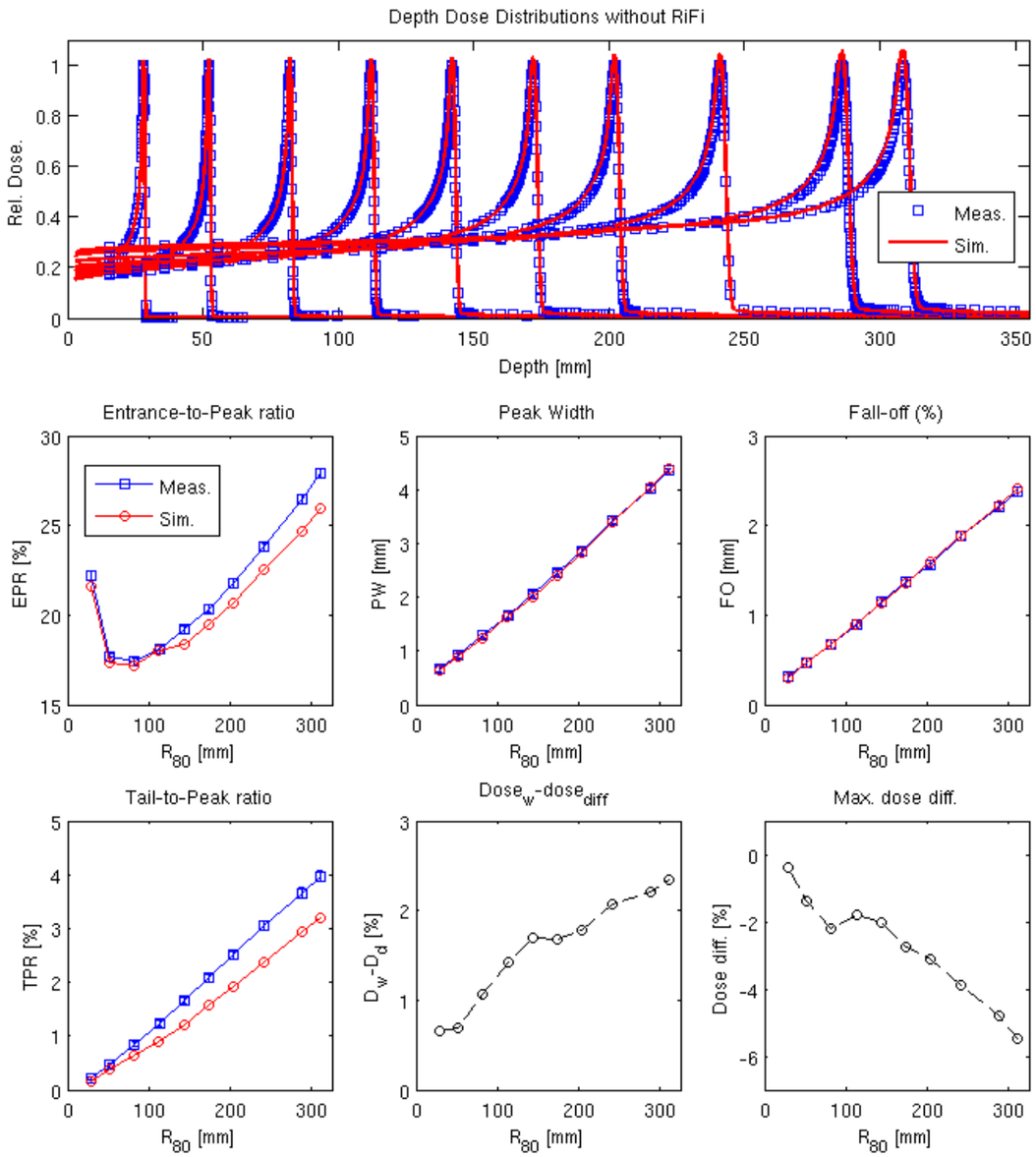
Monte Carlo calculation of RBE and in-vitro validation for helium ion-beam therapy

MCMA 2017, Napoli

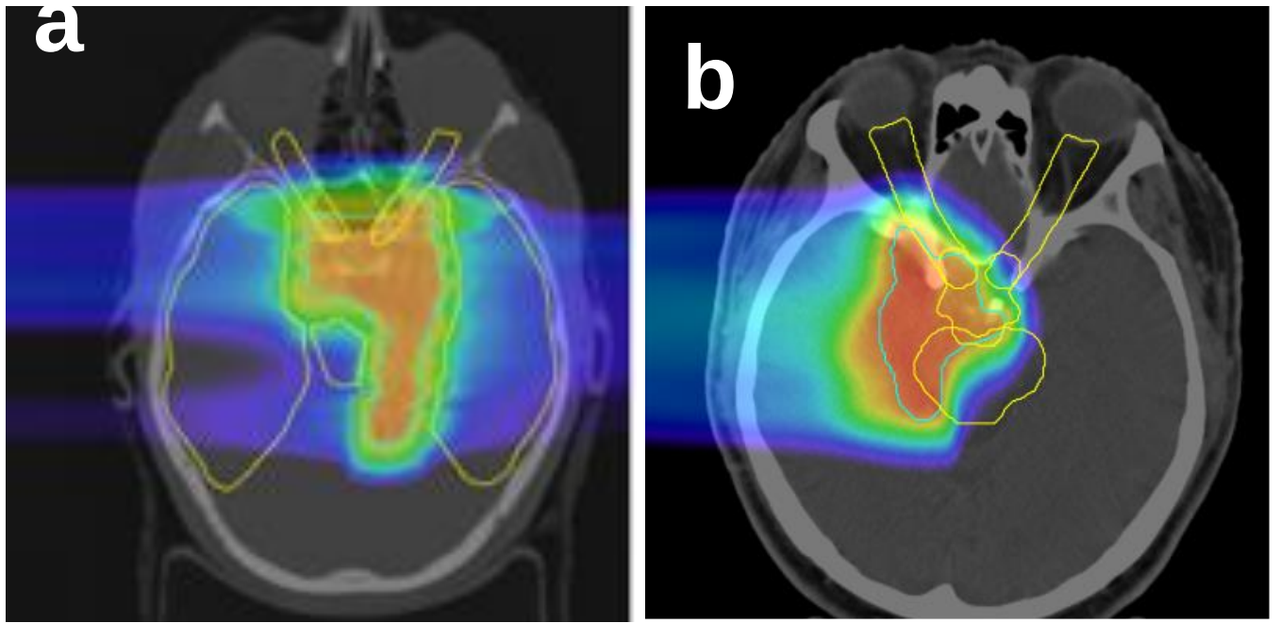
Stewart "Mac" Mein
PhD Student
German Cancer Research Center (DKFZ)
Translational Radiation Oncology Group — Dr. Amir Abdollahi
Heidelberg Ion-beam Therapy Center (HIT)
Biophysics in Particle Therapy Group — Dr. Andrea Mairani

Helium @ HIT

- ✦ Comprehensive dosimetric characterization @ HIT
- ✦ Validation of Monte Carlo Tx Planning (MCTP) platform
- ✦ Preliminary plan comparisons (p. vs. He)



Meningioma cases (He)

