ICTR-PHE 2016

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Investigation of the use of Inhomogeneous Fractional Dose (IFD) distributions in IMPT to improve the therapeutic index

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The Rationale for Inhomogeneous Fractional Dose (IFD)

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The emergence of nonuniform spatiotemporal fractionation schemes within the standard BED model

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Purpose: Nonuniform spatiotemporal radiotherapy fractionation schemes, i.e., delivering distinct dose distributions in different fractions can potentially improve the therapeutic ratio. This is possible if the dose distributions are designed such that similar doses ar... the fractionation effect) while hypofractiona...

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Simultaneous optimization of dose distributions and fractionation schemes in particle radiotherapy

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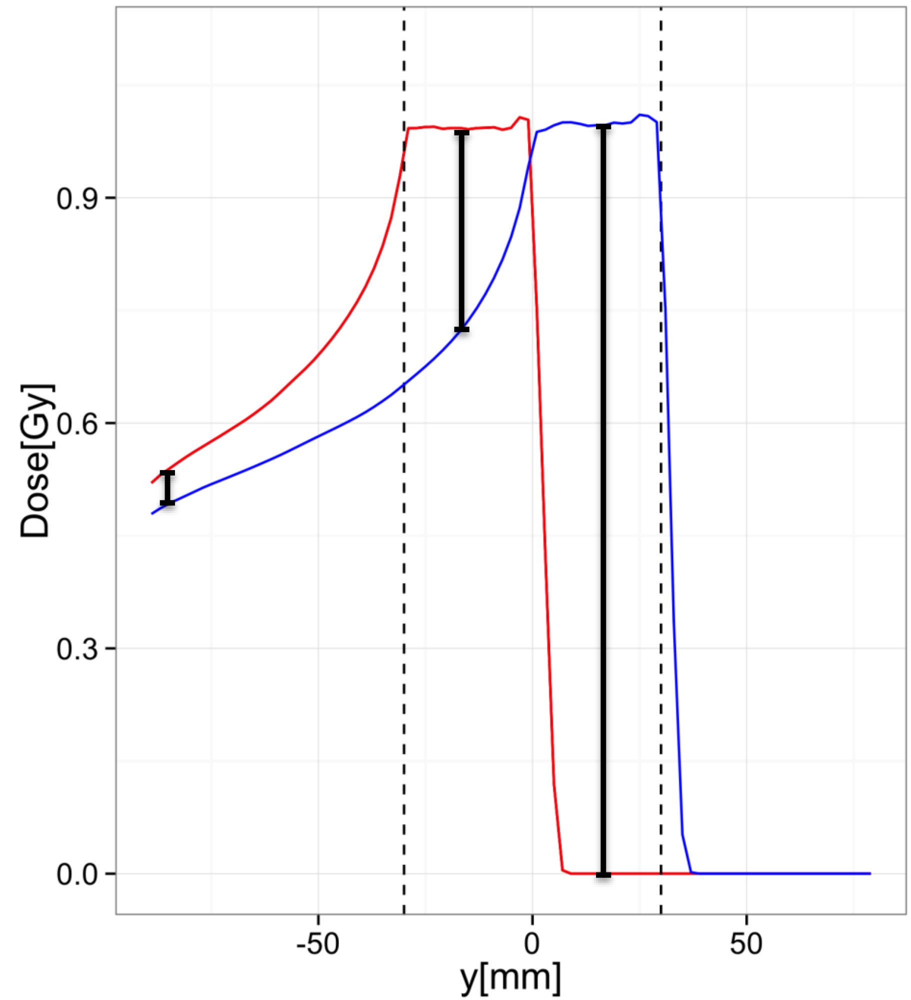
Purpose: The paper considers the fractionation ...



Purpose, Limits and Critical Issues

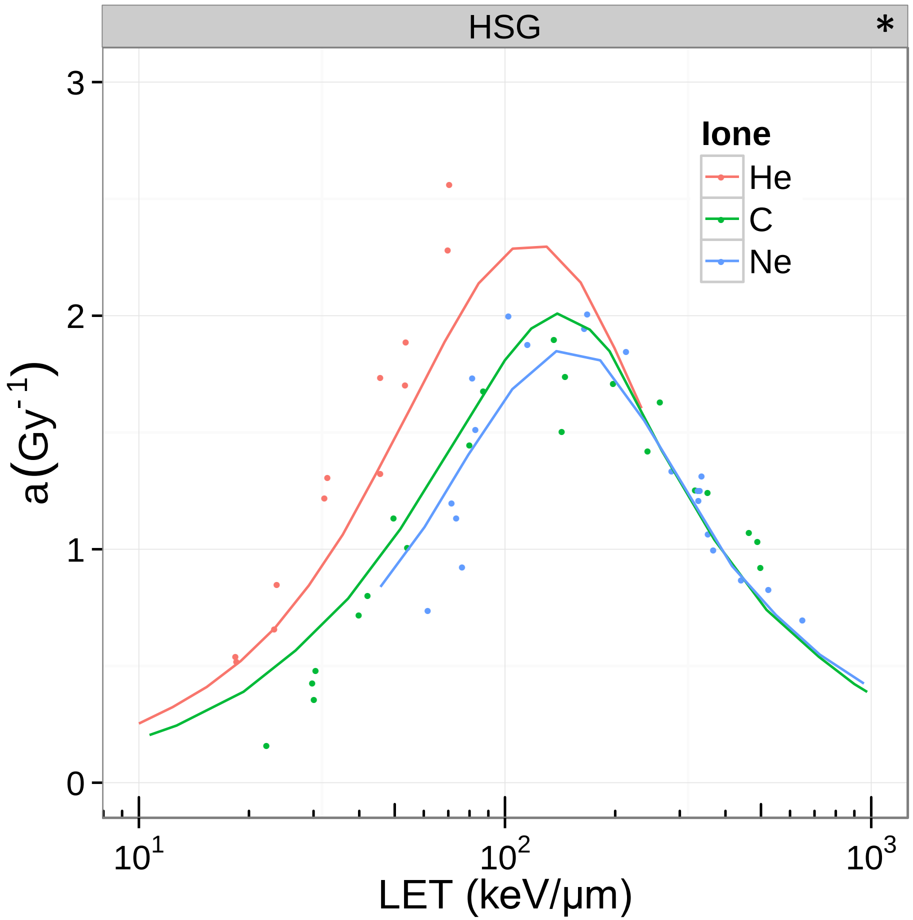
Purpose: To show the possible benefit achievable through the application of Inhomogeneous Fractional Dose distributions, comparing the effect of different primary ions.

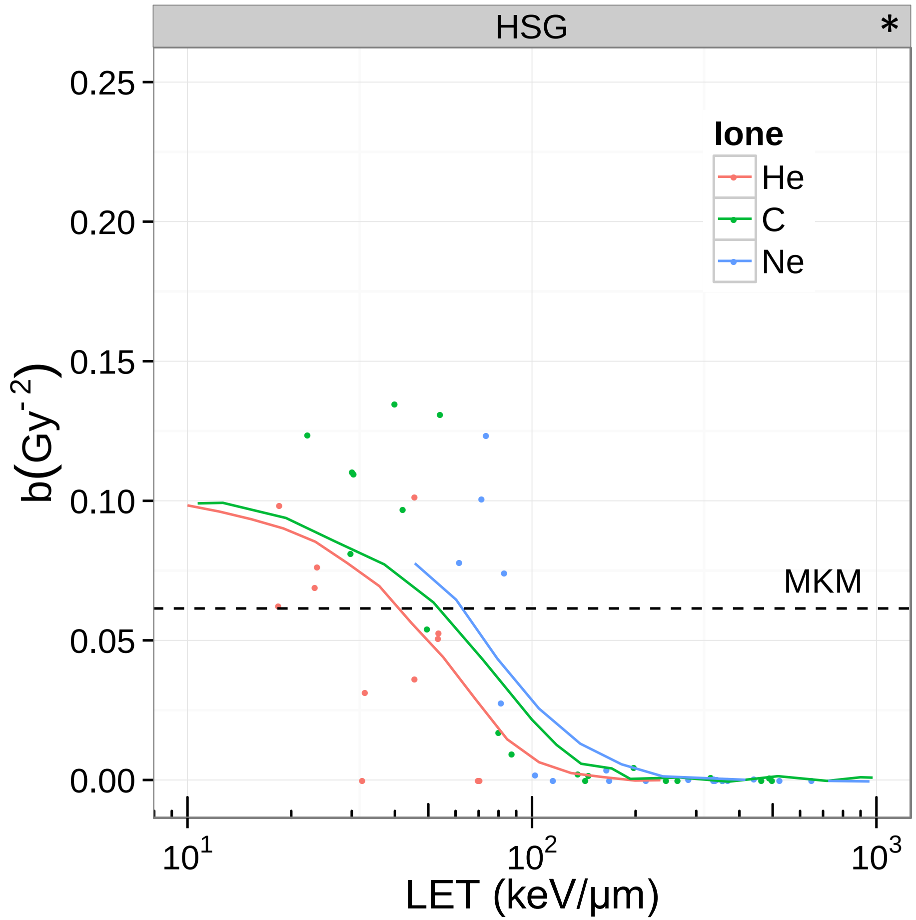
- Strong dependence on LQ parameters (α, β) variations in target
- Inadequacy of the standard BED (Biological Effective Dose) model: BED can't be defined due to the α dependence on the fractionation scheme:

