Supplementary Table 1. Characteristics of patients in the clinical trial of intraoperative gemcitabine infusion during surgery

Patient	*Sex*	*Age*	*Race*	*Tumor location*	*Tumor size (cm)*	*LN+*	*Differentiation /Histology*	*Ki67 (%)*	*KRAS Status*
1	Male	64	Caucasian	Head	3	15/43	Poor/Adeno	70%	G12D
2	Female	63	Black	Head	3	8/53	Poor/Adeno	30%	Q61H
3	Female	58	Caucasian	Tail	3.4	5/30	Poor/Adeno	50%	G12D
4	Male	56	Hispanic	Head	3.2	3/23	Mod/Adeno	10%	G12R
5	Female	68	Black	Tail	3.5	0/21	Mod/Adeno	30%	G12V
6	Female	69	Caucasian	Head	1.9	3/76	Mod/Adeno	20%	G12V
7	Female	63	Caucasian	Head	3.1	21/57	Mod/Adeno	60%	G12D
8	Male	64	Caucasian	Tail	3	0/14	Poor/Adeno	90%	G12D
9	Female	59	Caucasian	Body	2.2	0/40	Mod/Adeno	1%	WT
10	Female	55	Caucasian	Head	1.9	3/76	Mod/Adeno	70%	G12V
11	Male	76	Caucasian	Head	3.2	6/42	Poor/Adeno	20%	WT
12	Female	56	Caucasian	Head	1.3	0/23	Mod/Adeno	20%	WT

Abbreviations: LN+=lymph nodes positive divided by total lymph nodes evaluated, Mod=moderately differentiated, Poor=poorly differentiated, Adeno=Adenocarcinoma

Supplementary Table 2. Characteristics of patients who received gemcitabine-based chemoradiation for potentially resectable pancreatic cancer. For full details of the clinical trials, see references 19 and 20.

Characteristic	***Value***
Median age, range	64 (38-80)
Median OS time, mo.	23
Median follow up, range, mo.	20 (3-148)
Sex	
Male	63 (57%)
Female	47 (43%)
Race/ethnicity	
Caucasian	94 (85%)
Hispanic	9 (8%)
African American	4 (4%)
Asian	3 (3%)
Underwent curative-intent resection	
Yes	80 (73%)
No	30 (27%)
Cytotoxic regimen	
Gem-Cisplatin, Gem-XRT	79 (72%)
Gem-XRT	31 (28%)

Abbreviations: OS=overall survival, Gem=gemcitabine, XRT=radiotherapy (30 Gy in 10 fractions), mo.=months

Supplementary Table 3. Characteristics of patients who underwent surgical resection alone (the learning dataset for the CT mathematical model)

Characteristic	*No. of Patients (%)*
Sex	
Male	25 (45%)
Female	30 (55%)
Median age (range)	65 (25-85)
Race/ethnicity	
Caucasian	47 (85%)
Hispanic	4 (7%)
Black	2 (4%)
Asian	2 (4%)
Resectability	
Potentially resectable	54 (98%)
Borderline	1 (2%)

Supplementary Table 4. Ranges for R and R_c derived from learning dataset of 55 patients with a delay phase time point at t=180 s

Parameter	***Range***
R	0.02 to 0.12 s^{-1}
R_c	$2.0x10^{-6}$ to 0.08 s^{-1}

Supplementary Table 5. Distributions of CT-derived transport parameters by pancreatic tissue type

Parameter	***Normal pancreas***	***Tumor***	***P Value***
Median R (s^{-1}), range	0.06, 0.04-0.12	0.07, 0.03-0.12	0.12
Median R_c (s^{-1}), range	0.05, $2.0x10^{-6}$-0.06	0.02, $2.0x10^{-6}$-0.08	<0.0001
Median Y^T_{max} (HU), range	103.37, 45.49-207.88	54.69, 2.46-140.88	<0.0001
Median Y^V_{max} (HU), range	220.84, 58.62-526.19	81.51, 3.46-277.77	<0.0001

Supplementary Table 6. Ranked percentages of cells with a given level of hENT1 staining in samples from the phase 0 trial.

Patient	*Nuclear staining intensity*	*Cytoplasmic intensity*
3	80% 3+, 15% 2+, 5% 1+ and neg	20% 3+, 80% 2+
2	60% 3+, 40% 2+	60% 3+, 40% 2+
7	50% 3+, 35% 2+, 10% 1+, 5% neg	10% 3+, 50% 2+, 40% 1+
1	40% 3+, 50% 2+, 10% 1+ and neg	40% 3+, 40% 2+, 20% 1+
4	70% 2+, 25% 1+, 5% neg	90% 2+, 10% 1+
11	30% 3+, 60% 2+,10% 1+	40% 3+, 55% 2+, 5% 1+ and neg
9	30% 3+, 60% 2+, 5% 1+, 5% neg	70% 3+, 30% 2+
6	10% 3+, 50% 2+, 35% 1+, 5% neg	20% 2+, 70% 1+, 10% neg
5	5% 3+, 35% 2+, 55% 1+, 5% neg	30% 2+, 70% 1+
10	5% 3+, 30% 2+, 60% 1+, 5% neg	30% 2+, 70% 1+
12	40% 2+, 40% 1+, 20% neg	10% 2+, 50% 1+, 40% neg
8	20% 2+, 70% 1+, 10% neg	10% 2+, 70% 1+, 20% neg

Abbreviations: neg=negative

Supplementary Table 7. Univariate analyses of patients who received gemcitabine-based chemoradiation for potentially resectable pancreatic cancer.

Characteristic	*No. of patients*	*Univariate Hazard Ratio (95% CI)*	*Univariate P value*
Sex			
Male	63	0.99 (0.65-1.49)	0.94
Female	47	--	
Race/ethnicity			0.61
Caucasian	94	--	
Hispanic	9	1.10 (0.49-2.14)	0.81
African American	4	0.45 (0.07-1.43)	0.20
Asian	3	0.78 (0.13-2.49)	0.72
Cytotoxic regimen			
Gem-Cisplatin, Gem-XRT	79	0.77 (0.48-1.21)	0.27
Gem-XRT	31	--	
Underwent curative-intent resection			
Yes	80	0.12 (0.07-0.22)	<0.0001
No	30	--	
Normalized AUC	110	0.28 (0.11-0.69)	0.006

Abbreviations: No.=number, CI=confidence interval, Gem=gemcitabine, XRT=radiotherapy (30 Gy in 10 fractions), AUC=area under the curve

Supplementary Table 8. Univariate analyses of 80 patients with PDAC who underwent resection after gemcitabine-based chemoradiation.

