Joint optimization of photon–carbon ion treatment plans

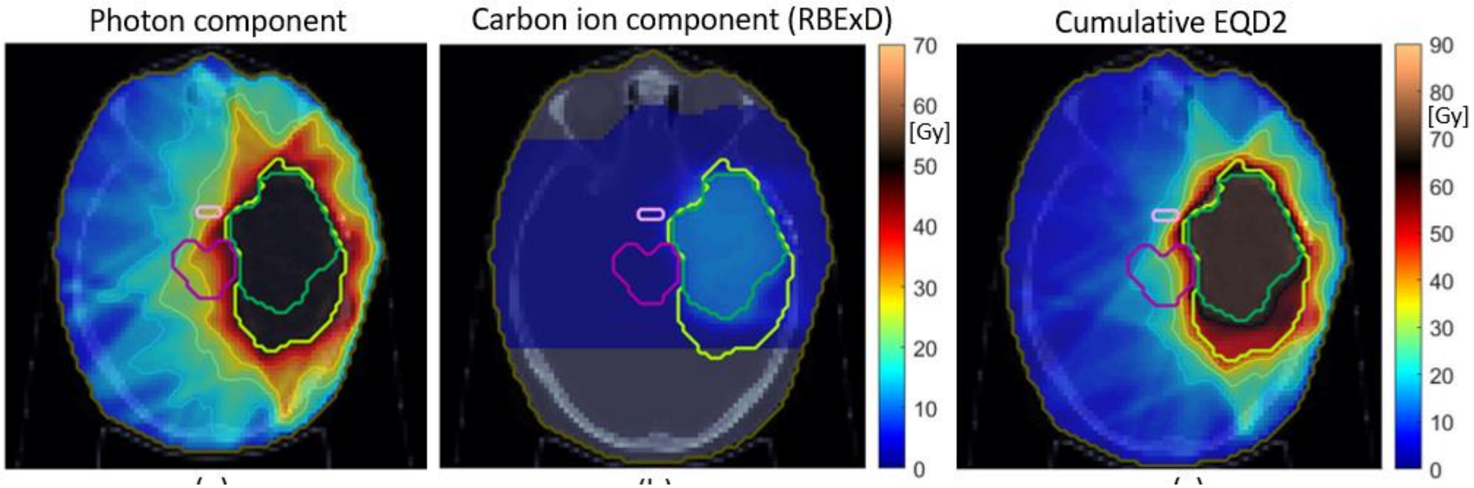
7th Annual Loma Linda Workshop

Amit Ben Antony Bennan,
Mark Bangert, Jan Unkelbach,
Niklas Wahl, Oliver Jaekel

HIRO Heidelberg Institute for Radiation Oncology
UniversitätsKlinikum Heidelberg
HIT Heidelberger Ionenstrahl-Therapiezentrum
GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION
Research for a Life without Cancer