$$\dot{D}_{vbt} \Rightarrow LET_{vt} \Rightarrow \begin{cases} \alpha_{v\{t\}} \equiv \tilde{\alpha}\{LET_{vt}\} \\ \beta_{v\{t\}} \equiv \tilde{\beta}\{LET_{vt}\} \end{cases}$$

v: voxel index
b: beam index
t: fraction index

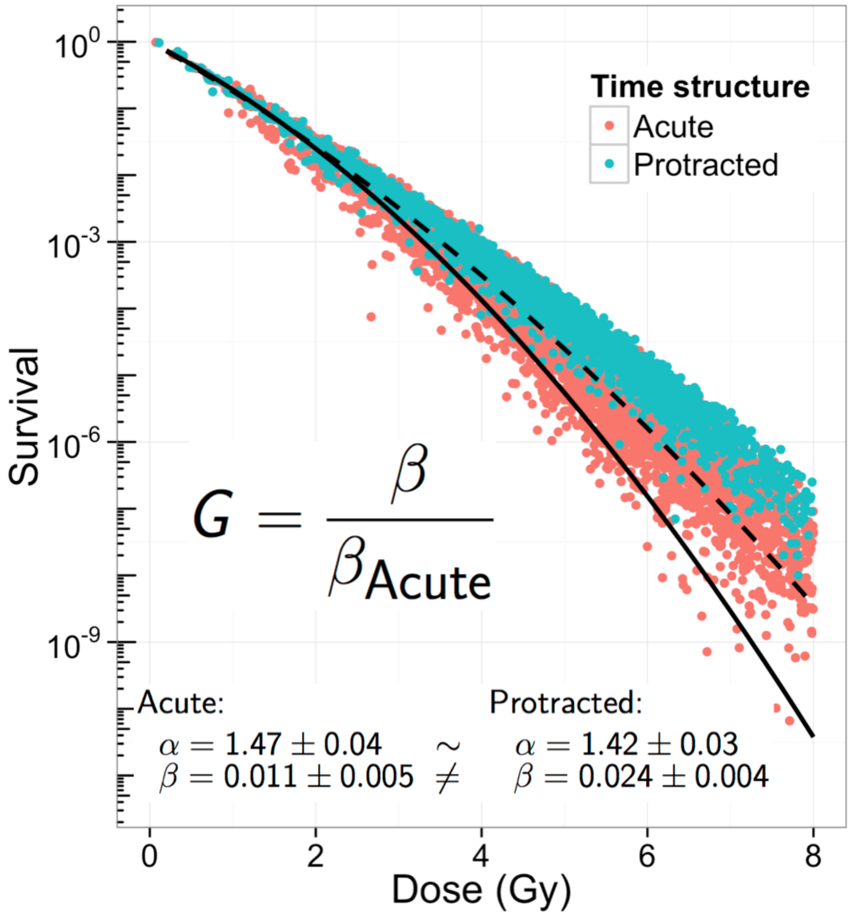
α & β Dependence on LET – MCt-MKM

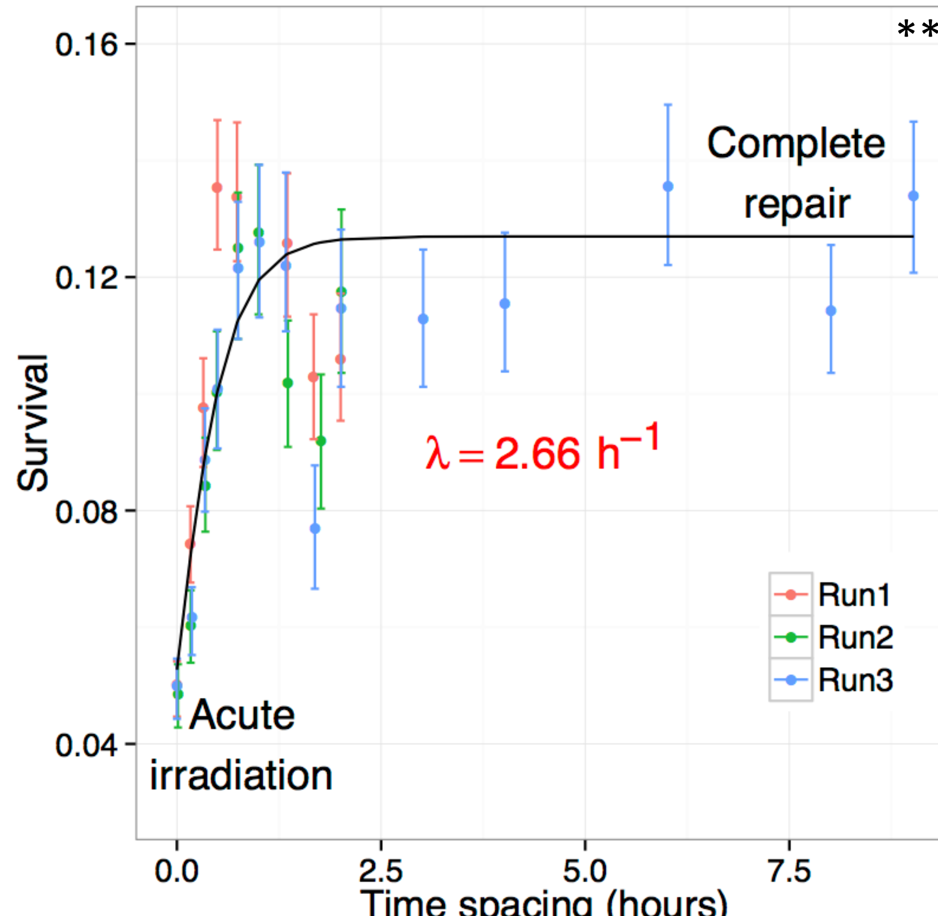




* L. Manganaro, 54° Annual Conference of PTCOG, San Diego (CA). Paper to be submitted.

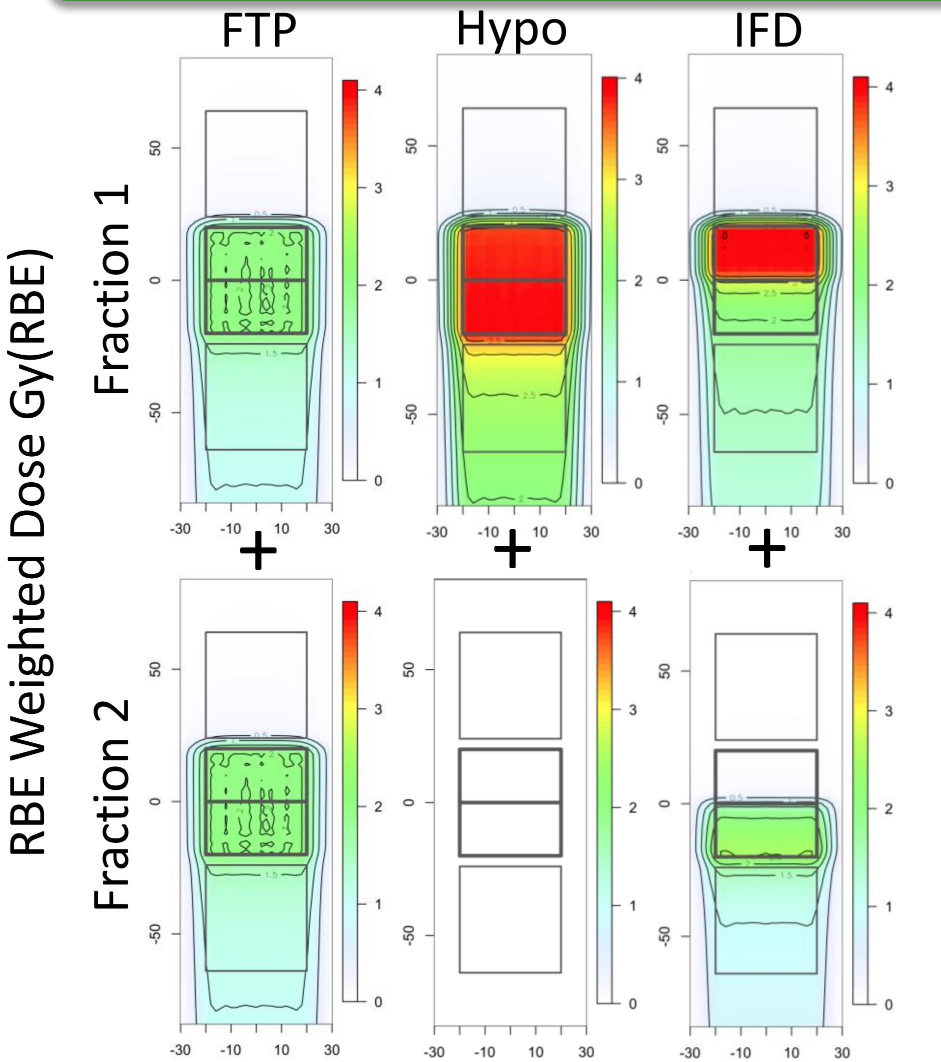
α & β Dependence on the Time Structure – MCt-MKM