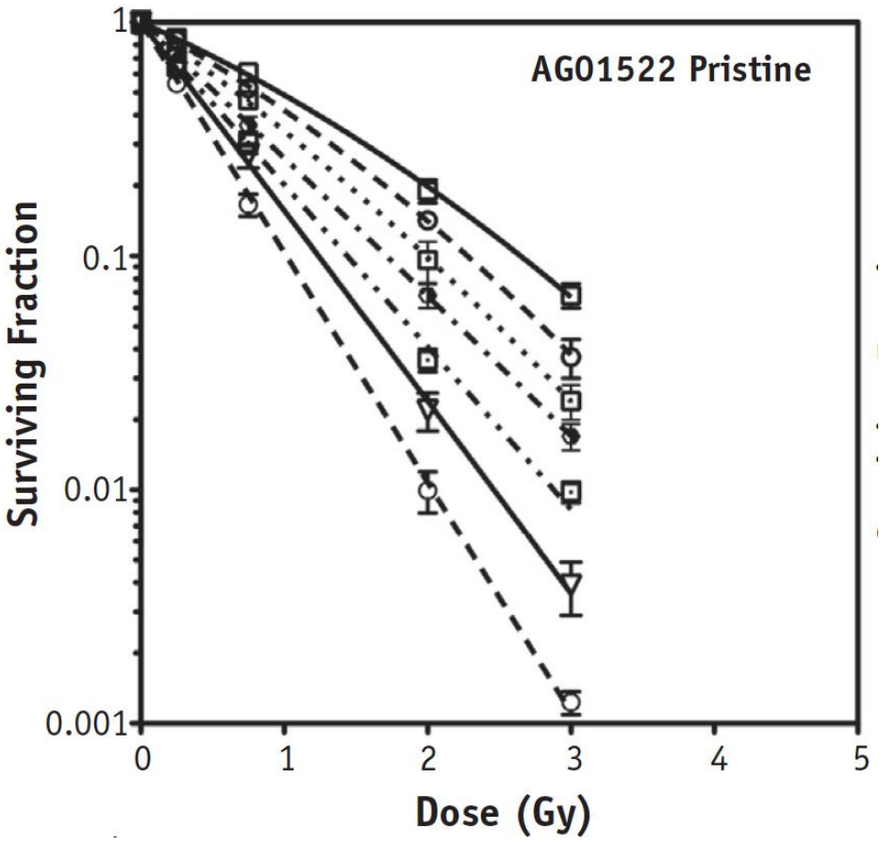


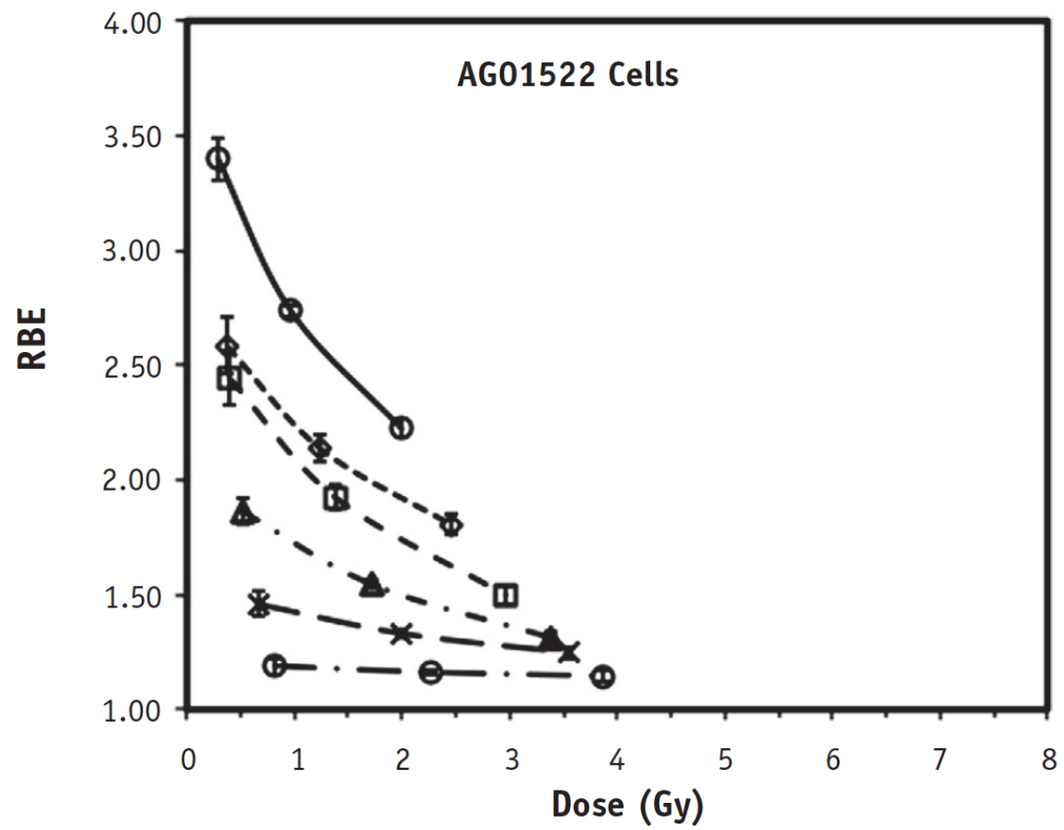
physical + biological

Tessonnier et al 2017

RBE Prediction

model **surviving fraction (SF)**





$$SF = e^{-\left(\alpha D + \beta D^2\right)}$$

$$RBE_{SF} = \frac{D^X_{SF}}{D^P_{SF}}$$

RBE(Dose, LET, [α/β]ph)

Chaudhary et al 2014

RBE Prediction

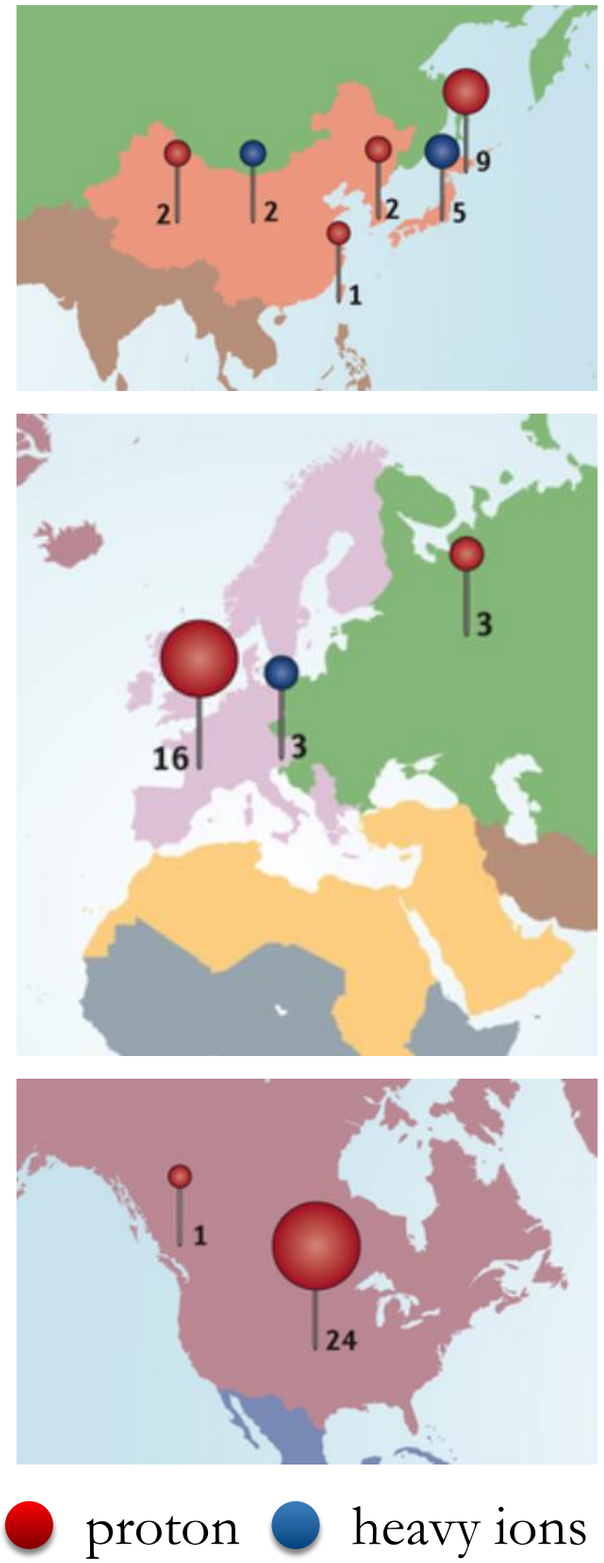
Methods:

1) Biophysical models (Theoretical)

- **MKM** = Microdosimetric Kinetic Model
- **LEM** = Local Effect Model

2) Phenomenological (Experimental)

- "Data-driven"
- Interpretation of collected data from the literature



Durante et al 2017

RBE Prediction

FLUKA-coupled D_{bio} Calculation

p 1999

C 2010

He 2016

Physical and biophysical characteristics of a fully modulated 72 MeV therapeutic proton beam: model predictions and experimental data

M. Biaggi [a], F. Ballarini [a,b], W. Burkard [c], E. Egger [c], A. Ferrari [b,d], A. Ottolenghi [a,b,*]

The FLUKA Monte Carlo code coupled with the local effect model for biological calculations in carbon ion therapy

A Mairani[1,2,6], S Brons[2], F Cerutti[3], A Fassò[4], A Ferrari[3], M Krämer[5], K Parodi[2], M Scholz[5] and F Sommerer[3,7]

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 Valle[3], T Tessonnier[7,8], R Galm[2,5,6,7], M Ciocca[1], K Parodi[2,7,8], A Ferrari[9], O Jäkel[2,6], T Haberer[2], P Pedroni[4] and T T Böhlen[10]

Optimizing the modified microdosimetric kinetic model input parameters for proton and ^{4}He ion beam therapy application

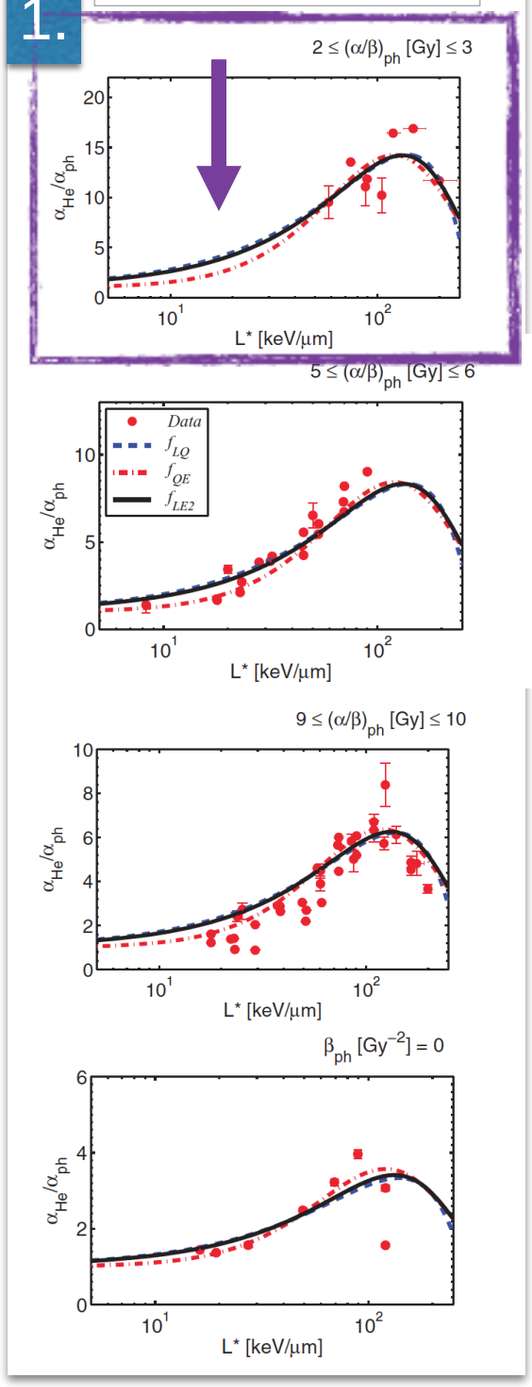
A Mairani[1,2], G Magro[1], T Tessonnier[3,4], T T Böhlen[5], S Molinelli[1], A Ferrari[6], K Parodi[2,3,4], J Debus[2,3] and T Haberer[2]