Characteristic	*No. of patients*	*Univariate Hazard Ratio (95% CI)*	*Univariate P value*
Cytotoxic regimen			
Gem-Cisplatin, Gem-XRT	54	1.12 (0.67-1.93)	0.68
Gem-XRT	26	--	
Surgical margin			
Positive	4	1.44 (0.44-3.53)	0.50
Negative	76	--	
N stage			
pN1	44	1.33 (0.81-2.22)	0.25
pN0	36	--	
Pathological response	65	5.68 (2.08-15.35)	0.0008
Normalized AUC	80	0.26 (0.09-0.80)	0.02

Abbreviations: No.=number, CI=Confidence Interval, Gem=gemcitabine, XRT=radiotherapy (30 Gy in 10 fractions), pN1=pathological stage N1, pN0=pathological stage N0, AUC=Area Under the Curve

Supplementary Table 9. Exploratory multivariate overall survival model for patients who received gemcitabine-based chemoradiation for potentially resectable pancreatic cancer using a cut-off of 0.6 for normalized AUC.

Characteristic	*No. of patients*	*Univariate Hazard Ratio (95% CI)*	*Univariate P value*	*Multivariate Hazard Ratio (95% CI)*	*Multivariate P value*
Normalized AUC with cut-off of 0.6	110				
High (normalized AUC>0.6)	22	0.47 (0.25-0.80)	0.005	0.49 (0.27-0.85)	0.009
Low (normalized AUC≤0.6)	88	--		--	
Underwent curative-intent resection					
Yes	80	0.12 (0.07-0.22)	<0.0001	0.12 (0.07-0.22)	<0.0001
No	30	--		--	

Abbreviations: No.=number, CI=confidence interval, AUC=area under the curve

Supplementary Table 10. Exploratory multivariate overall survival model for 80 patients with PDAC who underwent resection after gemcitabine-based chemoradiation using a cut-off of 0.6 for normalized AUC.

Characteristic	*No. of patients*	*Univariate Hazard Ratio (95% CI)*	*Univariate P value*	*Multivariate Hazard Ratio (95% CI)**	*Multivariate P value**	*Multivariate Hazard Ratio (95% CI)***	*Multivariate P value***
Normalized AUC							
High (normalized AUC>0.6)	18	0.44 (0.21-0.83)	0.01	--		0.45 (0.22-0.86)	0.01
Low (normalized AUC≤0.6)	62	--				--	
Surgical margin							
Positive	4	1.44 (0.44-3.53)	0.50	2.39 (0.56-7.06)	0.21	1.36 (0.41-3.32)	0.57
Negative	76	--		--		--	
N stage							
pN1	44	1.33 (0.81-2.22)	0.25	1.23 (0.66-2.36)	0.51	1.22 (0.73-2.04)	0.45
pN0	36	--					
Pathological response	65	5.68 (2.08-15.35)	0.0008	5.04 (1.72-14.93)	0.003	--	

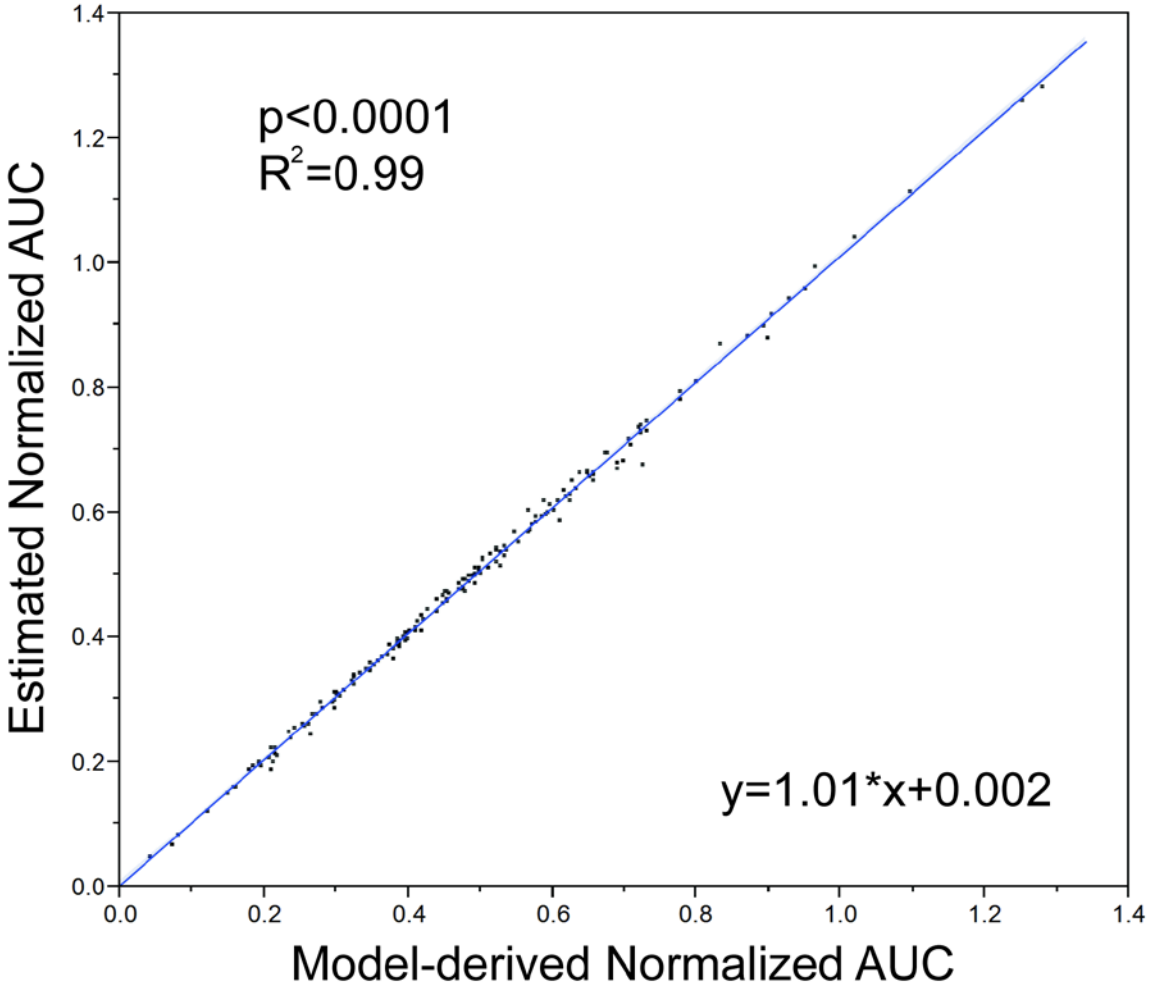
Abbreviations: No.=number, CI=Confidence Interval, pN1=pathological stage N1, pN0=pathological stage N0, AUC=Area Under the Curve, *=Multivariate model with Surgical Margin, N stage, and Pathological response, **=Multivariate model with Surgical Margin, N stage, and Normalized AUC

Supplementary Table 11: Tests of normality for data

Variable	**P value**
Normalized AUC	0.23
Normalized gemcitabine incorporation	0.49
Tumor gemcitabine incorporation	0.71
Stromal score	0.56
Pathological response	0.08

Abbreviation: AUC=Area Under the Curve
Note: A P value greater than 0.05 is considered to be consistent with a normal distribution.

