ProtOes: Consideration of interplay effects for the proposed oesophageal trial

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Background

Neoadjuvant chemoradiation prior to definitive surgery in locally advanced oesophageal cancer has shown improved outcomes in the CROSS trial. However, the anatomical position, size and proximity of the tumour to surrounding structures, poses a conundrum as there is a high integral dose to neighbouring organs, which may translate to an increased perioperative risk and worse long term outcomes.

ProtOes is a randomised, multi-centre phase II study, comparing protons and photons, which aims to evaluate a reduction in normal tissue toxicity whilst maintaining efficacy of delivering concurrent chemotherapy with hypofractionated treatment of 40Gy in 15#.

Methods

In preparation for the UK-based trial – ProtOes, a comparison of treatment plans with photons and protons was made in a patient with 'flip-flop' oesophageal tumour (as would represent extreme motion). The interval target volume (ITV) was delineated over ten 4DCT phases. One posterior and two posterior oblique single field optimisation (SFO) plan with pencil beam scanning was created on the maximal exhalation phase (MEP). For proton planning, CTVB and ITV target statistics have been evaluated under 0.3cm setup and 3.5% range uncertainty. Velocity 4.0 was used to study the effect of respiratory motion and change in water equivalent thickness (WET). The nominal proton plan with repainting was recalculated on each phase's adaptive CT and the dose was deformed back to MEP, equally summed and combined to approximate the dose over a free breathe treatment. The effect of interplay was studied by taking into account spot delivery time and breathing rate in seconds.

The V99 and V2 doses vary by ~1Gy from the original plan on the maximum exhale phase, particularly reducing the dose inferiorly (as shown by the arrow in Figure 1) due to the moving OAR. The ITV and CTVB are well covered by the 95% isodose.

Results

As shown in Table 1 and 2, the target doses between photons and protons were comparable, but reduced dose to the heart, liver and lung with protons. Photon plan used average 4DCT whereas proton plan used maximum exhale for planning, so table below are only representative of likely differences in dose statistics.

Structure	Volume	Photons (%) 41.4Gy/23#	Protons (%) 41.4Gy(CGE)/23#
ITV	99%	98.0	98.8
	95%	98.4	99.2
	Mean	100.3	100.0
PTV	99%	96.8	96.7
	95%	97.8	98.7
	Mean	100.0	99.9

Table 1 Difference in target doses between photons and protons, planned for 41.4Gy in 23# for comparison.

Structure	Statistic	Dose Constraints	Dose achieved		Units
			Photons	Protons	
Lungs	V20	<20%	12.1	6.8	%
	Mean	<1500cGy	1113.3	427.8	cGy
Heart	V30	<45%	18.1	8.1	%
	Mean	<2500cGy	1923.4	546.3	cGy
Liver	V30	<30%	14.4	6.9	%
	Mean	<2800cGy	1863.1	547.6	cGy
Spinal Cord	D 0.1cc	<2800cGy	2197.7	2273.8	cGy

Table 2 Difference in OARs statistics between photons and protons.

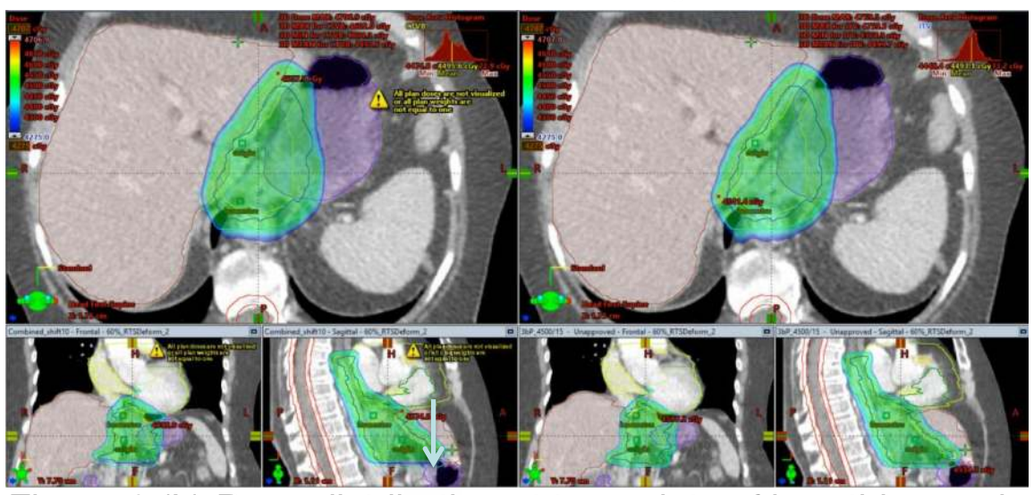

Figure 1 (L) Dose distribution at ten points of breathing cycle (R) Nominal plan on maximum exhale phase. Dose colour wash represents 95% isodose. ITV in blue, CTVB in yellow, PTV in light blue.

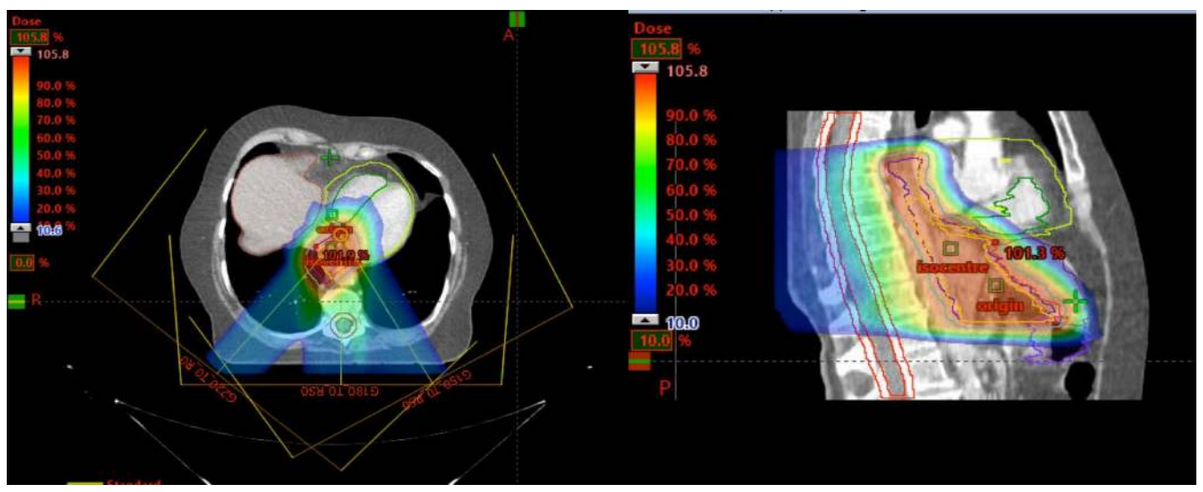

Figure 2 Field arrangement for proton plan – anterior field avoided due to uncertainty in chest movement and dose to lung. Dose colour wash represents 10% isodose. ITV in blue, CTVB in yellow, PTV in light blue.

Conclusion

This study describes a methodology to account for tumour motion in plan robustness considerations in the treatment of oesophageal cancer and may be applied to a hypofractionated treatment schedule. Further cases are being studied in order to validate this approach.