Phenomenological Approach

2016a 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 Valle[3], T Tessonnier[7,8], R Galm[2,5,6,7], M Ciocca[1], K Parodi[2,7,8], A Ferrari[9], O Jäkel[2,6], T Haberer[2], P Pedroni[4] and T T Böhlen[10]

1. parameterization



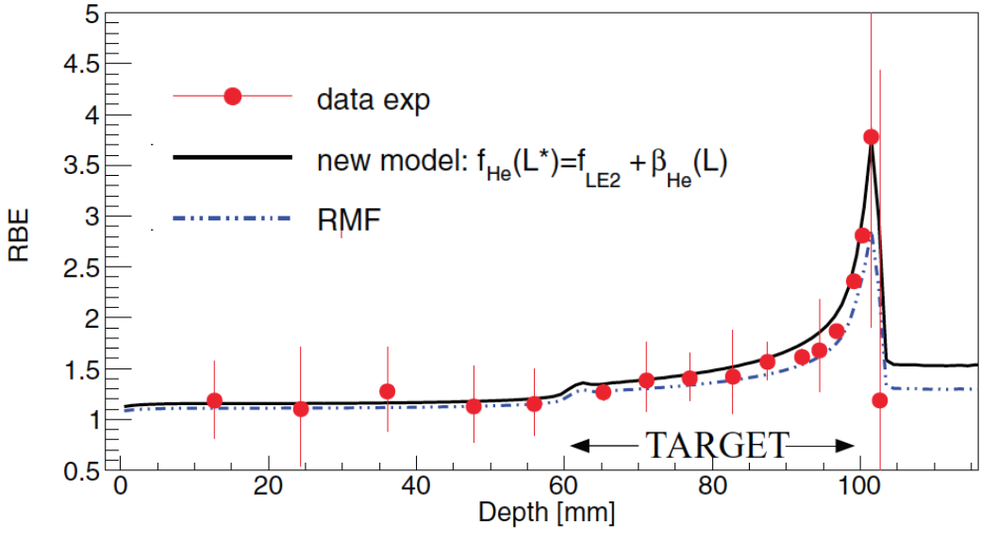
2016b Biologically optimized helium ion plans: calculation approach and its *in vitro* validation

A Mairani[1,2], I Dokic[2,3,4,5], G Magro[1], T Tessonnier[5,6], F Kamp[7], D J Carlson[8], M Ciocca[1], F Cerutti[9], P R Sala[10], A Ferrari[9], T T Böhlen[11], O Jäkel[2,4], K Parodi[2,5,6], J Debus[2,5], A Abdollahi[2,3,4,5] and T Haberer[2]

2. Experimental validation

Table 1. α_{ph} and β_{ph} values obtained by fitting the clonogenic A549 cell survival data with the linear-quadratic model are reported together with their uncertainties (one standard deviation, Mairani *et al* (2016) and Dokic *et al* (2016)).

Cell line	α_{ph} [Gy^{-1}]	β_{ph} [Gy^{-2}]
A549	0.173 ± 0.026	0.032 ± 0.004



3. Model Comparisons

Table 3. Summary of the mean survival absolu predictions and experimental data.

RBE model	$\mu_{\Delta S}$ (%)
$f_{QE} + \beta_{He}(L)$	9.8 ± 1.3
RBE = 1.3	18.8 ± 4.3
LEM D_t = 10.8 Gy	4.5 ± 0.8
LEM D_t = 15 Gy	6.7 ± 1.5
RMF	5.8 ± 1.1
New $f_{LE2} + \beta_{He}(L)$	5.3 ± 0.9
New $f_{LE2} + \beta_{He} = \beta_{ph}$	6.5 ± 0.9
LET_D-based	4.5 ± 0.8

RBE Prediction

2017

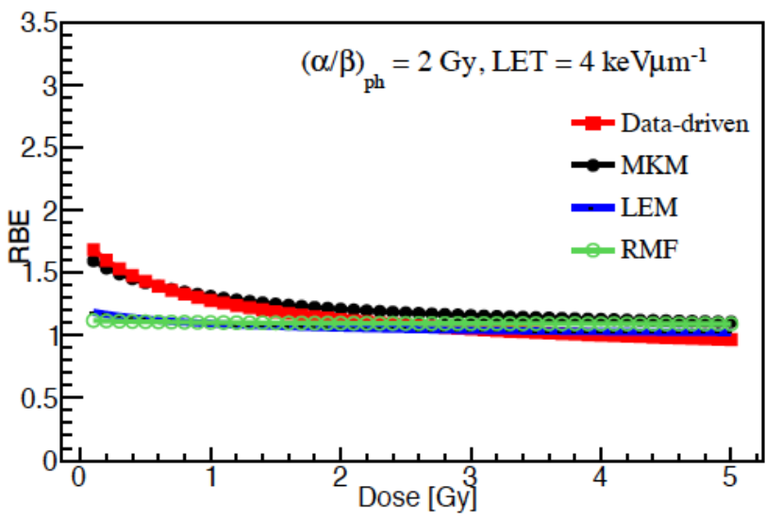
RBE models in 4-He ion beam therapy: predictions in clinically-relevant scenarios

