SUPPLEMENTAL TABLE 1: Initialization parameters for non-linear least squares fitting

Parameter	v_b *(mL/mL)*	K_1 *(mL/min/mL)*	k_2 *(min^{-1})*	k_3 *(min^{-1})*	k_4 *(min^{-1})*	*Delay (s)*
Initial value	0.01	0.01	0.01	0.01	-	0
Upper bound	1.0	5.0	5.0	1.0	-	50
Lower bound	0.0001	0.0	0.0	0.0	-	0

SUPPLEMENTAL TABLE 2: Absolute bias (s.d.) in seconds of LE and CFD delay estimates for 2- and 10-second frame lengths

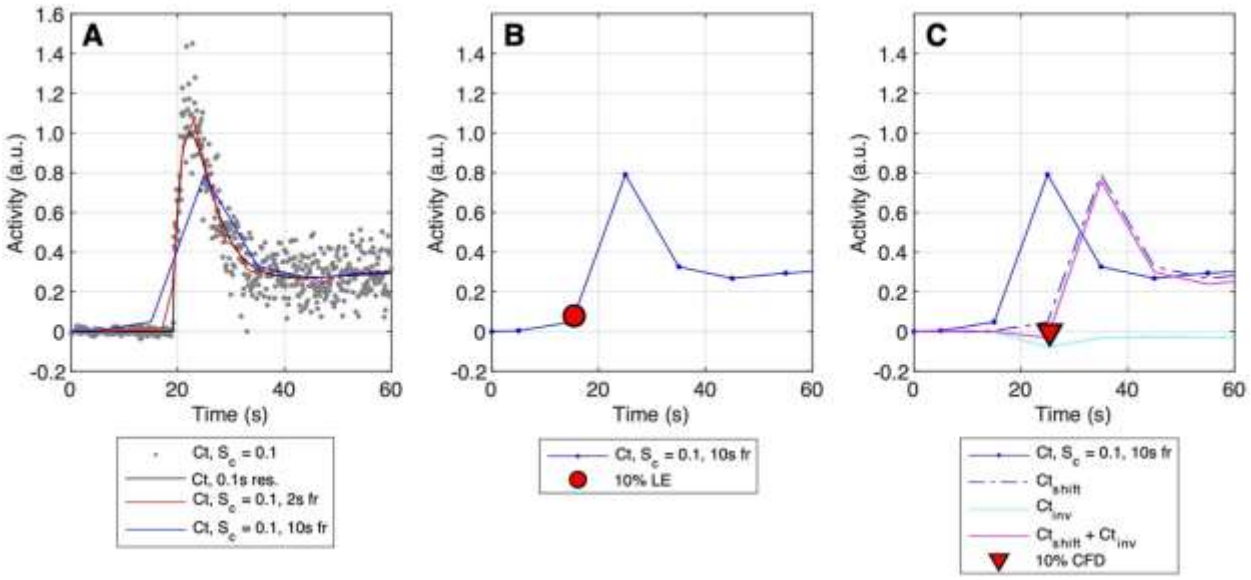
	LE								*CFD*							
Noise Level	0.03		0.1		0.2		0.3		0.03		0.1		0.2		0.3	
Threshold/ Attenuation fraction	**LE, 2 s frames**								**CFD, 2 s frames**							
2.5%	1.49	(0.38)	1.54	(0.39)	1.61	(0.63)	5.93	(9.99)	5.24	(13.14)	13.71	(19.38)	22.28	(20.22)	27.97	(18.52)
5%	1.23	(0.33)	1.25	(0.34)	1.29	(0.35)	1.33	(0.37)	0.74	(2.85)	5.63	(13.71)	11.75	(18.46)	16.62	(19.99)
10%	0.88	(0.24)	0.89	(0.25)	0.91	(0.27)	0.93	(0.29)	0.62	(0.41)	0.64	(0.98)	2.43	(8.30)	5.53	(13.29)
15%	0.61	(0.21)	0.62	(0.22)	0.63	(0.23)	0.64	(0.26)	0.67	(0.46)	0.69	(0.47)	0.71	(0.82)	1.19	(4.31)
20%	0.39	(0.17)	0.40	(0.18)	0.40	(0.20)	0.41	(0.22)	0.80	(0.53)	0.79	(0.52)	0.79	(0.52)	0.79	(0.72)
25%	0.20	(0.13)	0.21	(0.14)	0.22	(0.15)	0.24	(0.17)	0.87	(0.55)	0.87	(0.55)	0.87	(0.55)	0.86	(0.55)
