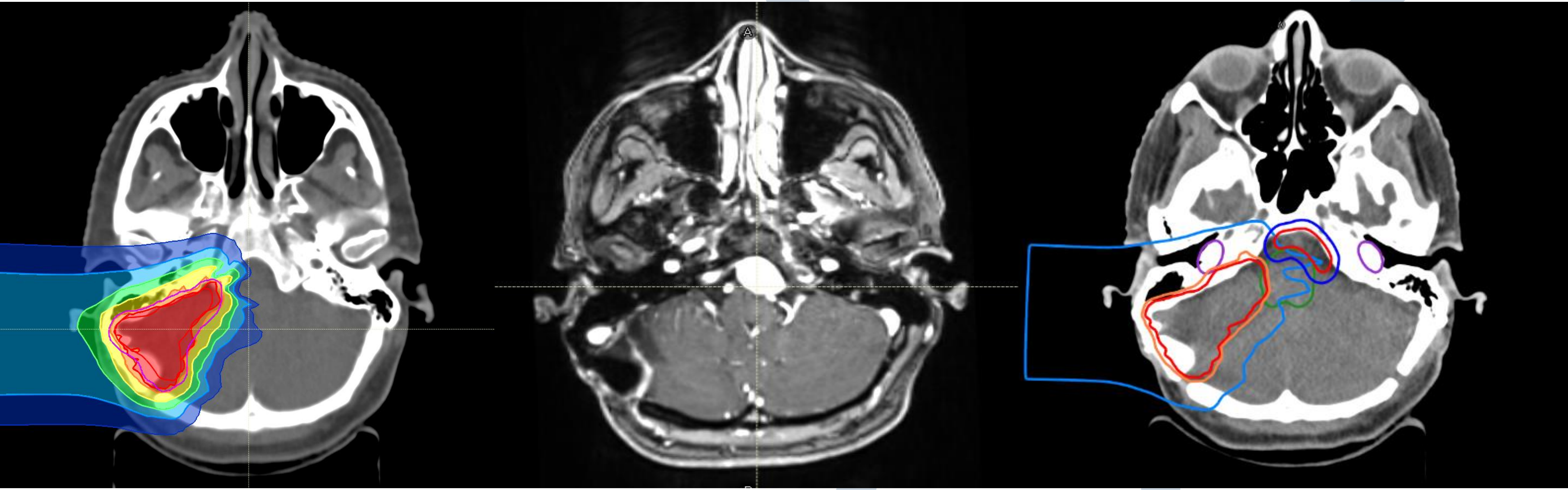


Figure 1. Roadmap for development, investigation and clinical translation of helium ion beams. Topics include the following: past, present and future clinical trials, physical characterization of helium ions, accelerator/facility start-up, imaging/verification techniques, dose calculation algorithms, TPS development and validation, biological effects (*in vitro* versus *in vivo*), clinical modeling and novel applications.

1st treatment with scanned helium beams

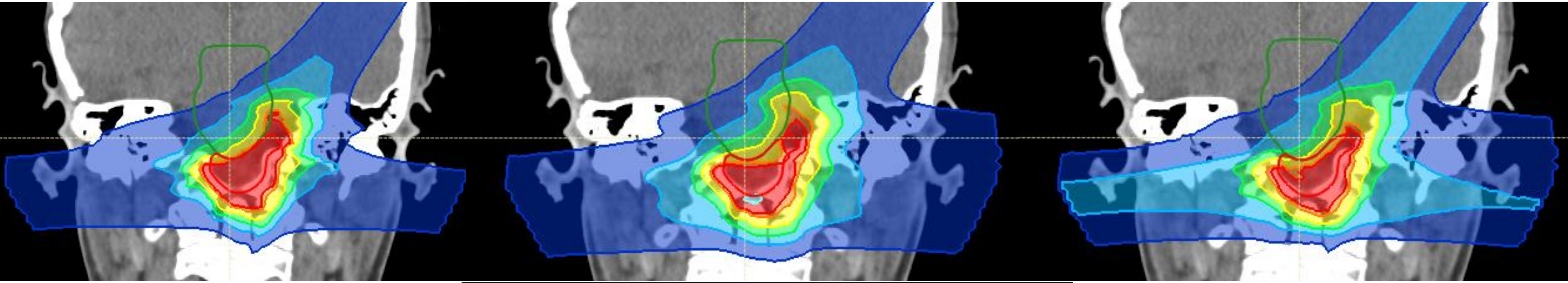


Intracranial anaplastic hemangiopericytoma

Summer 2021 – 60GyRBE – 30 fractions / Re-irradiation (1st treatment 60GyRBE-2015)

1st treatment with scanned helium beams

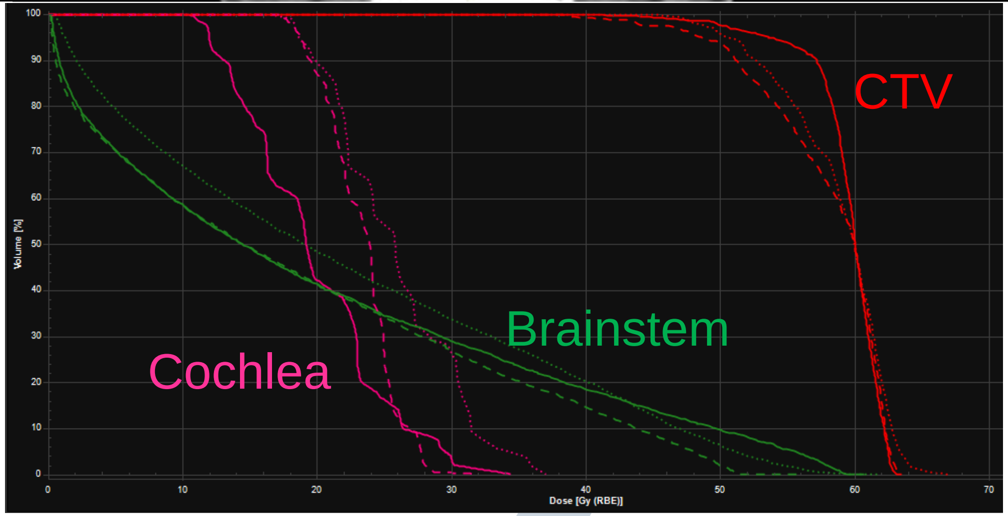
Helium (mMKM) | Protons (1.1) | Carbon (LEM I)



Helium

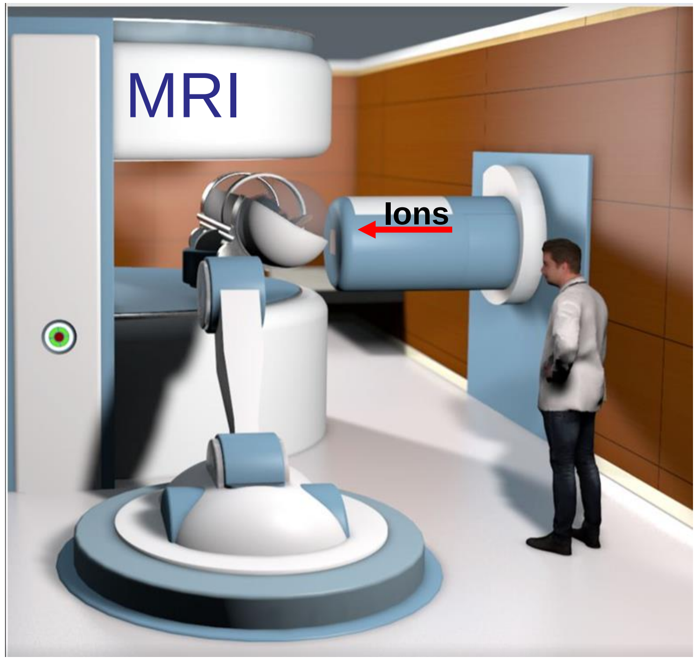
Protons

Carbon



ARTEMIS – MRI guided particle therapy

MR-guided proton and ion beam therapy (*with **MonteRay***) – ARTEMIS program @ HIT



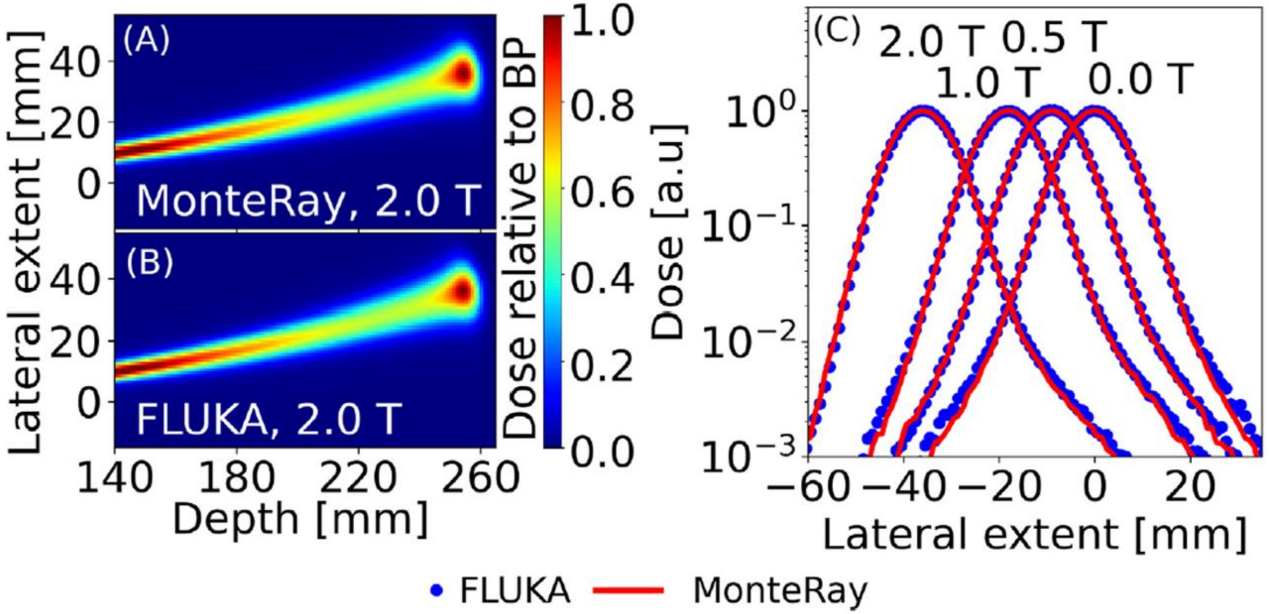


FIGURE 5 | For 200 MeV protons in water, 2D dose distributions calculated with MonteRay **(A)** and FLUKA **(B)** are shown in a plane perpendicular to the 2 T magnetic field. In **(C)**, Lateral profiles for 200 MeV protons in water and with magnetic field strengths of 0 T, 0.5 T, 1 T, and 2 T are displayed at the location of the BP. MonteRay's results are indicated by a red line while FLUKA's results are displayed as blue dots.

Particle Arc Therapy (PAT): delivery which makes use of rotational motion of gantry and/or patient (step-and-shoot or dynamic rotation).

Treatment Optimization:

Conventional vs. PAT

i. Improved target conformity +

ii. Improved Robustness +

iii. LET Redistribution +

iv. Delivery efficiency +

SCIENTIFIC ARTICLE | VOLUME 6, ISSUE 3, 100661, MAY 2021 Download Full Issue

Spot-Scanning Hadron Arc (SHArc) Therapy: A Study With Light and Heavy Ions

Stewart Mein, PhD • Thomas Tessonnier, PhD • Benedikt Kopp, MS • ... Jürgen Debus, MD, PhD • Thomas Haberer, PhD • Andrea Mairani, PhD • Show all authors

Open Access • Published: February 03, 2021 • DOI: https://doi.org/10.1016/j.adro.2021.100661 •
Check for updates

MEDICAL PHYSICS
The International Journal of Medical Physics Research and Practice

RESEARCH ARTICLE | Open Access

Spot-scanning hadron arc (SHArc) therapy: A proof of concept using single- and multi-ion strategies with helium, carbon, oxygen, and neon ions

Stewart Mein, Benedikt Kopp, Thomas Tessonnier, Jakob Liermann, Amir Abdollahi, Jürgen Debus, Thomas Haberer, Andrea Mairani

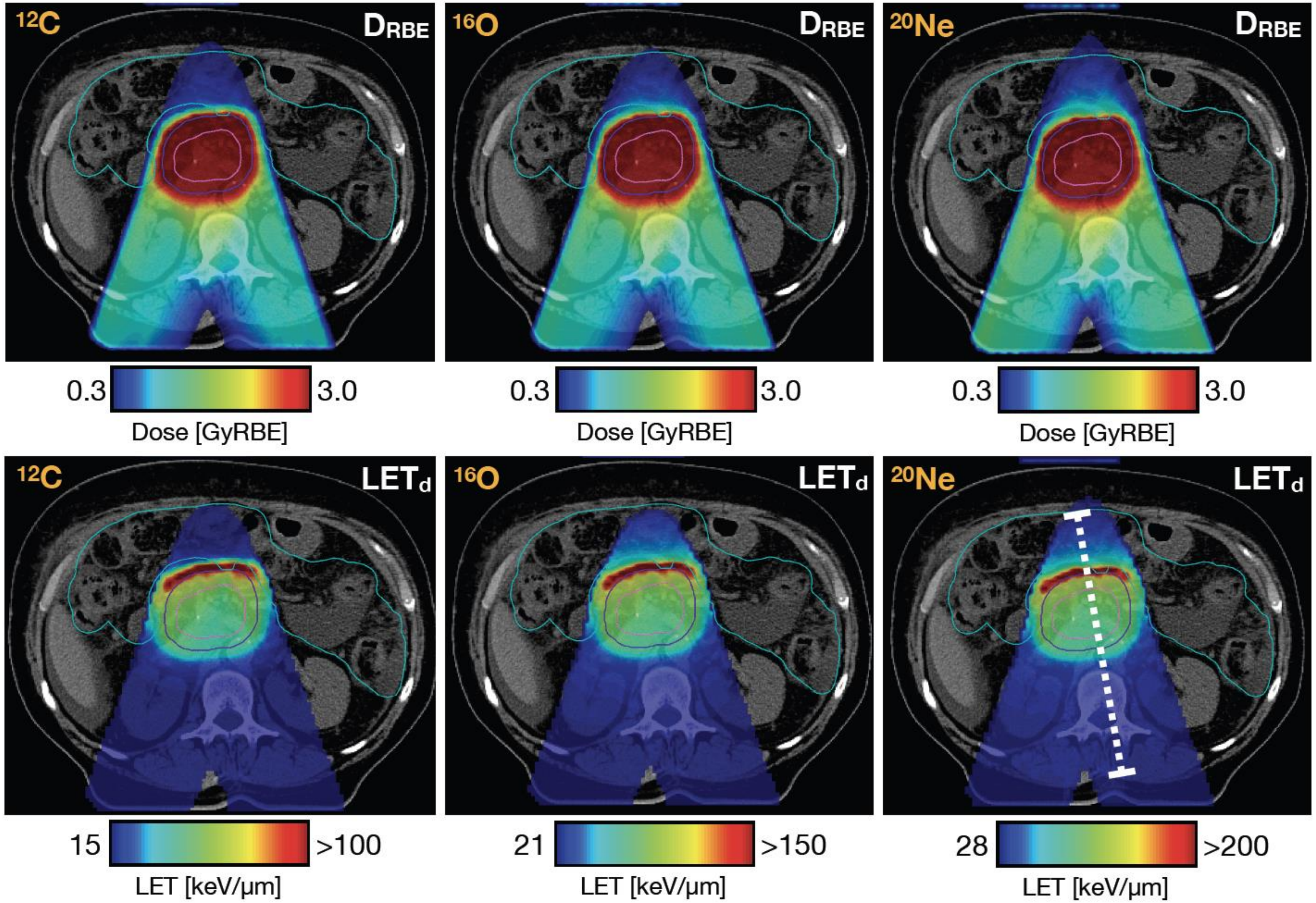
First published: 19 June 2022 | https://doi.org/10.1002/mp.15800 | Citations: 3

