A Framework for Iso-toxic Adaptive Replanning Using Biophysical Models

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INTRODUCTION

MR-guided online adaptive radiotherapy (MRgOART) allows iso-toxic treatments, i.e., adjusting fraction target dose based on daily anatomic and/or biologic changes while maintaining the same doses for organs at risk (OAR). This work describes a framework for such an iso-toxic planning in MRgOART using biophysical models.

METHOD

This adaptive framework focuses on calculating biologically effective dose (BED) for the target (T) and the OARs based on the adaptive plan optimized based on the daily anatomy.

The fractional target dose is rescaled such that the same OAR doses are maintained. BED for each fraction is determined using the uncomplicated tumor control probability (UTCP):

$$UTCP=TCP\cdot(1-NTCP),$$

where TCP is tumor control probability and NTCP is normal tissue complication probability (see description below). Target and organ specific model parameters derived from published dose-response data are used in the calculation.

Data for representative SBRT for prostate and pancreatic cancer patients treated with MRgOART were used to demonstrate the utility of the proposed framework.

RESULTS

The proposed framework allowed to increase/decrease fraction dose based on anatomy change (e.g., OAR moved away from the target), and to estimate fraction doses for the remaining fractions considering total BED.

The ratio of daily UTCP to originally planned UTCP ranged from 0.960-1.116 & 0.967-1.127 for the prostate and pancreas cases, respectively.

Plan Prescription

D (Gy)	33
N	5
d (Gy)	6.6
Volume (%	95.6
α/β (Gy)	10

BED_{plan} (Gy) 54.78

fx #	fx_i	BED_{fx_i}	BED remain (Gy)	$BED_{running\_total}$ (Gy)	BED remain (%)	fxs_left @ $d_{planned}$	fxs_left @ $d_{changec}$
1	6.6	10.96	43.82	10.96	80.00	4.00	4.00
2	9.6	18.82	25.01	29.77	45.65	2.28	1.33
3	9.6	18.82	6.19	48.59	11.30	0.57	0.33
4	9.6	18.82	-12.62	67.40	-23.04	-1.15	-0.67
5		0.00	-12.62	67.40	-23.04	-1.15	
total			67.40				

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fx #	fx_i	ULD_{fx_i}	ULD remain (Gy)	$BED_{running\_total}$ (Gy)	ULD remain (%)	fxs_left @ $d_{planned}$	fxs_left @ $d_{changec}$
1	6.6	10.96	43.82	10.96	80.00	4.00	4.00
2	6.6	10.96	32.87	21.91	60.00	3.00	3.00
3	6.6	10.96	21.91	32.87	40.00	2.00	2.00
4	6.6	10.96	10.96	43.82	20.00	1.00	1.00
5	6.6	10.96	0.00	54.78	0.00	0.00	0.00
total			54.78				

Figure 1. In-house software program for Biological Effective Dose (BED) Calculations. Example iso-toxic adaptive calculations for situations when the plan is assessed on the daily reference MRI and the Organs At Risk (OAR) & Target are well separated that increase in dose is allowed for several fractions enabling TX to reach BED_{plan} (Table on left) or the daily anatomy is consistent with the planning MRI (Table on Right).

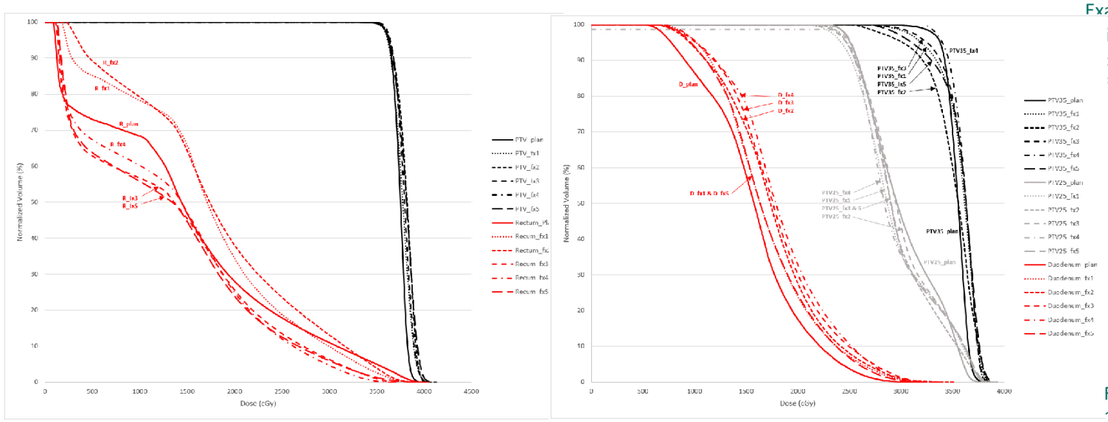

Figure 2. Prostate (figure on left) and Pancreas (figure on right) SBRT dose volume histogram (DVH). The radiation schedule for the prostate is 36.25 Gy in 5 fractions and 35 & 25 Gy in 5 fractions for the pancreas. The prostate DVH illustrates the daily variability in the rectum, which didn't influence a change in target coverage. The pancreas DVH illustrates the daily duodenum variability and the ensuing changes in target coverage.

		Target: PTV36.25Gy			Rectum				
		V(3625)	V(4350)	TCP	V(3806)	V(2900)	NTCP	UTCP	Ratio UTCP to $UTCP_{plan}$
Ideal		98%	0.0 cc		0.03 cc	15.00%			
Acceptable		95%	0.03 cc		1.00 cc	20.00%			
Plan	M1	95%	0 cc	93.00%	0.69 cc	12.27%	15.60%	84.400%	
	M1ADT03	93.80%	0 cc	93.67%	0.06 cc	11.49%	14.92%	85.691%	1.015
	M1ADT05	96.06%	0 cc	94.56%	0.08 cc	15.07%	19.71%	81.640%	0.967
	M1ADT07	96.78%	0 cc	94.13%	0.0 cc	7.59%	7.91%	93.206%	1.104
	M1ADT09	95.26%	0 cc	94.52%	0.0 cc	5.92%	6.38%	95.147%	1.127
	M1ADT11	96.19%	0 cc	94.68%	0.07 cc	7.15%	7.50%	94.171%	1.116

Figure 3. Prostate SBRT clinical plan (M1) and daily adaptive plan for fractions 1-5 (M1ADT03-11) DVH, tumor control probability (TCP), normal tissue control probability (NTCP) and uncomplicated tumor control probability (UTCP) values. Though most fractions were able to simultaneously increase target coverage without exceeding the plan NTCP value and indicates an improved therapeutic ratio (denoted as an UTCP ratio > 1). Additionally, the prescribed dose could have been increased to achieve the same level of NTCP (i.e. maintain same iso-toxic level adaptive planning) as the clinically approved plan. However, the second fraction (M1ADT05) the rectum's NTCP score was higher than plan indicates an increased risk of toxicity, which resulted in a decreased therapeutic ratio (denoted as an UTCP ratio < 1). This fraction could benefit from a dose reduction to the same NTCP level as the plan (i.e. maintain same iso-toxic level in adaptive planning).

CONCLUSIONS

A framework for iso-toxic adaptive planning is developed to account for biological effect of different fraction doses and to optimize the therapeutic ratio in MRgOART.

REFERENCES

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