Mixed modality treatments

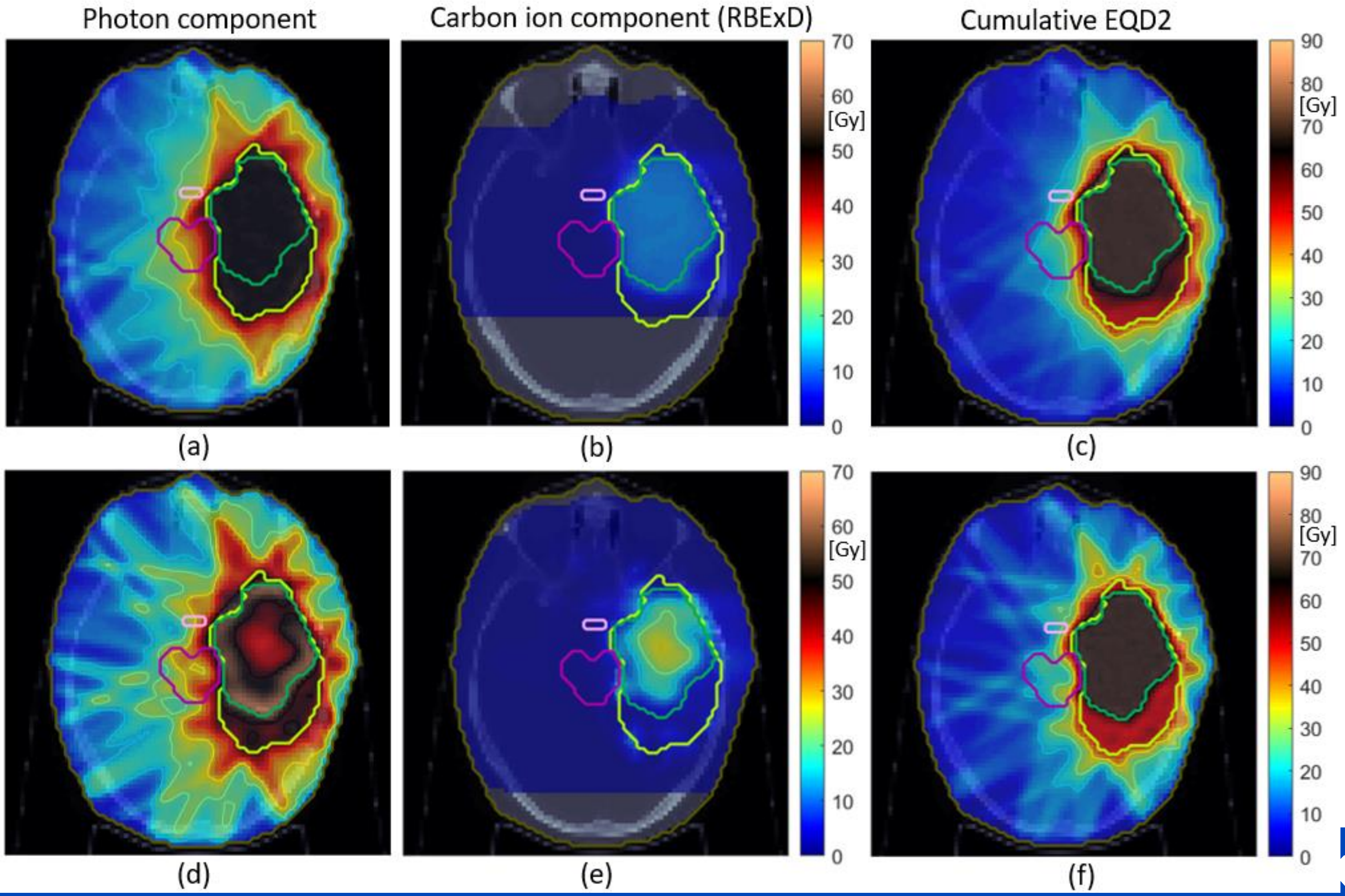
CLEOPATRA protocol



Mixed modality treatments

CLEOPATRA protocol

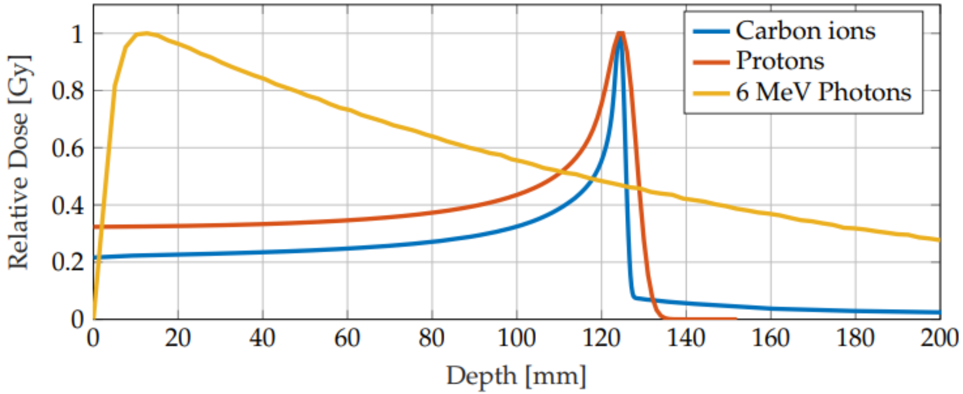
Joint Opt

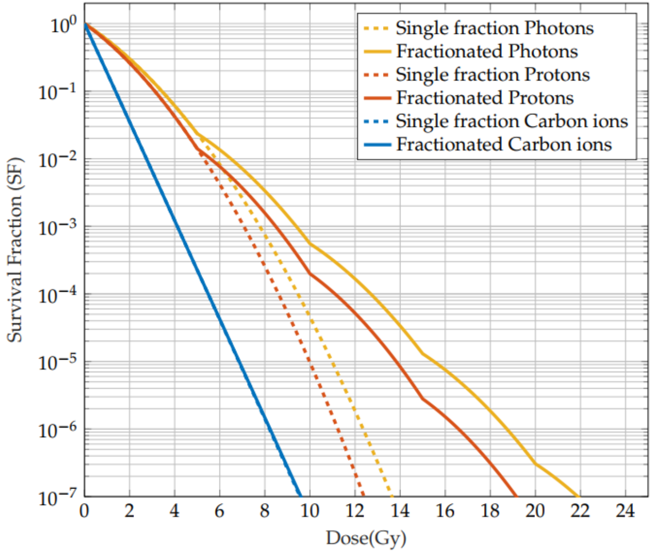


kfz.

Back to the Basics

- Carbon ions = protons + sharper Bragg peak + Fragmentation tail
- RBE: Protons ~1.1, Carbon ions: varies along the beam(~3)
- Protons and photons show some predicted fractionation benefit
- Carbon ions show almost no fractionation benefit at the Bragg peak





Rationale

- High RBE, hypoxia invariance, lower integral dose to NT
- Traditionally used for H&N, pediatric cases, lung, prostate, pancreas
- Ideally you would want to treat LARGE, HYPOXIC / RADIORESISTANT tumors with CIRT
- Downside: limited/no sparing by fractionation

RATIONALE for Carbon – photon joint optimization – Carbon ions to reduce integral dose and photons to fractionate dose to NT

Playing their strengths…

Photon – Proton combined treatments (BED)

ELSEVIER
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original article

Optimization of combined proton–photon treatments

Jan Unkelbach [a,*], Mark Bangert [b], Karen De Amorim Bernstein [c], Nicolaus Andratschke [a], Matthias Guckenberger [a]

[a] Department of Radiation Oncology, University Hospital Zürich, Switzerland; [b] Department of Medical Physics in Radiation Oncology, German Cancer Resear

International Journal of Radiation Oncology • Biology • Physics ASTRO

PHYSICS CONTRIBUTION | VOLUME 108, ISSUE 3, P792-801, NOVEMBER 01, 2020

Accounting for Range Uncertainties in the Optimization of Combined Proton-Photon Treatments Via Stochastic Optimization

Silvia Fabiano, MSc • Mark Bangert, PhD • Matthias Guckenberger, MD • Jan Unkelbach, PhD

Published: April 30, 2020 • DOI: https://doi.org/10.1016/j.ijrobp.2020.04.029 • Check for updates

IOP Publishing Phys. Med. Biol. 64 (2019) 065011 (21pp) https://doi.org/10.1088/13

Physics in Medicine & Biology IPEM Institut Engine

RECEIVED 14 June 2018
REVISED 8 January 2019
ACCEPTED FOR PUBLICATION 14 January 2019
PUBLISHED 11 March 2019

PAPER

Optimal combined proton–photon therapy schemes based on the standard BED model

S C M ten Eikelder [1,4], D den Hertog [1], T Bortfeld [2] and Z Perkó [2,3]

[1] Department of Econometrics and Operations Research, Tilburg University, Tilburg, The Netherlands
[2] Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States of America
[3] Department of Radiation Science and Technology, Delft University of Technology, Delft, The Netherlands
[4] Author to whom any correspondence should be addressed.

E-mail: s.c.m.teneikelder@tilburguniversity.edu

Keywords: proton therapy, intensity-modulated radiation therapy (IMRT), optimization, multi-modality treatment, biolo dose (BED)

Supplementary material for this article is available online

IOP Publishing Phys. Med. Biol. 64 (2019) 105003 (11pp) https://doi.org/10.1088/1361-6560/ab18c7

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

RECEIVED 10 January 2019
REVISED 25 March 2019
ACCEPTED FOR PUBLICATION 12 April 2019
PUBLISHED 8 May 2019

PAPER

Hybrid proton-photon inverse optimization with uniformity-regularized proton and photon target dose

Hao Gao

Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA 30322, United States of America