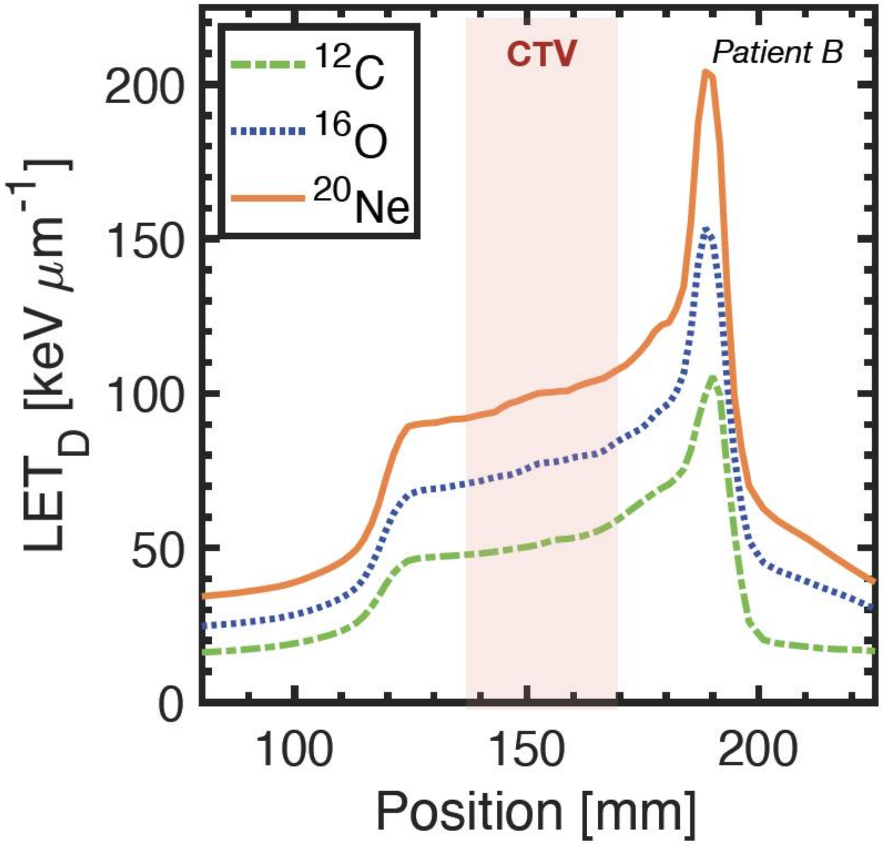
Biological Dose Optimization for Particle Arc Therapy Using Helium and Carbon Ions

Stewart Mein PhD *, †, ‡, §, Thomas Tessonnier PhD ‖, Benedikt Kopp PhD *, †, ‡, §, Christian Schömers PhD ‖, Semi Harrabi MD ‡, §, ‖, Amir Abdollahi MD, PhD *, †, ‡, §, Jürgen Debus MD, PhD *, †, ‡, §, ‖, ¶, Thomas Haberer PhD ‖, Andrea Mairani PhD *, ‖, ¶