** Experimental data from: Inaniwa *et al.*, Radiation Research, **180**(1): 44—59. 2013.

Fractionation Schemes Comparison



FTP (Full Target Plan): *

Fraction1 = Fraction2 = D = 2 Gy(RBE)

Target: PTV

Hypofractionation: *

Fraction2 = 0

Target: PTV

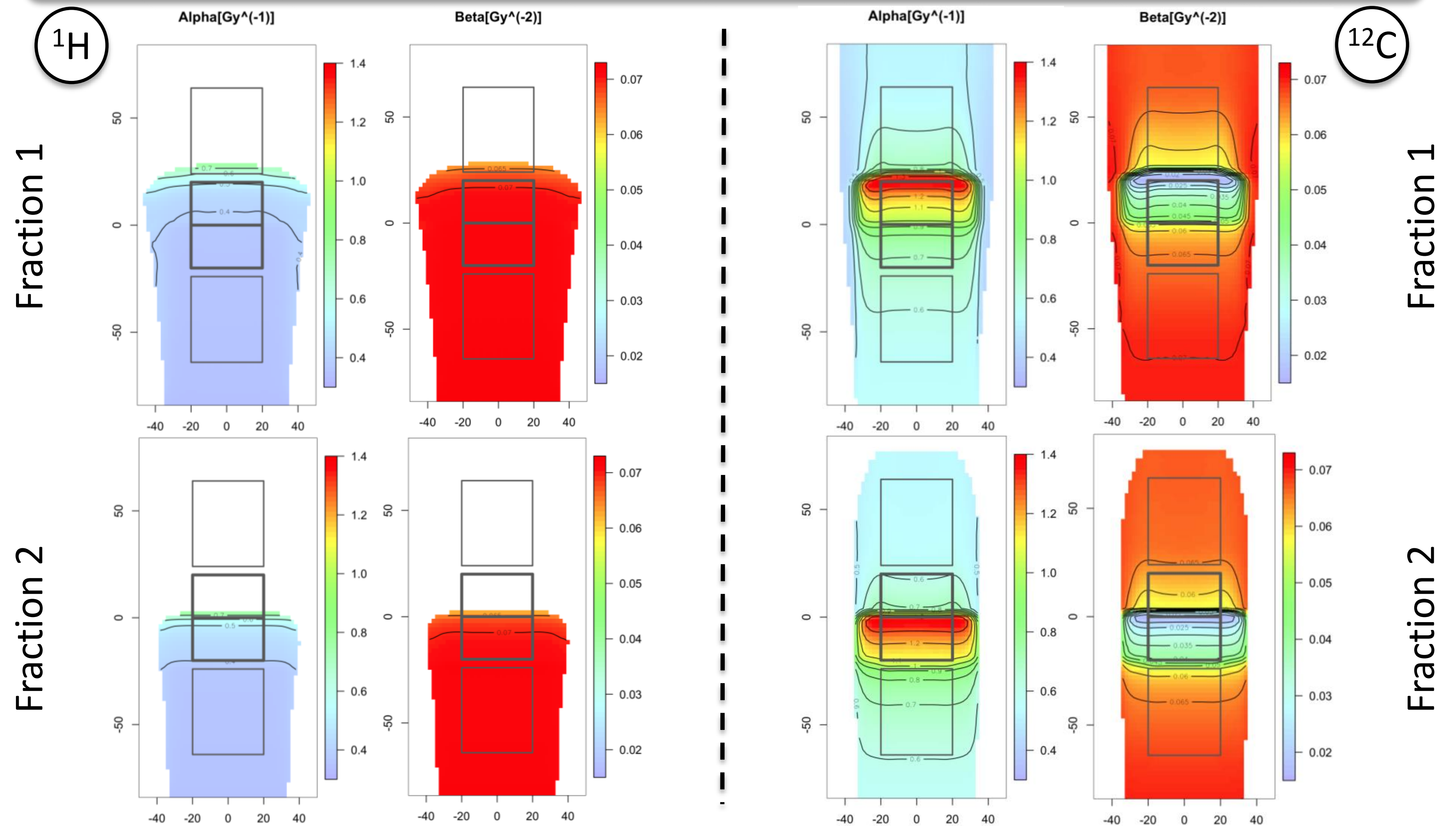
IFD (Inhomogeneous Fractional Dose): *

Fraction1 = D_p
Target: <u>Proximal</u> PTV subregion

Fraction2 = D_d
Target: <u>Distal</u> PTV subregion

* Plans evaluated using Rplanit, based on the TPS PlanKIT: Russo *et al.*, PMB, **61** (2016), 183—214