30%	**0.11**	**(0.05)**	**0.11**	**(0.07)**	**0.14**	**(0.10)**	**0.18**	**(0.13)**	0.94	(0.56)	0.93	(0.56)	0.93	(0.56)	0.93	(0.57)
40%	0.32	(0.09)	0.32	(0.12)	0.34	(0.17)	0.35	(0.21)	1.00	(0.56)	1.04	(0.57)	1.06	(0.58)	1.07	(0.59)
50%	0.63	(0.09)	0.63	(0.12)	0.65	(0.19)	0.67	(0.25)	1.18	(0.58)	1.18	(0.58)	1.20	(0.60)	1.20	(0.61)
Threshold/ Attenuation fraction	**LE, 10 s frames**								**CFD, 10 s frames**							
2.5%	8.46	(2.34)	8.64	(2.39)	8.95	(2.65)	15.13	(11.40)	4.27	(7.53)	7.36	(11.87)	14.44	(16.73)	20.69	(17.57)
5%	7.70	(2.22)	7.81	(2.25)	7.99	(2.28)	8.20	(2.32)	2.73	(1.59)	5.16	(9.26)	6.65	(11.03)	10.10	(14.31)
10%	6.65	(2.04)	6.74	(2.06)	6.86	(2.08)	6.99	(2.10)	2.78	(1.66)	2.78	(1.67)	4.08	(6.63)	5.02	(8.36)
15%	5.84	(1.94)	5.91	(1.96)	6.00	(1.99)	6.09	(2.00)	2.94	(1.86)	2.95	(1.86)	2.94	(1.86)	3.06	(2.59)
20%	5.14	(1.82)	5.20	(1.84)	5.28	(1.86)	5.35	(1.88)	3.01	(1.94)	3.01	(1.94)	3.01	(1.93)	3.01	(1.93)
25%	4.47	(1.71)	4.52	(1.73)	4.59	(1.75)	4.65	(1.77)	3.05	(1.98)	3.06	(1.98)	3.06	(1.98)	3.06	(1.98)
30%	3.80	(1.64)	3.85	(1.65)	3.91	(1.67)	3.96	(1.69)	3.10	(2.02)	3.10	(2.02)	3.09	(2.01)	3.09	(2.01)
40%	2.50	(1.59)	2.54	(1.60)	2.59	(1.62)	2.63	(1.63)	3.10	(2.02)	3.10	(2.02)	3.10	(2.02)	3.12	(2.04)
50%	1.58	(1.30)	1.61	(1.31)	1.64	(1.33)	1.66	(1.34)	3.21	(2.12)	3.18	(2.10)	3.21	(2.12)	3.25	(2.15)