Mein et al, *Adv. Rad. Onc.* ***2021***

IMPT for pancreatic cancer treatment

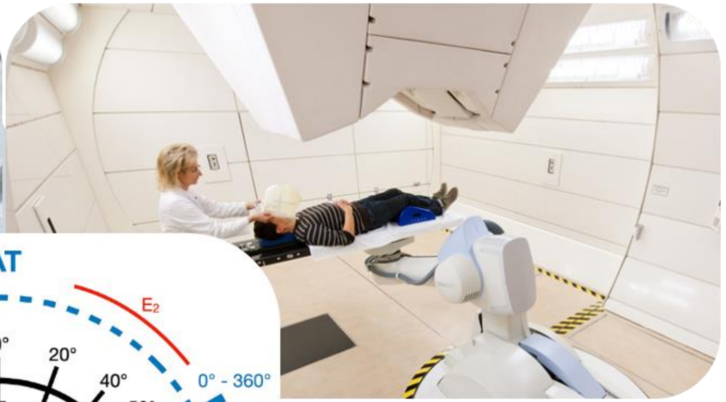


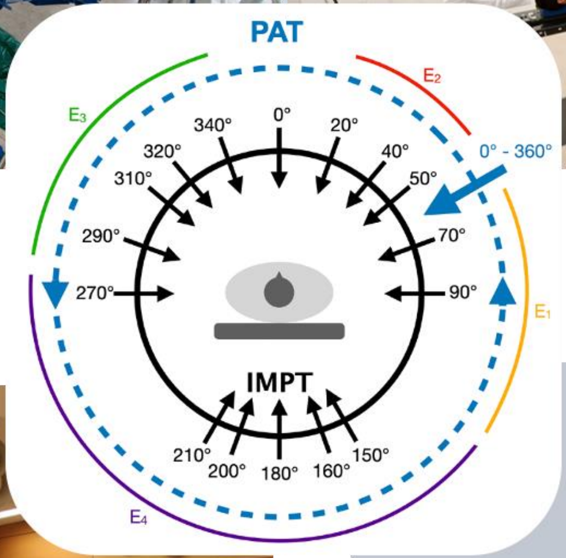


Mein et al ***2022b***

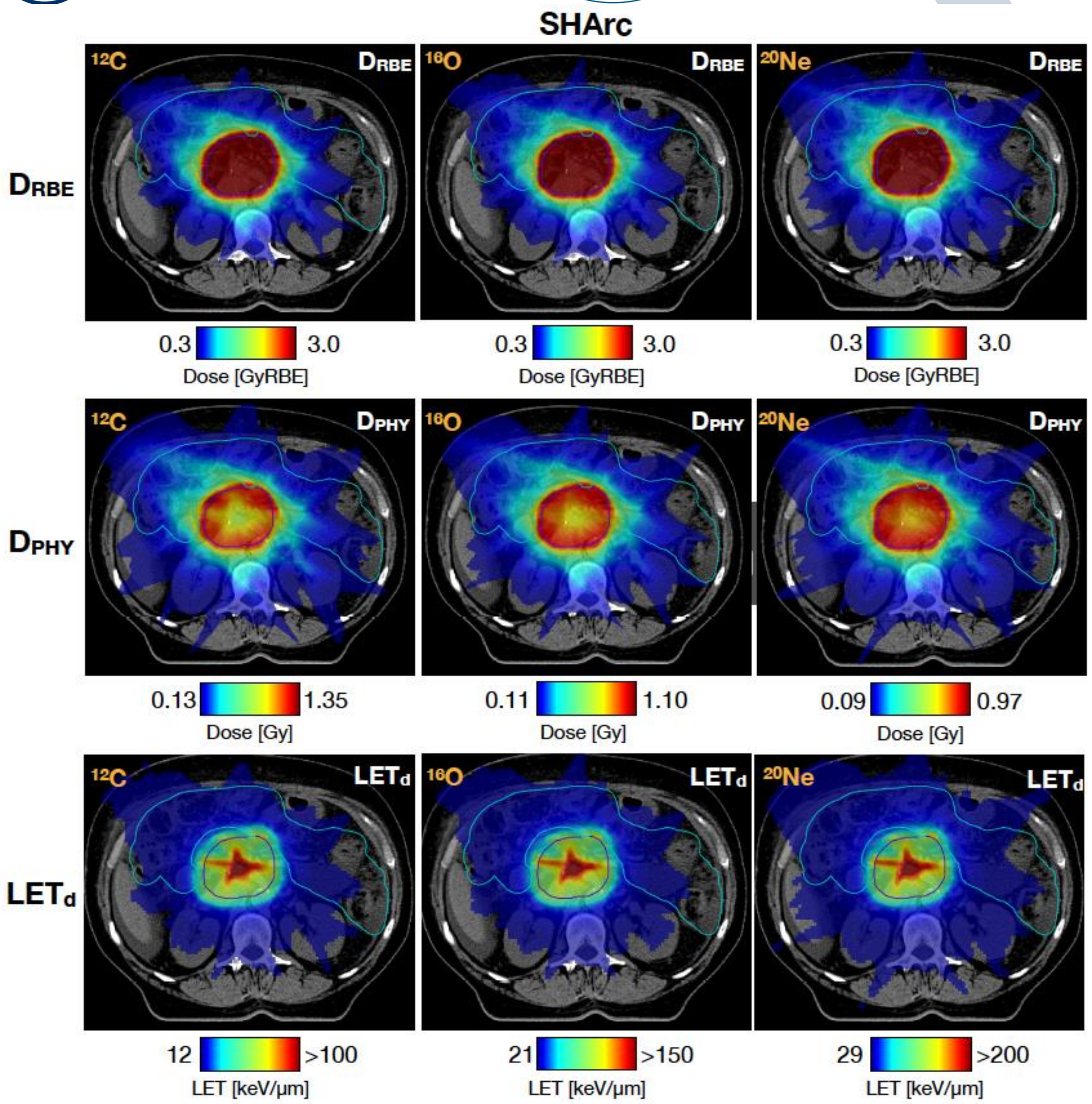
Pancreatic Adenocarcinoma

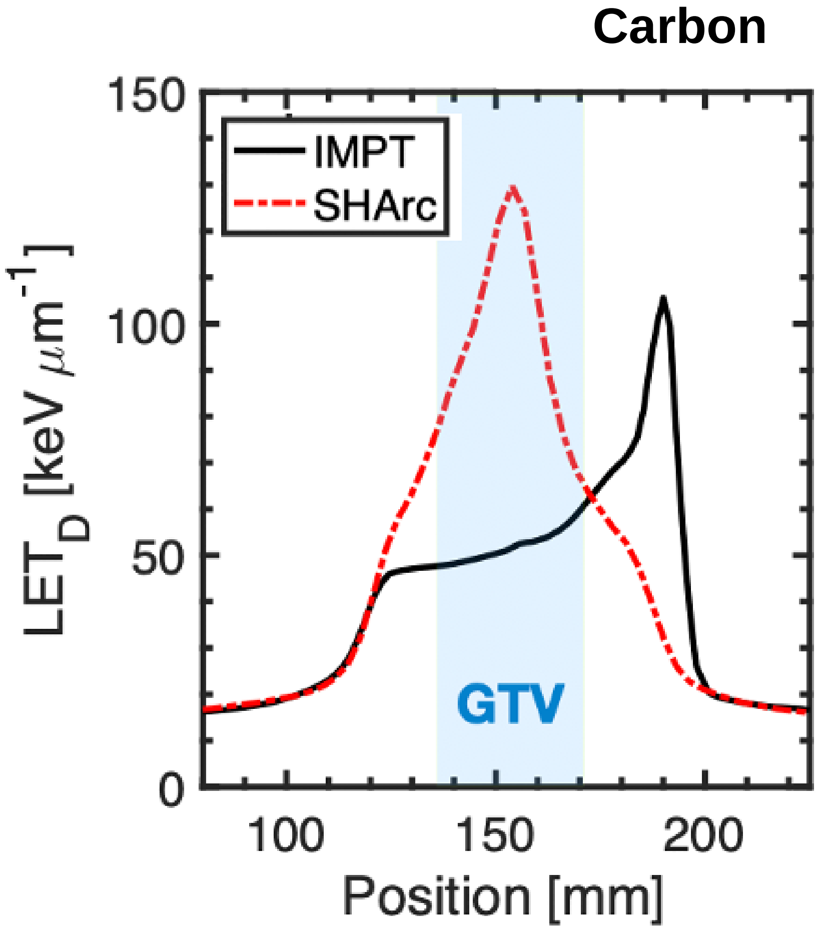
Gantry + Table





Horiz. Beam + Chair

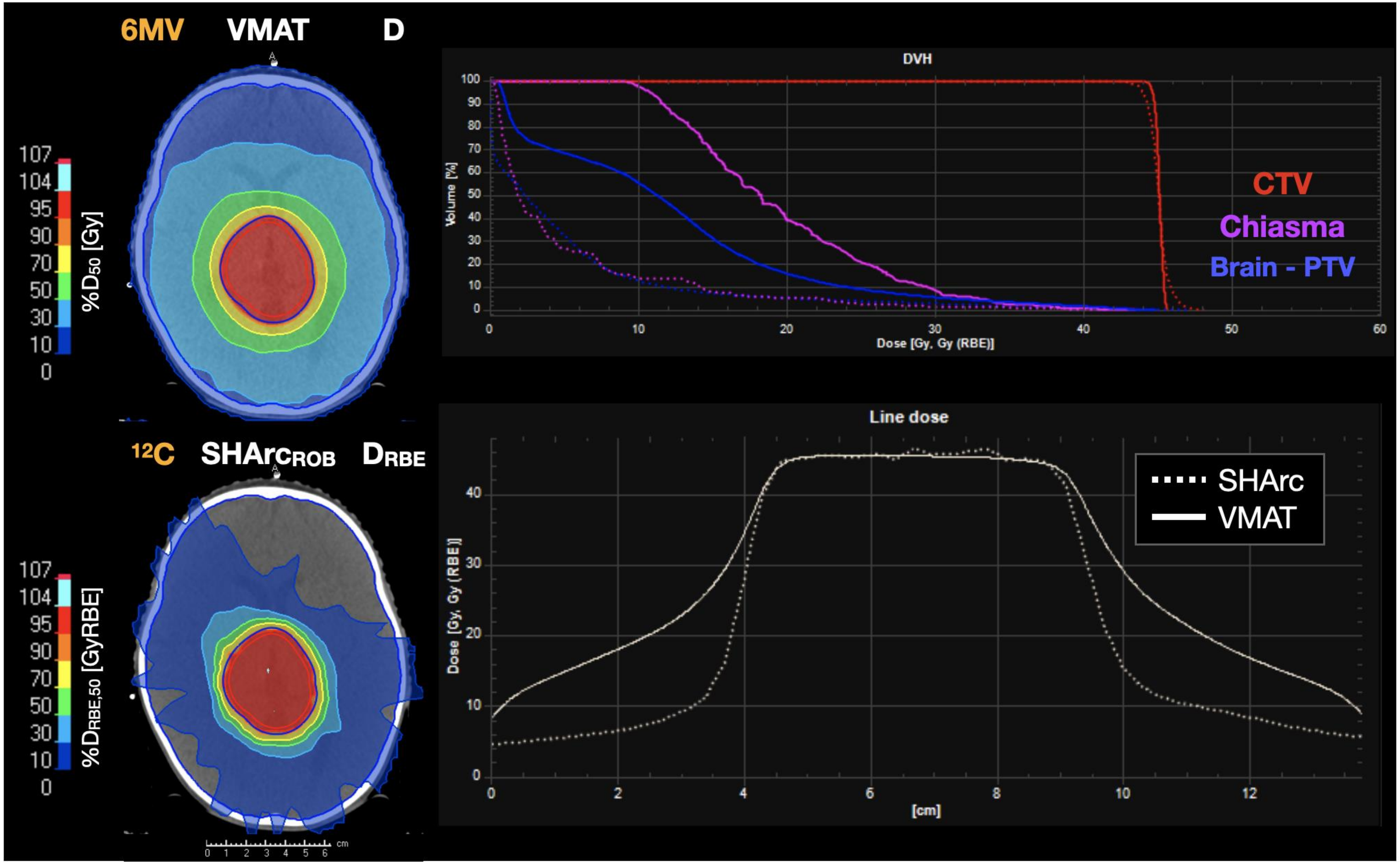




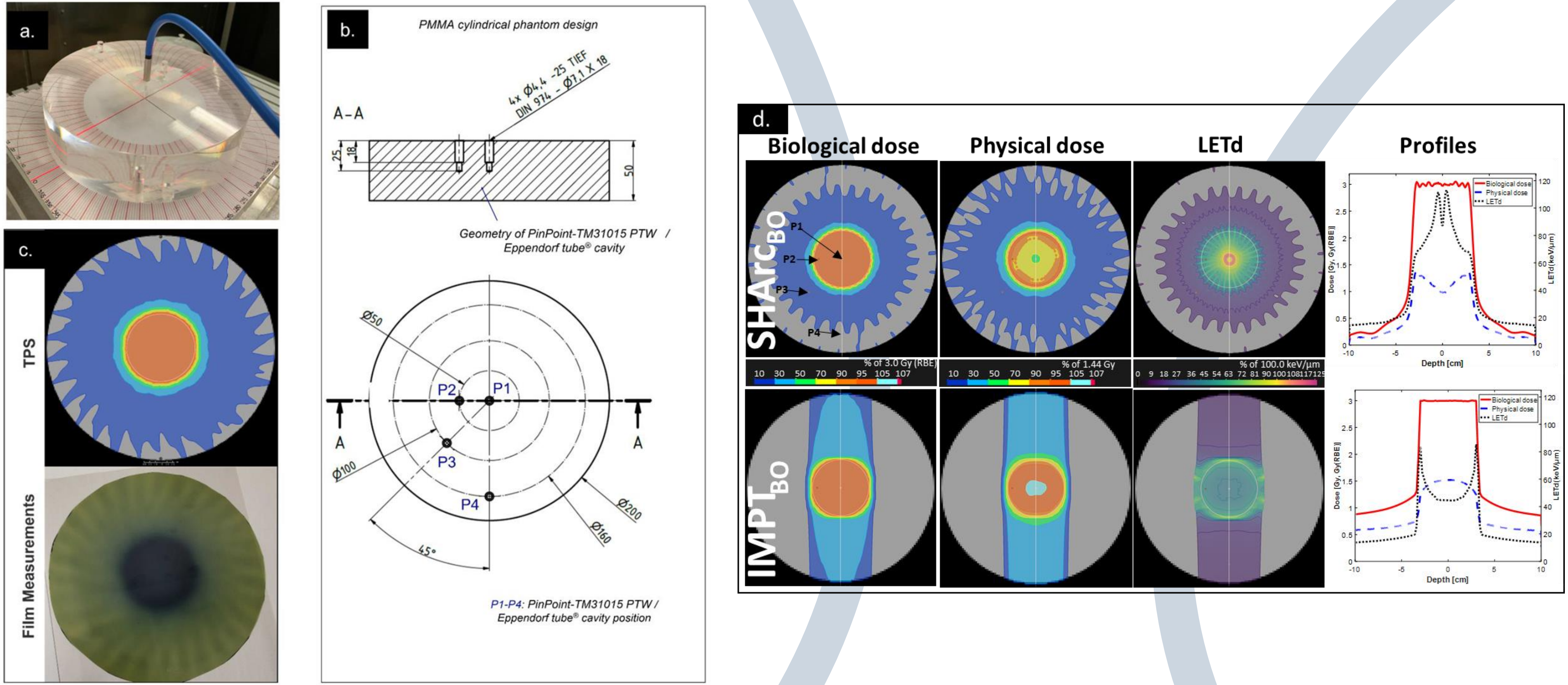
Target LET enhancement using arc delivery.

Mein et al ***2022b***

Pancreatic Adenocarcinoma


6MV VMAT D
107
104
95
90
70
50
30
10
0
%D50 [Gy]
12C SHArcROB DRBE
%DRBE,50 [GyRBE]
cm
DVH
Volume [%]
Dose [Gy, Gy (RBE)]
CTV
Chiasma
Brain - PTV
Line dose
Dose [Gy, Gy (RBE)]
[cm]
SHArc
VMAT

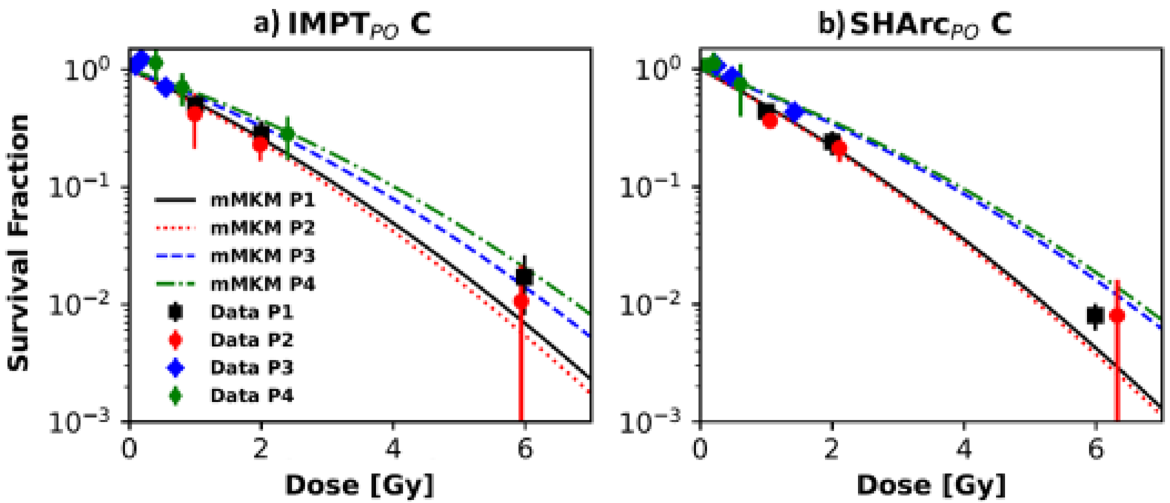
Biophysical Verification of Carbon Ion Arc Therapy

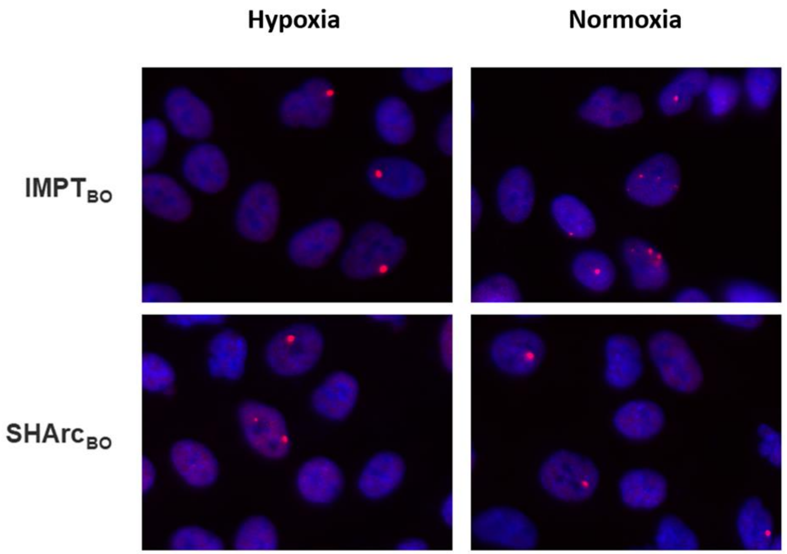


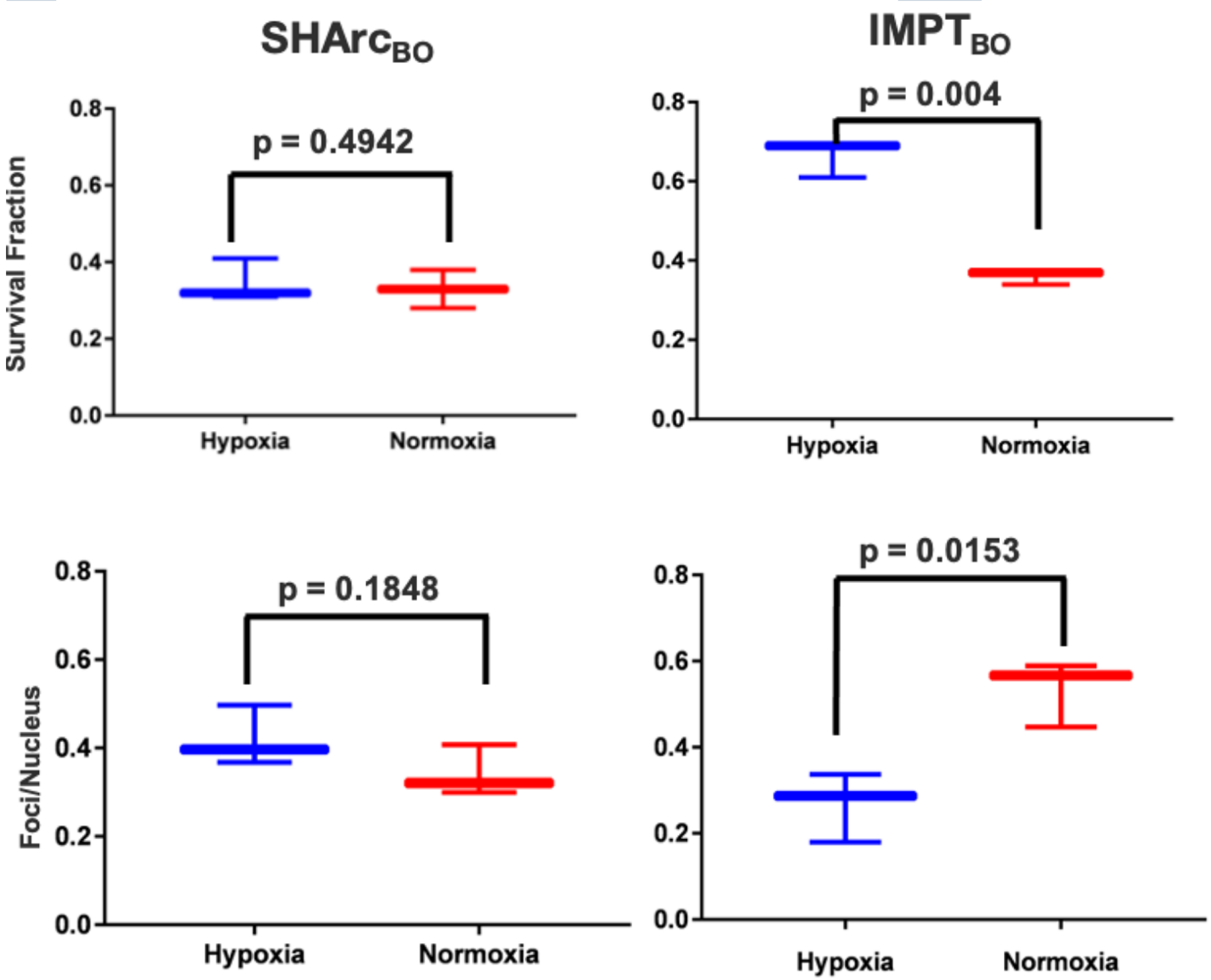
Tessonnier, Filosa et al, *Adv. Rad. Onc.* ***2024***

Biophysical Verification of Carbon Ion Arc Therapy

In vitro validation – A549

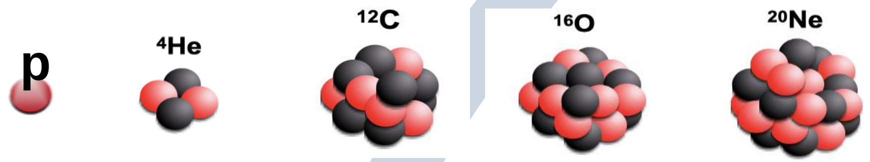






Tessonnier, Filosa et al, *Adv. Rad. Onc.* ***2024***

Multi-ion therapy (MIT): a particle therapy technique which involves the delivery of ≥2 charged particle species in a single fraction (e.g., p, He, C, O, and/or Ne ions)



Objective(s): design treatments which exhibit features unattainable using a single ion species — primary clinical aims are dependent on optimization/delivery technique (e.g., to improve dosimetric features, reduce physical and radio-biological uncertainties and/or improve TCP/NTCP)

Status: research and development, with one clinical program running for patient treatments

- **Ion selection**: end-point and optimization method dependent. However, in general, all proposed MIT techniques to-date involve mixture of 2 or more light and heavy ion species. Therefore, at the very least, combining a “lower” and “higher” LET particle is appropriate, in order to balance physical and biological properties (e.g., LET & RBE levels)

Examples:

Mairani et al **2022** PMB, *Roadmap: helium ion therapy*

• Optimization algorithm:

HIT (DE)

Combined ion-beam constant RBE (CICR)

Aim: robust physical/biological optimization and OAR sparing

robustness:

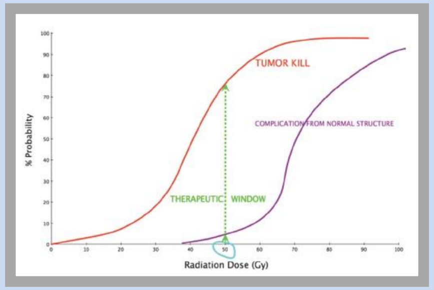
phys. bio.

