The use of non-invasive imaging biomarkers to predict outcomes in pancreatic cancer: A digital innovation project from the PURPLE pancreatic cancer platform

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Background

- Recently radiomics (a novel software -assisted imaging texture analysis) has shown promise as a non-invasive biomarker in pancreatic ductal adenocarcinoma (PDAC).
- It quantitatively extract features from conventional images and has the potential to develop tumour invasion models providing insights into aspects of tumour grade and heterogeneity.
- We sought to examine CT slice thickness and region of interest (ROI) dimensions to identify the optimal approach to developing this technology.

Aim

- To assess the impact of slice thickness in 2D & 3D CT-Based radiomics analysis on the feature robustness and prognostic values in patients with pancreatic adenocarcinoma

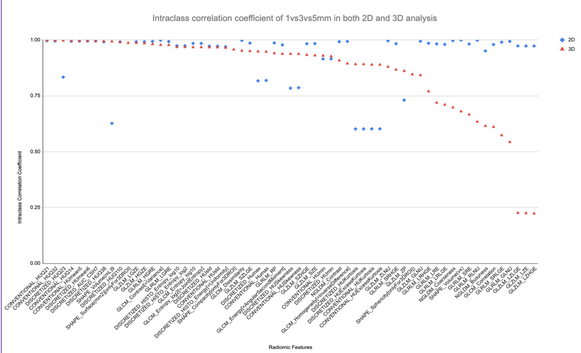
Methods

- Between January 2016 and June 2021, de-identified data and staging CTs were extracted from the PURPLE pancreatic cancer registry, for PDAC patients treated at Peter MacCallum Cancer Centre and Royal Melbourne Hospital.
- We evaluated radiomic feature (RF) robustness based on slice thickness, 2D and 3D segmentation of the ROI (PDAC tumour) on portal venous phase.
- CT images resampled into 1mm, 3mm and 5mm slice thickness. Sixty-one features were extracted using a radiomics software (LIFEx). Intraclass correlation coefficient (ICC) evaluated slice thickness robustness of each RF.
- Robust features were correlated with clinical and survival outcomes via univariate and multivariate models using IBM SPSS.

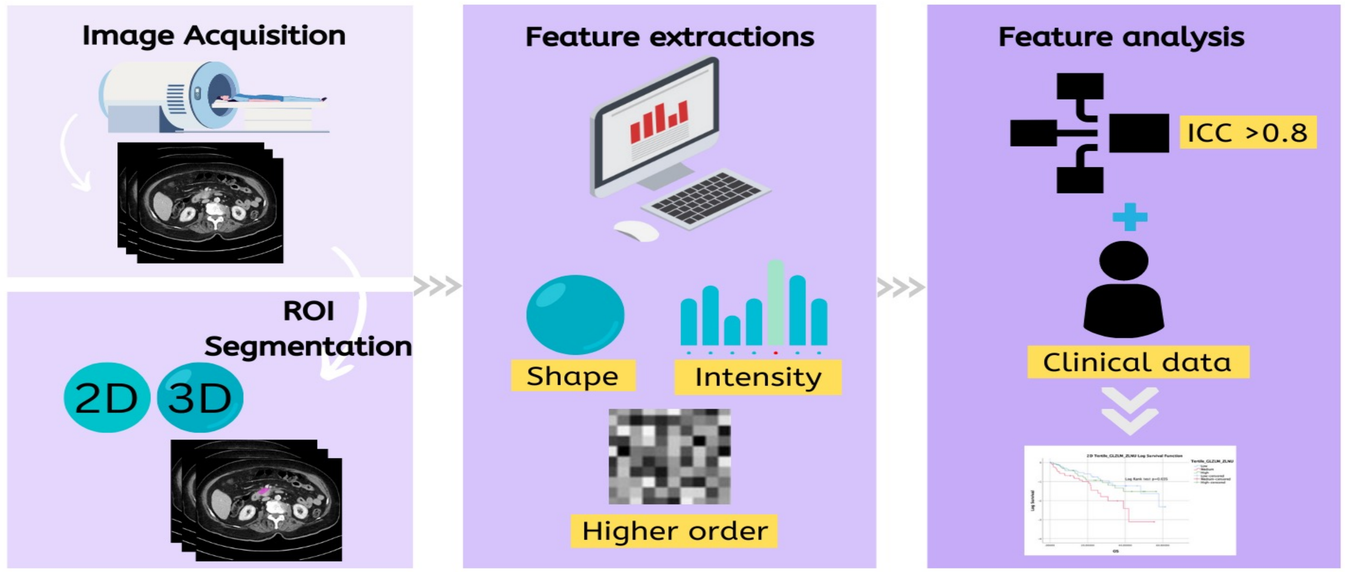
Results I

- 98 patients with PDAC (50 females; mean age 68 years): 42 had early-stage disease, 28 had advanced unresectable and 28 had metastatic disease at initial diagnostic imaging. CT slice thickness reconstruction resulted in 36 (1mm), 96 (3mm) and 98 (5mm) slice thicknesses, respectively.