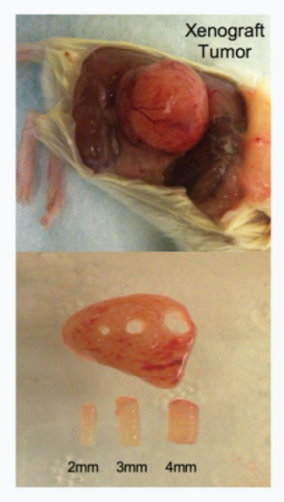
Supplementary Fig. 1. Appropriateness of CT mass transport model



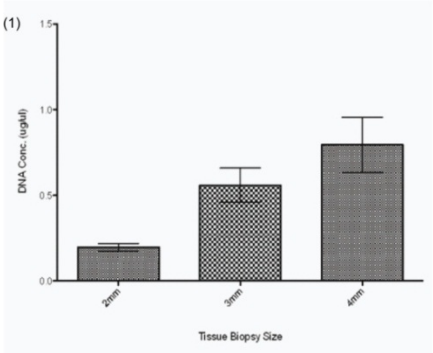
The estimated normalized AUC was calculated using a simple piece-wise linear equation, as illustrated in Fig. 1a, and compared with the model-derived normalized AUC. This demonstrated a 1:1 correlation between the estimated and model-derived values, illustrating how the continuous model function (Eq. 2) can be approximated using a straightforward calculation that can be applied at any institution.

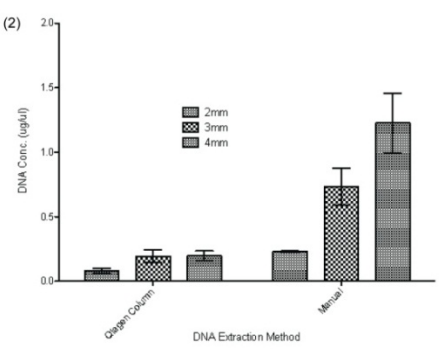
Supplementary Fig. 2. Pre-trial optimization of tissue processing in patient-derived PDAC xenografts

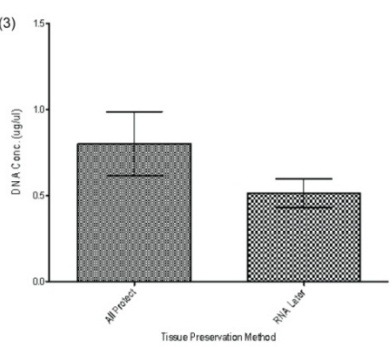
a.



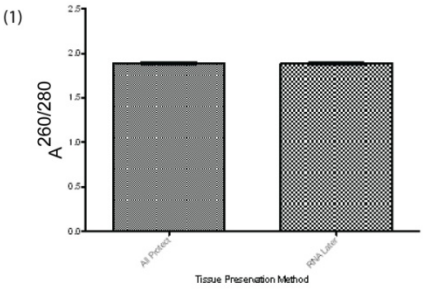
b.

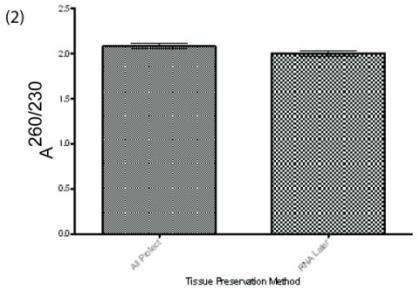


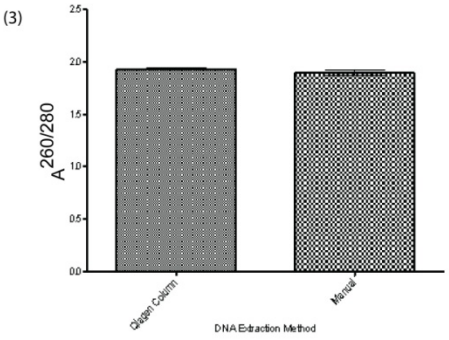


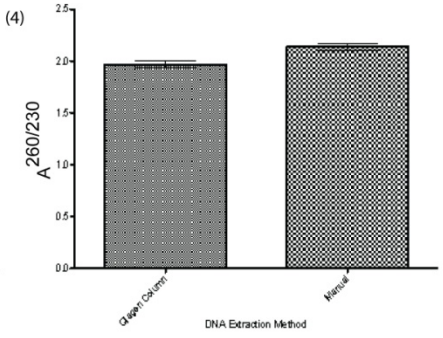


c.