T.T Böhlen et al **Phys. Med. Biol.** 2012
Kopp, Mein et al **IJROBP** 2020
Mein et al **Med Phys** 2022

NIRS (JP)

Intensity modulated composite particle therapy (IMPACT)

Aim: expand therapeutic window via optimization of physical dose and LET

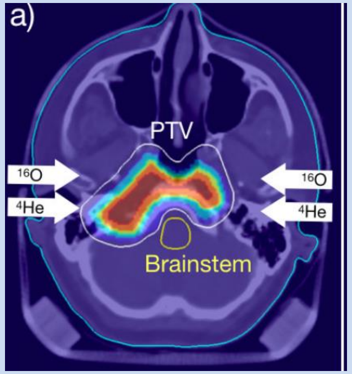


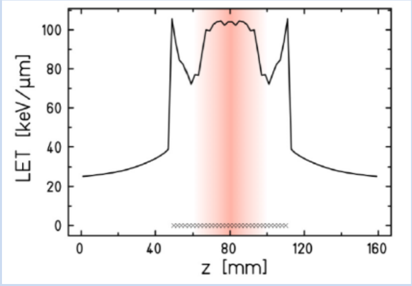
Inaniwa et al. **Phys. Med. Biol.** 2017, 2018, 2020, 2021

GSI (DE)

Multi-ion kill painting

Aim: overcome hypoxia-related tumor radio resistance



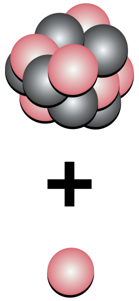


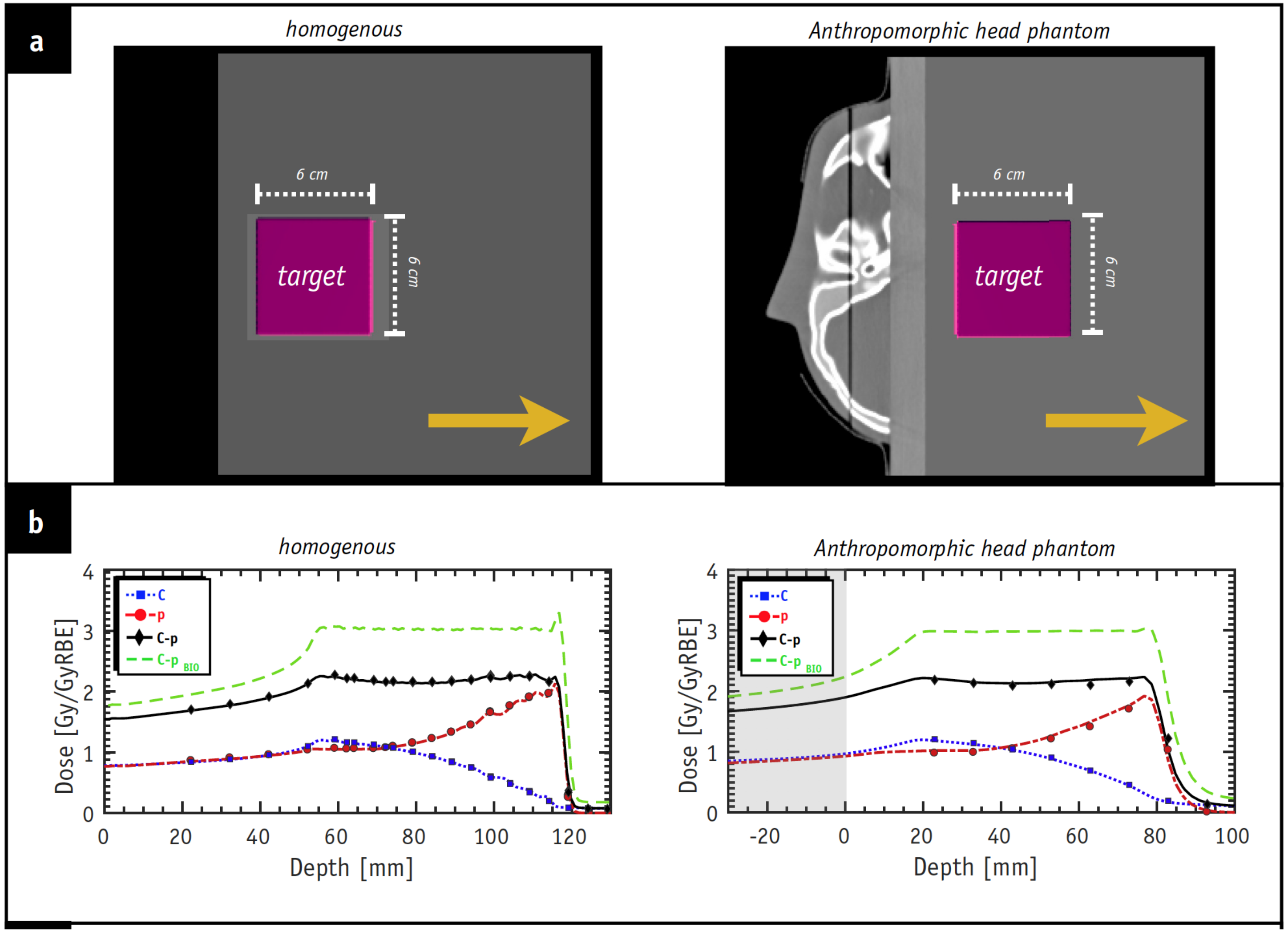
Tinganelli et al **Sci. Rep.** 2015
O Sokol et al **Phys. Med. Biol.** 2019

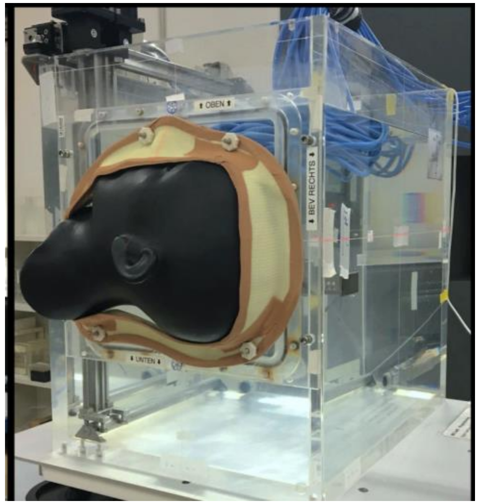
MIT Validations: *physics*

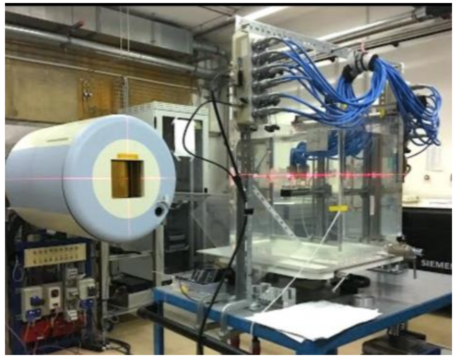
All new delivery methods must be verified experimentally

CICR$_{C\text{-}p}$





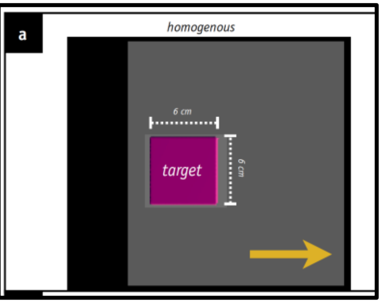




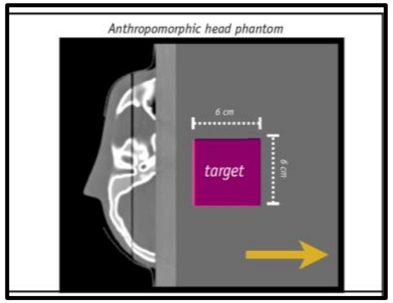
Kopp, Mein et al, *IJROBP* ***2020***

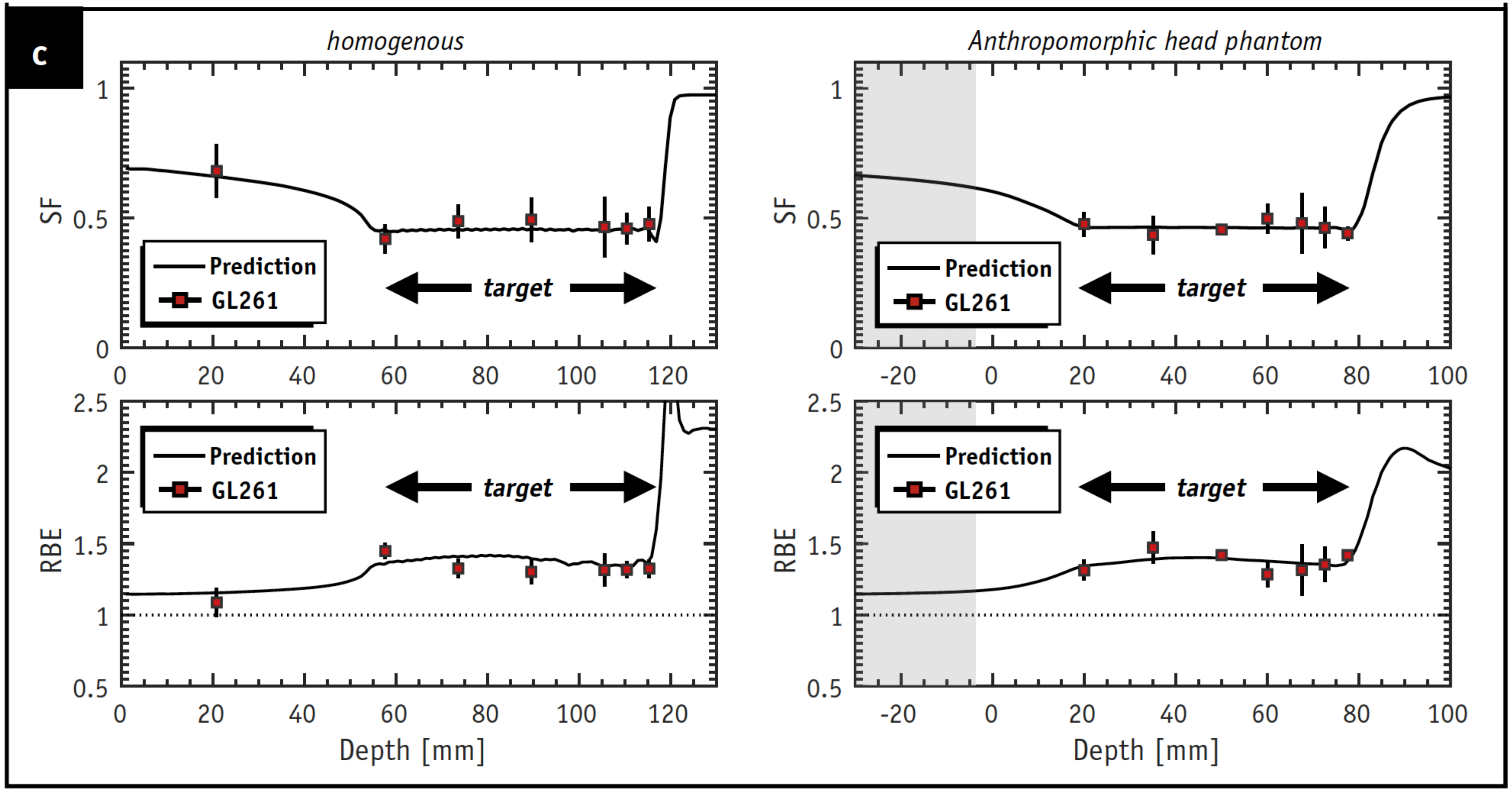
MIT Validations: *biology*

HEIDELBERG UNIVERSITY HOSPITAL

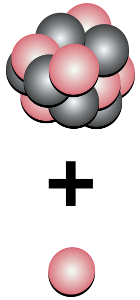


All new delivery methods must be verified experimentally





CICR$_{C\text{-}p}$

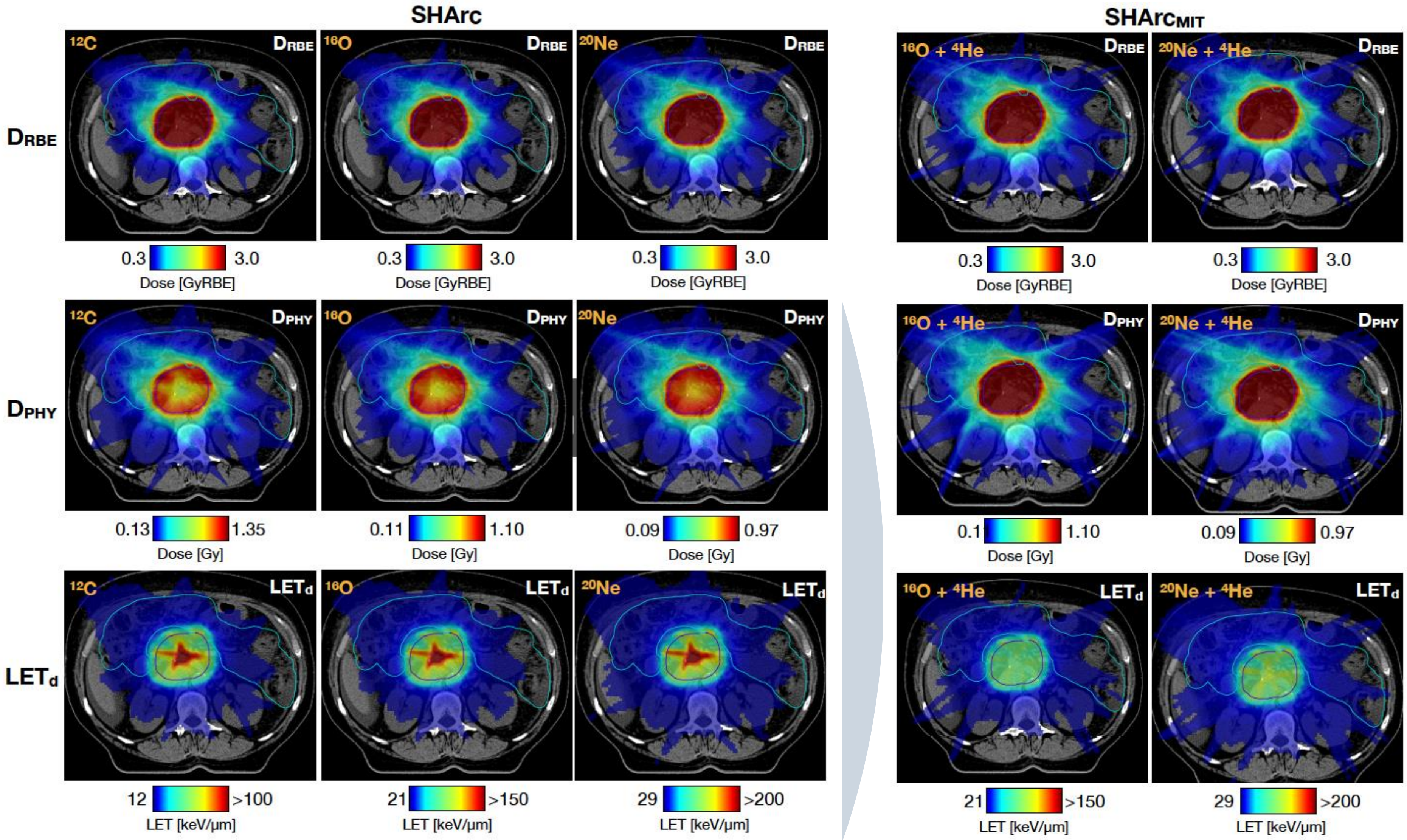


in vitro
clonogenic assay:

glioma cell line (GL261)

RBE$_{av}$ variation ~1-3 % in the target

Kopp, Mein et al, *IJROBP* ***2020***



SHArc (1-arc): target LET enhancement using arc delivery.