E-mail: hgao24@emory.edu

Keywords: hybrid proton-photon optimization, IMRT, IMPT, ADMM

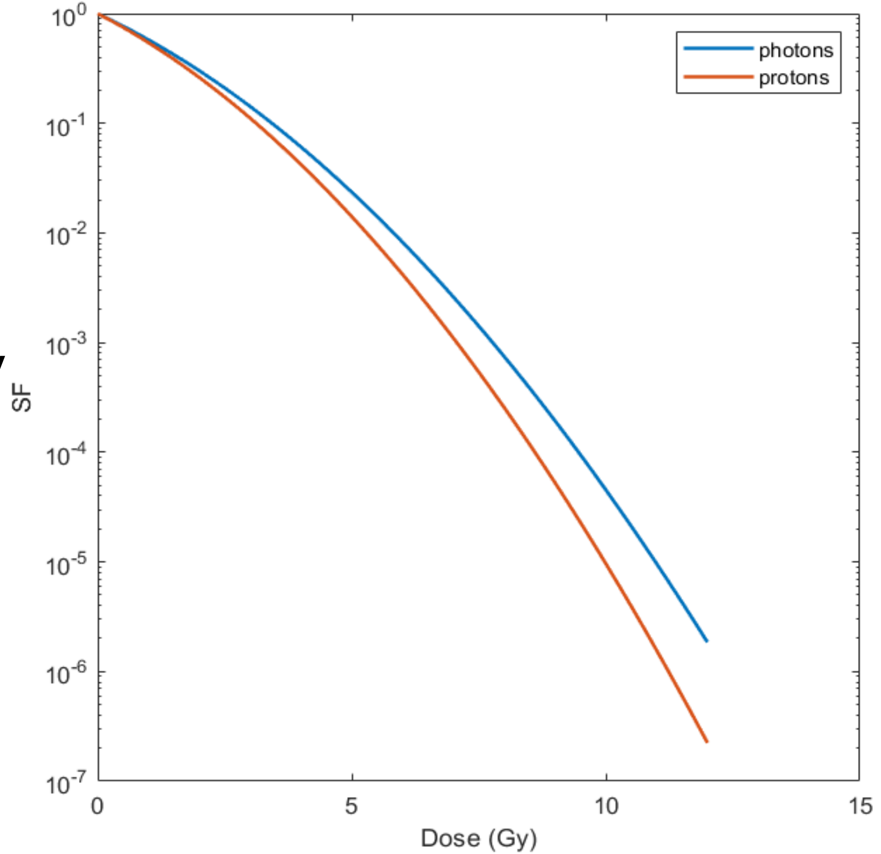
Linear Quadratic model

- Alpha / beta values describe the shape of the curve (fitting parameters)
- Depends on tissue and radiation quality

$$SF = e^{-n(\alpha d + \beta d^2)}$$

$$BED = nd\left(1 + \frac{d}{\alpha/\beta}\right)$$

$$\varepsilon = n(\alpha d + \beta d^2)$$



Linear Quadratic model

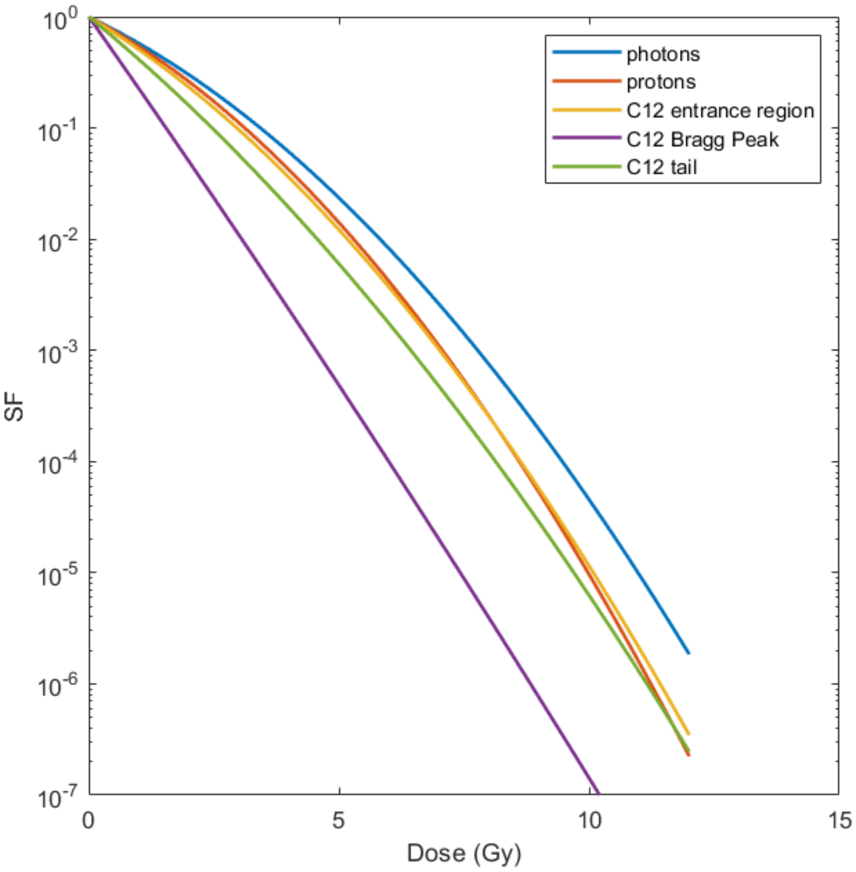
- Alpha / beta values describe the shape of the curve (fitting parameters)