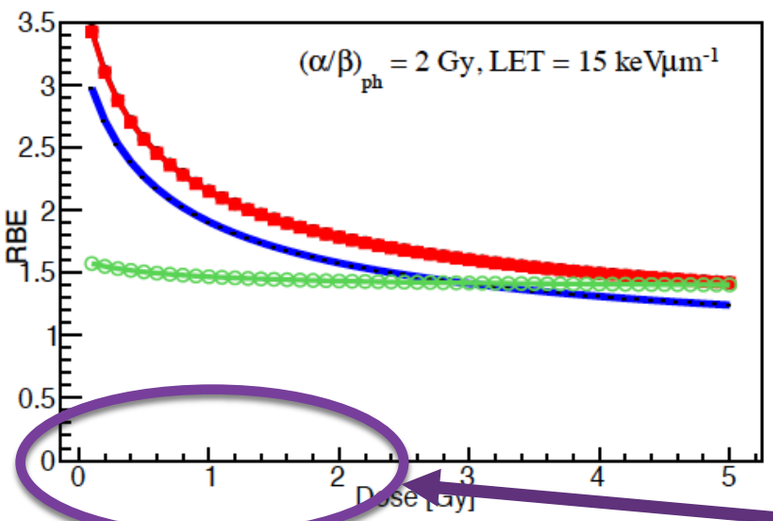
LET ↓

LET ↑

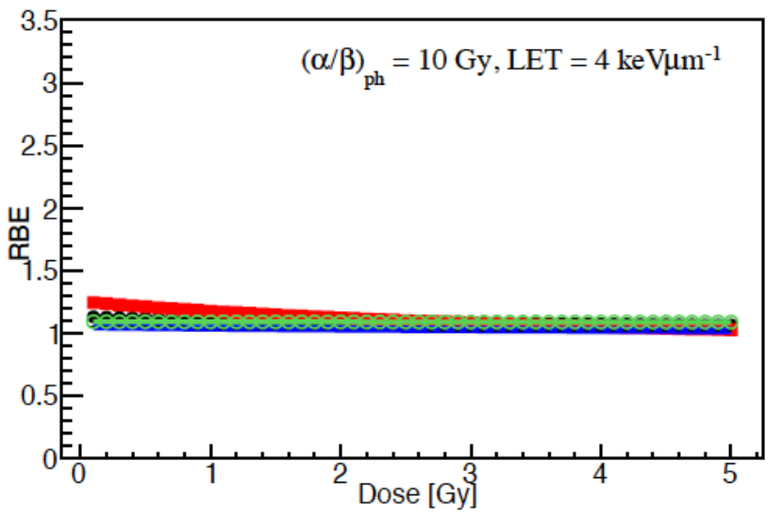
(α/β)γ ↓

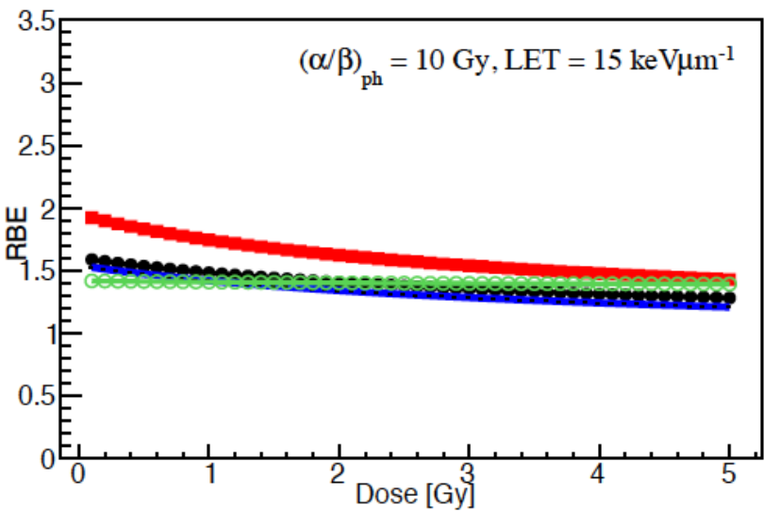
(α/β)γ ↑





clinical relevance



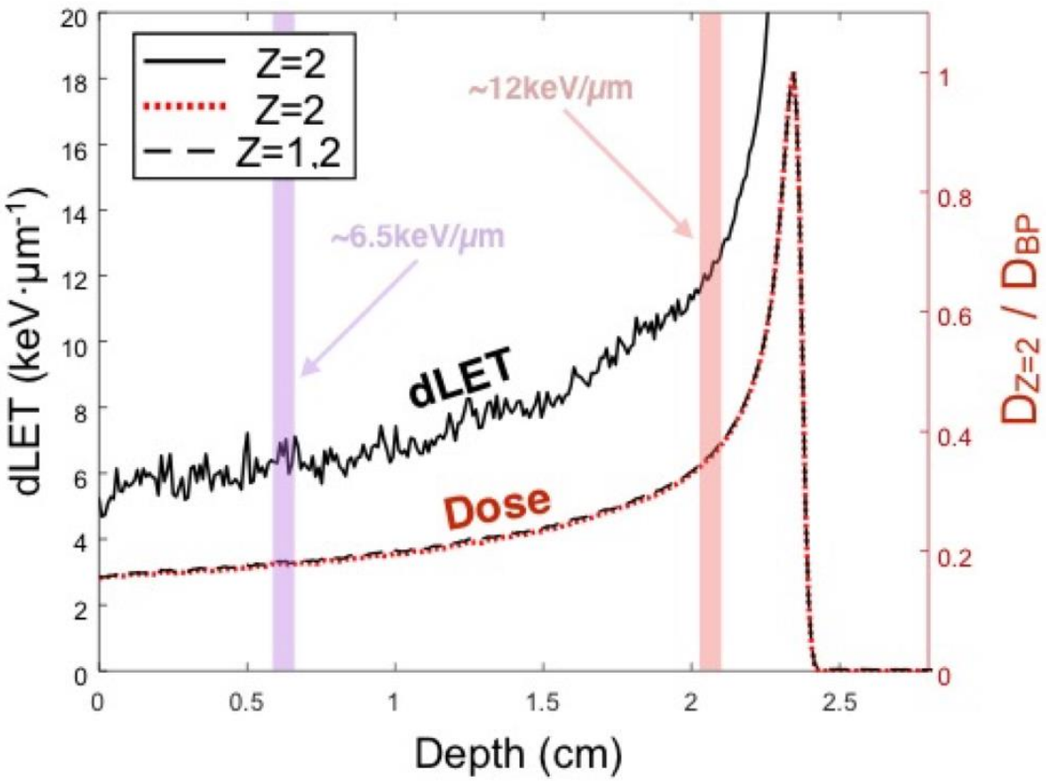


RBE(Dose, LET, [α/β]ph)

RBE Model Validation

Clonogenic Assay with Pristine Peaks:
RenCa cell-line

- Photon:[1 to 8 Gy]
- Determination of alpha (α_{ph}) and beta (β_{ph})
- 4He beam delivery: [0.25 to 3.3 Gy]
- E_{He} =56.65 MeV/u, BP depth = 24 mm
- Biol. measurements: 6 and 21mm
- FLUKA simulations: D_{eff} [DD, MKM, LEM-IV]



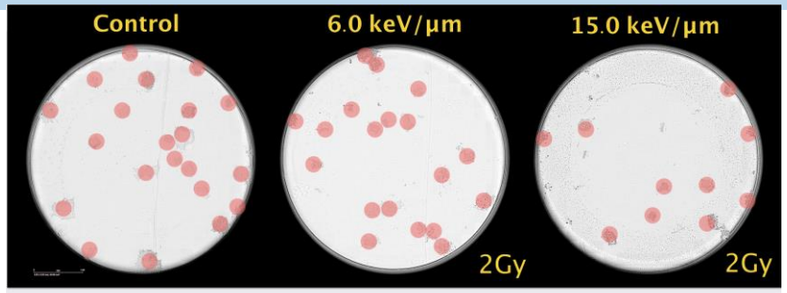


FIG 1: Clonogenic assay post-irradiation imaging with the Incucyte™ demonstrating enhanced cell kill with increased dLET.