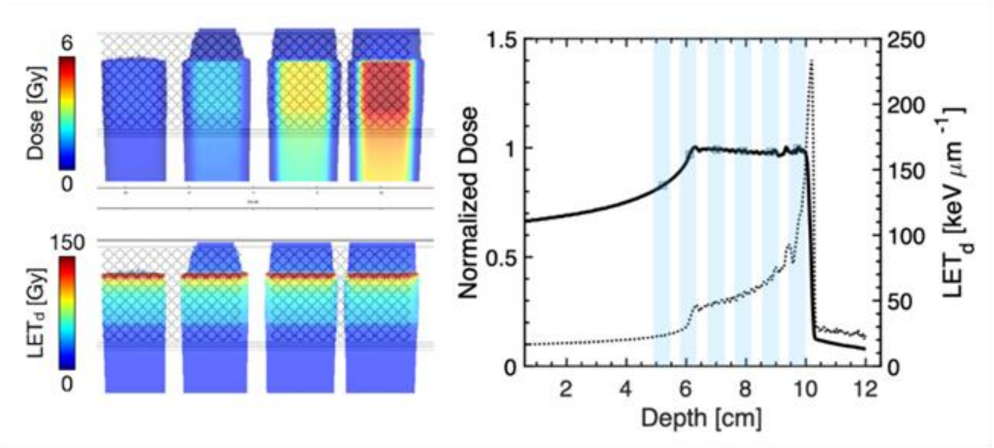
SHArc$_{MIT}$ (2-arc): improved physical dose and RBE homogeneity in the target

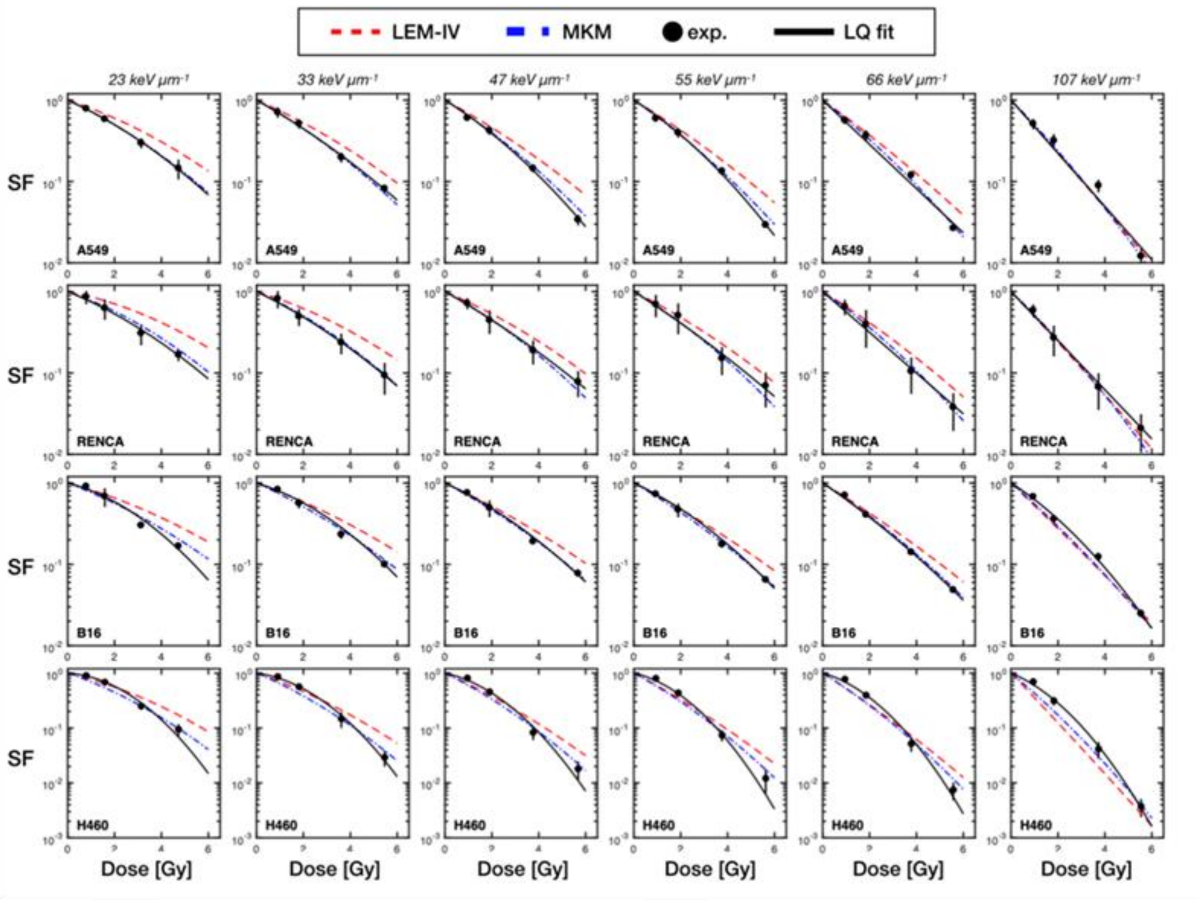
Mein et al ***2022b***

Pancreatic Adenocarcinoma

Which biological model?: ^{12}C ions *in vitro* considerations

- Clinical settings (SOBP)
- 4 cell lines *in vitro* (low and middle α/β values), 6 LET_d, 4 dose levels
- > 2 biological models
- Full Monte Carlo characterization

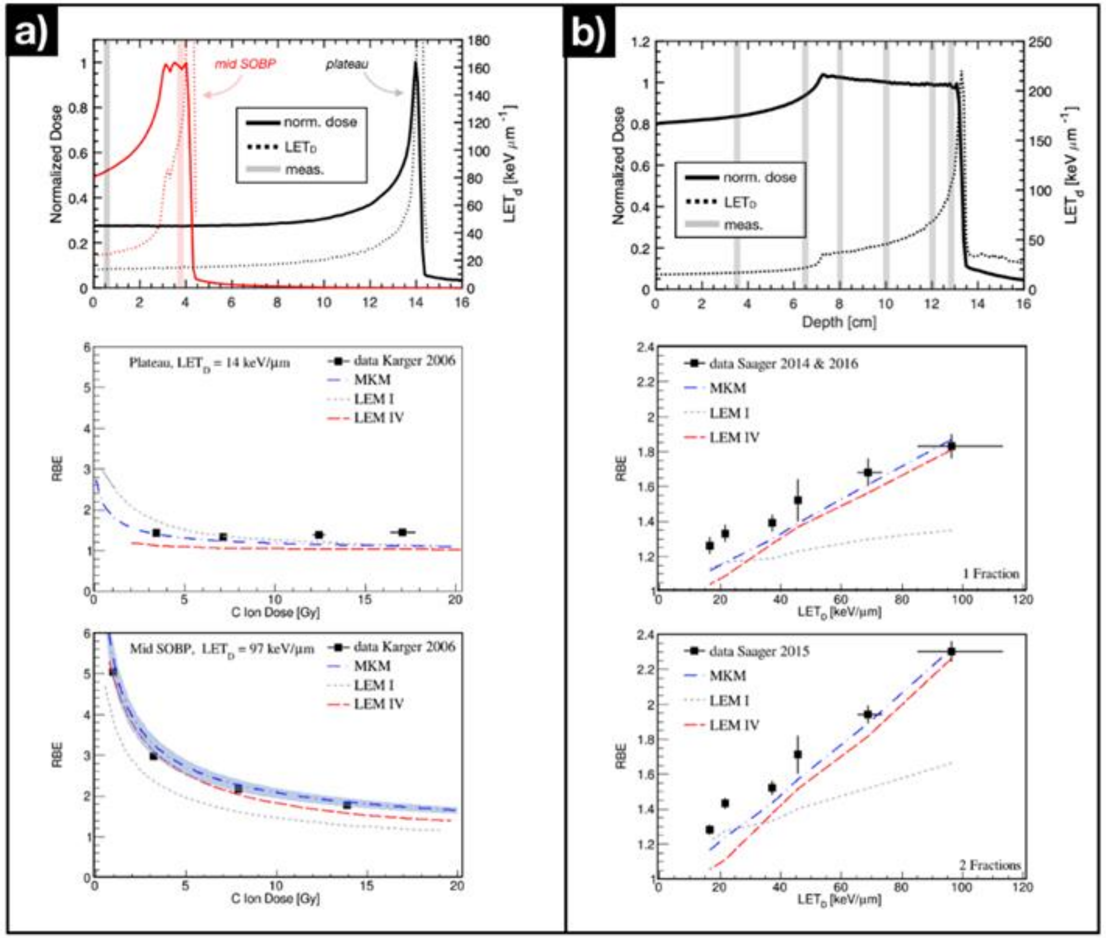




Mein, etl al 2019 IJROBP

Which biological model?: ^{12}C ions *in vivo* considerations

- Single energy slice and clinical settings (SOBP)
- Rat spinal cord irradiation (low α/β tissue)
- Full Monte Carlo characterization
- Same tendencies found *in vitro* (assuring)



Mein, et al 2019 IJROBP

Do we observe clinically the limitations of a biological model?

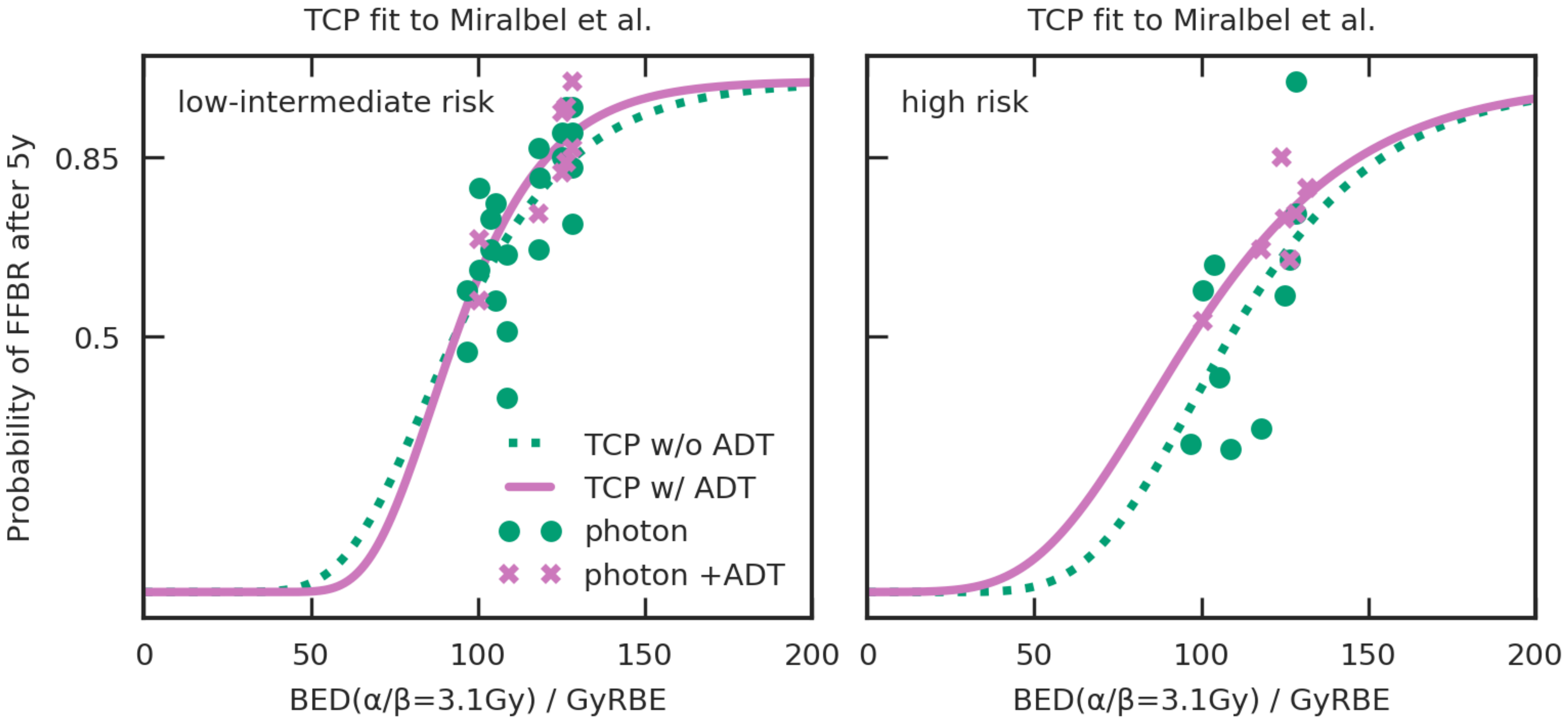
- Prostate Trial (IPI) (Habl et al. 2014, 2016, Eichkorn et al. 2022)
- **66 Gy (RBE), RBE = 1.1 1H** vs. **66 Gy (RBE) LEM I a/β = 2 Gy 12C** in 20 fx

	overall cohort n=91	**protons n=46**	**carbon ions n=45**
Median age (years)	68 (range 50-80)	69 (range 50-80)	67 (range 57-80)
Hormone therapy	21 [23%]	10 [22%]	11 [24%]
Initial PSA in median (range)	6.7 (2.4-26.6)	7.2 (2.9-26.6)	6.5 (2.4-16.8)
Gleason score			
5	2 [2.2%]	0 [0%]	2 [4%]
6	33 [36%]	17 [37%]	16 [36%]
7 (3+4)	28 [31%]	15 [33%]	13[29%]
7 (4+3)	22 [24%]	11 [24%]	11 [24%]
8	6 [7%]	3 [6.5%]	3 [7%]
9	1 [1%]	0 [0%]	1 [2%]
Clinical tumor stage			
T1a-b	2 [2%]	0 [0%]	2 [4%]
T1c	68 [75%]	37 [80%]	31 [69%]
T2a	14 [15%]	6 [13%]	8 [18%]
T2b-c	5 [6%]	3 [7%]	2 [4%]
T3a-b	3 [3%]	0 [0%]	3 [7%]
D'Amico score			
low risk	21 [23%]	8 [17%]	13 [29%]
intermediate risk	54 [59%]	30 [65%]	24 [53%]
high risk	16 [18%]	8 [17%]	8 [18%]
Mean Yale risk of lymph node involvement (range)	5.1 (0-13.2)	5.4 (0.1-13.2)	4.8 (0-12.7)

See also Habl et al. (IJROBP, 2016)

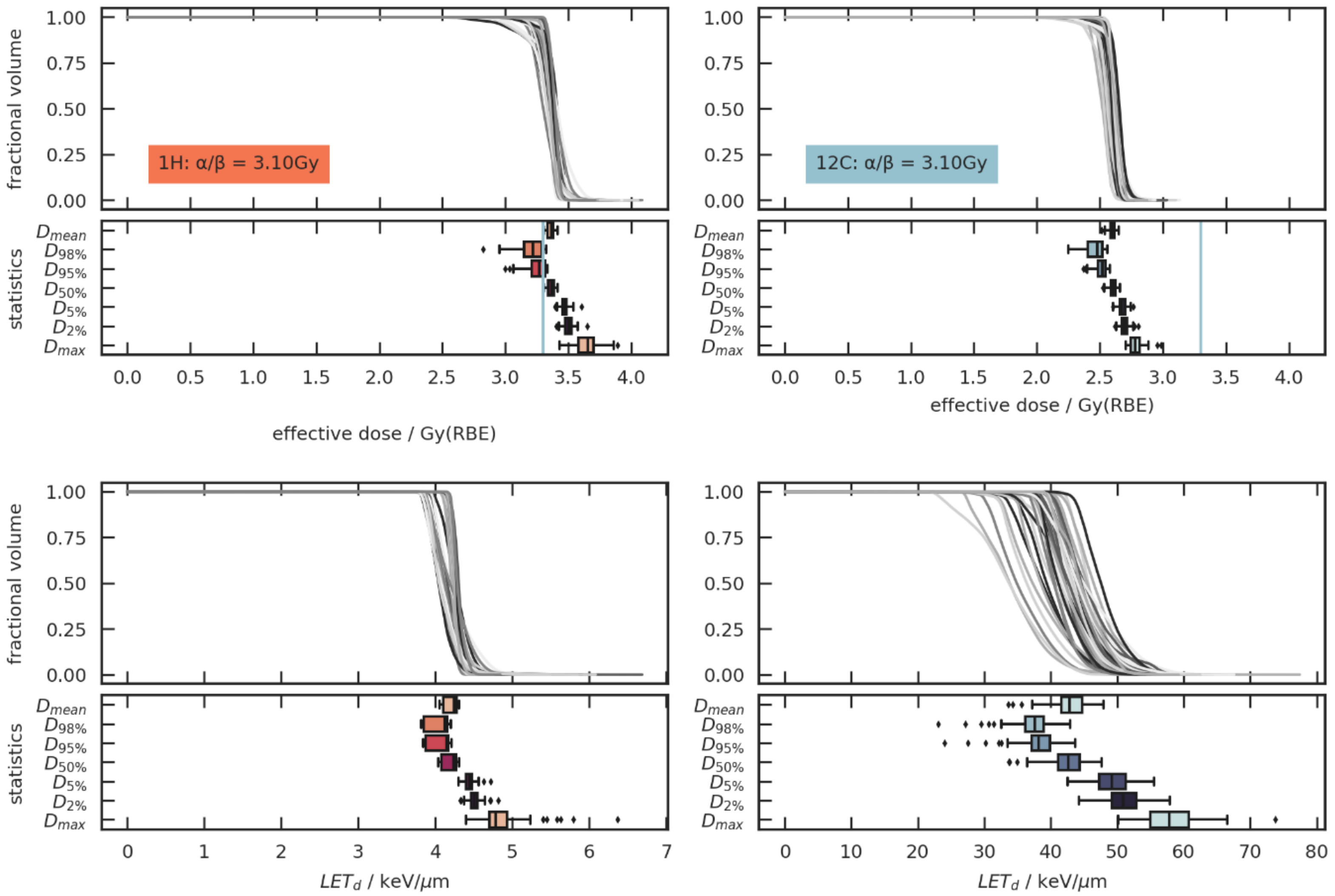
Improve the clinical outcome with a better biological framework