- Depends on tissue and radiation quality

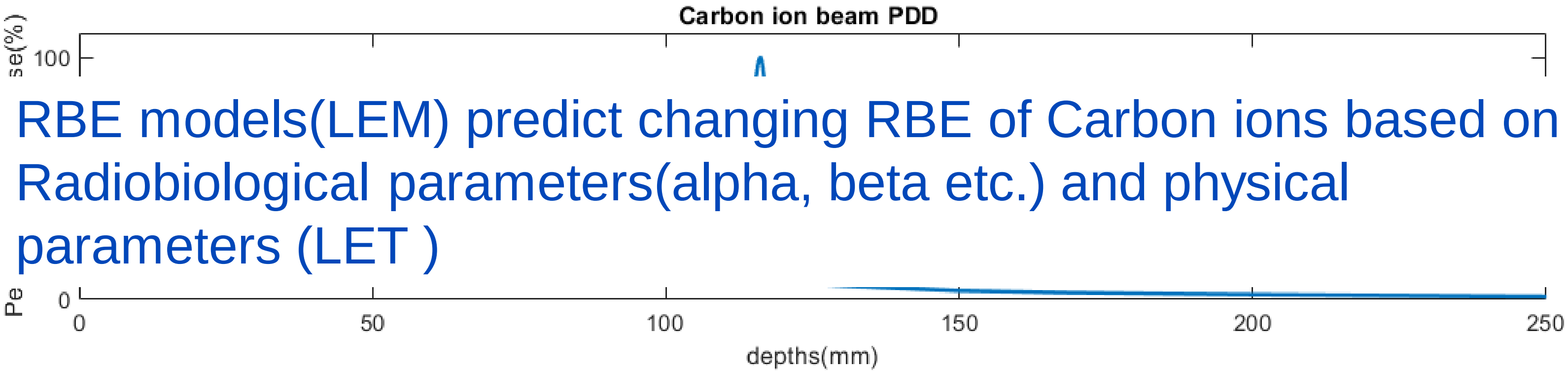
$$SF = e^{-n(\alpha d + \beta d^2)}$$

$$BED = nd\left(1 + \frac{d}{\alpha/\beta}\right)$$

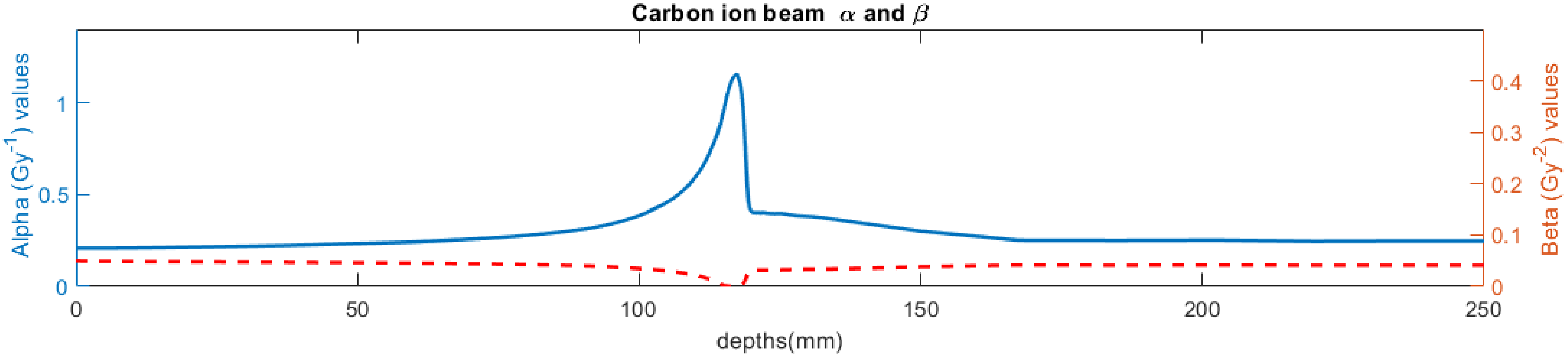
$$\varepsilon = n(\alpha d + \beta d^2)$$



Challenges with Carbon ions:
Carbon effective α,β depend on the position of voxel in the beam

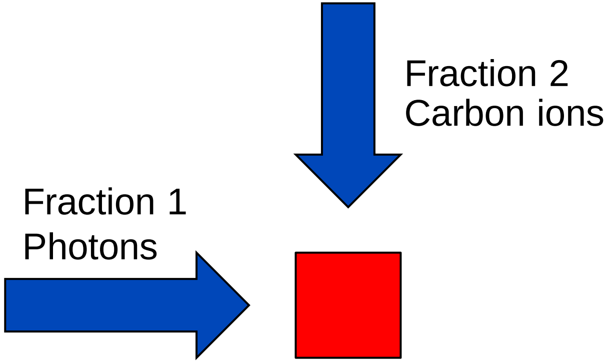


RBE models(LEM) predict changing RBE of Carbon ions based on Radiobiological parameters(alpha, beta etc.) and physical parameters (LET)



dkfz.

Mixed Modality Radiotherapy and variable RBE models



$$\min \quad f(w) = \sum_{n} p_n f_n(w)$$

Where eg.

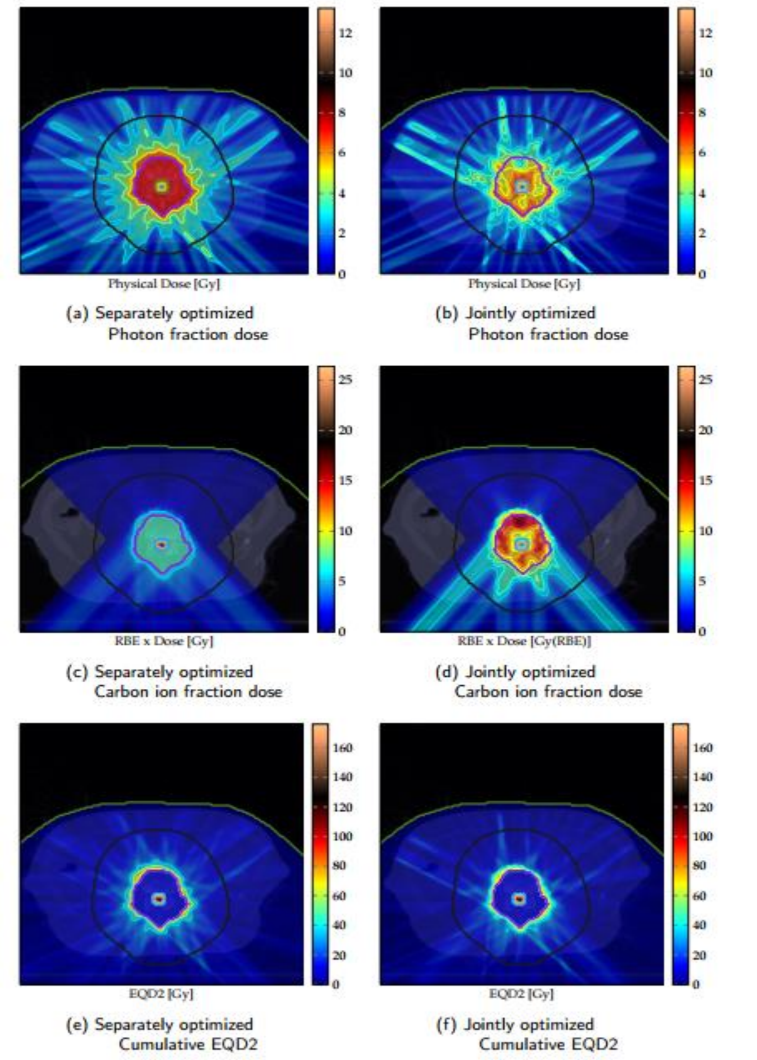
$$f_{sqdeviation} = \frac{1}{N_s} \sum_{i \in S} \left(\varepsilon_i^{Total} - \hat{\varepsilon}\right)^2$$

The plans are optimized on the total biological effect.

$$\varepsilon_i^{Total} = \left(n_\gamma\left(\alpha_\gamma d_{i\gamma} + \beta_\gamma d_{i\gamma}^2\right) + n_c\left(\alpha_{ic} d_{ic} + \beta_{ic} d_{ic}^2\right)\right), i \in V$$

Photon Effect Carbon Effect

dkfz.