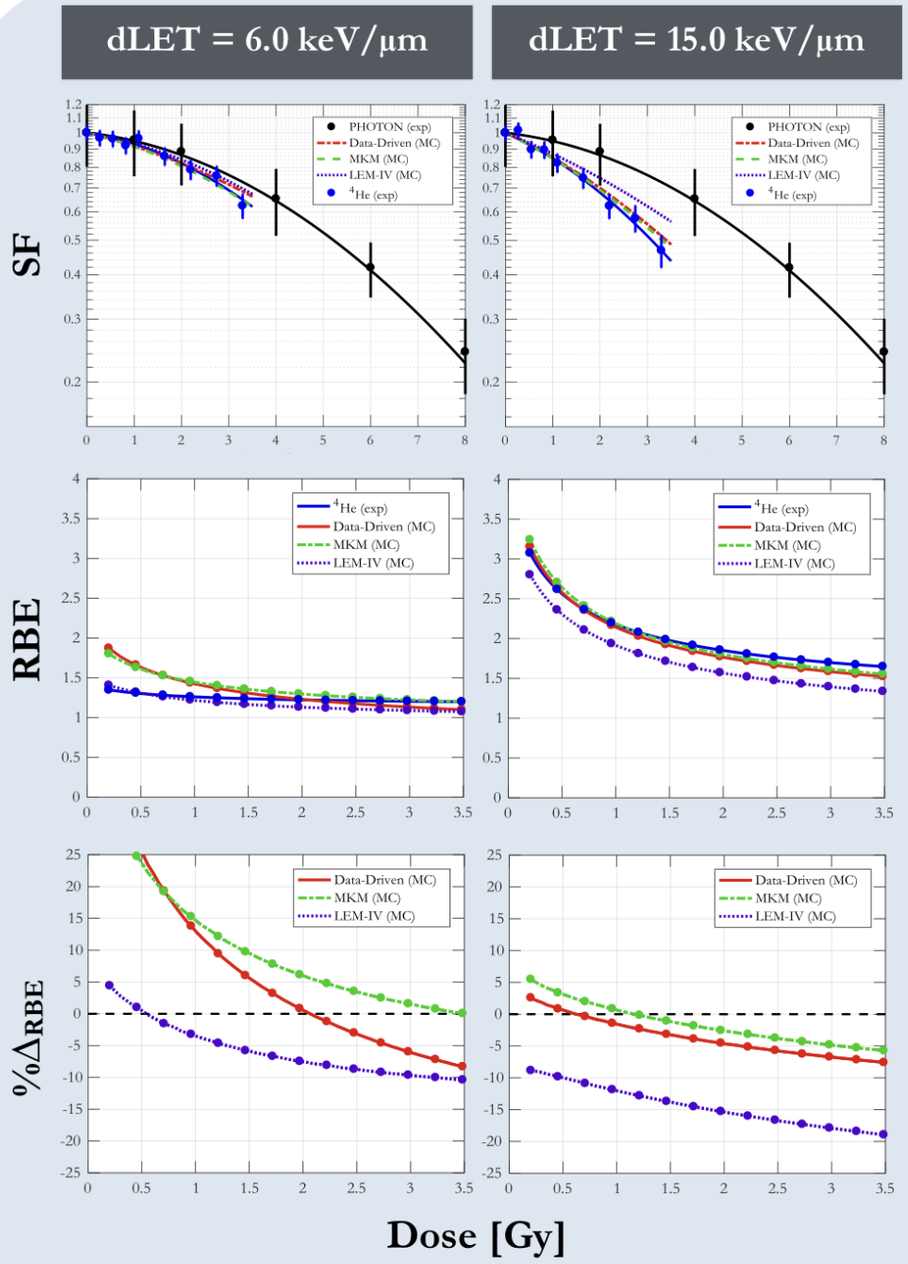


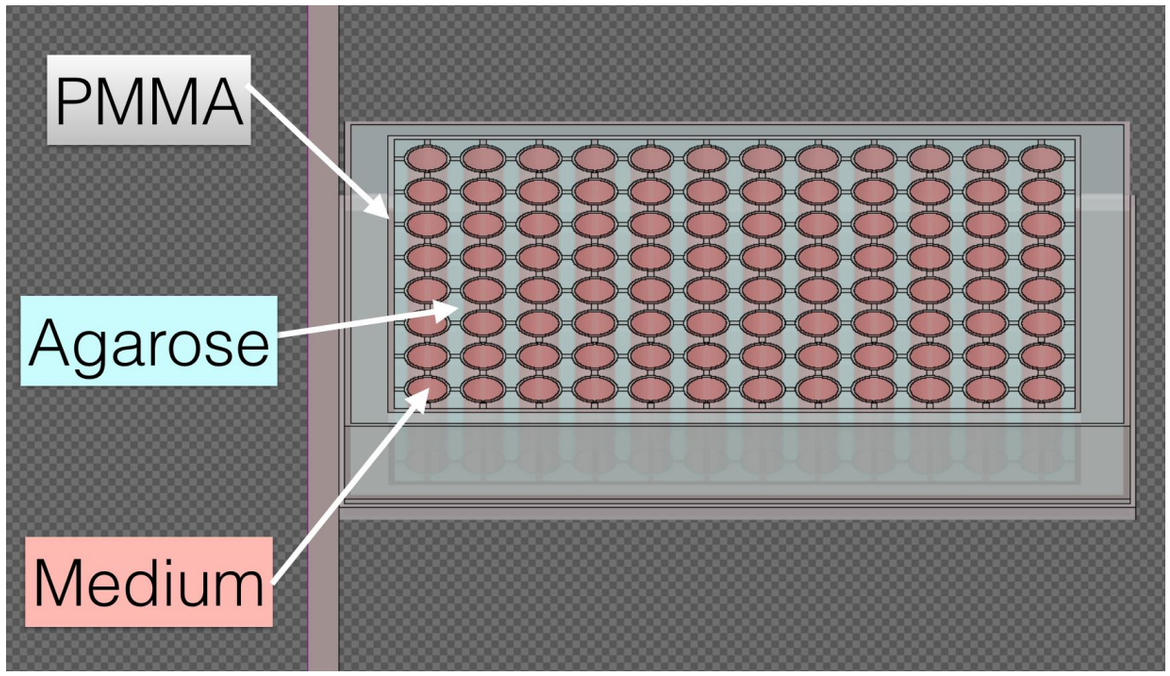
FIG 2 : Surviving Fraction (SF), RBE and local percent difference in RBE ($\%\Delta_{RBE}$) between predictions and experimental data.

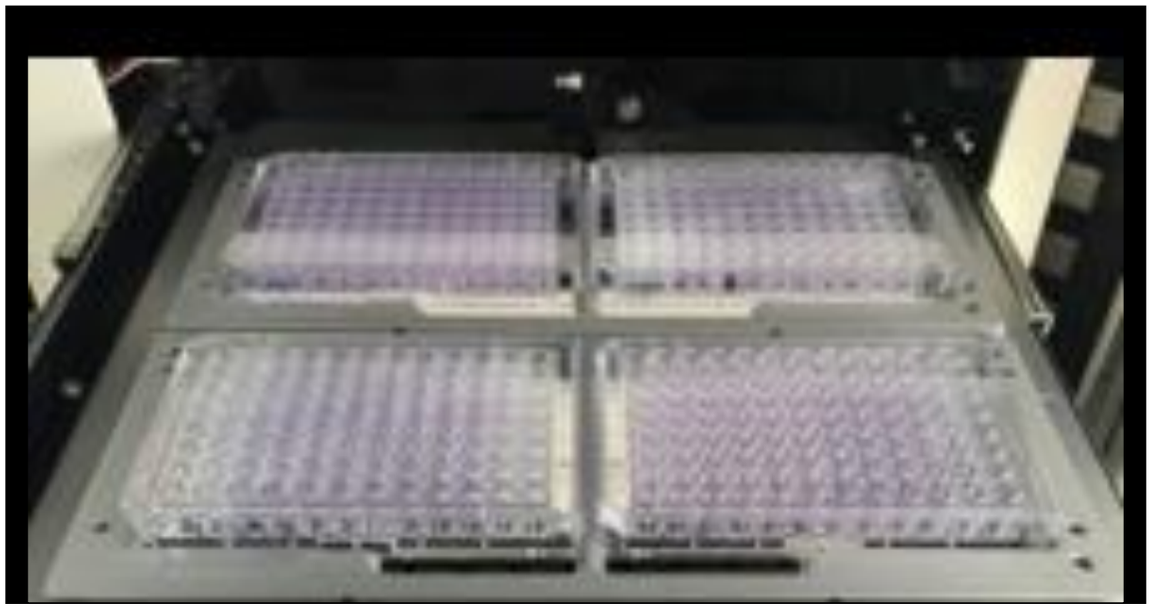
Mein et al 2017 @ PTCOG

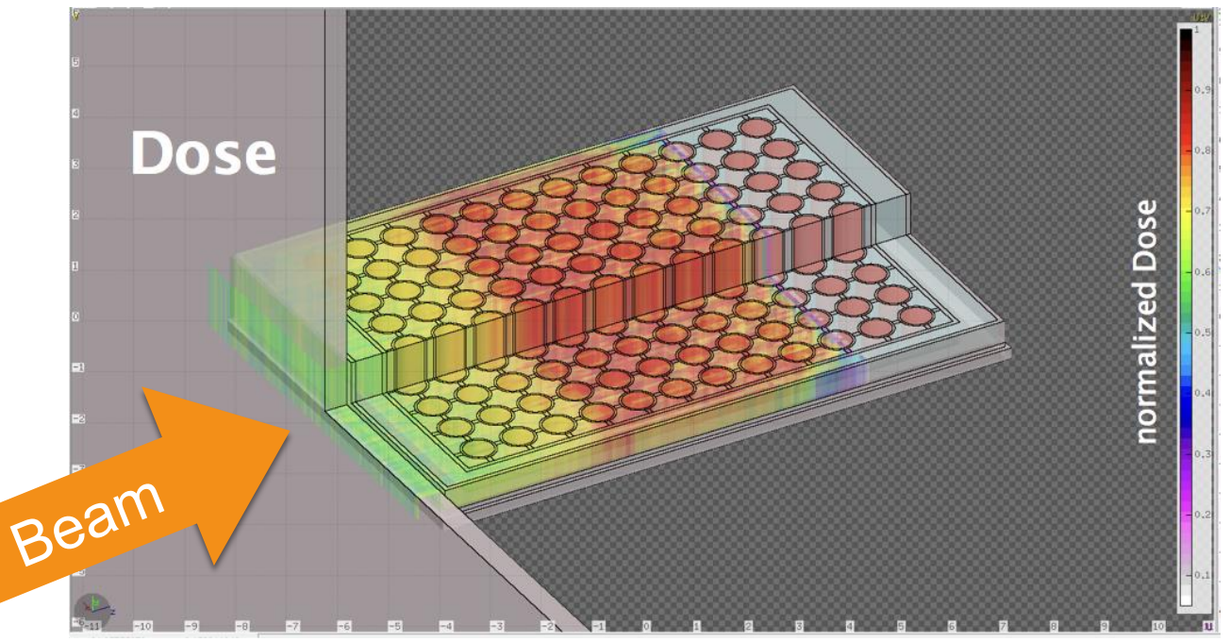
RBE Model Validation

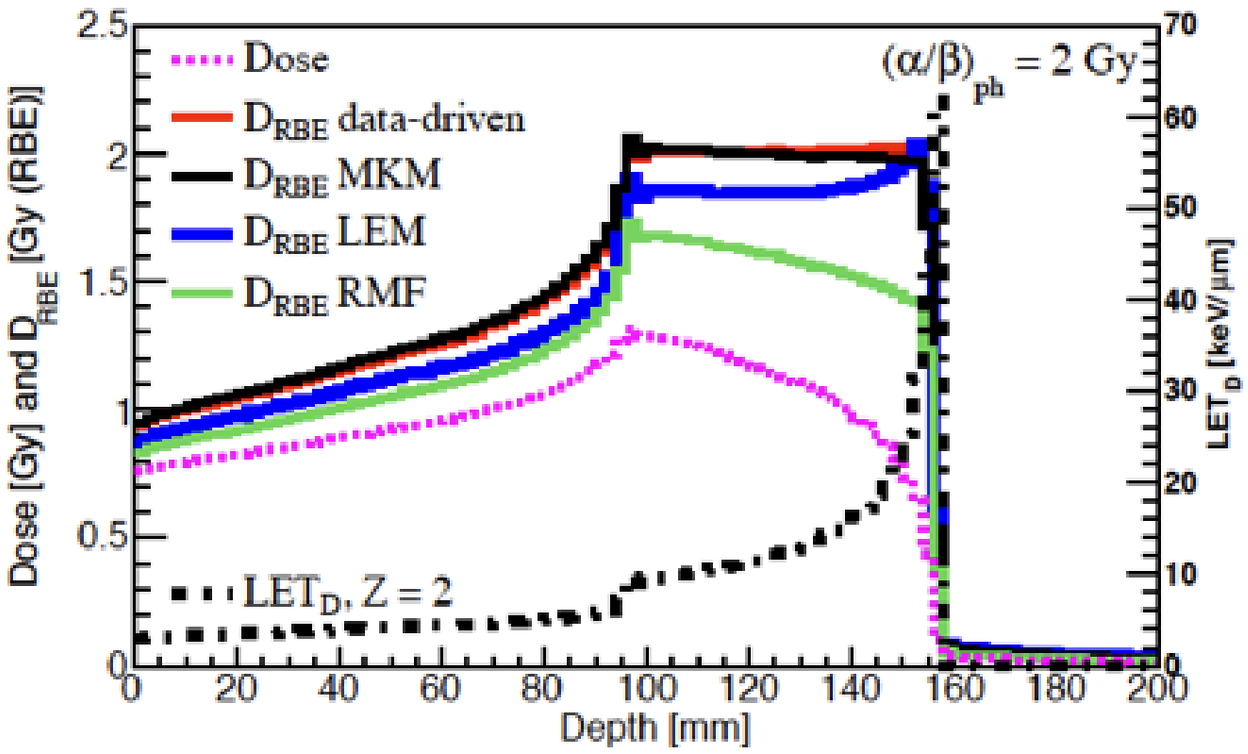
High-throughput *Clonogenic Assay — Clinical-like Fields (SOBPs)*