Photon clinical data from literature



J. Besuglow, …, A. Mairani 2023 IJROBP

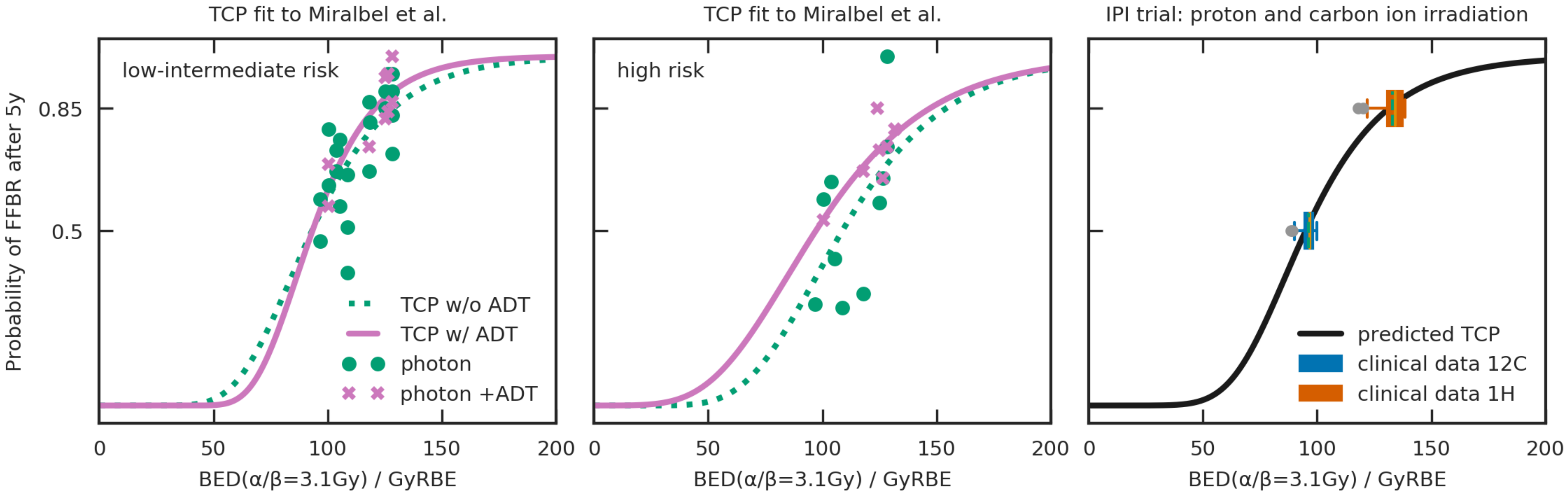
How do improve the clinical treatment ? Learning from the cohort



J. Besuglow, …, A. Mairani 2023 IJROBP

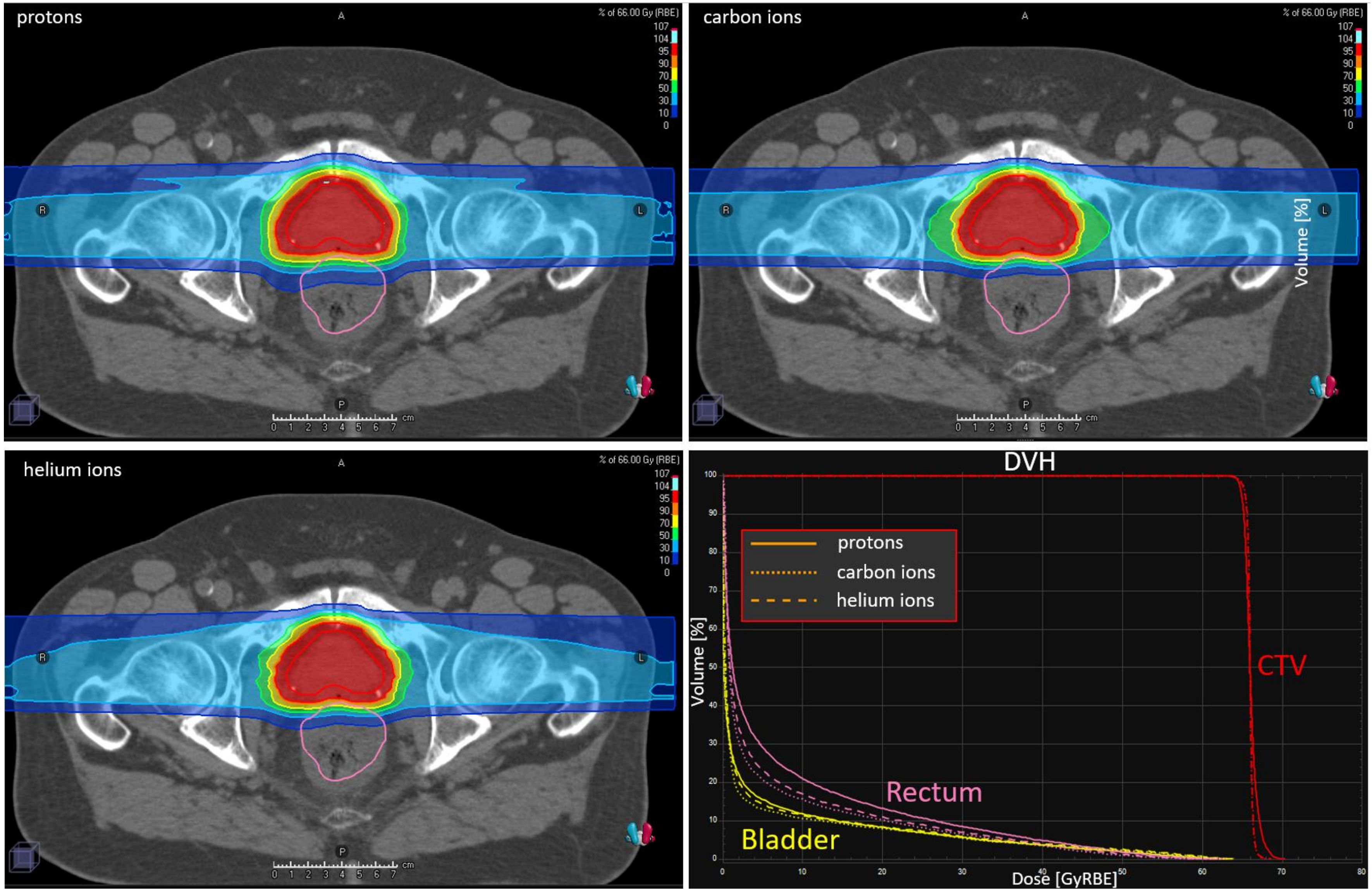
Do we observe clinically the limitations of a biological model?

- Prostate Trial (IPI) (Habl et al. 2014, 2016, Eichkorn et al. 2022)
- **66 Gy (RBE), RBE = 1.1 1H** vs. **66 Gy (RBE) LEM I a/β = 2 Gy 12C** in 20 fx



J. Besuglow, …, A. Mairani 2023 IJROBP

Learning from 1H and 12C patients cohort for 4He planning



J. Besuglow, …, A. Mairani 2023 IJROBP

The „UNIfied and VERSetile bio response Engine“ - UNIVERSE

- UNIVERSE: multipurpose mechanistic modelling framework of radiation action
- **Goal: Translating** the action of **“effect-modifiers”** (e.g., DNA damage inhibition) from readily available **photon data to charged particle scenarios**

Open Access Article

Modeling the Effect of Hypoxia and DNA Repair Inhibition on Cell Survival after Photon Irradiation

by Hans Liew [1,2,3,4,5,6], Carmen Klein [2,3,4,5], Frank T. Zenke [7], Amir Abdollahi [2,3,4,5], Jürgen Debus [1,2,3,4,5,6], Ivana Dokic [2,3,4,5,*,†] and Andrea Mairani [2,3,4,5,*,†]

Open Access Article

Modeling Direct and Indirect Action on Cell Survival After Photon Irradiation under Normoxia and Hypoxia

by Hans Liew [1,2,3,4,5,6], Stewart Mein [2,3,4,5], Jürgen Debus [1,2,3,4,5,6], Ivana Dokic [2,3,4,5] and Andrea Mairani [2,3,4,5,*]

International Journal of Radiation Oncology • Biology • Physics ASTRO

Physics Contribution

Deciphering Time-Dependent DNA Damage Complexity, Repair, and Oxygen Tension: A Mechanistic Model for FLASH-Dose-Rate Radiation Therapy

Hans Liew, MSc,[*,†,‡,§,‖] Stewart Mein, PhD,[*,†,‡,§] Ivana Dokic, PhD,[*,†,‡,§] Thomas Haberer, PhD,[¶] Jürgen Debus, MD, PhD,[†,§,‖,¶,#] Amir Abdollahi, MD, PhD,[*,†,‡,§] and Andrea Mairani, PhD[#,**]

Combined DNA Damage Repair Interference and Ion Beam Therapy: Development, Benchmark and Clinical Implications of a Mechanistic Biological Model

Hans Liew, MSc ** • Sarah Meister, MSc • Stewart Mein, PhD • ... Jürgen Debus, MD, PhD • Ivana Dokic, PhD • Andrea Mairani, PhD • Show all authors • Show footnotes

Open Access Article

Impact of DNA Repair Kinetics and Dose Rate on RBE Predictions in the UNIVERSE

by Hans Liew [1,2,3,4,5,6], Stewart Mein [2,3,4,5], Thomas Tessonnier [5], Christian P. Karger [3,7], Amir Abdollahi [2,3,4,5], Jürgen Debus [1,2,3,4,5,6], Ivana Dokic [2,3,4,5] and Andrea Mairani [2,3,4,5,*]

Open Access Article

Do We Preserve Tumor Control Probability (TCP) in FLASH Radiotherapy? A Model-Based Analysis

by Hans Liew [1,2,3], Stewart Mein [1,2,3,4], Thomas Tessonnier [5], Amir Abdollahi [1,2,3], Jürgen Debus [2,3,6,7], Ivana Dokic [1,2,3] and Andrea Mairani [5,8,*]

The „UNIfied and VERSetile bio response Engine“ - UNIVERSE

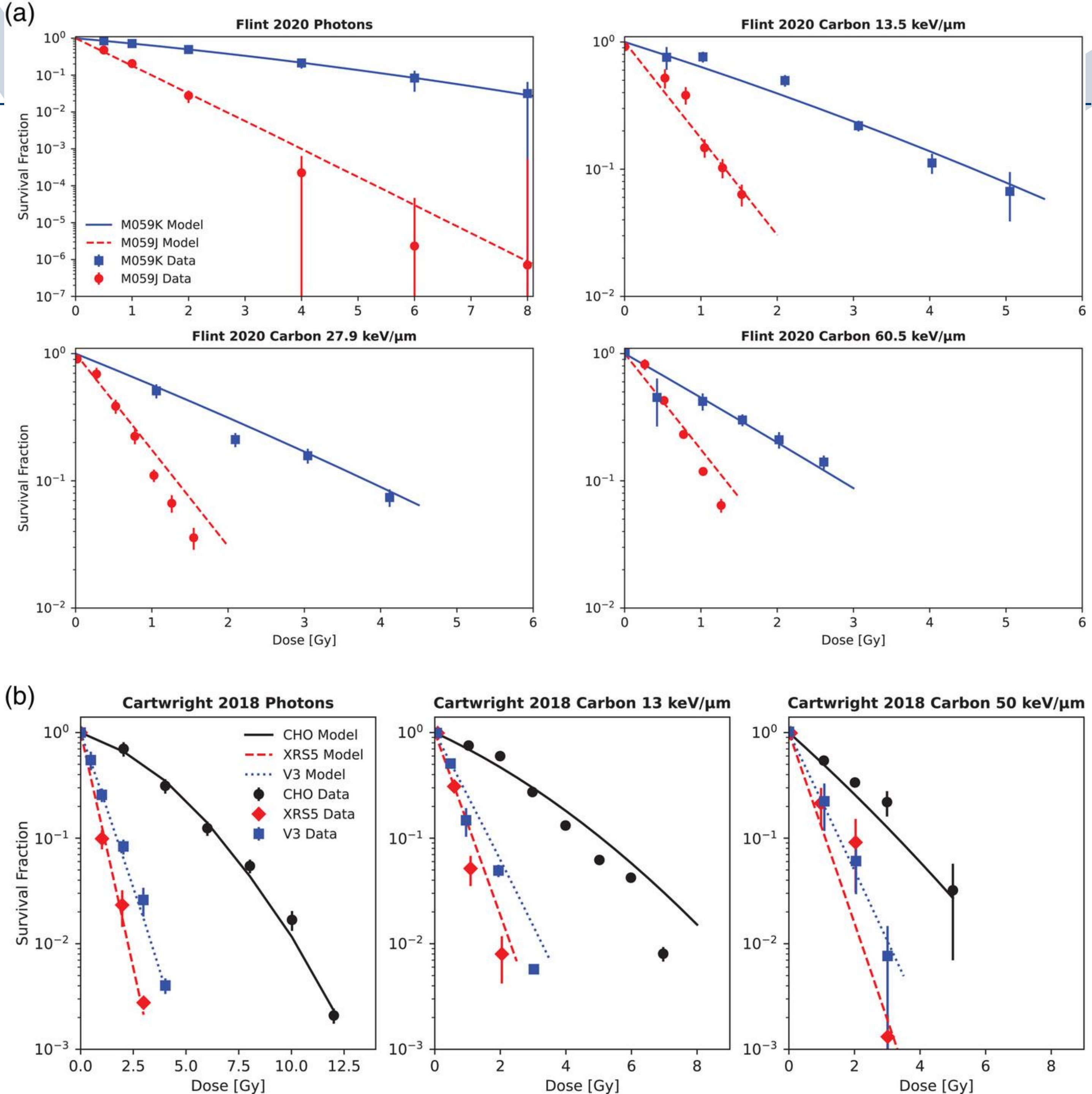
Hypothesis

RSF (as well as K_{iDSB}/K_{cDSB}) **values remain constant under change of radiation quality →** UNIVERSE can be extended to charged particles by solely implementing the heterogeneous dose distributions of ions (utilizing GPUs)