Proof of Concept

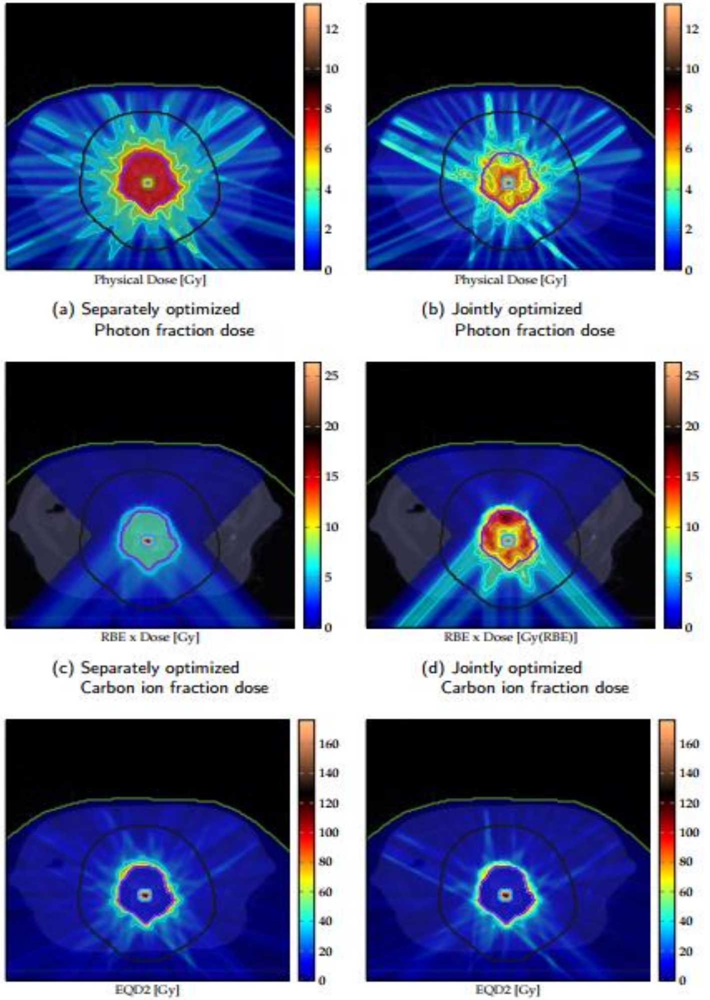
- Reproduce published results Unkelbach et al 2018

Fixed fraction allocation

- SBRT treatment
- Carbon ions: 1 fxn
- Photons: 4 fxn

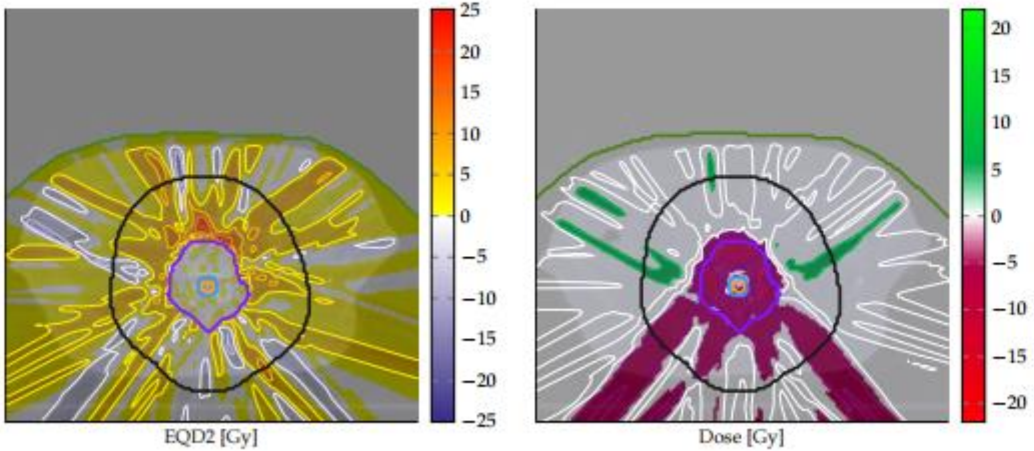
- Tumor α^T/β^T = 0.5/0.05 (10Gy)
- Healthy tissue α^{NT}/β^{NT}= 0.1/0.05 (2Gy)
- Fractionation benefit: $\alpha^T/\beta^T > \alpha^{NT}/\beta^{NT}$

Proof of Concept

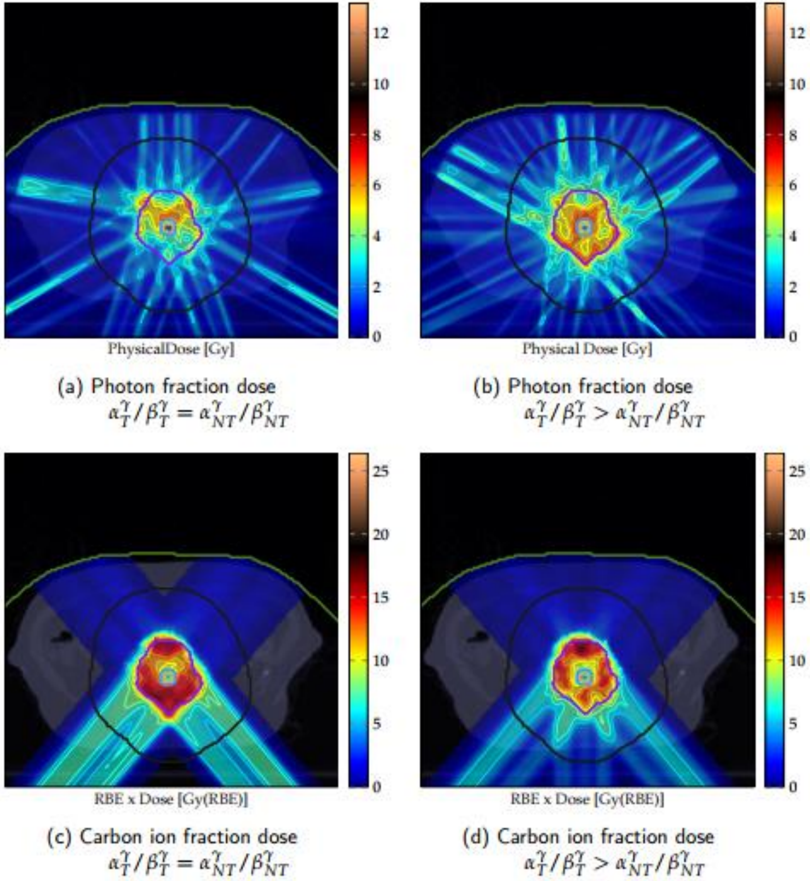


(a) Separately optimized Photon fraction dose
(b) Jointly optimized Photon fraction dose
(c) Separately optimized Carbon ion fraction dose
(d) Jointly optimized Carbon ion fraction dose
(e) Separately optimized Cumulative EQD2
(f) Jointly optimized Cumulative EQD2

- More conformal : additional degree freedom from both modalities
- Spatial distribution of fraction dose within the target
  = hypofractionation vs hyper fractionation



(a) EQD2 difference (Simple combination – Jointly optimized plan)
(b) Difference in fraction dose (Photon fraction – Carbon ion fraction)