SUPPLEMENTAL TABLE 3: Absolute bias (s.d.) of delay estimates (s) across different LE thresholds, framing protocols, noise levels

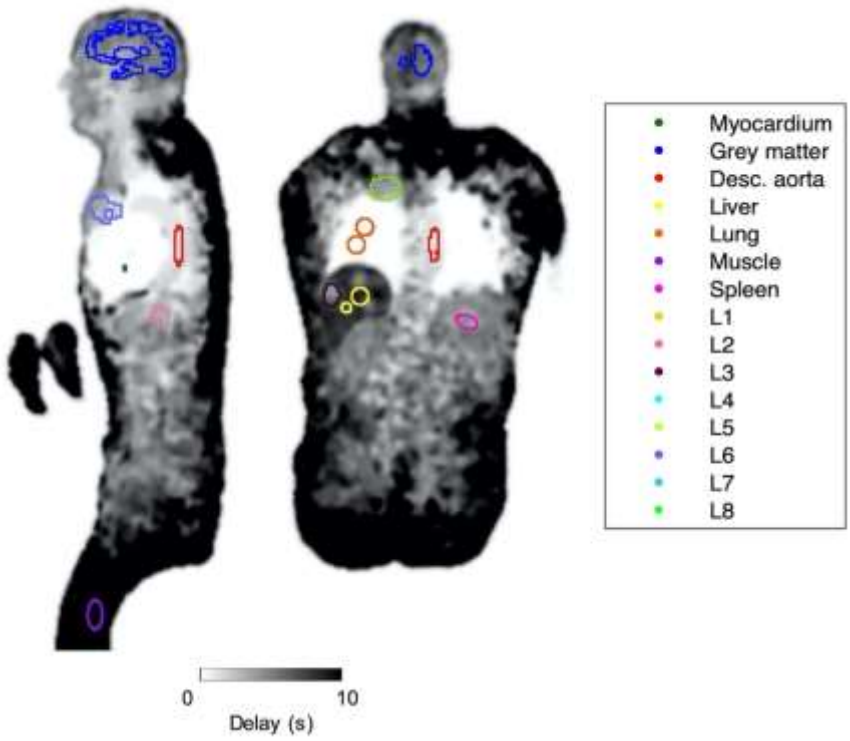
Noise Level (Sc)	0.03		0.1		0.2		0.3	
Framing (s)				**5% LE**				
0.1 (Native)	0.03	(0.01)	0.03	(0.02)	1.83	(6.89)	11.06	(15.0)
1	0.54	(0.14)	0.55	(0.15)	0.56	(0.17)	0.58	(0.27)
2	1.23	(0.33)	1.25	(0.34)	1.29	(0.35)	1.33	(0.37)
5	3.58	(0.85)	3.64	(0.86)	3.73	(0.90)	3.82	(0.94)
10	7.70	(2.22)	7.81	(2.25)	7.99	(2.28)	8.20	(2.32)
				10% LE				
0.1 (Native)	0.01	(0.01)	0.03	(0.03)	0.06	(0.06)	0.08	(0.09)
1	0.32	(0.10)	0.32	(0.11)	0.32	(0.13)	0.32	(0.16)
2	0.88	(0.24)	0.89	(0.25)	0.91	(0.27)	0.93	(0.29)
5	2.88	(0.72)	2.92	(0.74)	2.97	(0.76)	3.04	(0.78)
10	6.65	(2.04)	6.74	(2.06)	6.86	(2.08)	6.99	(2.10)
				20% LE				
0.1 (Native)	0.08	(0.02)	0.13	(0.07)	0.18	(0.12)	0.21	(0.15)
1	0.06	(0.04)	0.06	(0.05)	0.09	(0.07)	0.12	(0.09)
2	0.39	(0.17)	0.40	(0.18)	0.40	(0.20)	0.41	(0.22)
5	1.89	(0.65)	1.92	(0.66)	1.95	(0.67)	2.00	(0.69)
10	5.14	(1.82)	5.20	(1.84)	5.28	(1.86)	5.35	(1.88)
				25% LE				
0.1 (Native)	0.14	(0.03)	0.21	(0.09)	0.26	(0.15)	0.30	(0.19)
1	0.09	(0.05)	0.10	(0.06)	0.14	(0.09)	0.16	(0.13)
2	0.20	(0.13)	0.21	(0.14)	0.22	(0.15)	0.24	(0.17)
5	1.51	(0.64)	1.53	(0.64)	1.56	(0.65)	1.60	(0.67)
10	4.47	(1.71)	4.52	(1.73)	4.59	(1.75)	4.65	(1.77)
				30% LE				
0.1 (Native)	0.22	(0.04)	0.30	(0.11)	0.36	(0.18)	0.40	(0.22)
1	0.19	(0.05)	0.21	(0.07)	0.24	(0.12)	0.26	(0.16)
2	0.11	(0.05)	0.11	(0.07)	0.14	(0.10)	0.18	(0.13)
5	1.16	(0.61)	1.18	(0.61)	1.21	(0.63)	1.23	(0.64)
10	3.80	(1.64)	3.85	(1.65)	3.91	(1.67)	3.96	(1.69)
				40% LE				
0.1 (Native)	0.40	(0.05)	0.50	(0.14)	0.58	(0.24)	0.64	(0.30)
1	0.40	(0.04)	0.42	(0.07)	0.46	(0.14)	0.50	(0.21)
2	0.32	(0.09)	0.32	(0.12)	0.34	(0.17)	0.35	(0.21)
5	0.64	(0.40)	0.65	(0.42)	0.66	(0.45)	0.67	(0.48)
10	2.50	(1.59)	2.54	(1.60)	2.59	(1.62)	2.63	(1.63)
				50% LE				
0.1 (Native)	0.61	(0.06)	0.74	(0.18)	0.85	(0.31)	0.93	(0.40)
1	0.61	(0.05)	0.63	(0.09)	0.69	(0.17)	0.75	(0.27)
2	0.63	(0.09)	0.64	(0.12)	0.65	(0.19)	0.67	(0.25)
5	0.50	(0.30)	0.51	(0.30)	0.52	(0.30)	0.54	(0.32)
10	1.58	(1.30)	1.61	(1.32)	1.64	(1.33)	1.67	(1.35)