96 well plate approach (as in Guan et al 2015)







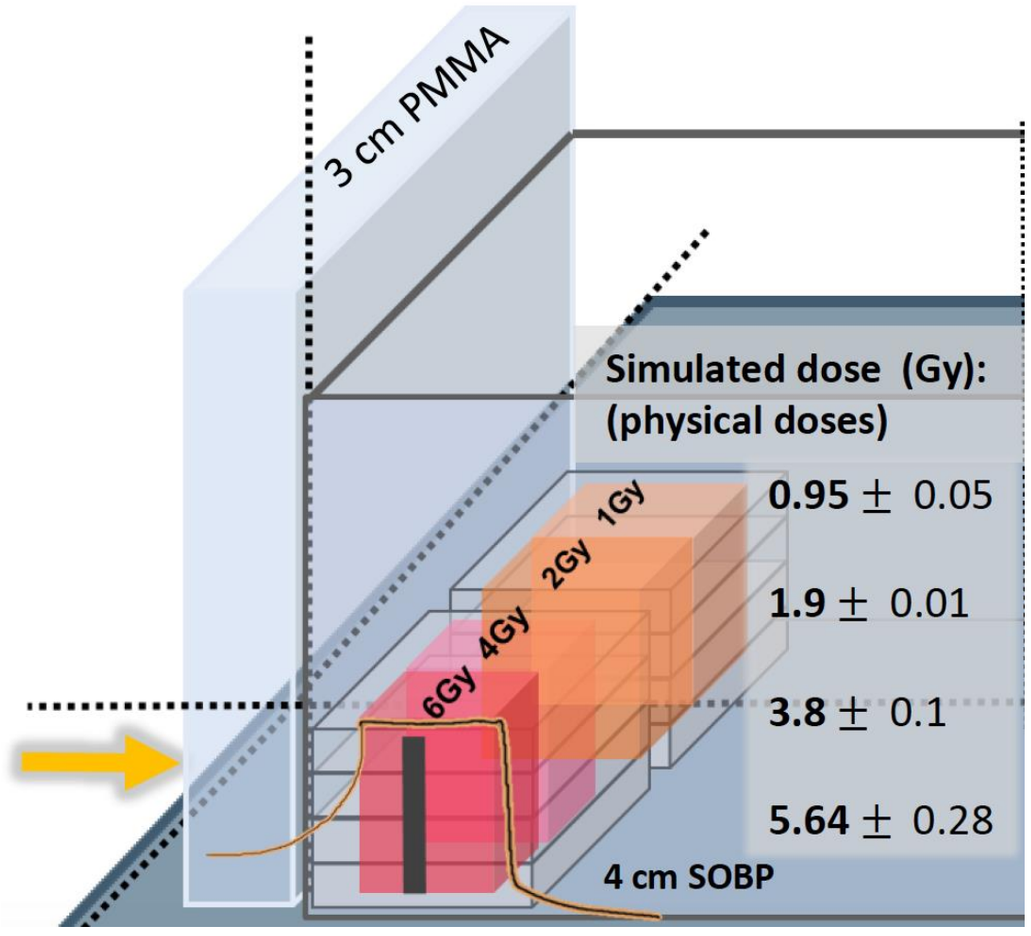


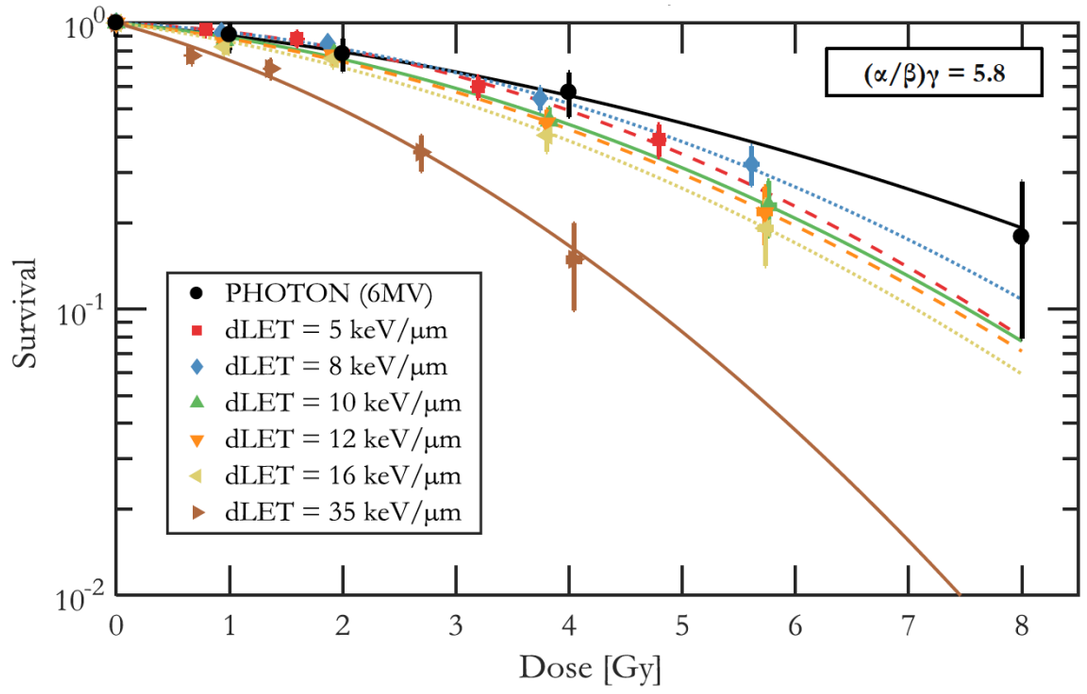
RBE Model Validation

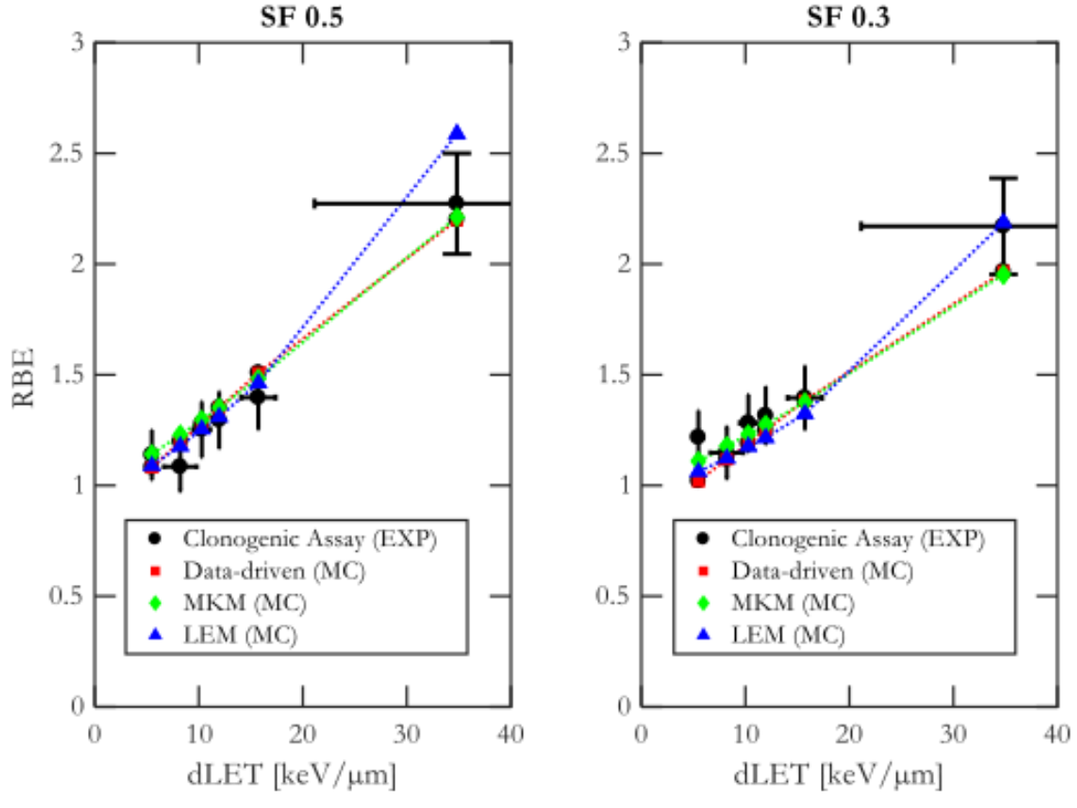
High-throughput *Clonogenic Assay — Clinical-like Fields (SOBPs)*

H1460 cell-line

$\alpha_{ph}/\beta_{ph} = 5.8$







✔ Validity of 96-well plate high-throughput approach

Klein et al 2017 (under revision)