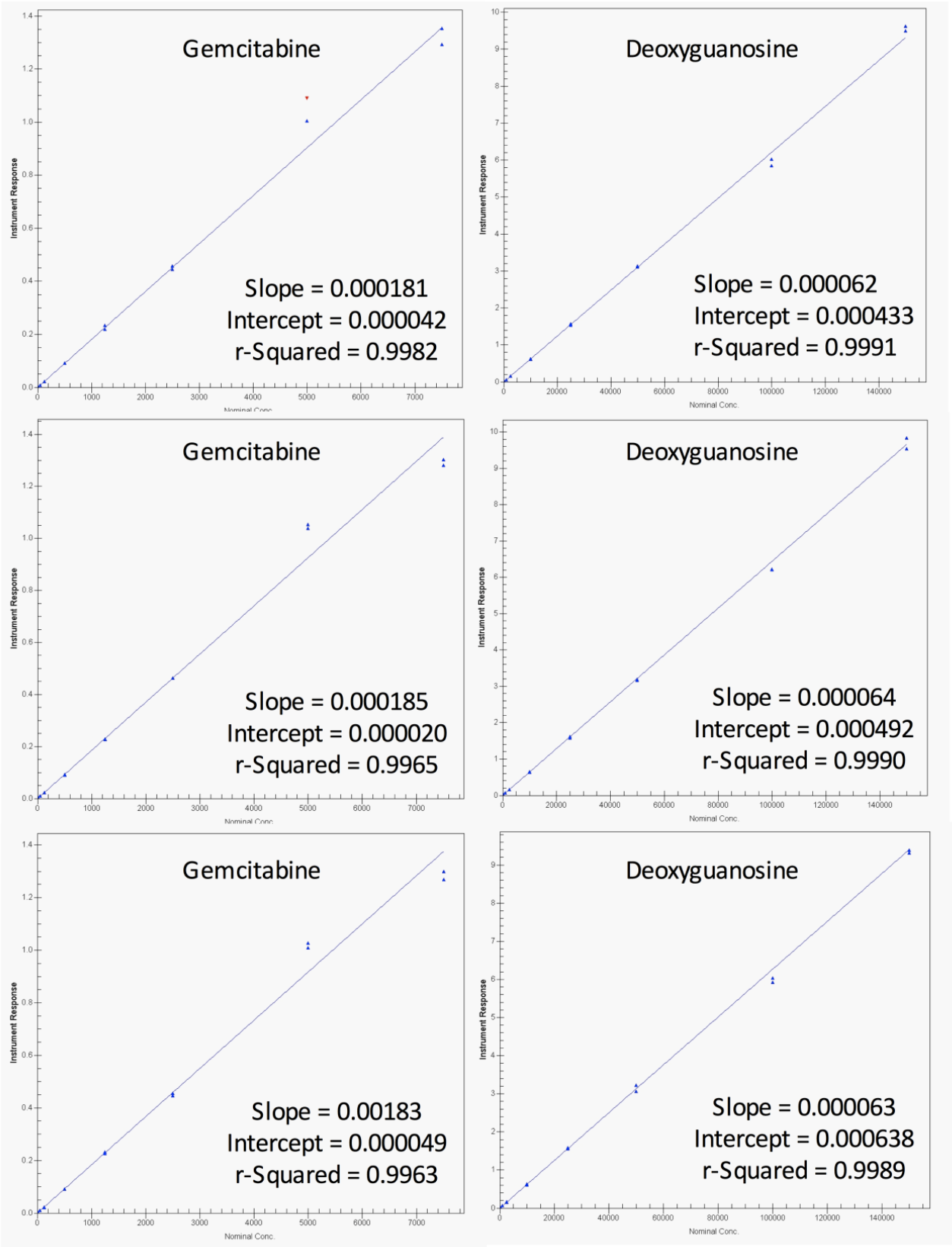




(a) With an approved Institutional Animal Care and Use Committee protocol and IRB-approved protocol, optimization of tissue processing obtained from the clinical trial of intraoperative gemcitabine infusion during PDAC resection was performed with samples of pancreatic tumorgrafts established from the resected human PDAC tumors and grown in NOD/SCID mice as previously described (1).

(b-c) Tissue samples were homogenized in a pre-cooled bead mill and subject to lysis buffer in water bath overnight. DNA was precipitated with chloroform-phenol extraction with isoproponal precipitation. Samples were quantified and quality determined with nanodrop analyzer (Thermo Scientific).The highest qualitative and quantitative DNA was obtained with 4mm core punch biopsy samples, placed in AllProtect preservation solution (Qiagen) and stored at -80^{o} C until processed utilizing a manual DNA extraction protocol (b[1-3] and c[1-4]).

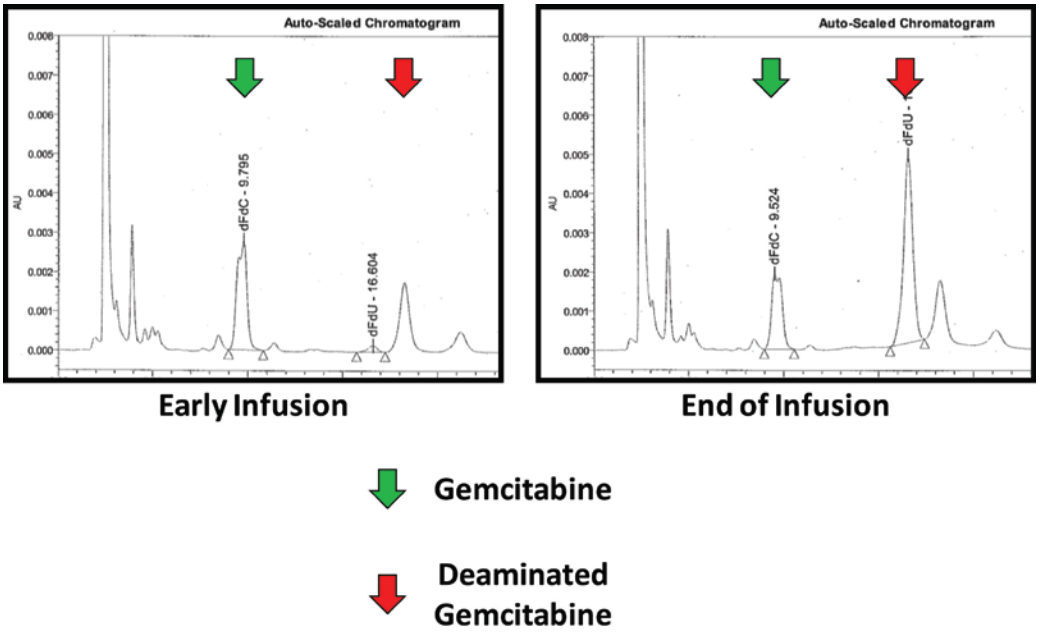
Supplementary Fig. 3. Gemcitabine incorporation calibration curve