(a) Photon fraction dose $\alpha_T^\gamma/\beta_T^\gamma = \alpha_{NT}^\gamma/\beta_{NT}^\gamma$

(b) Photon fraction dose $\alpha_T^\gamma/\beta_T^\gamma > \alpha_{NT}^\gamma/\beta_{NT}^\gamma$

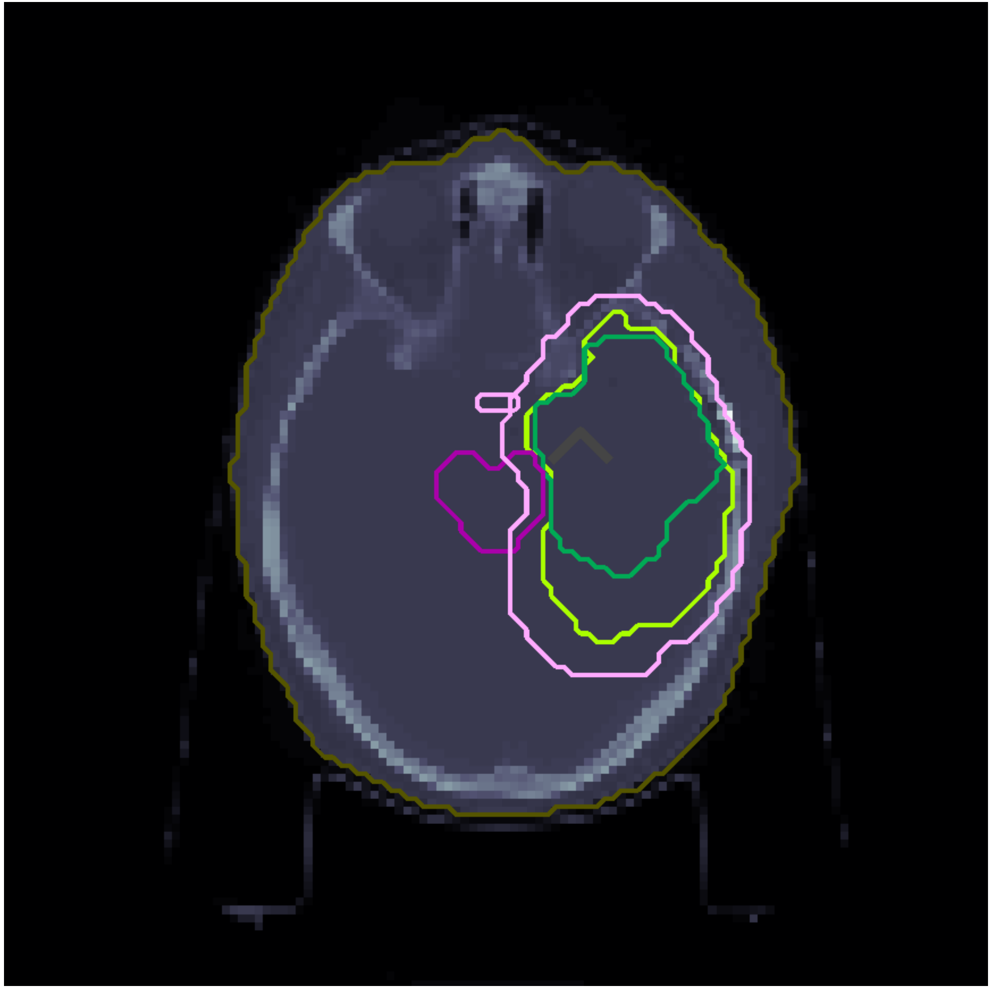
(c) Carbon ion fraction dose $\alpha_T^\gamma/\beta_T^\gamma = \alpha_{NT}^\gamma/\beta_{NT}^\gamma$

(d) Carbon ion fraction dose $\alpha_T^\gamma/\beta_T^\gamma > \alpha_{NT}^\gamma/\beta_{NT}^\gamma$

Impact of LQ model Parameter selection

- Without a fractionation benefit:
  $$\alpha^T/\beta^T \leq \alpha^{NT}/\beta^{NT}$$
- joint optimization result is based on physical dose characteristics

dkfz.



Glioblastoma

Assumption: the CTV is comprised of a combination of tumor and normal tissue.

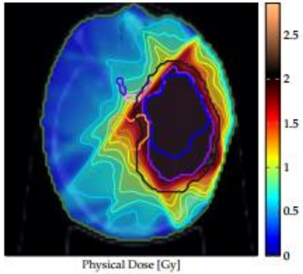
Carbon ions : 6 fxns (18 Gy(RBE))
Photons: 25 fxns (50 Gy)

Tumor α^{T}/β^{T} = 0.5/0.05 (10Gy)
Healthy tissue α^{NT}/β^{NT}= 0.1/0.05 (2Gy)

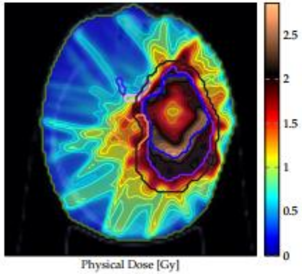
Prescriptions:
GTV: 50 Gy + 18 Gy (boost)
CTV: 50 Gy

Glioblastoma

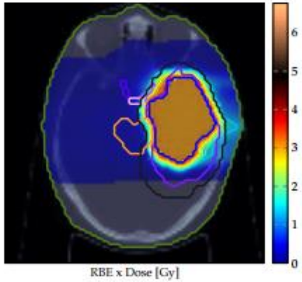
- Carbon ions at the core (almost x2)
- Photons at CTV + all interfaces with NT
- Improved Conformity



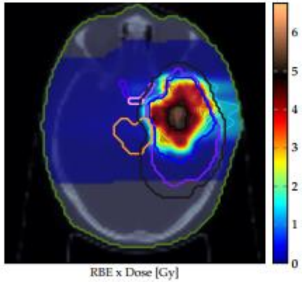
(a) Photon fraction dose
Reference plan



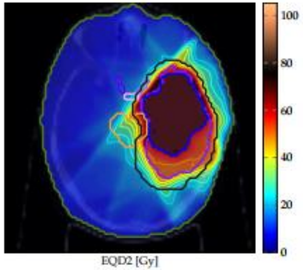
(b) Photon fraction dose
Jointly optimized plan



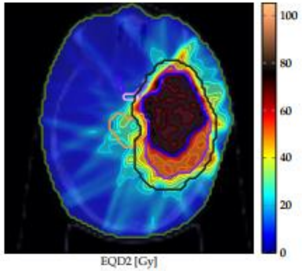
(d) Carbon ion fraction dose
Reference plan



