FLASH Radiotherapy Optimization

TEAM 17

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1 Introduction

FLASH Radiotherapy (FLASH-RT) is a promising new modality delivering radiation at ultra-high dose rates ($> 40\,\mathrm{Gy/s}$) to minimize normal tissue toxicity while maintaining effective tumor control [2]. This optimization problem involves three key goals: (i) maximize tumor control probability (TCP), (ii) minimize normal tissue complication probability (NTCP), and (iii) ensure that irradiation satisfies FLASH dose-rate thresholds [3, 2].

2 Relevant Parameters from RadBioDB

The key fields used from the RadBioDB [1] for optimization include:

- **CellClass**: Tumor (t) or Normal (n) classification.
- **DoseRate (Gy/min)**: Rate of radiation delivery per minute.
- α **(Gy^{-1})**: Linear coefficient in the Linear-Quadratic (LQ) model.
- β **(Gy^{-2})**: Quadratic coefficient in the LQ model.
- **LET (keV/µm)**: Linear Energy Transfer (not primarily needed unless incorporating LET effects).
- **Energy (MeV)**, **Source**, **IrradiationConditions**: Assumed constant during modeling.

3 Mathematical Formulation

3.1 1. Survival Probability per Voxel

Based on the LQ model [4, 2]:

$$S_i = \exp\left\{\left(-\alpha_i D_i - \beta_i D_i^2\right)\right\} \tag{1}$$

where D_i is the dose to voxel i, α_i and β_i are the radiosensitivity parameters from RadBioDB.

3.2 2. Tumor Control Probability (TCP)

Assuming Poisson statistics for tumor clonogenic survival [4]:

$$\text{TCP} = \exp\left(-N_0 \prod_{i \in T} S_i\right) \tag{2}$$

where N_0 is the number of clonogenic cells in the tumor.

Alternatively, approximating:

$$\text{TCP} \sim \frac{1}{1 + (TCD_{50}/EUD_T)^{\gamma_{50}}} \tag{3}$$

where EUD_T is the Equivalent Uniform Dose to the tumor.

3.3 3. Normal Tissue Complication Probability (NTCP)

Using the Lyman-Kutcher-Burman (LKB) model [4]:

$$EUD_o = \left(\frac{1}{|O|} \sum_{i \in O} D_i^{n_o}\right)^{1/n_o} \tag{4}$$

$$\text{NTCP}_o = \frac{1}{2}\left[1 + \text{erf}\left(\frac{EUD_o - TD_{50,o}}{\sqrt{2} m_o TD_{50,o}}\right)\right] \tag{5}$$

where $TD_{50,o}$ is the tolerance dose for 50% complication probability.

3.4 4. FLASH Dose-Rate Satisfaction

To model FLASH satisfaction, define:[1]

$$\Omega(D_{rate}) = \frac{1}{|H|} \sum_{i \in H} \Theta(R_i - R_{thr}) \tag{6}$$

where R_i is the DoseRate field (converted to Gy/s).

3.5 5. Final Objective Function

Combining the above:[2, 3, 4]

$$\max_{D} \quad F = w_T \cdot \text{TCP} - \sum_{o} w_o \cdot \text{NTCP}_o + w_R \cdot \Omega(D_{rate}) \tag{7}$$

where w_T, w_o, and w_R are scalar weights adjusting priorities.

[1] Typical FLASH threshold: $R_{thr} \approx 40$ Gy/s [2]

4 Formulation in Terms of Dataset Parameters

Every voxel i uses:

- α_i, β_i $\rightarrow$ From RadBioDB.
- D_i $\rightarrow$ Decision variable.
- R_i $\rightarrow$ From DoseRate column.
- CellClass $\rightarrow$ Tumor (for TCP) or Normal (for NTCP/FLASH).

Thus,

$$S_i = \exp\left\{\left(-\alpha_i D_i - \beta_i D_i^2\right)\right\} \tag{8}$$

for TCP calculation, and

$$EUD_o = \left(\sum_{i \in O} D_i^{n_o}\right)^{1/n_o} \tag{9}$$

for NTCP calculation, and

$$R_i \geq R_{thr} \tag{10}$$

for FLASH condition.

5 QUBO Formulation

5.1 1. Binary Variables

- $x_i = 1$ if voxel i receives sufficient dose (tumor or organ).
- $y_i = 1$ if voxel i satisfies FLASH dose-rate condition.

5.2 2. TCP Term

$$\text{TCP} \sim \sum_{i \in T} x_i \tag{11}$$

5.3 3. NTCP Term

$$\text{NTCP}_o \sim \sum_{i \in O} x_i \tag{12}$$

5.4 4. FLASH Satisfaction Term

$$\Omega \sim \sum_{i \in H} y_i \tag{13}$$

5.5 5. Full QUBO Objective

$$\min_{\{x_i, y_i\}} Q(x, y) = -w_T \sum_{i \in T} x_i + \sum_{o} w_o \sum_{i \in O} x_i - w_R \sum_{i \in H} y_i + P(x, y) \tag{14}$$

where $P(x, y)$ includes penalty terms enforcing:

- Dose delivery constraints.
- FLASH constraint: $x_i = 1 \implies y_i = 1$.
- Minimum tumor coverage.

Penalty example for FLASH violation:

$$P_{FLASH} = \lambda \sum_{i \in H} (x_i - y_i)^2 \tag{15}$$

where λ is a large constant.

6 References

References

[1] G. L. L. Seuntjens *et al.*, "Encyclopedia of Radiation Oncology: Radiobiological Database for FLASH-RT", 2021.

[2] Favaudon *et al.*, "Ultrahigh dose-rate FLASH irradiation minimizes the side effects of radiotherapy," *Sci Transl Med*, 2014.

[3] Ramesh *et al.*, "FLASH radiotherapy treatment planning: considerations for clinical implementation," *Med Phys*, 2022.

[4] J. T. Lyman, "Complication Probability as Assessed from Dose-Volume Histograms," *Radiat Res*, vol. 104, 1985.