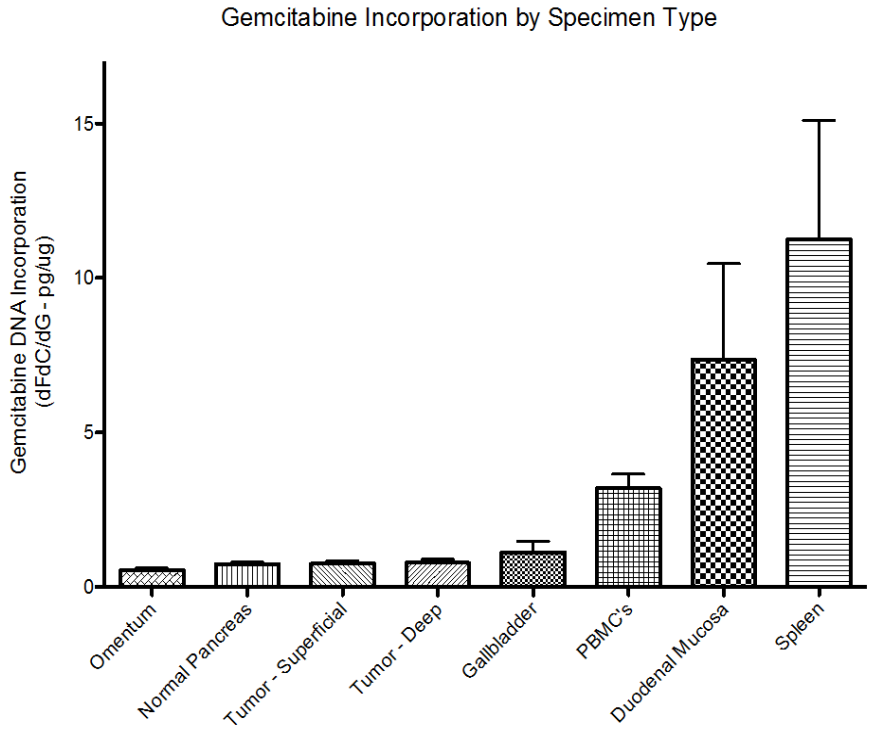
Purified extracted DNA from tissues was diluted in a hydration buffer within the concentration range of 0.087µg/µL to 0.22 µg/µL (i.e. 10 µg/115 µL to 25 µg /115 µL) according to assay requirements and sent to an outside facility for quantification (Advion Bioservices). Gemcitabine DNA incorporation was then determined by hydrolysis of samples using a two-step enzymatic procedure releasing bound dFdC (gemcitabine) which was subsequently quantified by LC-ESI-MS/MS using stable isotope labeled internal standards and selected reaction monitoring (SRM). dFdC was quantitated and reported relative to deoxyguanosine (dG), the complementary base for both dFdC and deoxycytosine (dC) (2). Calibration for the concentration determination of each sample was performed using a standard curve for dFdC (5.0 – 7500 pg/mL) and dG (0.100 – 150 µg/mL) normalized by use of stable labeled internal isotope standards. The calibrated response is the ratio of sample chromatographic peak area to internal standard chromatographic peak area. The standards and quality controls (QCs) were prepared in a surrogate matrix, which contains deoxyadenosine, deoxycytidine, and thymidine in concentrations that track with the deoxyguanosine concentration. There were 3 QC concentrations, one at ~3 times the lower limit of quantification, one at mid-curve range, and one in the upper quartile of the curve.

Supplementary Fig. 4. Gemcitabine detection in serum and gemcitabine incorporation in different tissues.

a.



b.

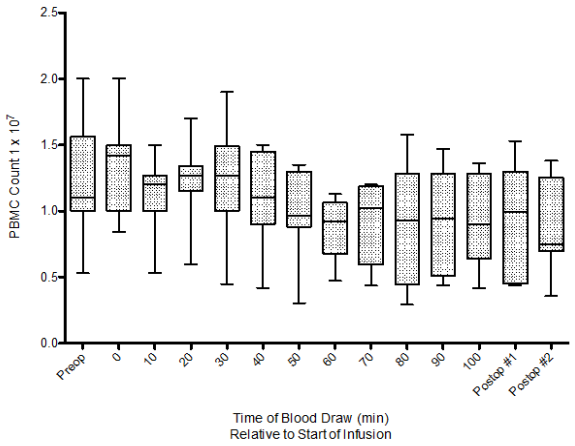


(a) Samples were collected, processed, and analyzed in a single laboratory (W.P.) as previously described (3). Briefly, from each patient studied, 10ml of blood was taken into tubes containing heparin and 5 μmol/L tertrahydrouridine at preinfusion and then at 10 minutes intervals until gemcitabine infusion was complete. Plasma was obtained by centrifugation of a portion of blood samples at various times during infusion, and gemcitabine (dFdC) and its deaminated metabolite (dFdU) were separated and visualized by reversed-phase high-performance liquid chromatography with detection wavelengths of 262nm (dFdU) and 275nm (dFdC). Mononuclear cells were isolated from a separate portion of blood by Ficoll-Hypaque step density centrifugation and quantified (Supplementary Fig. 6). After extraction of nucleotides with $HClO_4$, gemcitabine triphosphate was quantified by anion-exchange high-performance liquid chromatography.

(b) Genomic DNA was extracted from different tissue samples and the amount of incorporated gemcitabine was measured by a proprietary assay developed by Advion BioServices. The differences in gemcitabine incorporation into the DNA by tissue type may be related to differences in organ perfusion.

Supplementary Fig. 5. Hematological evaluation in the clinical trial of intraoperative gemcitabine infusion

a.



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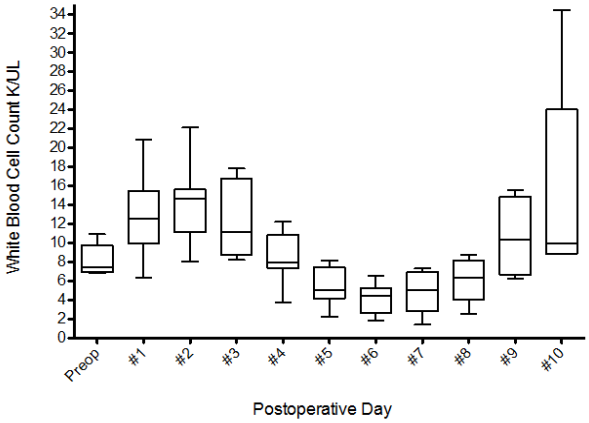
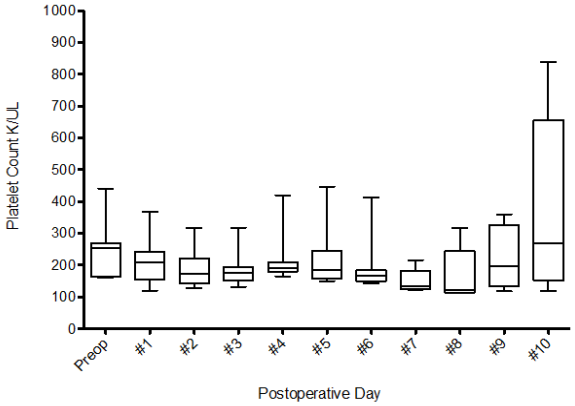


c.