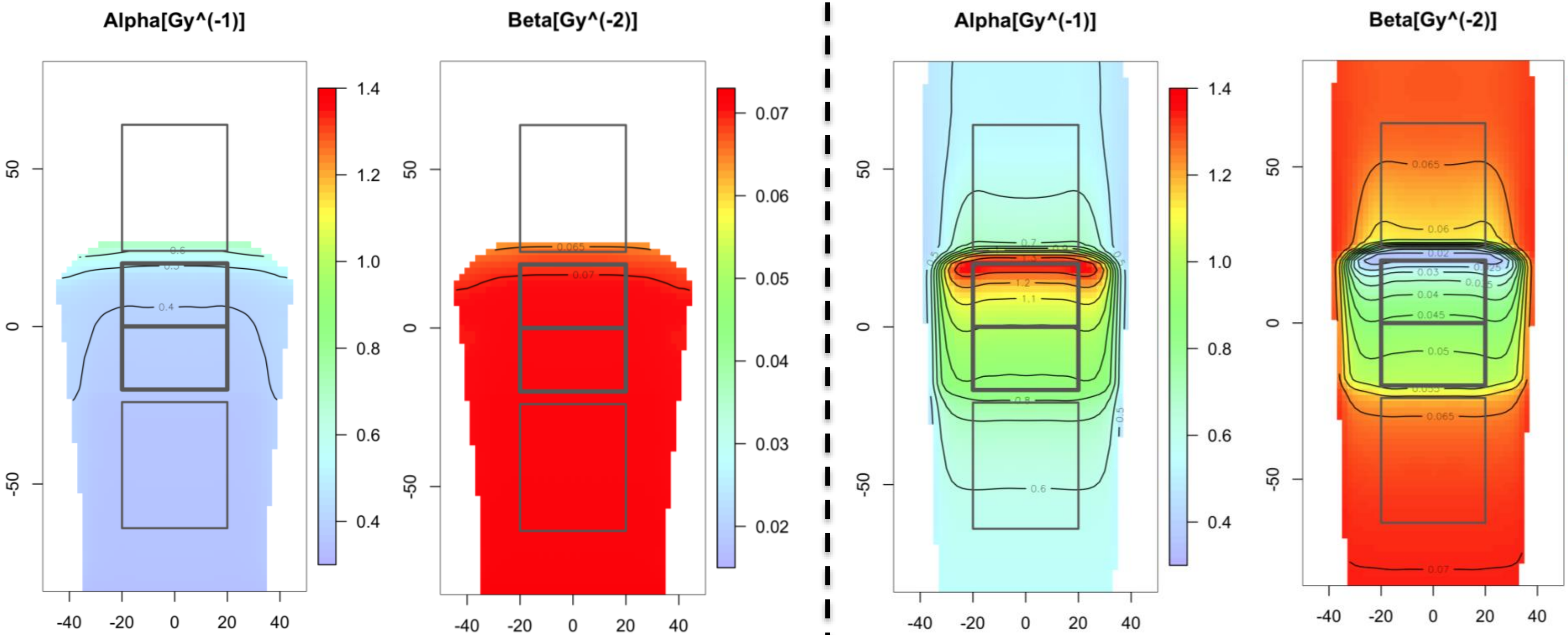
α & β Modulations



α & β Modulations

^{1}H ^{12}C

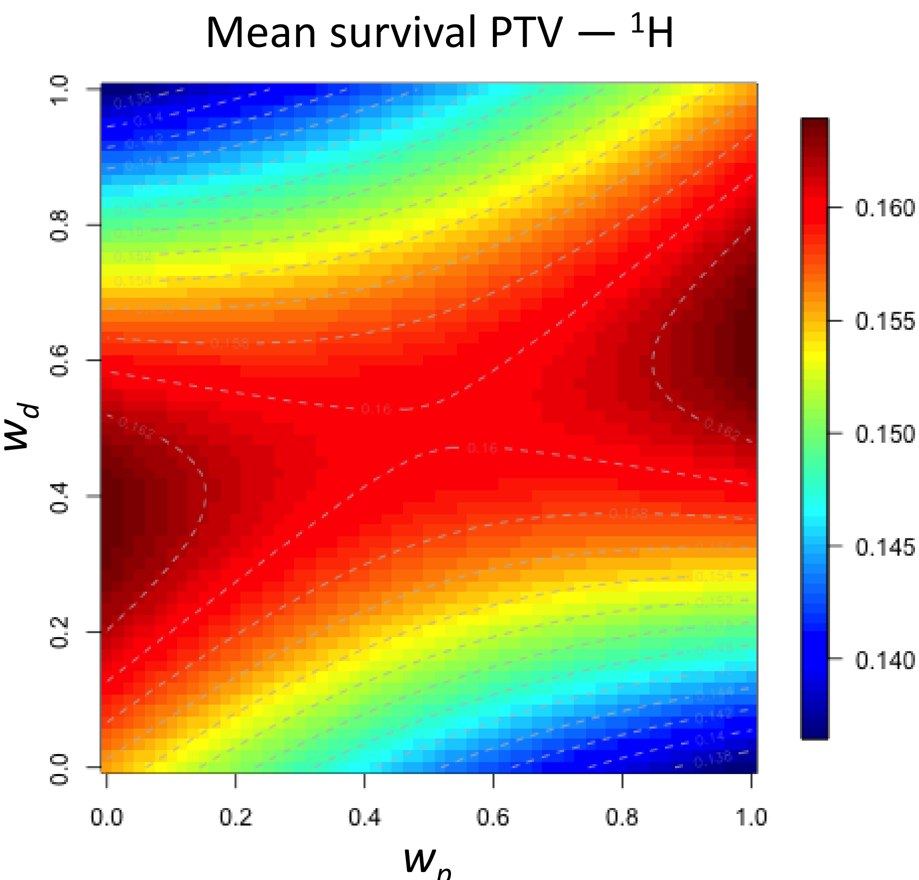
Combined Fractions — IFD



PTV: $\bar{R} = 5.7$ Gy
OAR1: $\bar{R} = 5$ Gy

PTV: $\bar{R} = 22$ Gy
OAR1: $\bar{R} = 9.6$ Gy

Weights variations



Fraction 1

$$w_n\left(w_p D_p + w_d D_d\right)$$

Fraction 2

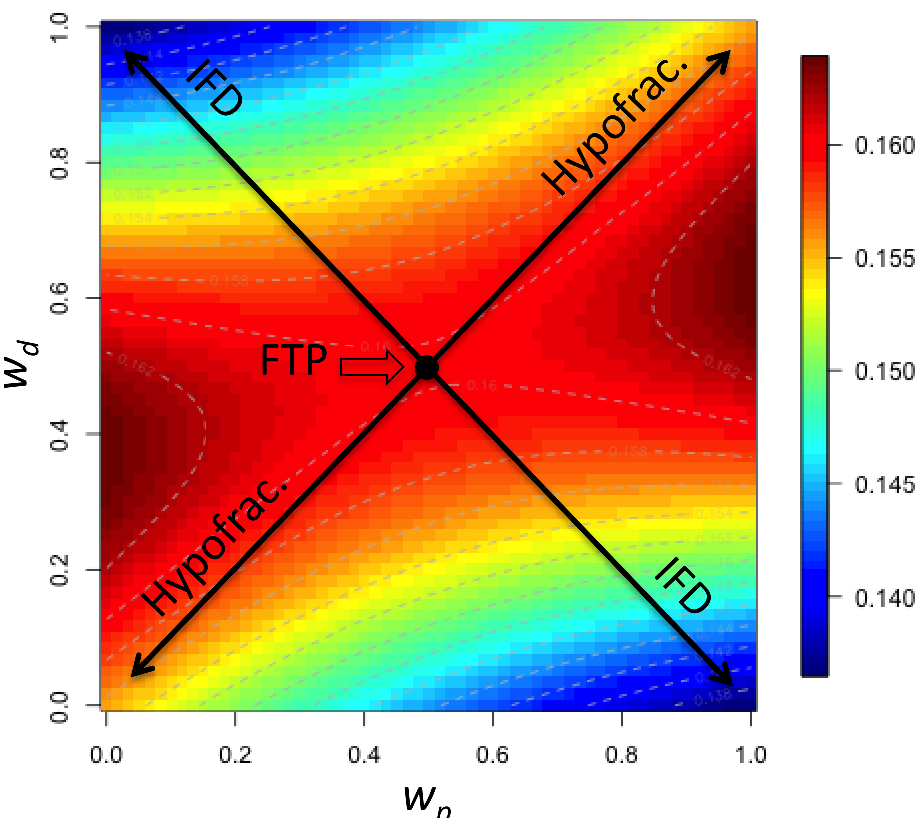
$$w_n\left[\left(1 - w_p\right)D_p + \left(1 - w_d\right)D_d\right]$$

Normalization:

$$w_n : \quad S_{OAR}^{IFD} = S_{OAR}^{Hypo} = S_{OAR}^{FTP}$$

Weights variations

Mean survival PTV — ^{1}H



Fraction 1

$$w_n\left(w_p D_p + w_d D_d\right)$$

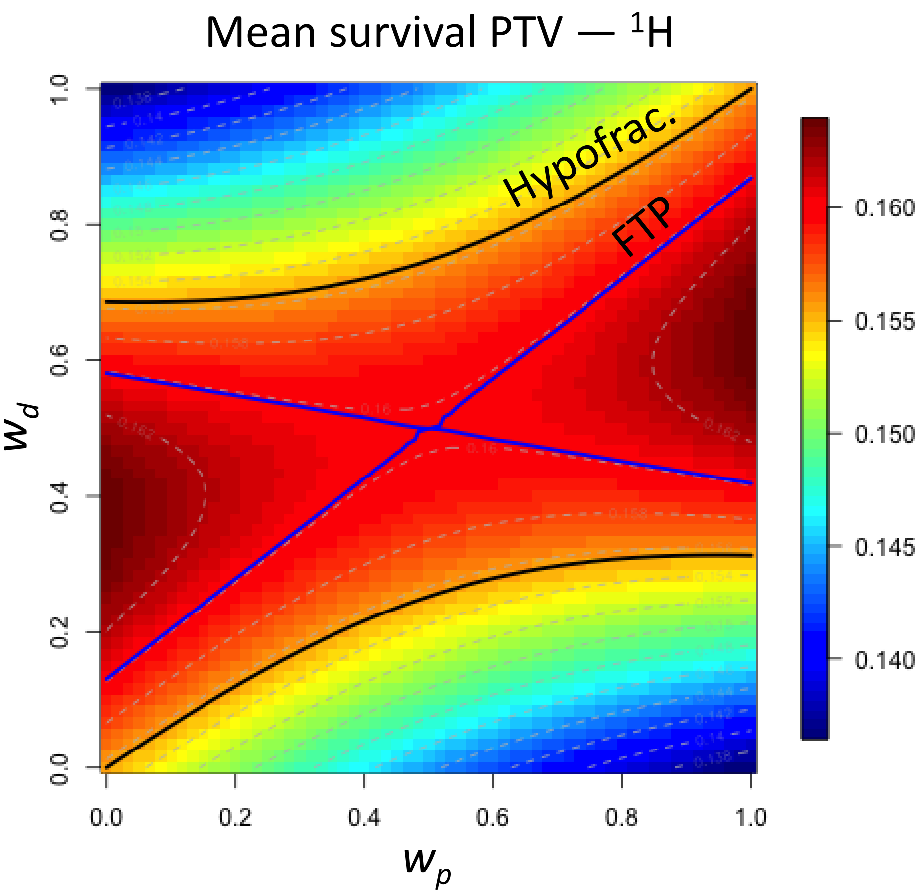
Fraction 2

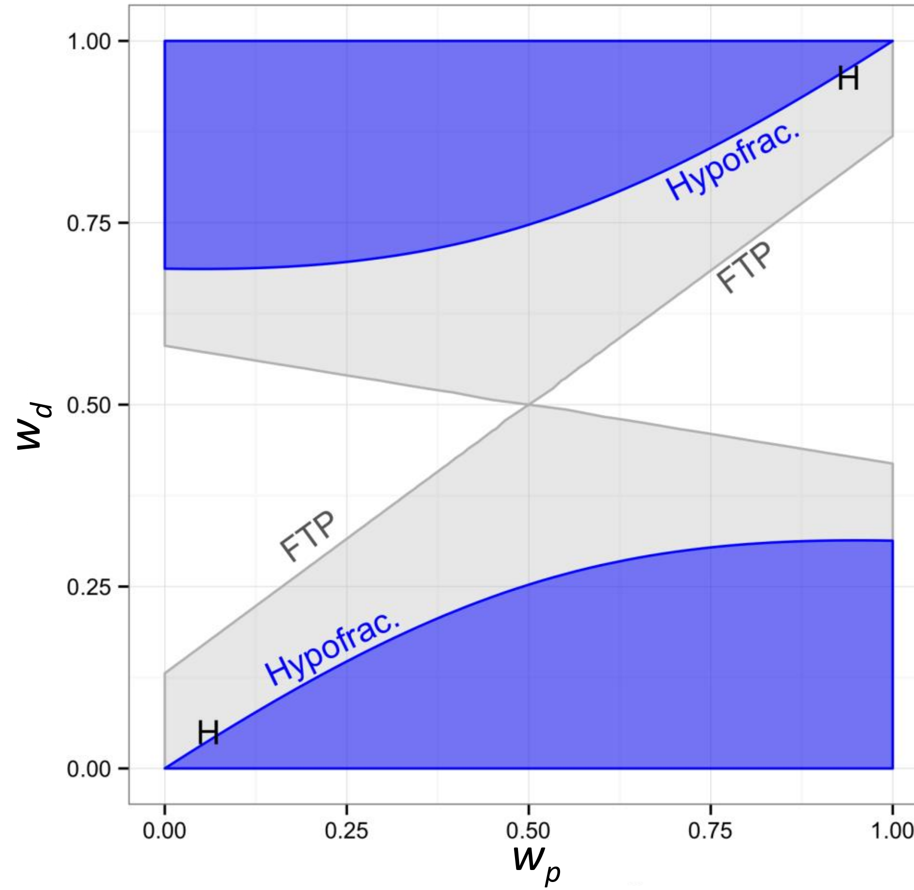
$$w_n\left[\left(1 - w_p\right) D_p + \left(1 - w_d\right) D_d\right]$$

