Adaptive MR-guided stereotactic ablative body radiotherapy (MRgSABR) for pancreas cancer: dosimetric evaluation from EMERALD trial

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INTRODUCTION

One in three pancreas adenocarcinoma patients die of local progression[1]. SABR may be a treatment option, however target motion and critical organ at risk (OAR) proximity are major obstacles in achieving acceptable PTV coverage and severe toxicity has been reported[2,3]. MR-guided SABR (MRgSABR) allows beam-gating, real-time tracking, and daily plan adaptation based on changes in tumour or OAR, showing promise results in this setting[4].

The EMERALD trial evaluated the feasibility and safety of ultra-hypofractionation with MRgSABR in pancreatic cancer. As BED_{10} >70 Gy has been associated with improved survival[5] this dose range was investigated in the three dose levels (BED_{10} 87.5 - 100 Gy). Each of the arms was assessed as an independent cohort. The primary endpoint of EMERALD was dose limiting toxicity (DLT).

AIM

We present the dosimetric impact of adaptive MRgSABR from the EMERALD trial. We also evaluated the GTV and PTV coverage within the BED 70 Gy isodose

METHOD

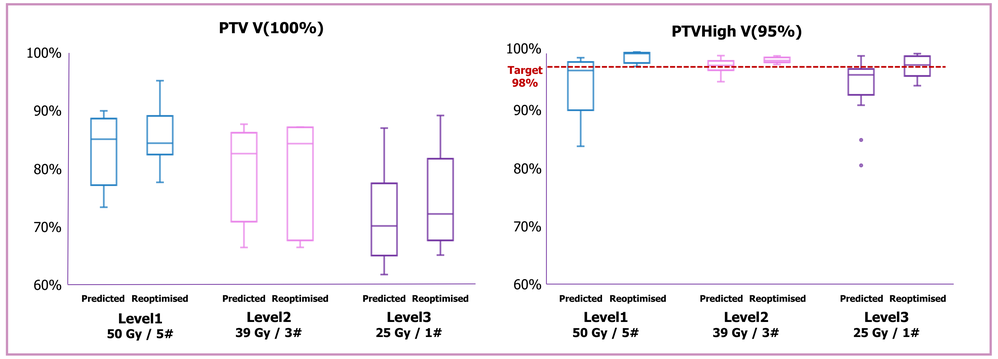
- Single-centre three-arm phase 1 non-randomised safety study (ISRCTN10557832)[6]
- Localised (locally advanced and inoperable) or locally recurrent pancreatic cancer
- All patients were treated with daily online adaptive MRgSABR (MRIdian Linac, ViewRay Systems Inc, OH)
- Induction chemotherapy was recommended but not mandatory
- **Three dose levels** were evaluated:
  - **Level1: 50 Gy / 5#** (BED_{10} 100 Gy)
  - **Level2: 39 Gy / 3#** (BED_{10} 90 Gy)
  - **Level3: 25 Gy / 1#** (BED_{10} 87.5 Gy)
- The planning objectives were:
  - 98% of PTVHigh receives ≥95% of the prescribed dose
  - Minimum PTV V(100%) ≥60%
  - Maximum PTV V(1 cc) ≥125% and ≤ 140%

RESULTS

Between **August 2022 to October 2023, 20 patients** underwent MRgSABR

- (Level1 n = 4, Level2 n = 8, Level3 n = 8)
- One patient in Level1 did not complete the treatment course due to development of obstructive jaundice requiring stenting
- Of the total of 49 fractions, 100% were successfully delivered using daily adaption
- Retrospective dosimetric data was available from 37 plans
  - Baseline → treatment plan produced from simulation imaging
  - Predicted → baseline plan recomputed on anatomy of the day
  - Reoptimised → treatment plan reoptimised on the anatomy of the day
- 76% of predicted plans failed to meet OAR constraints
- Following daily adaption:
  - All reoptimised plans met mandatory OAR dose constraints
  - PTVHigh V(95%) was maintained across all dose levels
- Despite larger tumour size in Level3, mean PTVHigh coverage remained >95%

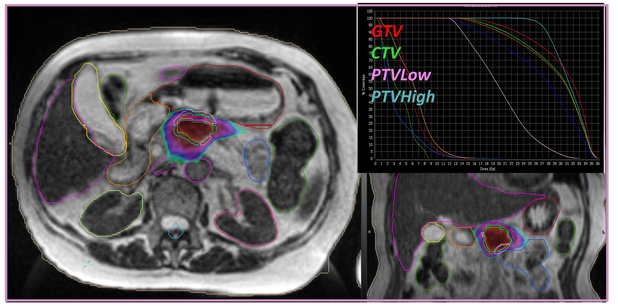
Boxplot of daily adaption impact: change in PTV and PTVHigh coverage between predicted and reoptimised plans



Summary of key dosimetric statistics for each dose level

Level	PTV V (100%) % mean (range)			PTVHigh V (95%) % mean (range)			GTV V(BED_{10}70)% median (range)		PTV V(BED_{10}70)% median (range)		GTV (cc) mean (range)		PTV (cc) mean (range)	
	Baseline	Predicted	Reoptimised	Baseline	Predicted	Reoptimised	Predicted	Reoptimised	Predicted	Reoptimised	Baseline	Adapted	Baseline	Adapted
1 (50 Gy/5)	88.32 (80-93.54)	85.05 (73.2-93.5)	84.24 (77.5-95)	99.78 (99.5-99.6)	96.75 (83.7-99)	99.67 (97.5-99.9)	99.17 (96.8-100)	99.3 (96.7-100)	94.35 (88.8-99.5)	94.8 (88.35-99)	31.91 (16-54.1)	35.64 (18.5-64.5)	70.15 (41.7-117.5)	76.33 (45.2-134.2)
2 (39 Gy/3)	82.9 (66.3-89.5)	82.44 (66,3-87,5)	83.57 (60-92.3)	99.37 (96.6-99.9)	97.62 (94.8-99.3)	98.76 (97.8-99.7)	96.6 (86.4-99.9)	95.2 (86.5-99.9)	91.6 (77.5-95.7)	88.8 (78.2-96.1)	30.67 (14.6-115.3)	34.12 (18.2-120.3)	73.08 (39.7-210.5)	80.21 (70.3-205.6)
3 (25 Gy/1)	77.45 (66.8-85.2)	67.91 (61.6-86.8)	72.72 (64.9-89)	99.3 (96.8-99.9)	94.78 (80.4-99.3)	96.98 (94.1-99.7)	86.13 (71.7-90.6)	84 (71.1-94.5)	78.13 (72.7-81.8)	79 (72.5-85.5)	42.19 (8.63-79.1)	48.70 (10.7-93.6)	89.16 (21.9-154.7)	83.70 (11.5-170.8)

BED_{10}: Biological Effective Dose; BED 70= 39.5Gy/5#; BED 70= 33.2 Gy/3#; BED 70Gy= 22Gy/1#.



Representative Level3 (25 Gy, single fraction) plan. MIM® 7.2.8. 1 Planning System

CONCLUSIONS

In the EMERALD trial, daily adaptive MRgSABR achieved optimal PTV_High V(95%) coverage whilst maintaining all mandatory OAR dose constraints across all dose levels. This was true even in the Level3 (25 Gy, single fraction) despite larger average tumour size and extreme hypofractionation.

EMERALD clinical outcomes will be reported shortly.

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