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Supplementary Materials

Fluorothymidine Positron Emission Tomography (FLT-PET) Repeatability and Response Evaluation in Advanced Pancreatic Cancer Patients Treated with Gemcitabine-Based Chemotherapy

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ABSTRACT

Purpose: This study aimed to evaluate the feasibility and repeatability of [^{18}F]-fluorothymidine positron emission tomography (FLT-PET) and its utility as a proliferative imaging marker to evaluate response in patients with advanced pancreatic adenocarcinoma (PDAC) receiving gemcitabine-based chemotherapy.

Methods: PDAC patients due to commence gemcitabine-based chemotherapy underwent FLT-PET over 60 minutes, before (baseline) and after 28 days of chemotherapy. Repeatability was assessed by a second FLT-PET scan within 7 days of baseline scan and before starting chemotherapy. Scans were assessed by two independent physician's to determine inter-reporter concordance. FLT-PET uptake over 45-60 minutes was estimated as maximum and mean standardised uptake values (SUVmax and SUVmean). Exploratory analysis of tissue biomarkers was performed from archival tissue samples.

Results: All 18 of the 21 patients consented who were imaged had primary tumour in-situ and 83% had metastases with 60% in liver. 17 patients received gemcitabine-based treatment. Thirty-five FLT-PET scans were acquired (89% evaluable) and 26 lesions delineated (17 primary tumours, 9 liver metastases). At baseline, liver metastases showed higher uptake compared with primary tumour with mean (SD) SUVmax [7.2 (1.1) vs 4.5 (1.3); $p < 0.001$] and SUVmean [4.7 (0.6) vs 2.1 (0.6); $p < 0.001$)]. There was good intra-patient repeatability and inter-reporter concordance with mean (SD) test-retest difference and inter-reporter Lin's concordance coefficient being 4.9% (17.6) and 0.703 for SUVmax and -5.4% (SD 9.8) and 0.710 for SUVmean, respectively. However, gemcitabine-capecitabine combination therapy resulted in a higher FLT uptake compared to gemcitabine alone, although this did not translate to clinical benefit. No relationship was observed between tissue markers and FLT in half of the subjects imaged whose tissue was available.

Conclusions: FLT-PET is a feasible and reproducible imaging technique in patients with PDAC to evaluate proliferation-targeting therapy, using a simplified imaging protocol in well-designed clinical trials.

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Supplementary Material A: Case Report

Changes to FLT uptake (SUV) of patient 4 who had a PET scan within three hours after gemcitabine administration are listed in Table S1. The results were very different from the mean treatment responses of other patients in Table 4. All tissues showed a decrease in SUV after treatment, except kidneys, with vertebrae having the largest decrease (-91.3%). Both kidneys showed minimal responses in SUV, except that the SUV_{max} increased by 37.0% in the left kidney.

	SUV_{mean}			**SUV_{max}**		
	Baseline	Treatment	Response (%)	Baseline	Treatment	Response (%)
Pancreatic tumour	2.14	1.73	-19.2	3.60	2.86	-20.5
Liver metastasis	4.62	3.20	-30.8	7.29	4.44	-39.1
Liver	7.94	3.01	-62.0	9.70	4.04	-58.4
Vertebrae	9.77	0.85	-91.3	13.44	3.59	-73.3
Spleen	1.53	0.85	-44.5	2.03	1.17	-42.2
Right Kidney	2.52	2.35	-6.9	4.32	4.07	-5.9
Left Kidney	2.44	2.46	0.9	3.91	5.36	37.0

Supplementary Material B: Relationship between baseline primary tumour SUVmax and clinical and pathological parameters, hENT1: Human equilibrative nucleoside transporter 1; RRM: Ribonucleotide reductase subunit M; TK1: Thymidine kinase 1; HUR: human antigen R; Ki67: protein Ki-67; %: percentage; vs: versus

	Univariate Linear Regression		**Multivariable Linear Regression**	
	OR (95% CI)	P-value	OR (95% CI)	p-value
Age	1.05 (0.95, 1.15)	0.305	-	
Gender (Female (vs Male))	4.04 (1.20, 13.58)	0.027	4.80 (0.77-29.96)	0.076
Performance Status	1.08 (0.32, 3.62)	0.897	-	
Stage (Metastatic (vs Locally advanced))	4.23 (0.79, 22.55)	0.086	-	
Size of primary tumour	1.03 (0.61, 1.75)	0.908	-	
hENT1 (%)	1.01 (0.97, 1.05)	0.508	-	
RRM (%)	1.01 (0.97, 1.06)	0.375	-	
TK1 (%)	1.03 (1.01, 1.06)	0.028	1.04 (0.99-1.09)	0.857
HUR (%)	1.14 (1.03, 1.25)	0.017	1.04 (0.99-1.09)	0.121
Ki67 (%)	1.03 (7.79, 13.00)	0.330	-	