Normalization:

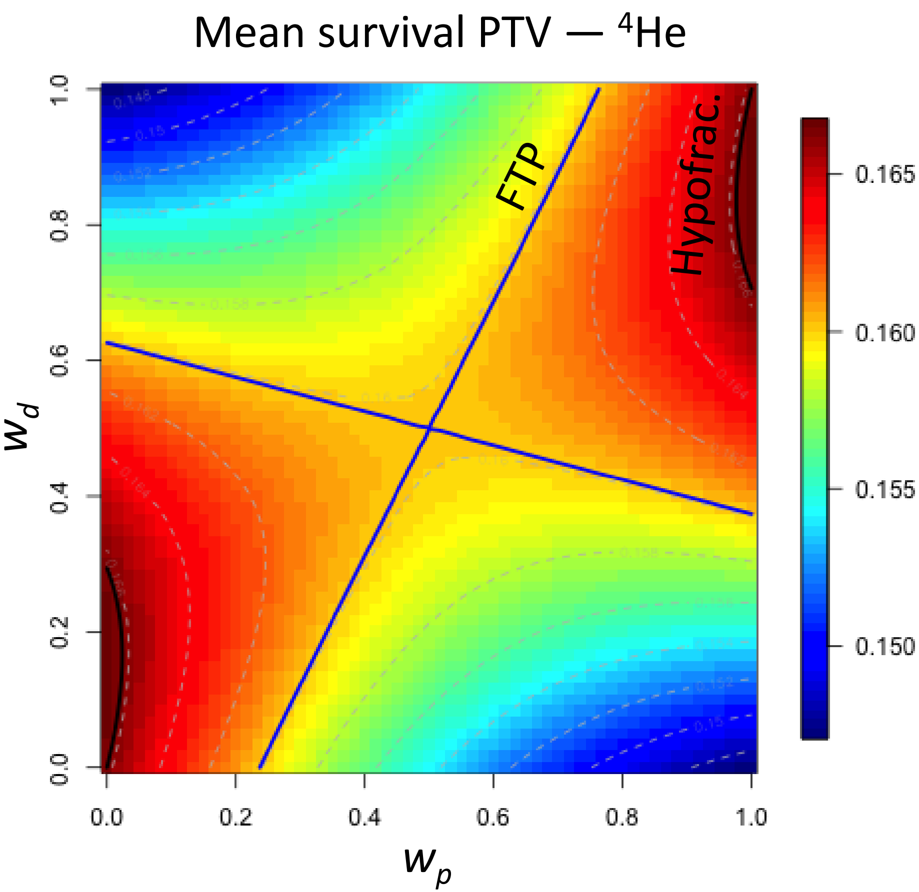
$$w_n : \quad S_{OAR}^{IFD} = S_{OAR}^{Hypo} = S_{OAR}^{FTP}$$

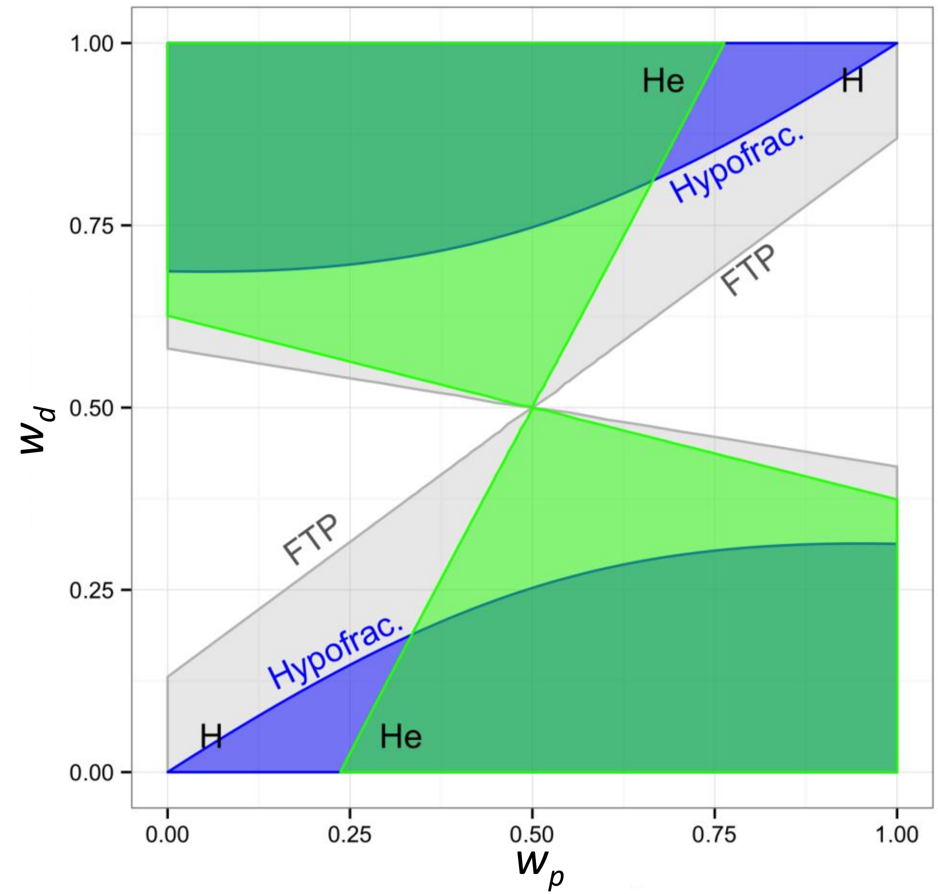
Fractionation Schemes Comparison – ^{1}H