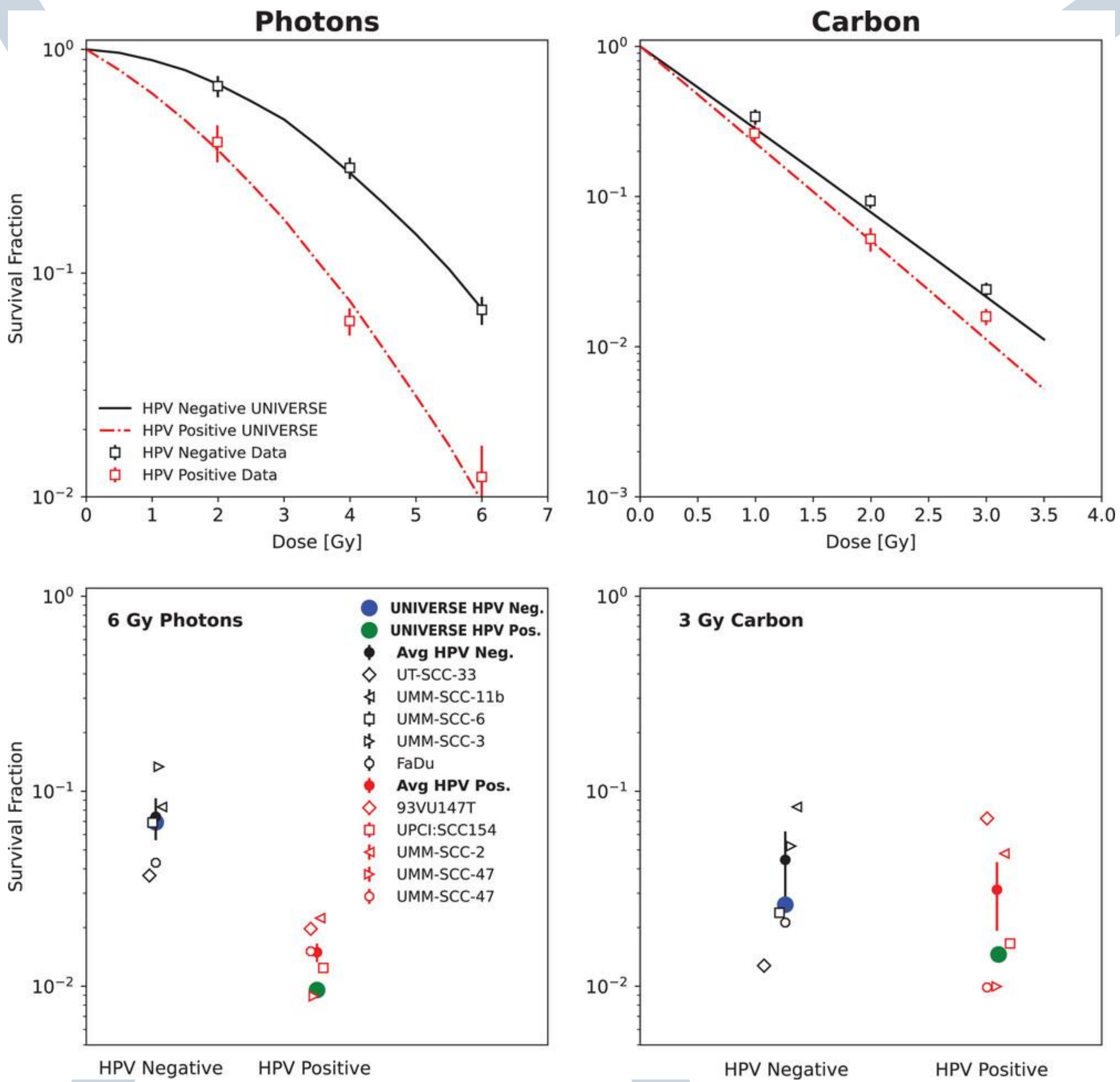
Combined DNA Damage Repair Interference and Carbon Ion Beam Therapy

(a)M059K cells and their DNA-dependent protein kinase (DNA-PK)-deficient mutant (M059J)

(b) CHO cells and their two NHEJ response-deficient mutants (V3 cell line is DNA-PKcs-deficient and xrs-5 cell line is Ku80-deficient)



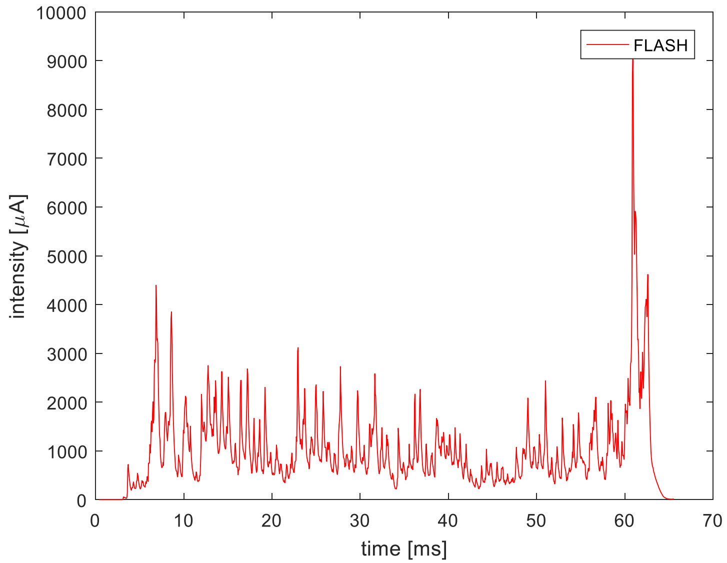
Carbon Ion Beam Therapy
and
HPV status



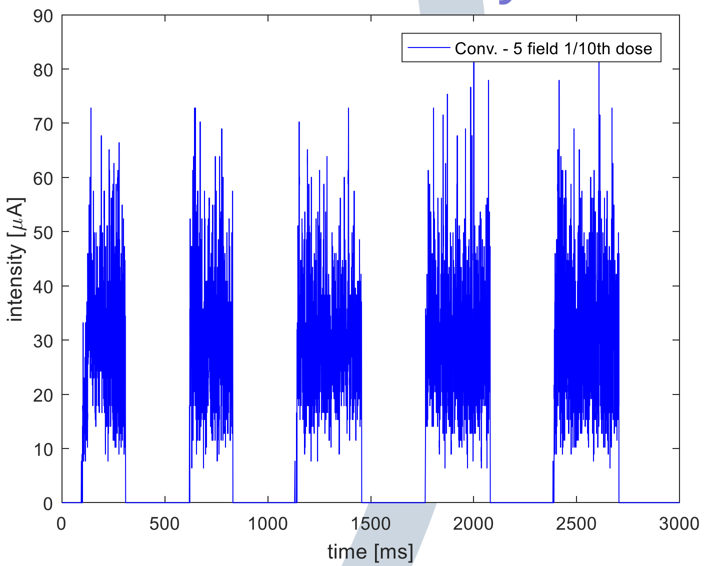
FLASH Radiotherapy

- Mostly with electrons and protons
- Great advantage: very fast (< 0.1 s) ➡ **Reduced effect of moving targets**
- Coupled with heavier ions characteristics (RBE and OER) could be the ultimate radiation therapy technique

FLASH: 186 Gy/s



SDR: 0.12 Gy/s



Helium Ion FLASH

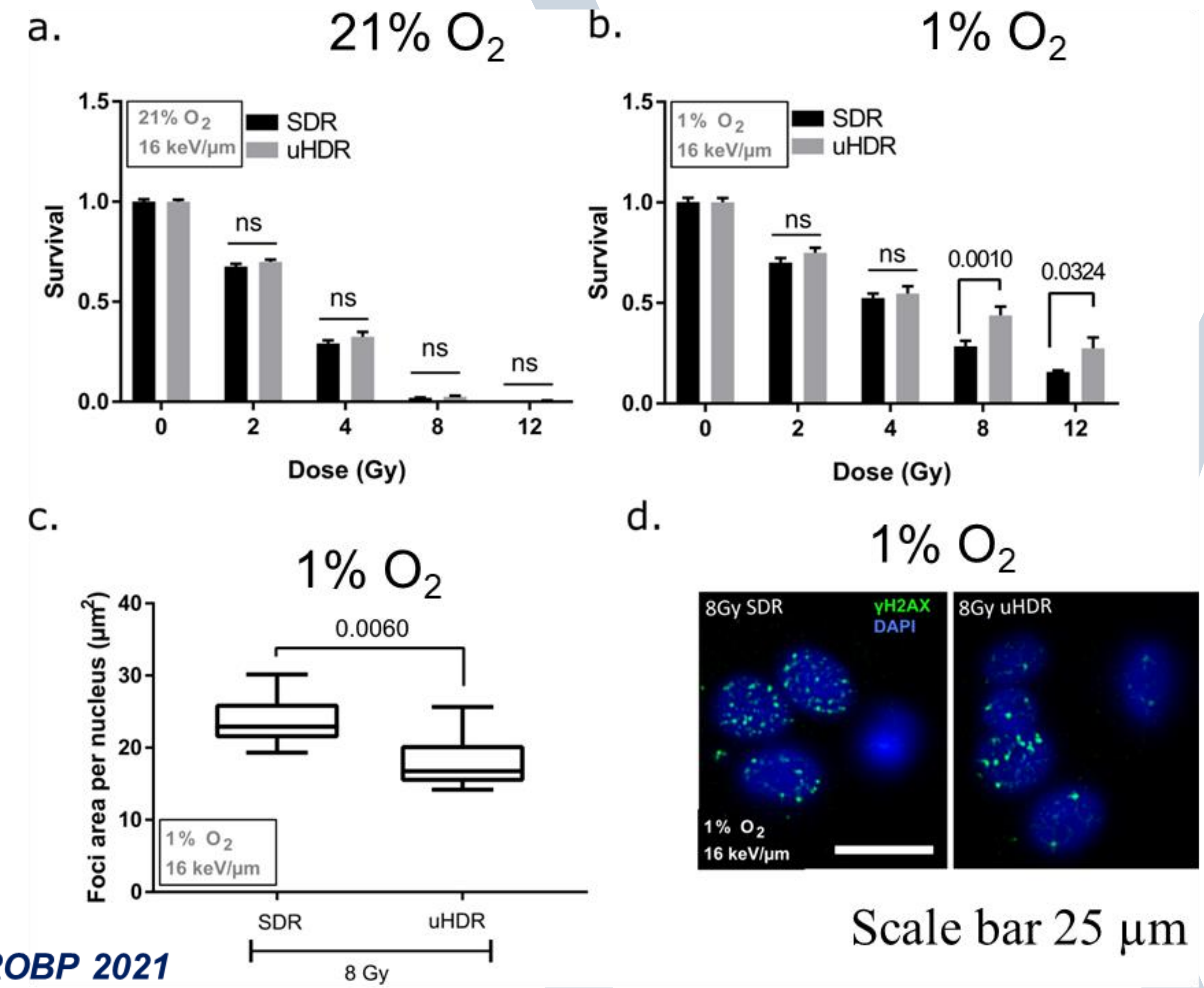
Tessonnier, Mein, Walsh et al. IJROBP 2021

