Dosimetric outcomes of ultra-hypofractionated adaptive MR-guided SABR for pancreatic cancer: EMERALD Phase 1 trial

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Introduction

Pancreatic cancer is one of the most aggressive malignancies, with poor survival rates. Considering that one in three patients with locally advanced pancreatic cancer (LAPC) succumb primarily to local progression, alongside recent improvements in systemic therapies, local control is likely to become increasingly important.

In this context, stereotactic MR-guided adaptive radiotherapy (SMART) has emerged as a promising treatment option. Daily online treatment adaption, real-time tumour tracking, and beam gating have enabled doses of 50 Gy in 5# to be safely delivered, with dosimetric and clinical benefits being demonstrated (1).

Leveraging the strengths of SMART, the EMERALD trial evaluated dosimetric impact of SMART in pancreatic cancer, using five, three and single ultra-hypofractionated schedules (2).

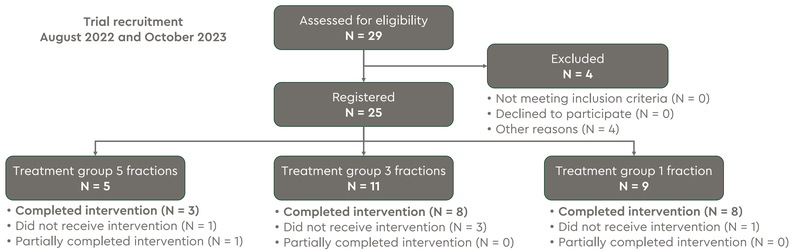
Material and methods

This was a single-centre, three-arm, phase 1 non-randomised safety study. Patients with localised or locally recurrent pancreatic cancer were treated with SMART at one of three different dose levels:

- Level 1: 50 Gy in 5 fractions (BED_{10} = 100 Gy)
- Level 2: 39 Gy in 3 fractions (BED_{10} = 90 Gy)
- Level 3: 25 Gy in a single fraction (BED_{10} = 87.5 Gy)

All patients were treated SMART a 0.35 T MR-guided linac (ViewRay Systems Inc., MRIdian, OH, USA). During the on-set adaptive process, contours were adjusted and a reoptimised plan calculated to meet dose constraints whilst maximizing target coverage on the daily anatomy. This resulted generating three plans for each treatment fraction:

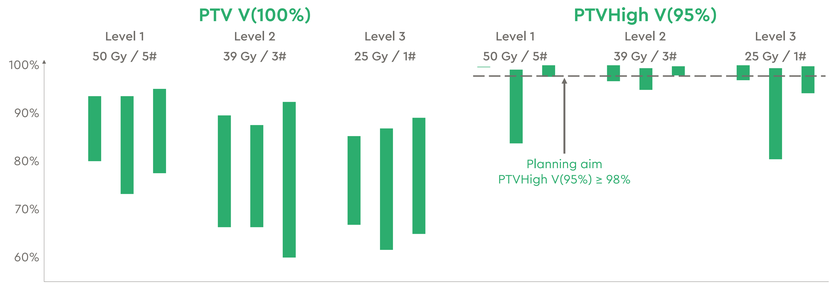
- Baseline plan (BP) was created off-line from the simulation image
- Predicted plan (PP) generated by recalculating the baseline plan onto the patient's anatomy of the day
- Reoptimised plan (RP) produced as an online adaptive plan based on anatomy of the day



Dosimetric benefit

Differences between baseline, predicted, and re-optimized SMART plans were assessed by comparing changes in PTV V(100%) and PTVHigh V(95%). Additionally, gross tumour volume (GTV) and planning target volume (PTV) coverage within the BED_{10} 70 Gy isodose line were analysed. Dosimetric data was available from 37 delivered fractions.

PTV and PTVHigh coverage from baseline, predicted and adapted plans



	PTV V(100%)									PTVHigh V(95%)								
	Level 1 50 Gy / 5#			Level 2 39 Gy / 3#			Level 3 25 Gy / 1#			Level 1 50 Gy / 5#			Level 2 39 Gy / 3#			Level 3 25 Gy / 1#		
	BP	PP	RP	BP	PP	RP	BP	PP	RP	BP	PP	RP	BP	PP	RP	BP	PP	RP
Min	80.0	73.2	77.5	66.3	66.3	60.0	66.8	61.6	64.9	99.5	83.7	97.5	96.6	94.8	97.8	96.8	80.4	94.1
Mean	88.3	85.1	84.3	82.9	82.4	86.3	77.5	67.9	72.7	99.8	96.8	99.7	99.4	97.6	98.8	99.3	94.8	97.0
Max	93.5	93.5	95.0	89.5	87.5	92.3	85.2	86.8	89.0	99.6	99.0	99.9	99.9	99.3	99.7	99.9	99.3	99.7

Detailed dosimetric data from analysis of all available fractions

	GTV $V(BED_{10}70)$% median (range)		PTV $V(BED_{10}70)$% median (range)		GTV (cc) mean (range)		PTV (cc) mean (range)	
	Predicted	Reoptimised	Predicted	Reoptimised	Baseline	Reoptimised	Baseline	Reoptimised
Level 1 (50 Gy/5#)	99.2 (96.8-100)	99.3 (96.7-100)	94.4 (88.8-99.5)	94.8 (88.4-99)	31.9 (16-54.1)	35.6 (18.5-64.5)	70.2 (41.7-117.5)	76.3 (45.2-134.2)
Level 2 (39 Gy/3#)	96.6 (86.4-99.9)	95.2 (86.5-99.9)	91.6 (77.5-95.7)	88.8 (78.2-96.1)	30.7 (14.6-115.3)	34.1 (18.2-120.3)	73.1 (39.7-210.5)	80.21 (70.3-205.6)
Level 3 (25 Gy/1#)	86.1 (71.7-90.6)	84.0 (71.1-94.5)	78.1 (72.7-81.8)	79.0 (72.5-85.5)	42.3 (8.63-79.1)	48.7 (10.7-93.6)	89.2 (21.9-154.7)	83.7 (11.5-170.8)

Deliverability and feasibility

Technical plan parameters such as the estimated delivery treatment time, the beam-on time (BOT), the number of segments, monitor units (MU) and beams were read out from treatment plan documentation files (Table 3). The 'time in' and 'time out', marking when the patient entered and exited the treatment room, were taken from the record and verify system for each fraction to accurately calculate the total treatment time.

Treatment delivery summaries

	Level 1 (50Gy/5#)	Level 2 (39Gy/3#)	Level 3 (25Gy/1#)
Total MU	4,006	6,063	11,158
Segments	76.5	75.5	105.5
Beams	19	19	47
Planned gantry, MLC and beam on time	12 minutes	15 minutes	22 minutes
Total in room time	1 hour 21 minutes	1 hour 23 minutes	2 hours 12 minutes

Single fraction treatments were delivered as two 12.5 Gy semi-fractions delivered back-to-back. The second delivery utilised contours from the first adaption, with optional re-adaption if required. Therefore, MU, segment and beam numbers are the summation of both plans. Extended in-room times represent repeat contouring and plan adaption phases.

Conclusions

In the EMERALD trial, daily adaptive SMART achieved excellent PTVHigh V(95%) coverage whilst maintaining all mandatory organ at risk dose constraints across all dose levels. This was true even in Level 3 (25 Gy, single fraction) despite larger average tumour size and extreme hypofractionation. Total in-rooms times are not prohibitive to delivering treatment

References

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