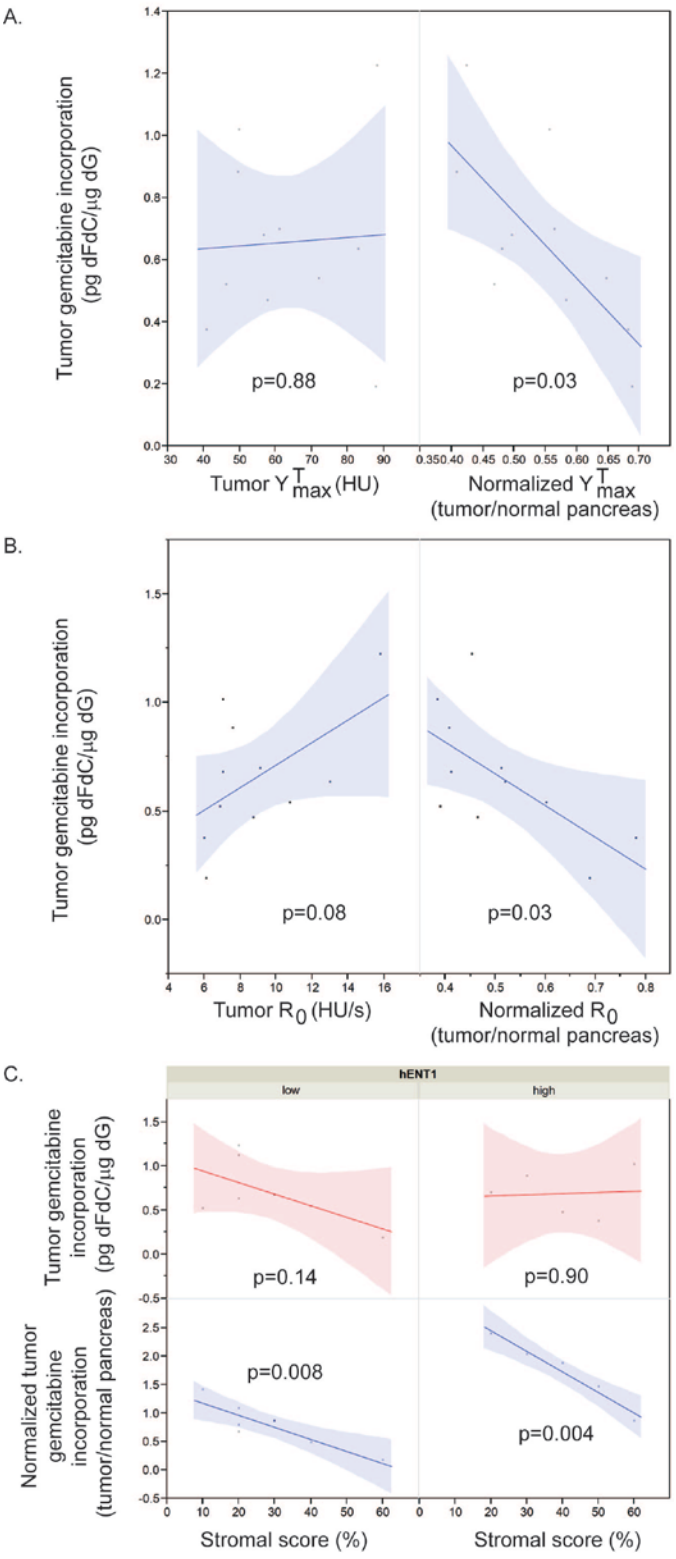


(a) The figure shows the peripheral blood monocyte (PBMC) yields during the intraoperative infusion of gemcitabine.

(b) For all patients on the clinical trial, the white blood cell count exhibited a nadir at postop day 6-7.

(c) The platelet counts were relatively stable for all patients after surgery.

Supplementary Fig. 6. Effect of normalization on correlations



(a) The CT-derived parameter Y^{T}_{max} is plotted against the average tumor gemcitabine incorporation in the tumor. After normalization with the Y^{T}_{max} in the normal pancreas for each patient, the correlation becomes statistically significant.

(b) Another CT-derived parameter, R_0, the initial influx rate of contrast, is plotted against the corresponding average tumor gemcitabine incorporation in the tumor. After normalization, the correlation becomes a significant inverse relationship, as opposed to a non-significant positive correlation.

(c) The un-normalized tumor gemcitabine incorporation and normalized gemcitabine incorporation are plotted against the corresponding stromal score for each patient in the clinical trial. This demonstrates how one variable in the correlations of a transport property (dependent or independent) needs to be normalized. Stromal score is a parameter specific to the tumor and cannot be normalized.

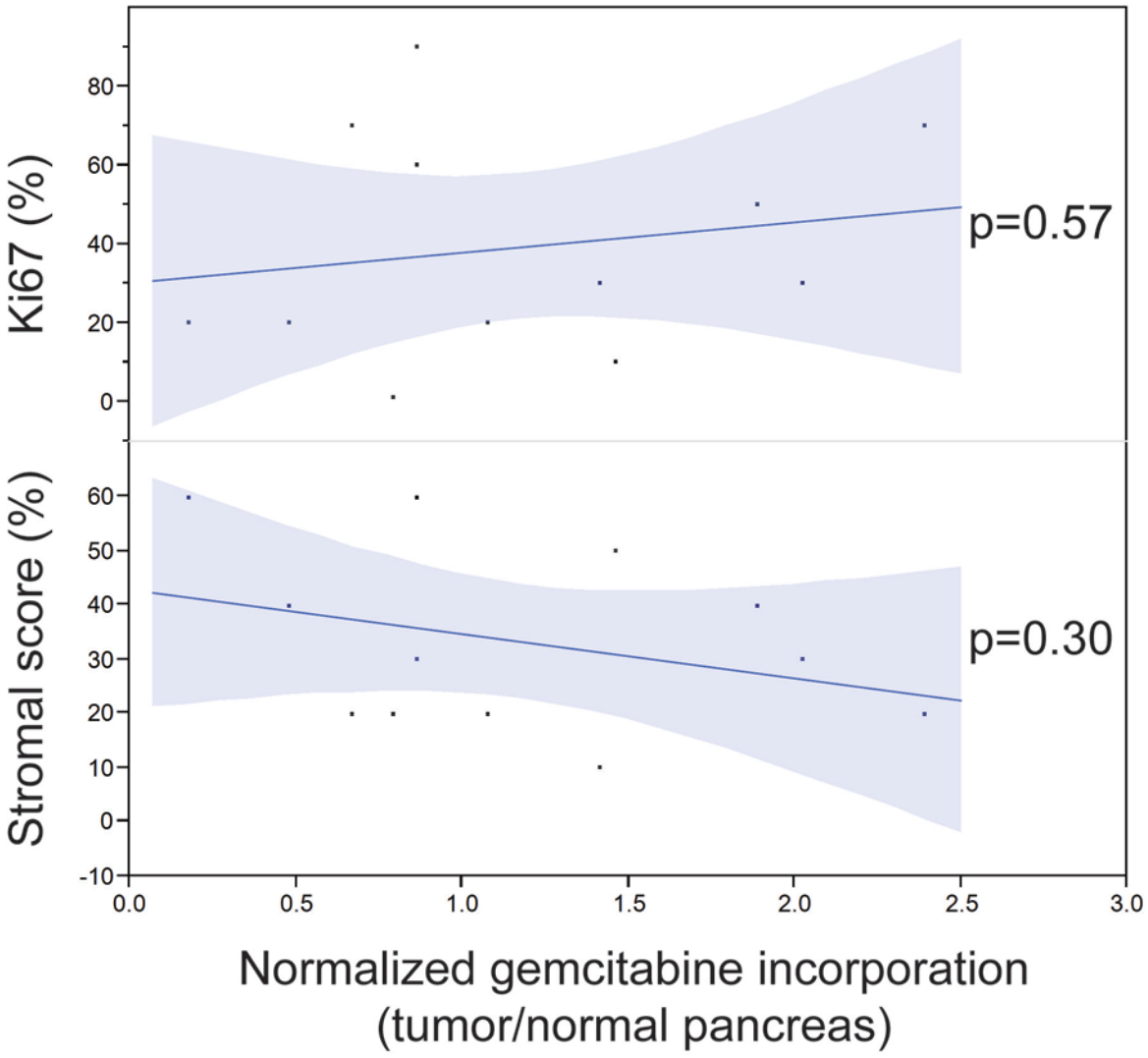
Part of the reason that normalization improves the correlations is that it eliminates minor variations in the acquisition times of the phases of the CT scan. It is recognized that there may be minor deviations in the timing of the arterial and portal venous phases, which is estimated to be ±5 seconds for each phase at M.D. Anderson. Two possible scenarios may occur. One is where the actual timing differs by the same amount at the arterial and portal venous phases. Another is where the actual timing of only one phase is different from the assumed timing.