Ion FLASH Radiotherapy: *in vitro*

H1437

Clonogenics

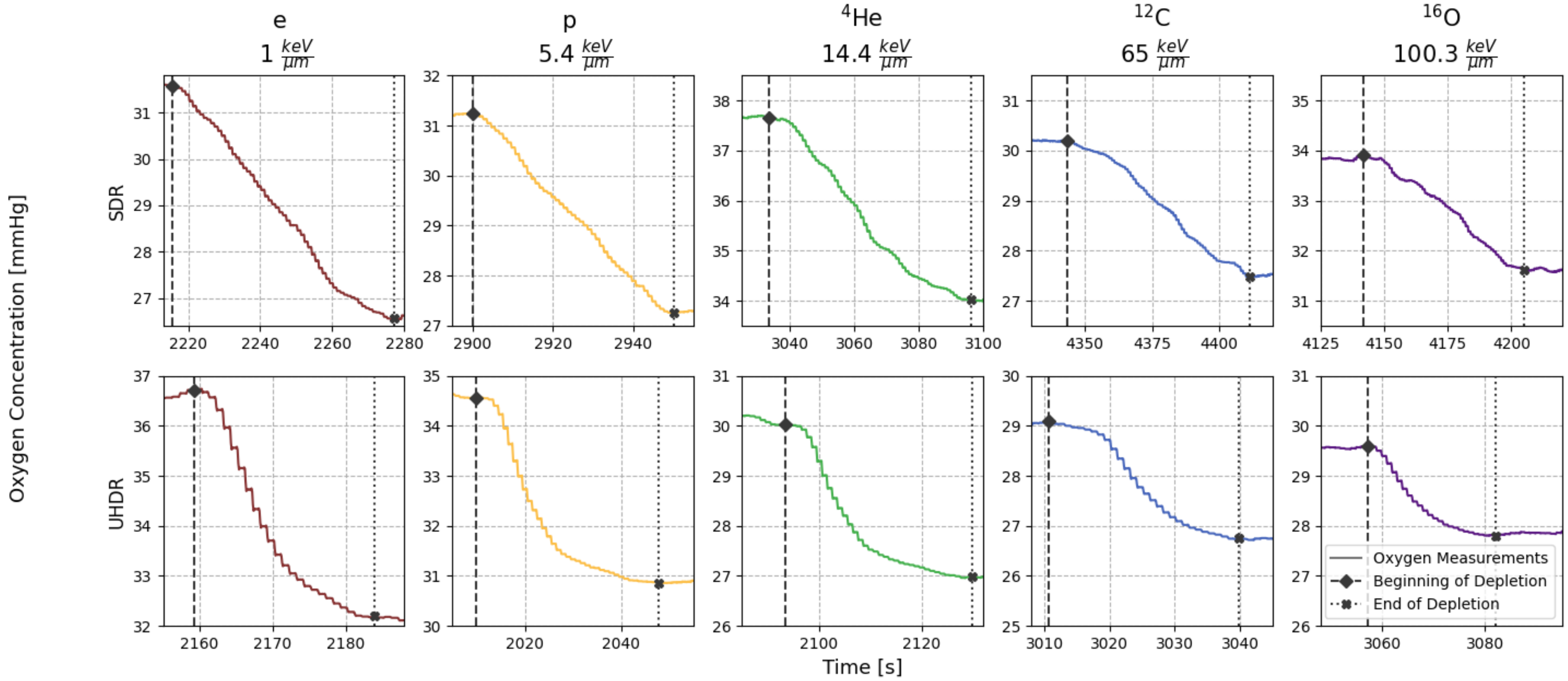
γH2AX foci



Tessonnier, Mein, Walsh et al, IJROBP 2021

FLASH Radiotherapy

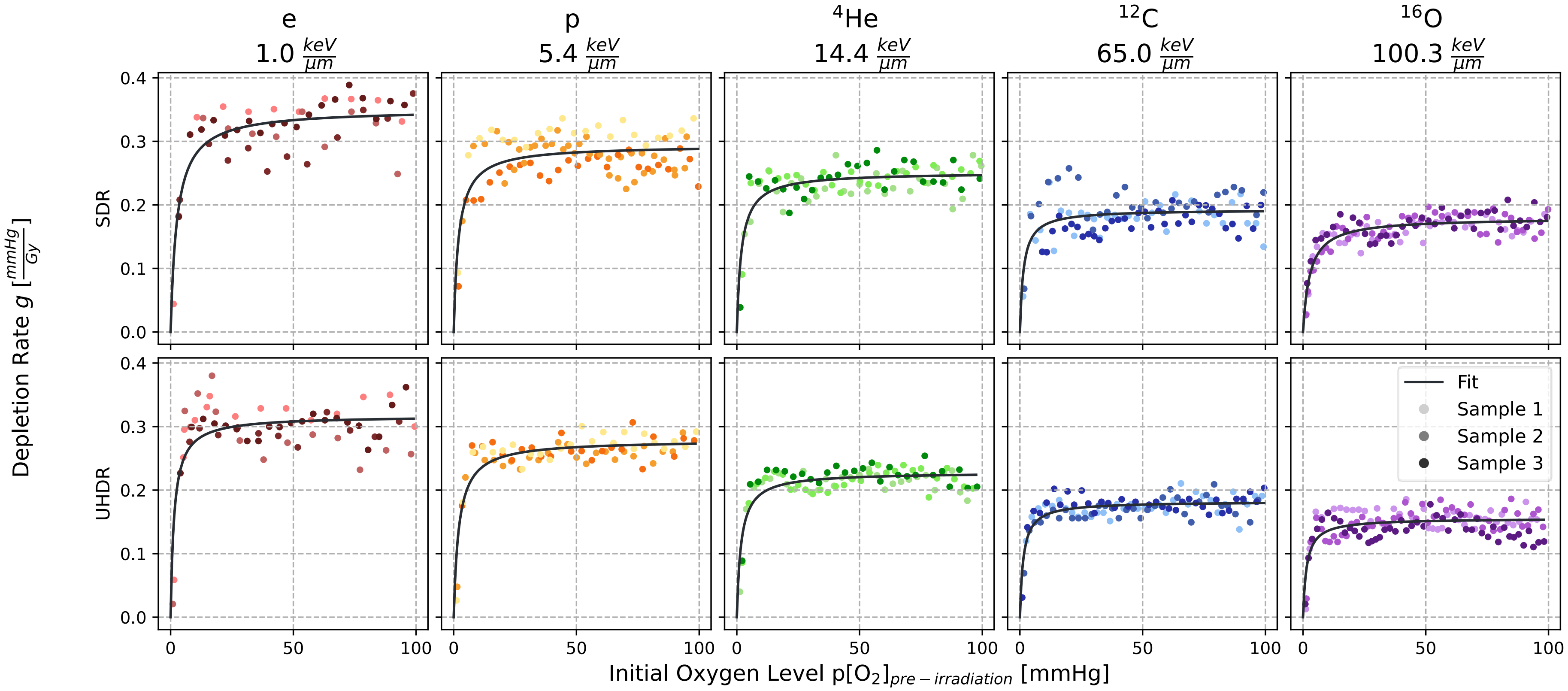
- mechanisms behind FLASH: Investigate oxygen consumption during UHDR irradiation across large LETd range: with electrons, proton, helium, carbon and oxygen ions



Karle, Liew, Tessonnier et al, J. Med. Phys., 2024, accepted Manuscript

FLASH Radiotherapy

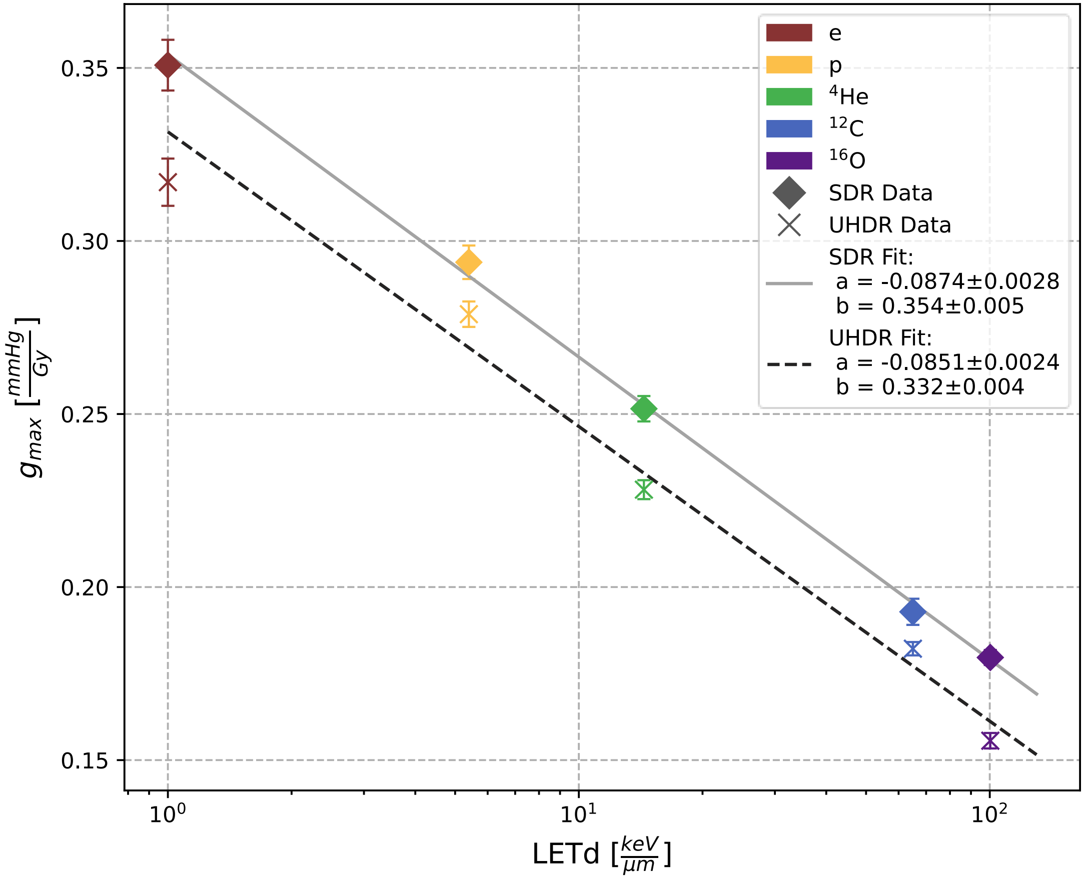
- mechanisms behind FLASH: Investigate oxygen consumption during UHDR irradiation across large LETd range: with electrons, proton, helium, carbon and oxygen ions



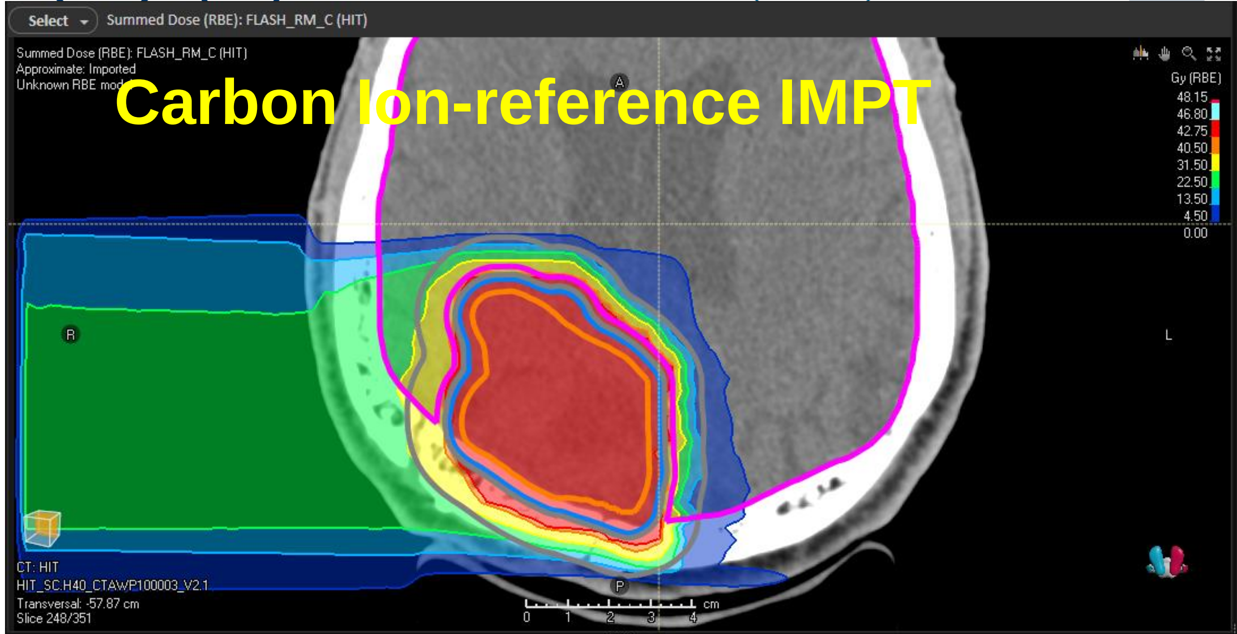
Karle, Liew, Tessonnier et al, J. Med. Phys., 2024, accepted Manuscript

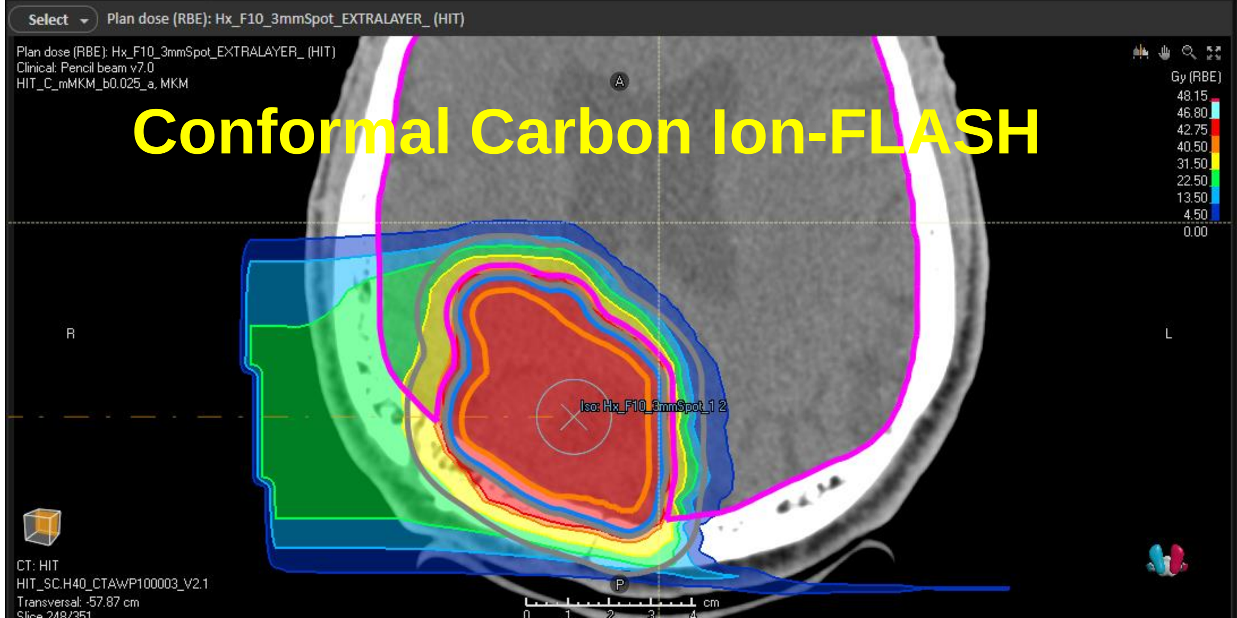
FLASH Radiotherapy

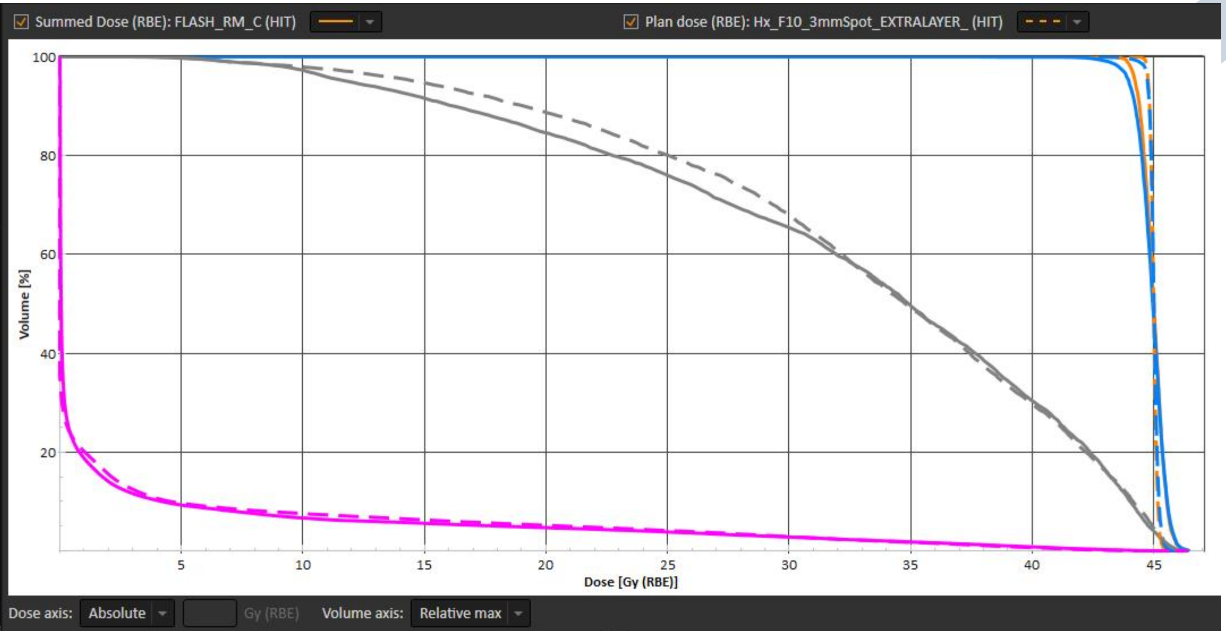
- mechanisms behind FLASH: Investigate oxygen consumption during UHDR irradiation across large LETd range: with electrons, proton, helium, carbon and oxygen ions



Karle, Liew, Tessonnier et al, J. Med. Phys., 2024, accepted Manuscript







Difference: Current - Co... | DVH | Dose statistics | Clinical goals | Objectives/constraints (... | Beams (Compare 1) | Energy layers (Compare... | BEV (Compare 1)

ROI statistics / POI statistics

Name	ROI	ROI vol. [cm³]	Dose [Gy (RBE)] D99	D98	D95	Average	D50	D2	D1	% outside grid
Summed Dose (RBE):...	Brain-PTV5	1372.59	0.00	0.01	0.01	2.29	0.05	33.96	39.02	0 %
Plan dose (RBE): Hx_...	Brain-PTV5	1372.59	0.00	0.00	0.00	2.42	0.00	33.70	38.34	0 %
Summed Dose (RBE):...	CTV	45.96	43.94	44.04	44.24	44.99	45.00	45.90	46.00	0 %
Plan dose (RBE): Hx_...	CTV	45.96	44.67	44.71	44.77	45.00	44.99	45.31	45.37	0 %
Summed Dose (RBE):...	h_Saum	128.85	7.05	9.24	11.89	32.49	34.92	45.40	45.64	0 %
Plan dose (RBE): Hx_...	h_Saum	128.85	7.00	9.93	14.77	33.18	34.78	45.44	45.67	0 %
Summed Dose (RBE):...	PTV	72.30	43.16	43.56	43.98	44.91	44.96	45.91	46.03	0 %
Plan dose (RBE): Hx_...	PTV	72.30	44.41	44.63	44.74	45.01	45.01	45.39	45.47	0 %

Conclusions

- Many technological and biological advancements are possible in ion beam therapy
- Clinical employment of novel approaches is undergoing at HIT
- Several clinical indications would benefit from a modernization of ion beam therapy
- Our mission at HIT is to facilitate and to support this modernization.

Thank you for your attention!

BioPT