Figure 1: Overall feature robustness assessed by intraclass correlation coefficient between 1vs3vs5mm groups in both 2D and 3D analysis



Radiomics workflow



Results II

- **Feature robustness :** CONVENTIONAL_HUQ2, CONVENTIONAL_HUQ3, DISCRETISED_HUmean, and DISCRETIZED_AUC_CSH were features in the top ranked ICC comparison between 2D and 3D**.**
- **Feature survival analysis:** Both 2D and 3D survival analysis showed GLZLM_ZLNU (heterogeneity related feature) to have significant correlation with survival in the univariate Cox-regression analysis. CONVENTIONAL_HUmean, and GLZLM_SZHGE were found significant in predicting survival outcome in Cox regression multivariate analysis.

Figure 2: Kaplan Meier's survival curve of significant radiomic features in tertiles in both 2D and 3D 3mm univariate analysis

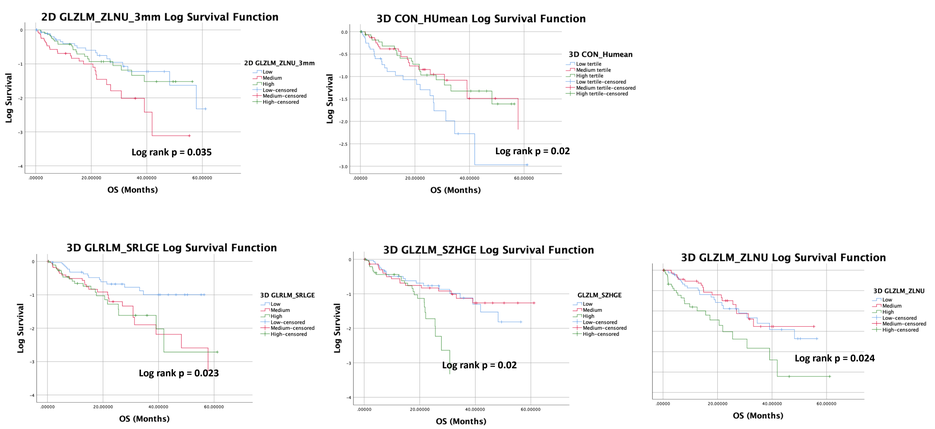


Table 1. Multivariable Cox Regression Analysis of significant clinical parameters and 3D 3mm radiomic features: Conventional_HUmean and GLZLM_SZHGE

Variable	HR	95% CI	p-value
Sex			
Male			
Female			
Age at Diagnosis tertiles			
<64	1		
64-72	1.64	0.77 - 3.49	0.199
>72	2.76	1.40 - 5.45	0.003
ECOG			
0	1		
1	1.73	0.95 - 3.15	0.074
2	1.83	0.78 - 4.27	0.162
3	5.13	1.36 - 19.36	0.016
Stage			
Stage 2 or less	1		
Stage 3	2.01	1.06 - 3.84	0.034
Stage 4	3.98	1.98 - 8.02	<0.001
CA 19_9* median			
≤800	1		
>800	2.71	1.41 - 5.19	0.003
Unknown	1.02	0.49 - 2.13	0.953
3D AUC CSH 3mm			
<1066	2.07	1.10 - 3.87	0.024
1066 - 1088	1.03	0.50 - 2.13	0.93
>1088	1		
3D GLZLM SZHGE 3mm			
<6568	1.53	0.77 - 3.07	0.226
6568-7000	1		
>7000	2.47	1.32 - 4.61	0.005

n=96 cases
**Cancer Antigen 19_9 (CA19_9)*
Reference category is the group with the highest survival.

Key take-home message

- 2D analysis provides more robust radiomic features than 3D analysis due to greater intrinsic dependency on the number of voxels in 3D analysis. (1)
- 1st order features were the common high robust features in both 2D and 3D analysis between different slice thicknesses.
- 3D analysis provides more prognostic values than 2D analysis, supported by other radiomic study. (2)
- Heterogeneity related radiomic features were significant features associated with survival outcome

Limitations:

- Relatively small sample size may have reduced statistical power.
- Real-world CT imaging used in this study was derived from multiple radiological centres with various scanning techniques and image quality that may have introduced RF biases but reflects real-world practice and challenges
- Manual lesion segmentation was performed by 2 different operators which may introduce operator-dependent variability; however, this limitation was mitigated by quality control by centralised review by an experienced subspecialist radiologist.

Conclusion

- 3D ROI analysis and slice thickness data harmonisation has high impact on radiomic results
- Further work to expand our PDAC cohort is underway to investigate the best radiomic analysis methodology
- This will lead to new models of PDAC risk stratifications to improve clinical outcomes.

References:

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2. Xu L, Yang P, Yen EA, Wan Y, Jiang Y, Cao Z, et al. A multi-organ cancer study of the classification performance using 2D and 3D image features in radiomics analysis. Phys Med Biol. 2019;64(21):215009.

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