In the first, more likely scenario where the timing is different by the same amount, a rescaling factor for the absolute value of R and R_c would be needed to obtain the correct absolute values for these parameters. By simply taking ratios of the correct timing and the assumed timing in Eq. 2 (see Methods), the rescaling factor for the absolute value of R and R_c would be: rescaling factor = assumed timing/correct timing. R_0 and AUC would have the same percentage change in value because the former is proportional to R and the latter is proportional to time. By their definitions, Y^{V}_{max} and Y^{T}_{max} would not change because they are not dependent on time. Additionally, in all correlations, normalization was used by taking the CT-derived parameter for the tumor and dividing by the normal

pancreas. If there was a slight deviation in the timing of the phases, the rescaling factors would cancel out. Thus, the normalization procedure (Supplementary Fig. 7) served to minimize the effects of minor deviations in the timing of the phases of the pancreatic protocol CT.

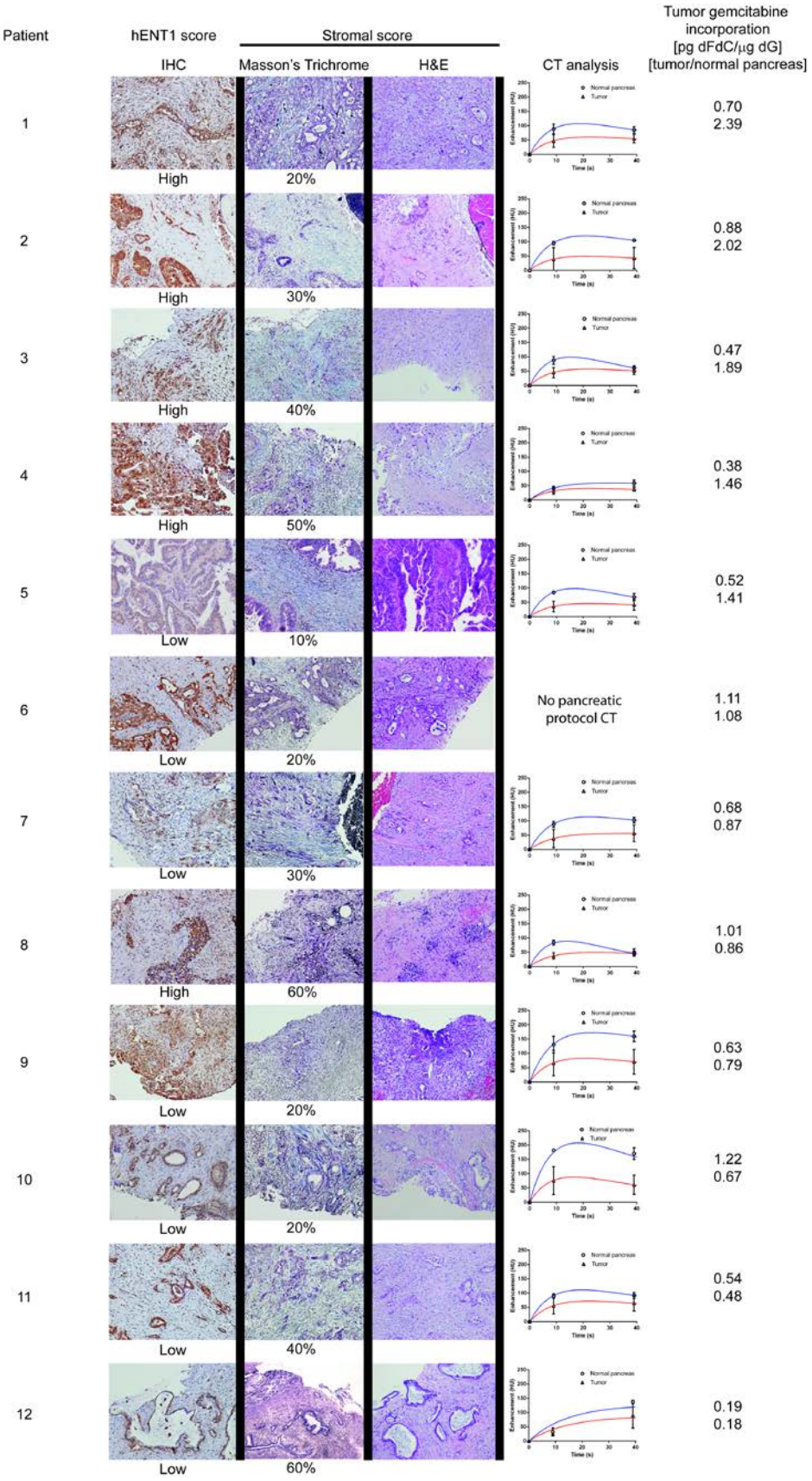
In the second scenario where the timing of only one phase is slightly different, a simple correction factor would be needed. For example, in the case where the portal-venous phase is slightly different from the assumed timing, it can be shown by a simple perturbation analysis of Eq. 3 (see Methods) that the correction factor for the absolute value of Y^{V}_{max} would be: correction factor=$1+R_c$*(actual t_{venous}-assumed t_{venous}). For the majority of patients, this would amount to at most a 5% change in the absolute value of Y^{V}_{max}, assuming a time differential of 5 s.

Supplementary Fig. 7. Pathological variables and normalized gemcitabine incorporation.



The Ki67 score (top panel) and stromal score (bottom panel) were assessed by a pathologist, independently of the gemcitabine incorporation. These pathological scores were plotted against the normalized gemcitabine incorporation. The results show that the pathological variables by themselves do not correlate with gemcitabine incorporation.

Supplementary Fig. 8. Histology, enhancement patterns, and gemcitabine incorporation in clinical trial of intraoperative gemcitabine infusion for resectable PDAC



Representative histology is shown for the patients on the clinical trial of intraoperative gemcitabine infusion during PDAC resection. The CT profiles and gemcitabine incorporation values for each patient are also shown.