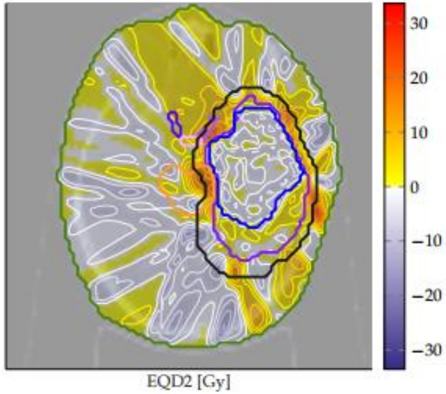
(e) Carbon ion fraction dose
Jointly optimized plan



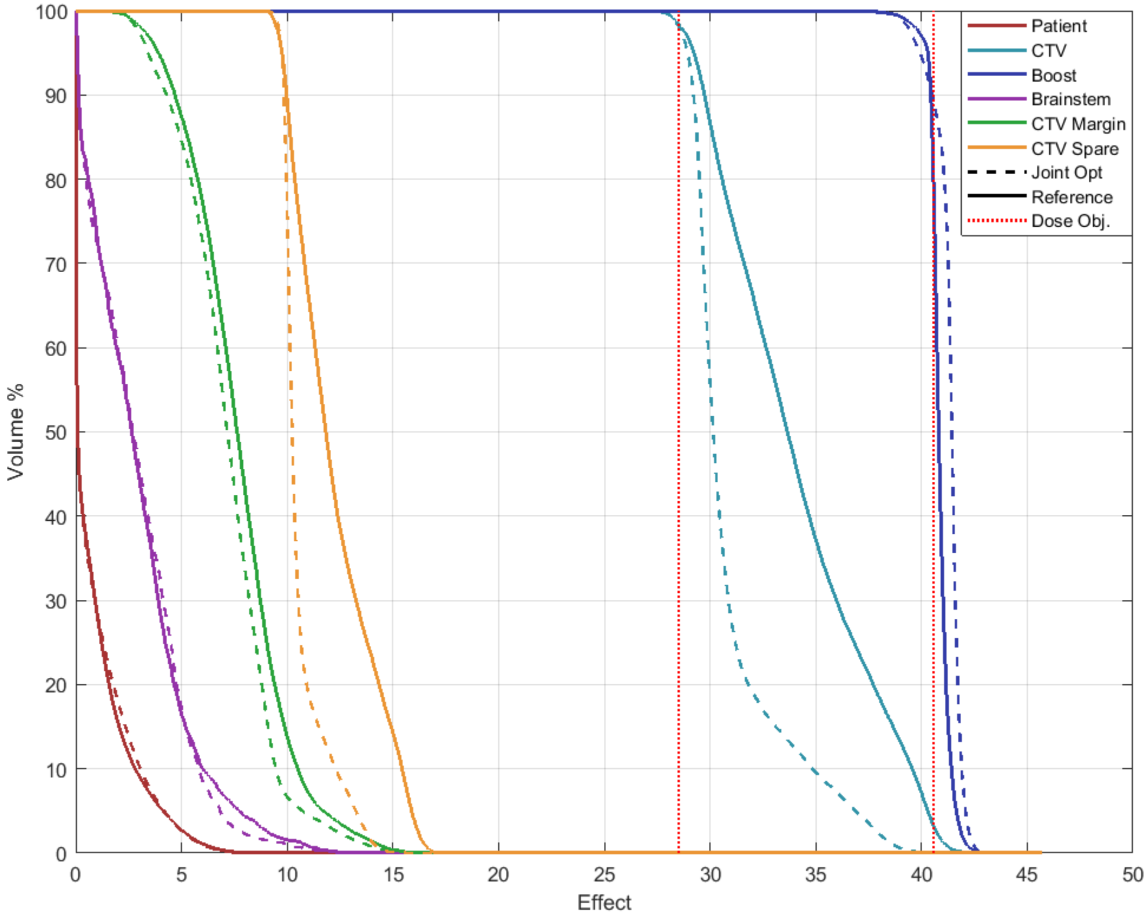
(g) Cumulative EQD2
Reference plan

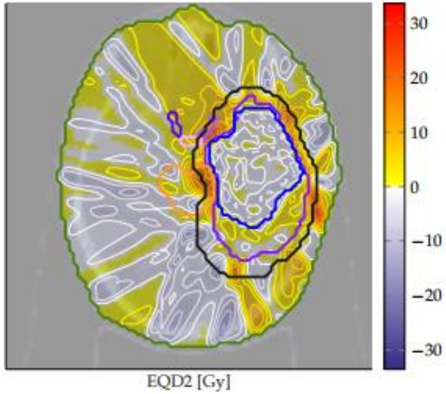


(h) Cumulative EQD2
Jointly optimized plan



(a) EQD2 Difference
(Reference plan – Jointly optimized plan)

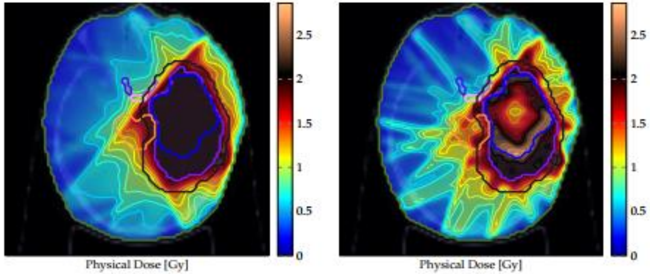




(a) EQD2 Difference
(Reference plan − Jointly optimized plan)

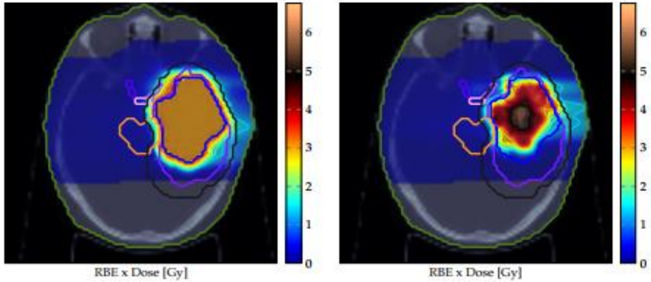
Glioblastoma

- Implicit redistribution of LET



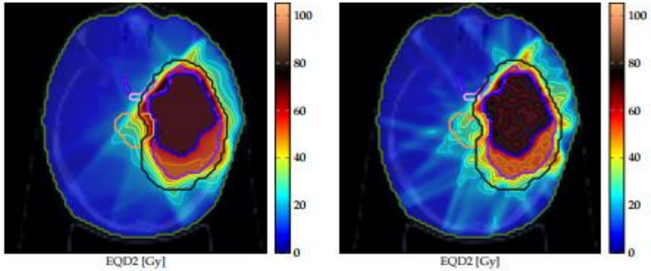
(a) Photon fraction dose Reference plan

(b) Photon fraction dose Jointly optimized plan



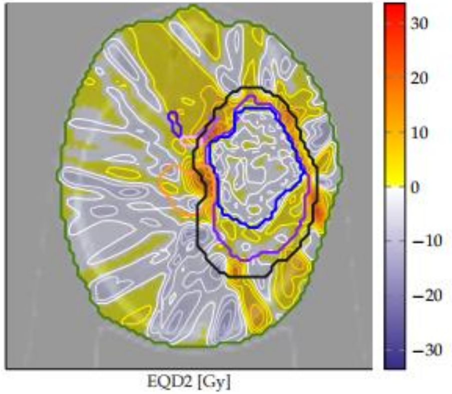
(d) Carbon ion fraction dose Reference plan