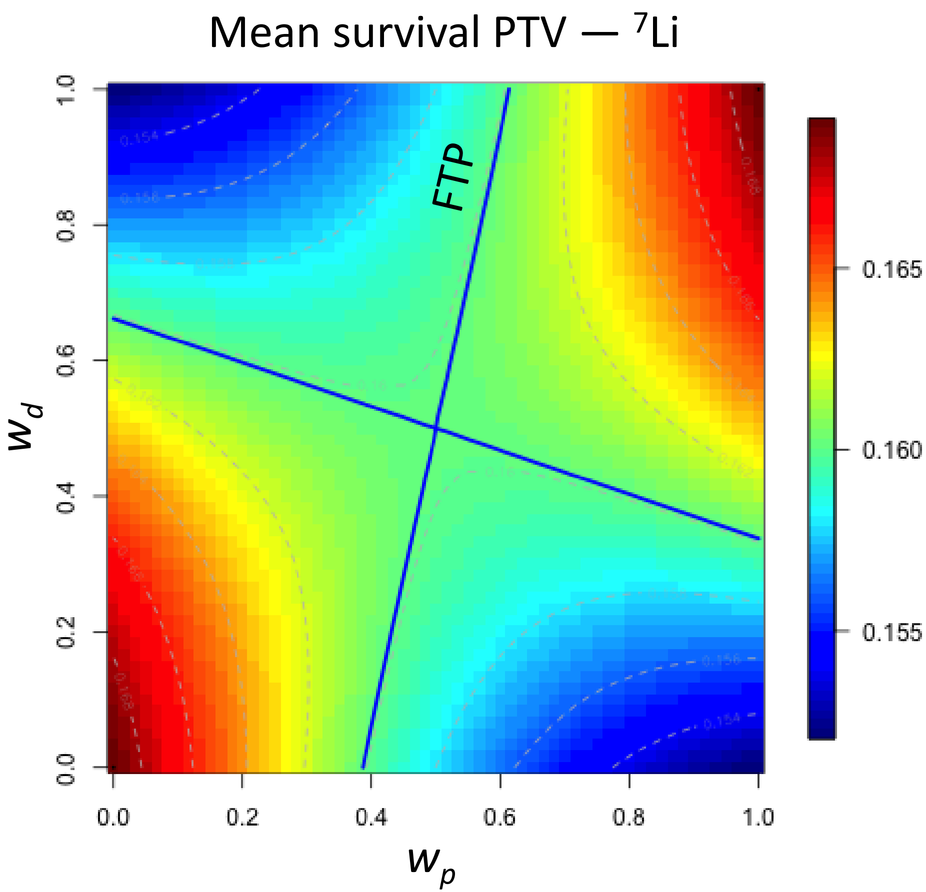


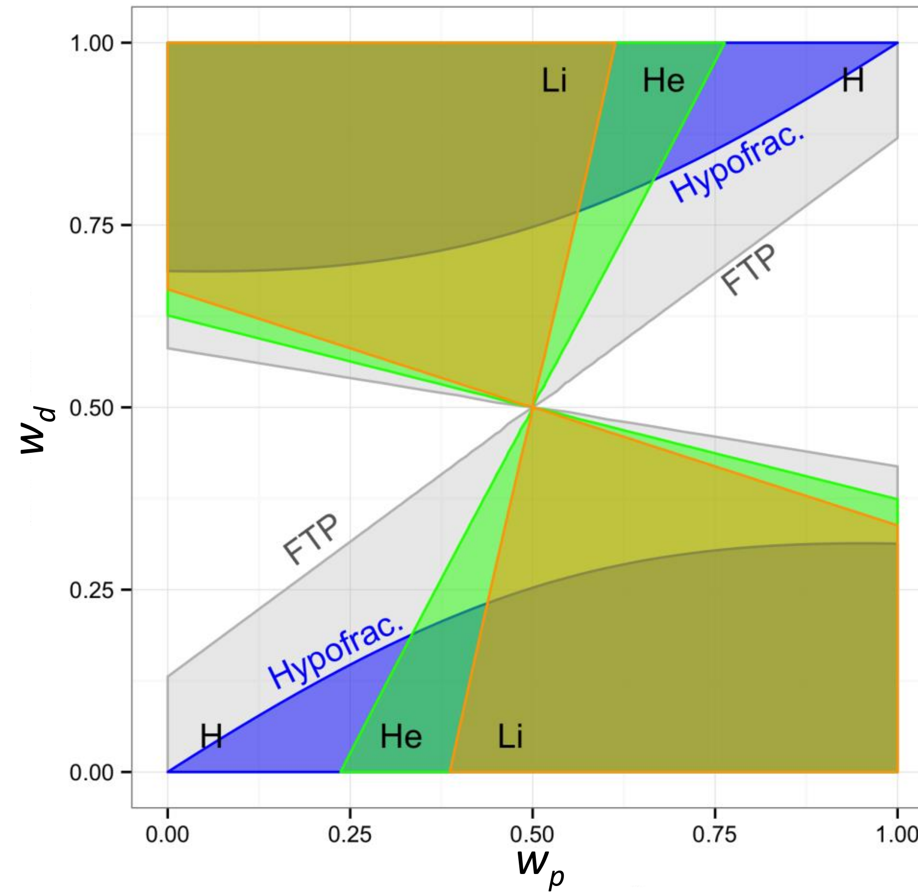
Fractionation Schemes Comparison – ^{4}He



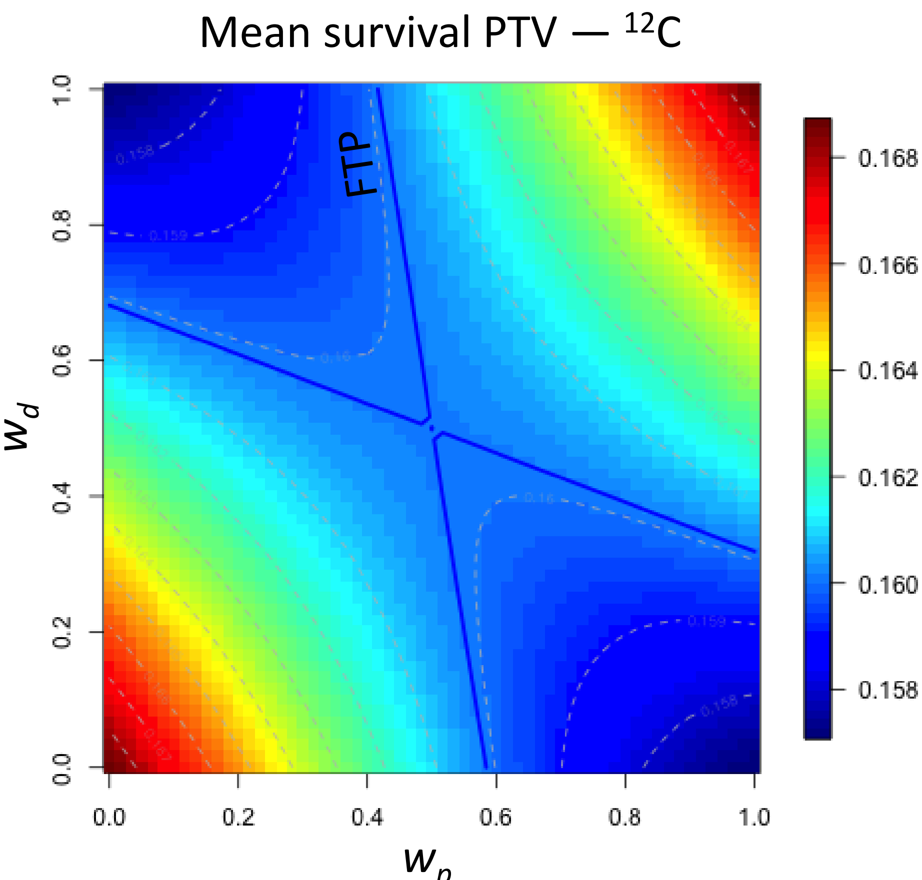


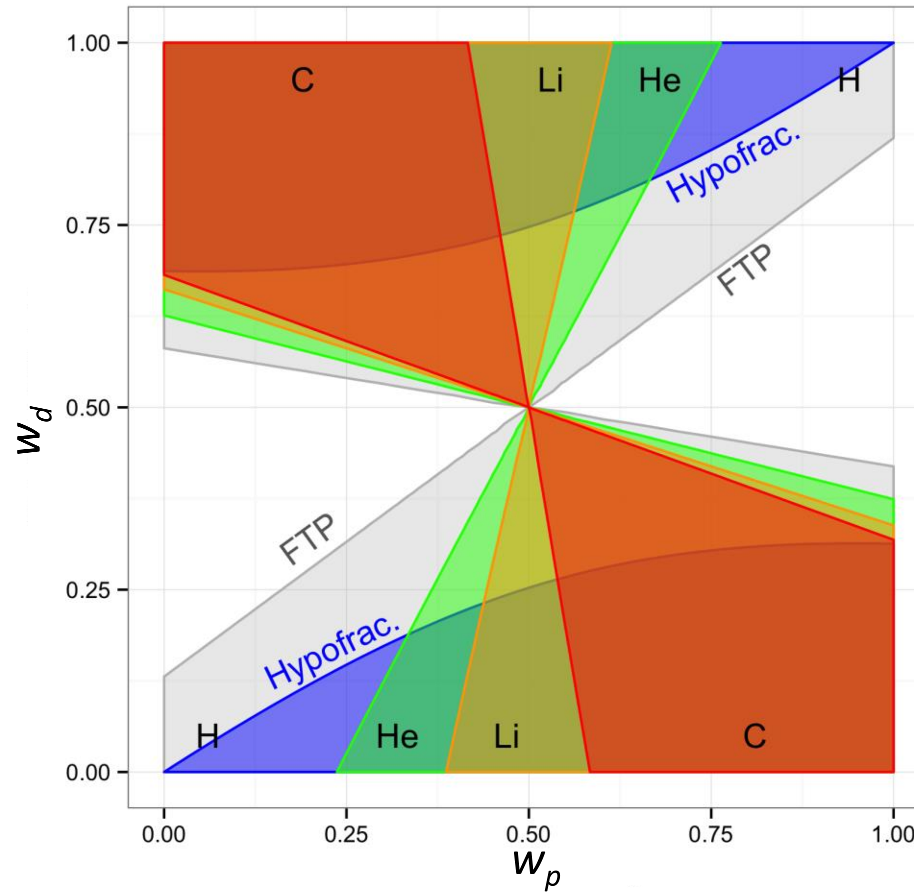
Fractionation Schemes Comparison – ^{7}Li