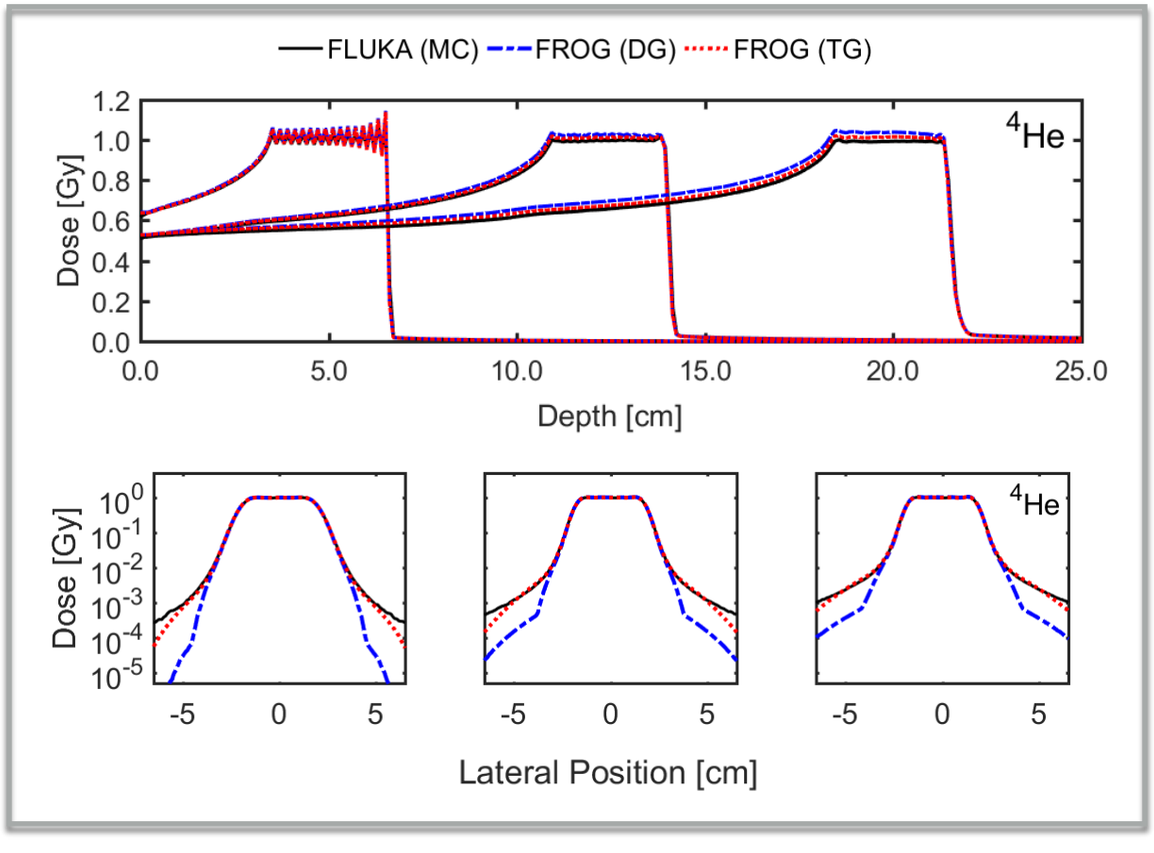
Application

Validation of clinical TPS

FROG

Fast **R**ecalculation & **O**ptimization on **G**PU

- **In-house** development
- **Fast** performance (~minutes)
- **Excellent** agreement with Monte Carlo
- **GPU-based** dose calculation
  - with **ray tracing** [1]
  - and **pencil beam splitting** [2,3]
  - HIT physics database [p, He, C, O]
    - Monte Carlo Calculated

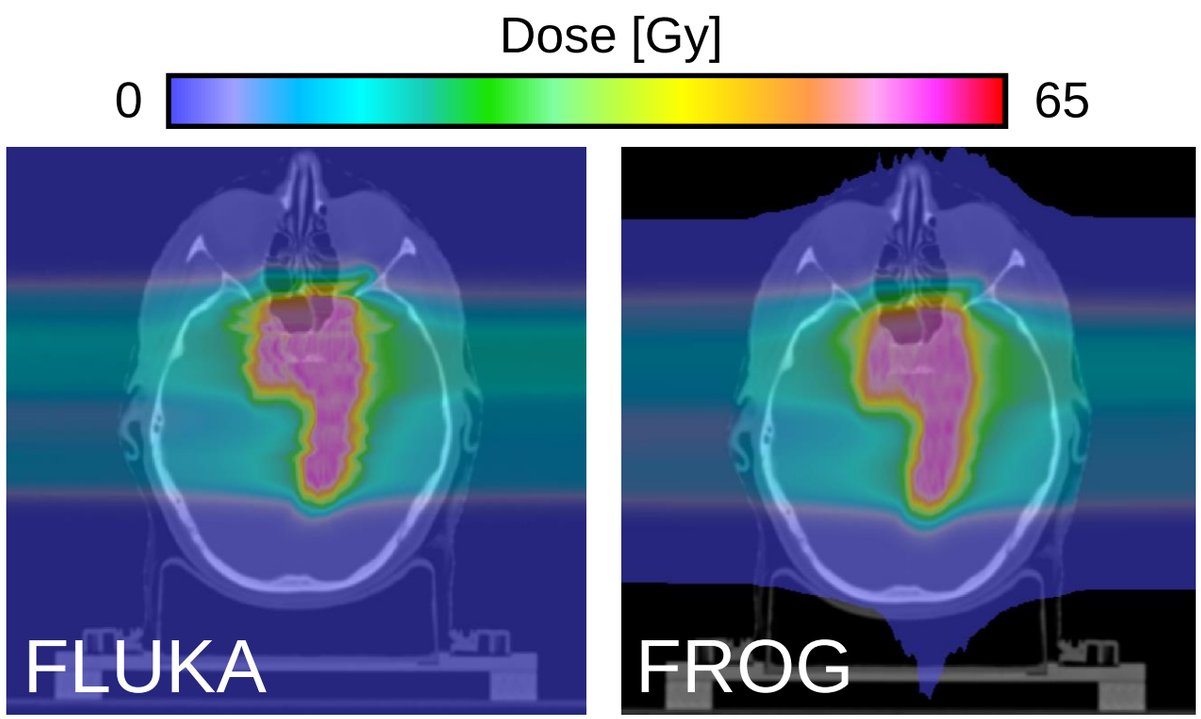


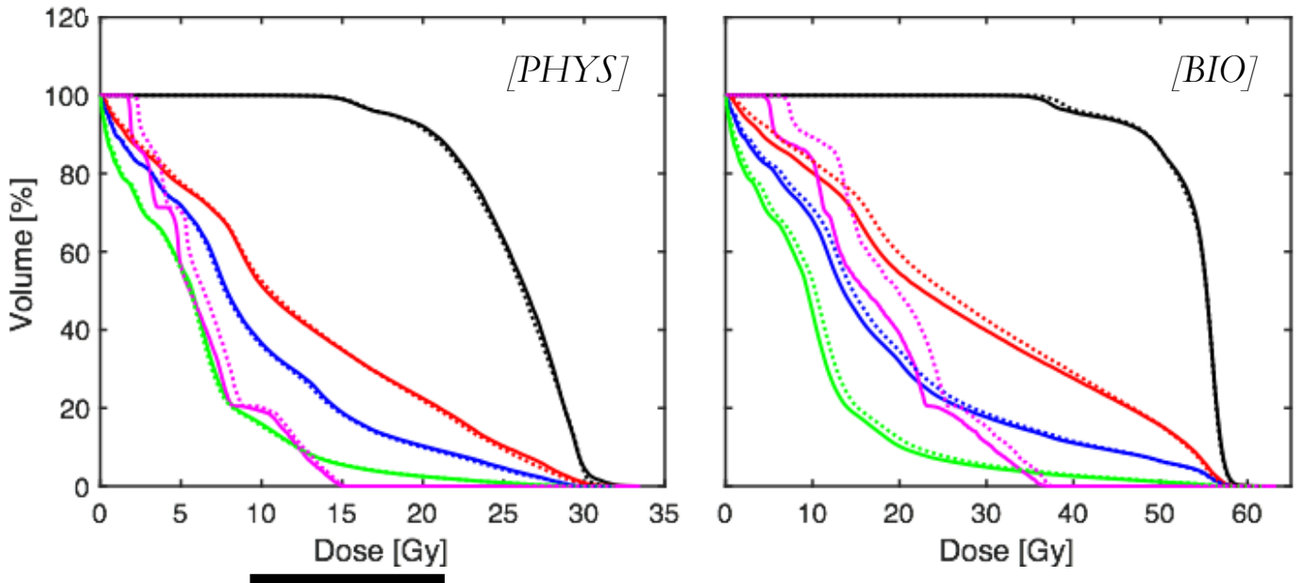
Validation against FLUKA — SOBPs in water

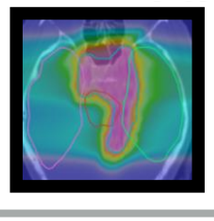
[1] Siddon, Prism representation: a 3D ray-tracing algorithm for radiotherapy applications, (1985)
[2] Kanematsu et al. Dynamic splitting of Gaussian pencil beams in heterogeneity-correction algorithms, (2009).
[3] Russo et al. A novel algorithm for the calculation of physical and biological irradiation quantities in scanned ion beam therapy: the beamlet superposition approach, (2016)