Author contribution statement

E.K. prepared the manuscript, main figures, and supplements with guidance from J.F. and assistance from M.T., V.C., H.S., and M.F. All other co-authors contributed to editing and revisions. E.K. conceived the idea to derive physical transport properties from contrast-enhanced CT scans as part of postdoctoral training focusing on the Transport Oncophysics theory of M.F. with oversight from H.S. P.B. and E.K. performed the CT measurements. V.C. developed the mathematical model with assistance from E.K. E.K. developed the methods to validate and apply the model. E.K. and V.C. generated and tested the associated biophysical/biological hypotheses of correlation between CT-derived transport properties with histopathology, gemcitabine delivery, and chemoradiation response with assistance from J.F, H.W., C.C., E.T. and M.F, as well as data obtained by M.T. E.K. discovered the association between gemcitabine incorporation, fibrosis, hENT1, and the CT-derived parameters after input and work by J.F., M.F.,V.C., D.C., H.W., and M.T. M.T. and J. F. conceived the idea of an intraoperative gemcitabine clinical trial for resectable pancreatic cancer to assess drug delivery and tissue pharmacokinetics. M.T. wrote, developed, and implemented the human trial protocol as part of a clinical investigator program focusing on Translational Oncology with oversight by G.V, W.P, and J.F. G.V., W.P., J.A., R.W., M.J. provided chemotherapeutic expertise and toxicity monitoring. M.K, J.L, M.T., R.T. and J.F. provided surgical planning, and perioperative safety monitoring for all trial participants. V.G. and M.R. delivered the intraoperative chemotherapy and provided intraoperative monitoring. M.T., R.C, Y.K., and Y.C. provided all pre-trial biospecimen processing optimization experiments. M.T., R.T., R.C., and Y.C. collected, processed, and analyzed all clinical biospecimens and data accrued from the trial. H.W. and D.C. provided all histopathologic analysis and immunohistochemical grading and scoring.

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1. Kim, M.P., Evans, D.B., Wang, H., Abbruzzese, J.L., Fleming, J.B., and Gallick, G.E. 2009. Generation of orthotopic and heterotopic human pancreatic cancer xenografts in immunodeficient mice. *Nat Protoc* 4:1670-1680.
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ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): James
2. Surname (Last Name): Abbruzzese
3. Date: 30-September-2013

4. Are you the corresponding author? ☐ Yes ☑ No Corresponding Author's Name:

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Dr. Abbruzzese has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Priya
2. Surname (Last Name): Bhosale
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No
Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Patent?	Pending?	Issued?	Licensed?	Royalties?	Licensee?	Comments	
System and Methods for Quantitatively Describing Biological Markers	☑	☐	☐	☐		CT analysis method	

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Dr. Bhosale reports no financial conflicts of interest. Dr. Bhosale has a patent "System and Methods for Quantitatively Describing Biological Markers" pending.

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Section 1. Identifying Information

1. Given Name (First Name): Deyali
2. Surname (Last Name): Chatterjee
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Dr. Chatterjee has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name): Rong
2. Surname (Last Name): Chen
3. Date: 30-September-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason B. Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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1. Given Name (First Name): Yuling
2. Surname (Last Name): Chen
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Corresponding Author's Name: Jason B. Fleming, M.D.

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

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Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Christopher
2. Surname (Last Name): Crane
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Patent?	Pending?	Issued?	Licensed?	Royalties?	Licensee?	Comments	
System and Methods for Quantitatively Describing Biological Markers	☑	☐	☐	☐		CT analysis method	

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Section 5. Relationships not covered above

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Section 6. Disclosure Statement

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Dr. Crane reports no financial conflicts of interest. Dr. Crane has a patent "System and Methods for Quantitatively Describing Biological Markers" pending.

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Vittorio
2. Surname (Last Name): Cristini
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Mauro
2. Surname (Last Name): Ferrari
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No
Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Jason
2. Surname (Last Name): Fleming
3. Date: 01-October-2013

4. Are you the corresponding author? ☑ Yes ☐ No

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Vijaya
2. Surname (Last Name): Gottumukkala
3. Date: 28-September-2013

4. Are you the corresponding author? ☐ Yes ☑ No Corresponding Author's Name:

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

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Dr. Gottumukkala has nothing to disclose.

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Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Milind
2. Surname (Last Name): Javle
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

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Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Javle has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Ya'an
2. Surname (Last Name): Kang
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Section 6. Disclosure Statement

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Dr. Kang has nothing to disclose.

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Matthew
2. Surname (Last Name): Katz
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Section 6. Disclosure Statement

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Dr. Katz has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Eugene
2. Surname (Last Name): Koay
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Patent?	Pending?	Issued?	Licensed?	Royalties?	Licensee?	Comments	
System and Methods for Quantitatively Describing Biological Markers	☑	☐	☐	☐		CT analysis method	

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Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Koay reports no financial conflicts of interest. Dr. Koay has a patent "System and Methods for Quantitatively Describing Biological Markers" pending.

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Jeffery
2. Surname (Last Name): Lee
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Dr. Lee has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): William
2. Surname (Last Name): Plunkett
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

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Section 6. Disclosure Statement

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Dr. Plunkett has nothing to disclose.

Evaluation and Feedback

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4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Marc
2. Surname (Last Name): Rozner
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Rozner has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Haifa
2. Surname (Last Name): Shen
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Patent?	Pending?	Issued?	Licensed?	Royalties?	Licensee?	Comments	
System and Methods for Quantitatively Describing Biological Markers	☑	☐	☐	☐		CT analysis method	

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Dr. Shen reports no financial conflicts of interest. Dr. Shen has a patent "System and Methods for Quantitatively Describing Biological Markers" pending.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Eric
2. Surname (Last Name): Tamm
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Tamm has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Ryan
2. Surname (Last Name): Thomas
3. Date: 30-September-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason B. Fleming, MD

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Thomas has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name): Mark
2. Surname (Last Name): Truty
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Truty has nothing to disclose.

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4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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Section 1. Identifying Information

1. Given Name (First Name): Gauri
2. Surname (Last Name): Varadhachary
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

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Dr. Varadhachary has nothing to disclose.

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1. Identifying information.

2. The work under consideration for publication.

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Section 1. Identifying Information

1. Given Name (First Name): Huamin
2. Surname (Last Name): Wang
3. Date: 28-September-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jasson Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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Section 1. Identifying Information

1. Given Name (First Name): Robert
2. Surname (Last Name): Wolff
3. Date: 01-October-2013

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Jason Fleming

5. Manuscript Title: Transport properties of pancreatic cancer describe gemcitabine delivery and response

6. Manuscript Identifying Number (if you know it):

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