Joint optimization of photon–carbon ion treatment plans

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Mixed modality treatments

CLEOPATRA protocol
Mixed modality treatments

CLEOPATRA protocol

Joint Opt
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)
Linear Quadratic model

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

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

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

\[ \varepsilon = n(\alpha d + \beta d^2) \]
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\[ \varepsilon = n(\alpha d + \beta d^2) \]
Challenges with Carbon ions: Carbon effective $\alpha, \beta$ 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)
Mixed Modality Radiotherapy and variable RBE models

\[
\begin{align*}
\text{min } f(w) &= \sum_n p_n f_n(w) \\
\text{Where } f_{\text{sqdeviation}} &= \frac{1}{N_s} \sum_{i \in S} (\varepsilon_i^{\text{Total}} - \hat{\varepsilon})^2 \\
\varepsilon_i^{\text{Total}} &= \left( n_\gamma (\alpha_\gamma d_\gamma + \beta_\gamma d_i^{\gamma}) + n_c (\alpha_{ic} d_{ic} + \beta_{ic} d_{ic}^{2}) \right), i \in V
\end{align*}
\]

The plans are optimized on the total biological effect.

**Photon Effect**

**Carbon Effect**
Proof of Concept

- Reproduce published results
  Unkelbach et al 2018

Fixed fraction allocation
- SBRT treatment
- Carbon ions: 1 fxn
- Photons: 4 fxn

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

- More conformal: additional degree freedom from both modalities

- Spatial distribution of fraction dose within the target
  
  = hypofractionation vs hyper fractionation
Impact of LQ model Parameter selection

- Without a fractionation benefit:
  \[ \frac{\alpha^T}{\beta^T} \leq \frac{\alpha^{NT}}{\beta^{NT}} \]

- joint optimization result is based on physical dose characteristics
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 $\alpha_T^T/\beta_T^T = 0.5/0.05$ (10Gy)
Healthy tissue $\alpha_{NT}^{NT}/\beta_{NT}^{NT} = 0.1/0.05$ (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) EQD2 Difference
(Reference plan – Jointly optimized plan)
Glioblastoma

- Implicit redistribution of LET
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
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
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
Thank you