Validation of clinical TPS

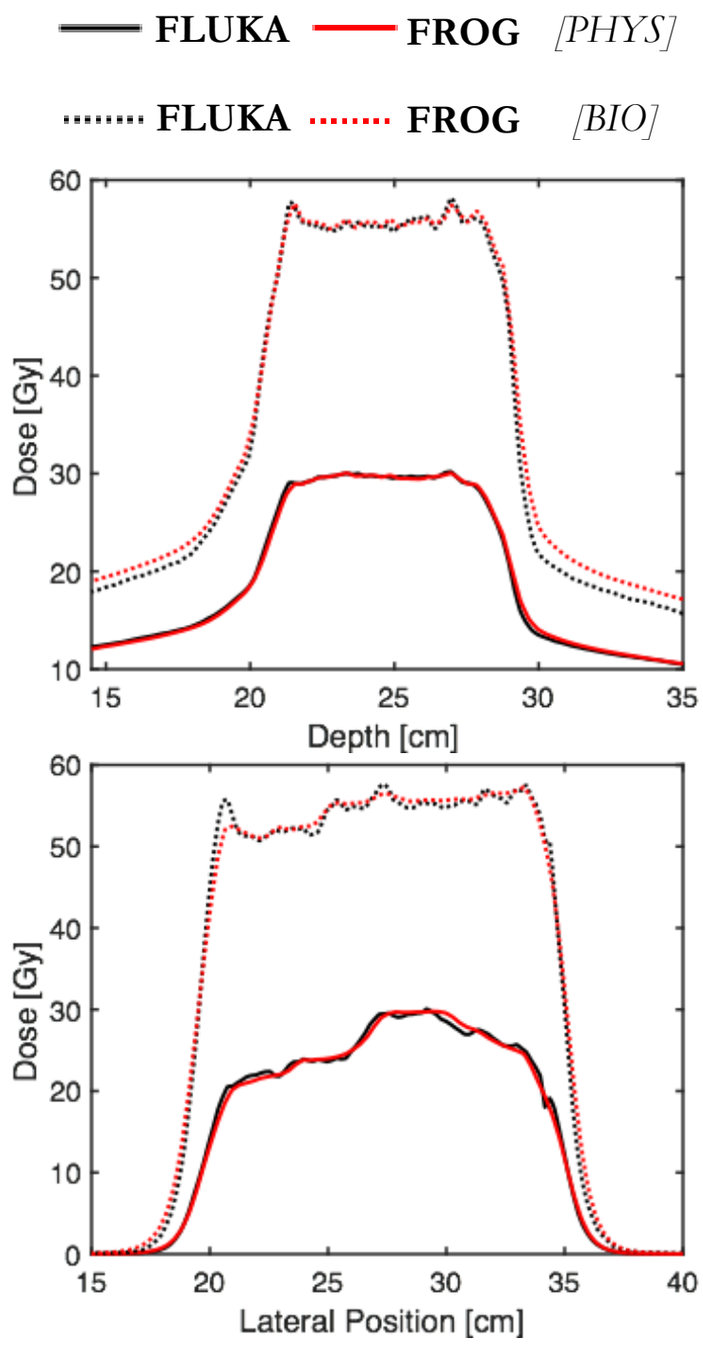
Meningioma cases (He)







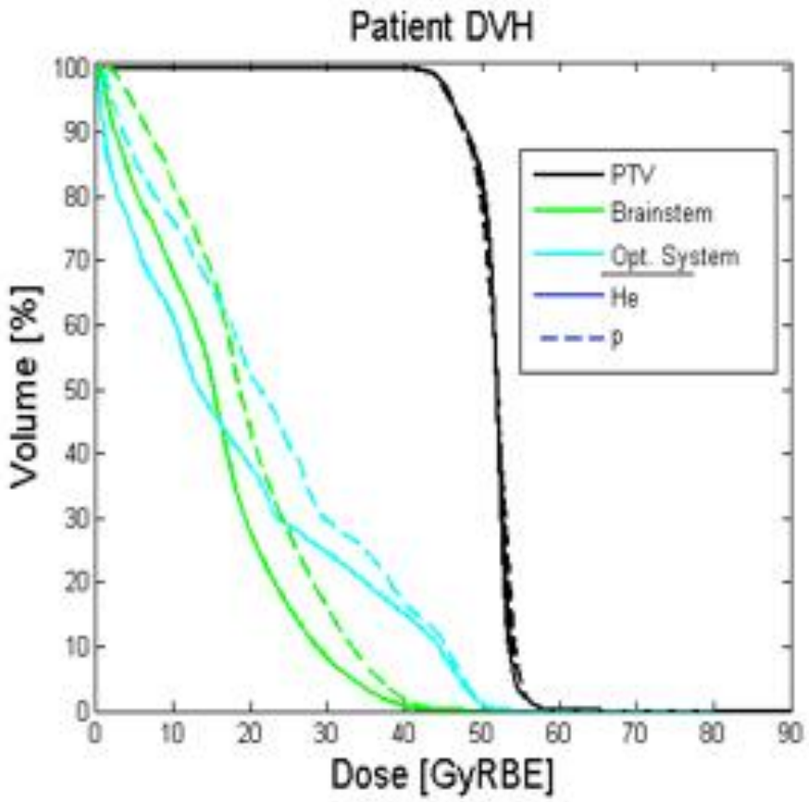
PTV
Brainstem
Chiasma
Temporal Lobe (L)
Temporal Lobe (R)

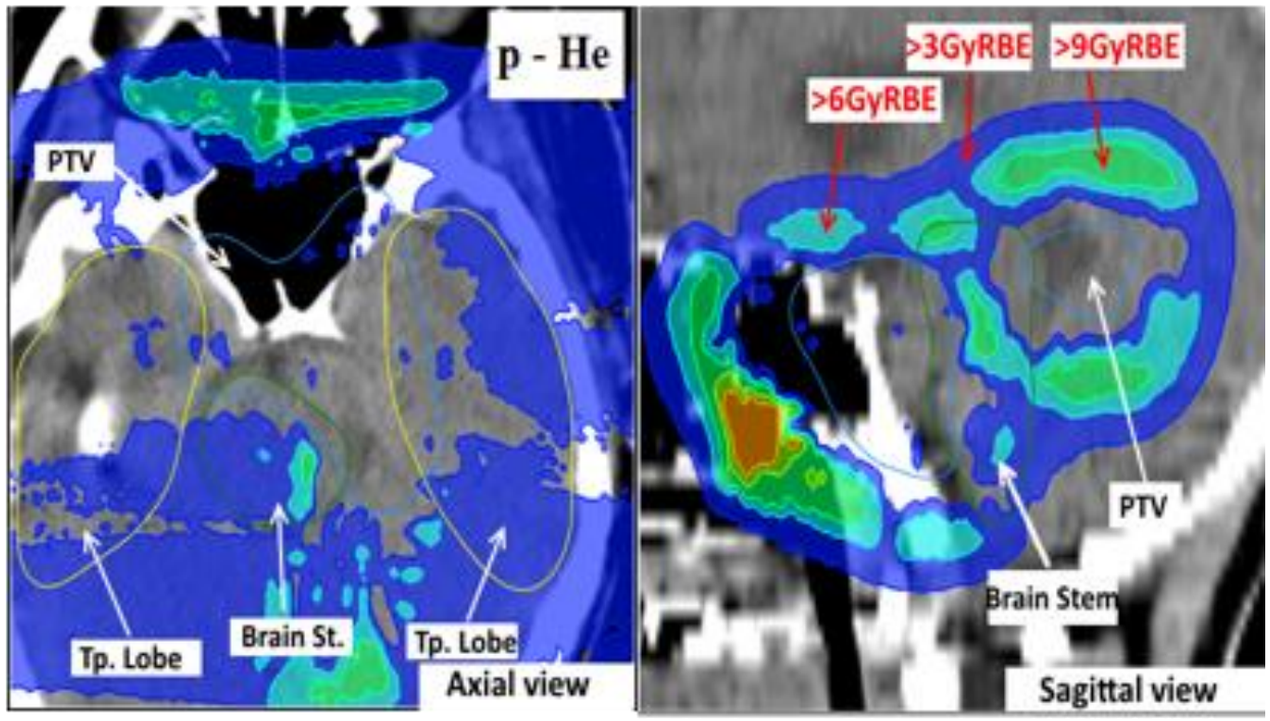


optimized via MCTP

Summary

Preparation for first He^4 treatments





Tessonnier et al 2017 (under review)

comprehensive characterization and benchmarking:

- He^4 RBE prediction with D_{bio} calc in FLUKA
- physical and biological calculation of FROG (in-house TPS) and future commercial TPS

Acknowledgments

German Cancer Research Center (DKFZ)

Translational Radiation Oncology Group

Dr. Amir Abdollahi
Dr. Ivana Dokic
Carmen Klein

Heidelberg Ion-beam Therapy Center (HIT)

Dr. Stephan Brons
Benjamin Ackerman
Dr. Thomas Haberer

Heidelberg University Clinic

Dr. Jurgen Debus

Biophysics in Particle Therapy Group

Dr. Andrea Mairani
Benedikt Kopp
Dr. Julia Bauer
Dr. Emanuel Bahn
Dr. Markus Alber

CNAO

Kyungdon Choi
Dr. Giuseppe Magro

LMU

Dr. Katia Parodi
Dr. Thomas Tessonnier