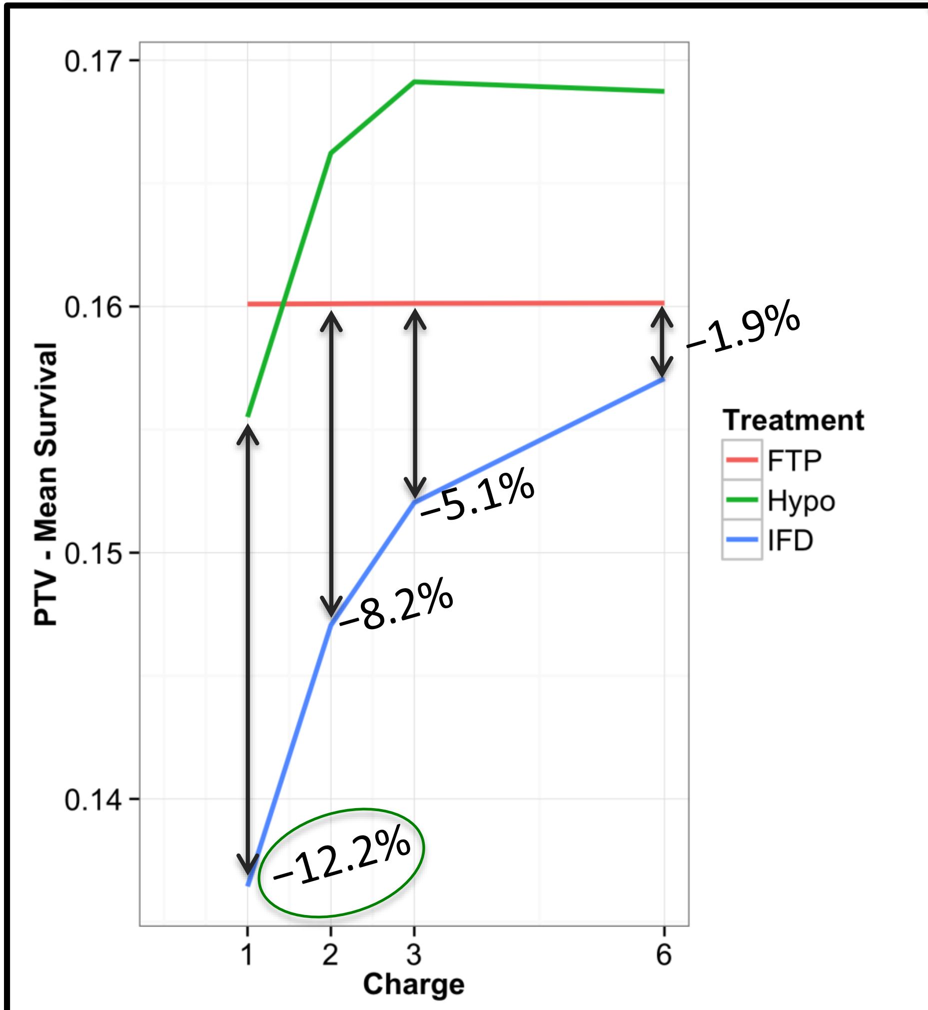


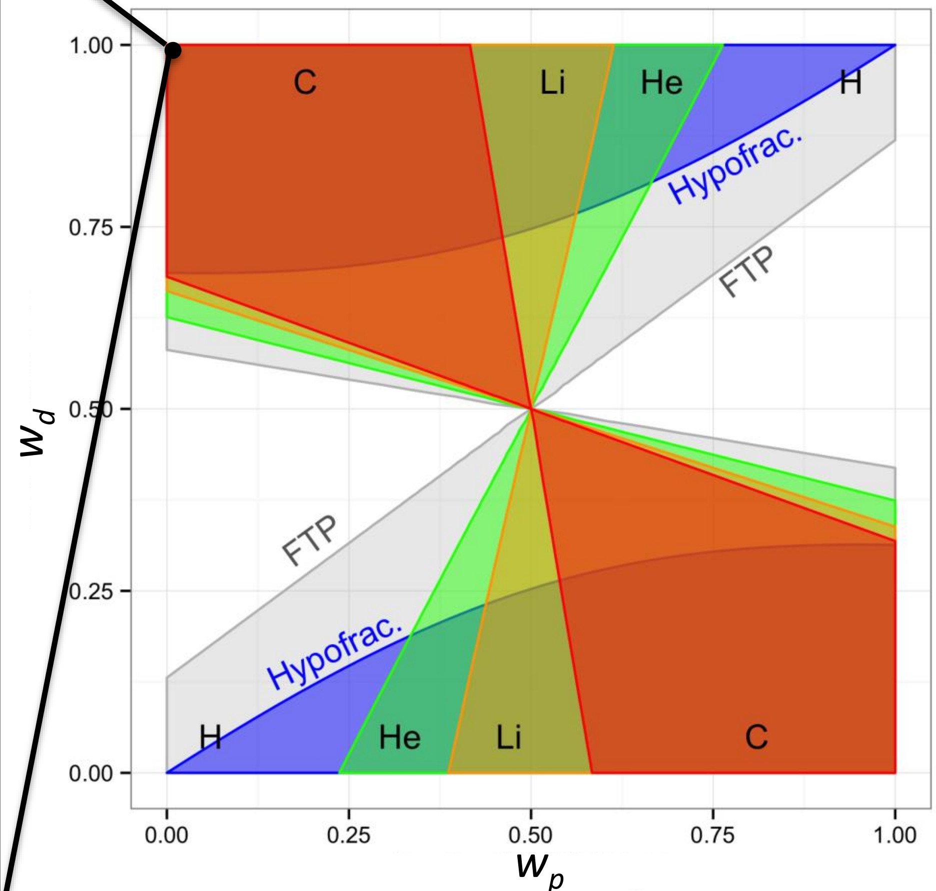
Fractionation Schemes Comparison – ^{12}C





Ions Comparison





Conclusions

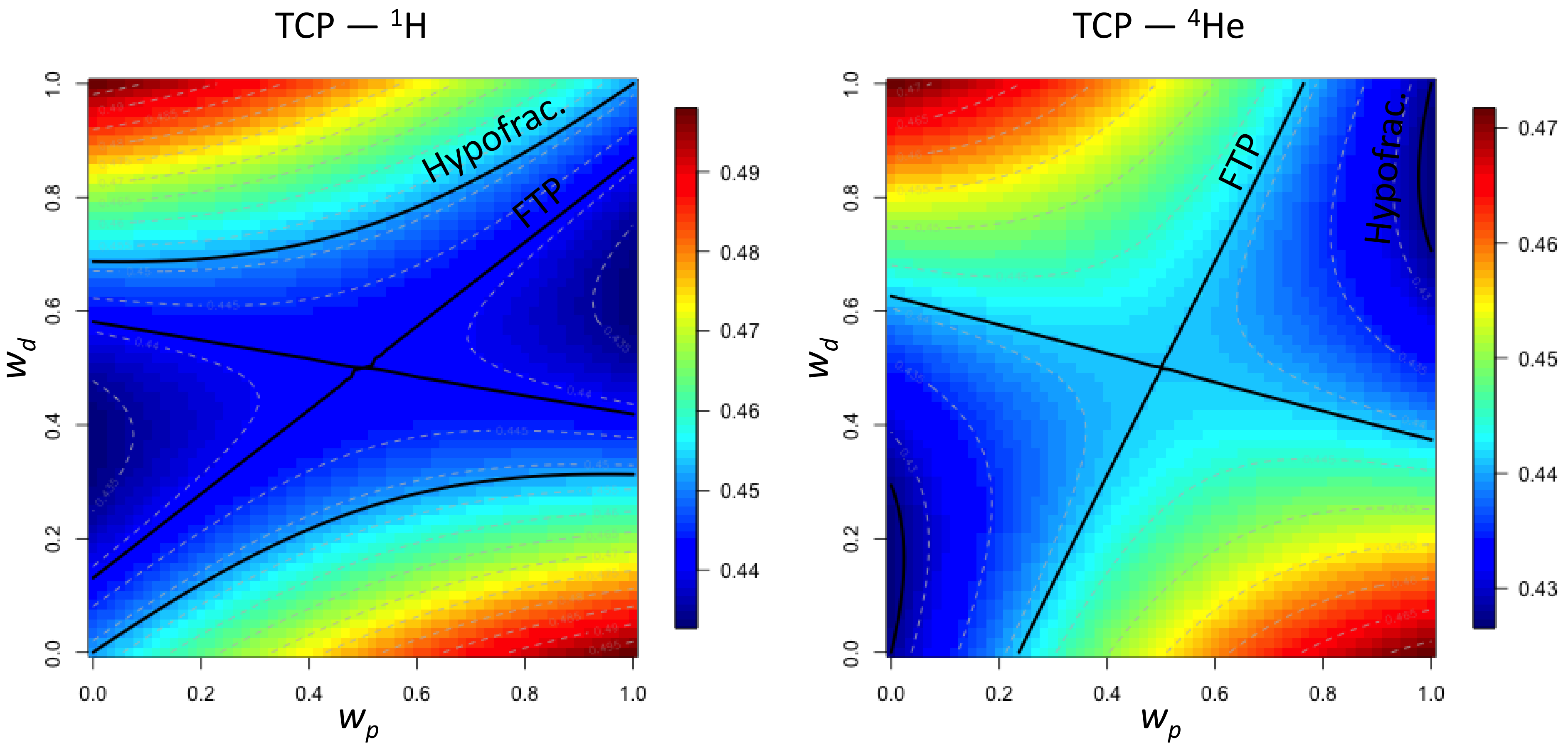
- The effectiveness of Inhomogeneous Fractional Dose distributions was proven
- A comparison between different ions showed a decrease of the effect with increasing LET (maximum benefit for protons)
- The effect is strongly dependent on α and β modulation in target: a complete biological model was introduced (MCt-MKM) to account for α and β spatio-temporal distributions.
- BED can't be defined due to the α variability from the fractionation scheme

Work in progress…
… Development of a pencil beam optimization algorithm to perform a systematic analysis of different clinical cases
… Tissue-dependent characterization
… Robustness analysis