(e) Carbon ion fraction dose Jointly optimized plan

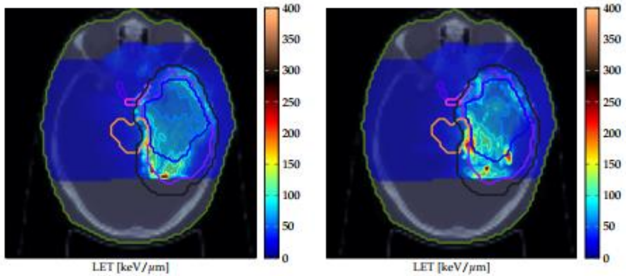


(g) Cumulative EQD2 Reference plan

(h) Cumulative EQD2 Jointly optimized plan

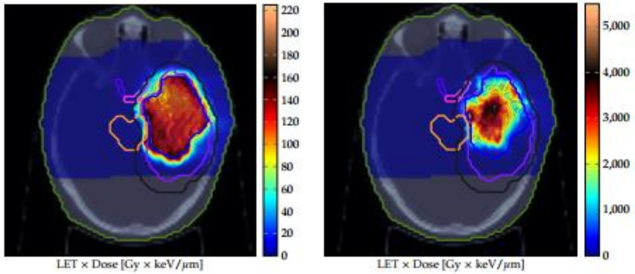


(a) EQD2 Difference (Reference plan – Jointly optimized plan)



(a) Dose averaged LET Reference plan

(b) Dose averaged LET Jointly optimized plan



(d) LET weighted dose Reference plan

(e) LET weighted dose Jointly optimized plan

dkfz.

Assumptions / Raised questions

- LQ model describes the iso effective dose-fxn translations accurately (therefore d/fxn heterogeneity is acceptable)

- Alpha Beta values “accurately” model the radiosensitivity of the tissue : definitely not true

- Not considering robustness of the plans

PHYSICS CONTRIBUTION | VOLUME 108, ISSUE 3, P792-801, NOVEMBER 01, 2020

Accounting for Range Uncertainties in the Optimization of Combined Proton-Photon Treatments Via Stochastic Optimization

Silvia Fabiano, MSc • Mark Bangert, PhD • Matthias Guckenberger, MD • Jan Unkelbach, PhD

Published: April 30, 2020 • DOI: https://doi.org/10.1016/j.ijrobp.2020.04.029 • Check for updates

Take home message – Joint optimization because…

- Aim is to investigate the possibilities **of mathematically combining different radiation modalities** in the LQ based biological effect space.

- Physical DOF from cumulative spatial dose redistribution
- Temporal DOF from local dose per fraction modulation

- Use **Photons for fractionation** and sparing, **use carbon ions to hypofractionate/ for high LET** and reduce integral dose

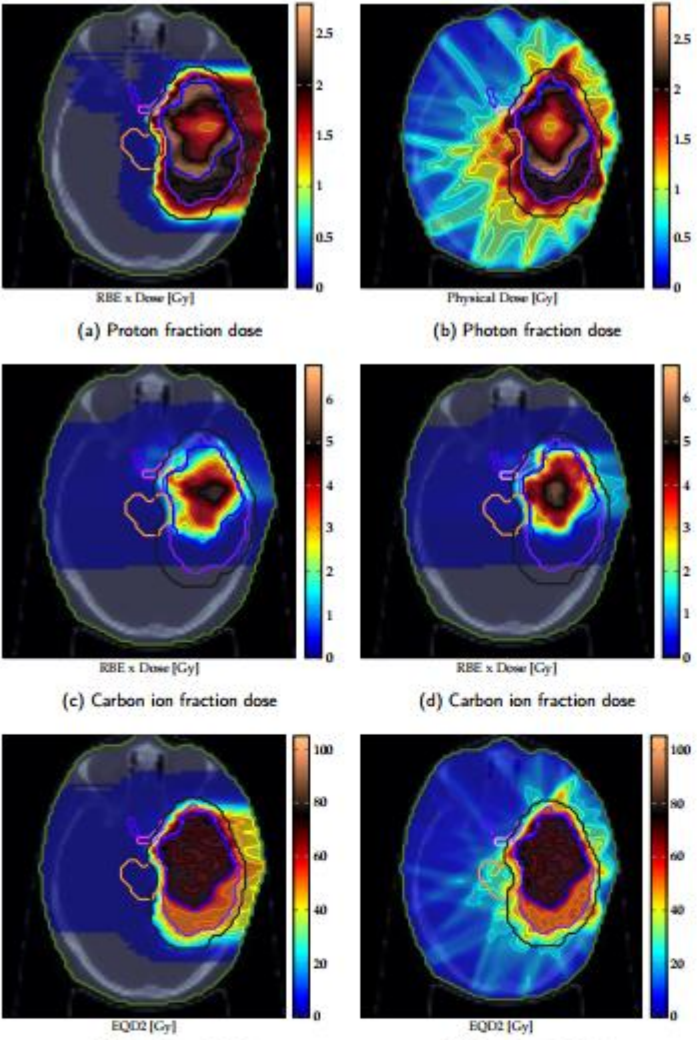
- Easily incorporate other RBE models and dose accumulation models

PHYSICS CONTRIBUTION | ARTICLES IN PRESS

Joint Optimization of Photon–Carbon Ion Treatments for Glioblastoma

Amit Ben Antony Bennan, MSc • Jan Unkelbach • Niklas Wahl • Patrick Salome, MSc • Mark Bangert

Open Access • Published: May 28, 2021 • DOI: https://doi.org/10.1016/j.ijrobp.2021.05.126



(a) Proton fraction dose (b) Photon fraction dose
(c) Carbon ion fraction dose (d) Carbon ion fraction dose
(e) Cumulative EQD2 (f) Cumulative EQD2

Proton – Carbon ion joint optimization

- Protons are assumed to be radiobiologically similar to photons i.e. constant RBE
- Qualitatively similar to photon-carbon ion treatment

Thank you

dkfz.

Thank you