Conclusions

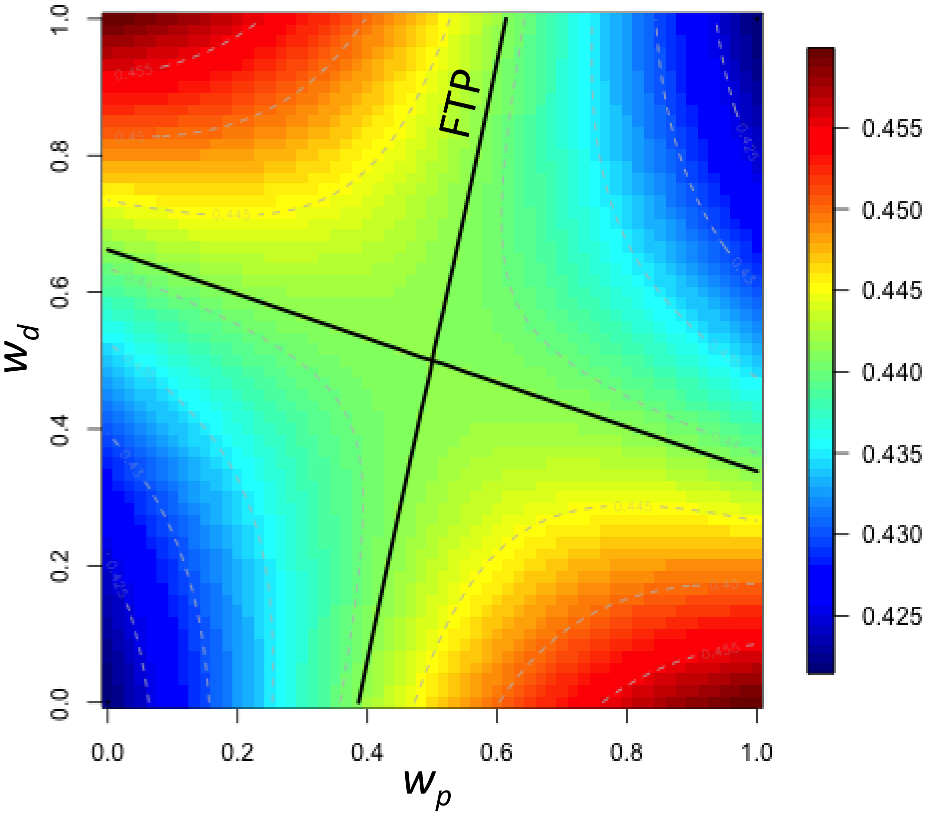
Thank you for your attention!

Spares...

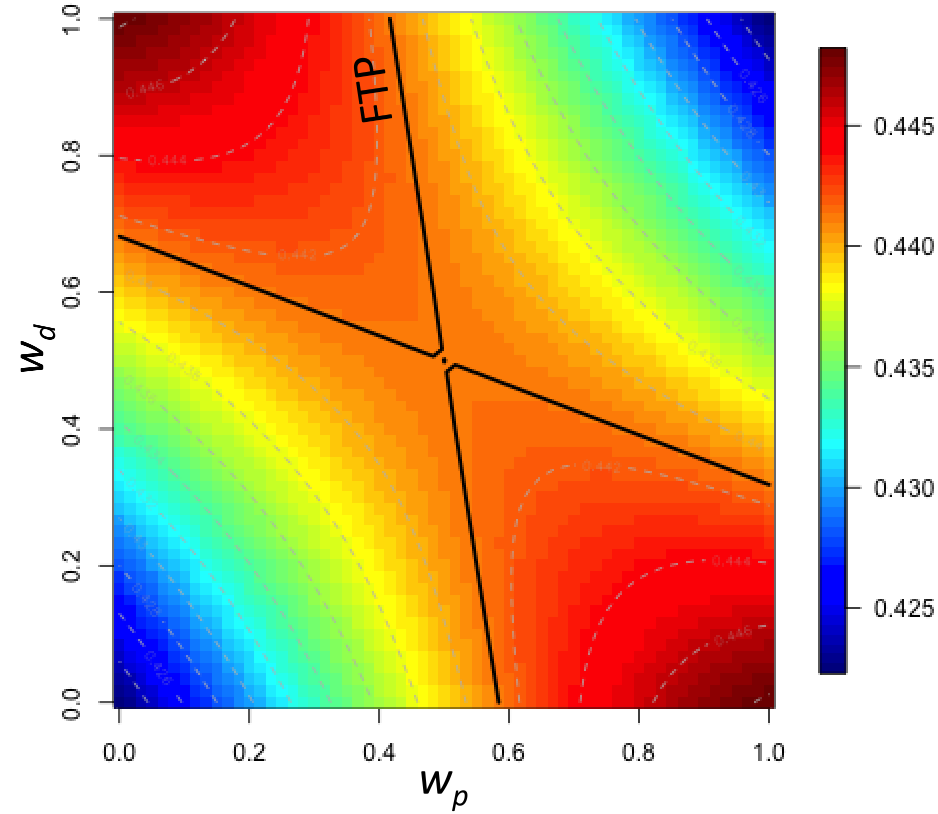

TCP — ^{1}H
Hypofrac.
FTP
w_d
w_p
0.0
0.2
0.4
0.6
0.8
1.0
0.49
0.48
0.47
0.46
0.45
0.44
TCP — ^{4}He
FTP
Hypofrac.
w_d
w_p
0.47
0.46
0.45
0.44
0.43

Spares…

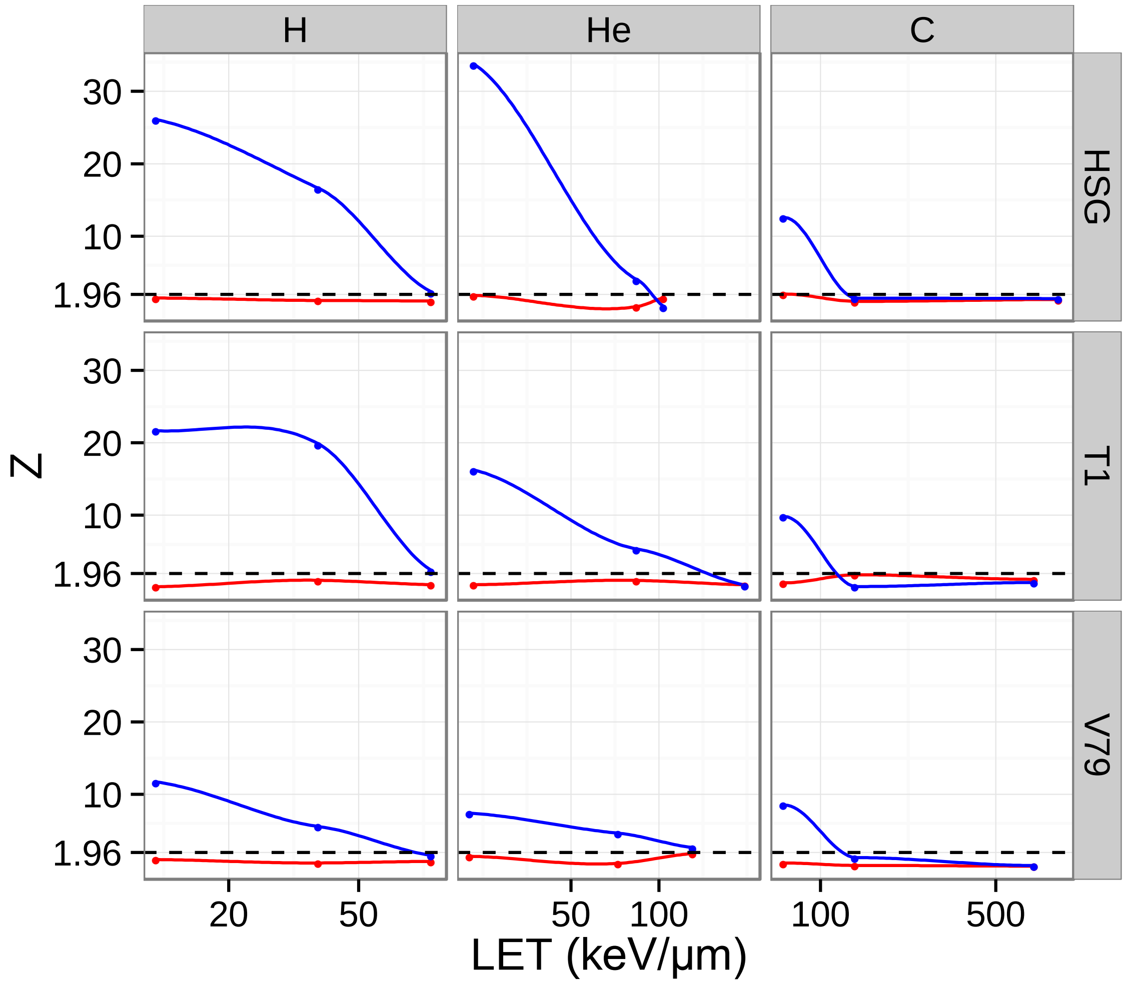
TCP — ^{7}Li



TCP — ^{12}C



Spares...



$$Z_x = \frac{\left| x_{\text{Acute}} - x_{\text{Protracted}} \right|}{\sqrt{s^2_{x_{\text{Acute}}} + s^2_{x_{\text{Protracted}}}}}$$

x Î $\{a, b\}$