SUPPLEMENTAL TABLE 4: Impact of delay correction on mean parametric Patlak K_i (mL/min/100 mL) for representative GUC patient

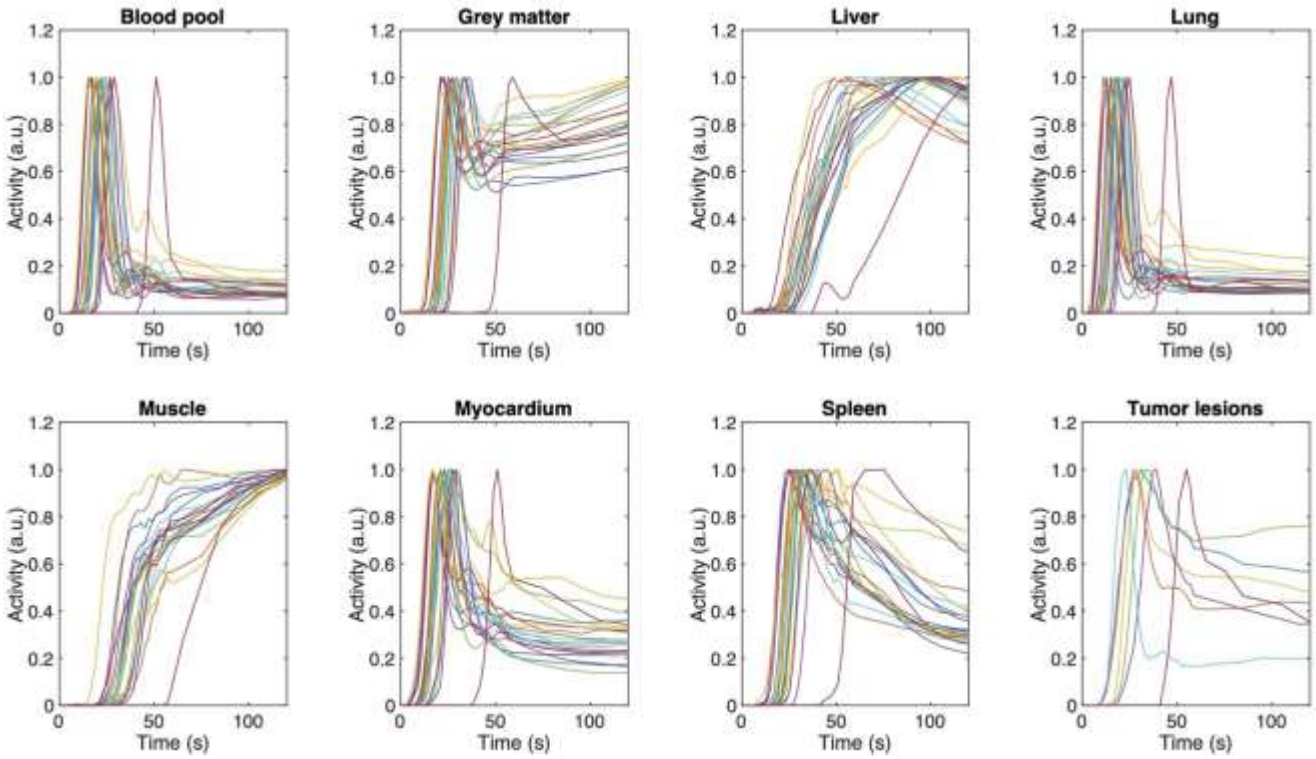
Tissue	*JE*	*LE*	*No delay correction*
Grey matter	1.253	1.250	1.249
Liver	0.118	0.116	0.113
Lung	0.094	0.094	0.094
Muscle	0.051	0.050	0.049
Myocardium	0.252	0.252	0.252
Spleen	0.302	0.302	0.301
L1	0.300	0.300	0.299
L2	0.187	0.187	0.186
L3	0.309	0.308	0.306
L4	0.214	0.213	0.211
L5	0.270	0.269	0.268
L6	0.317	0.316	0.316
L7	0.130	0.129	0.128
L8	0.277	0.277	0.276



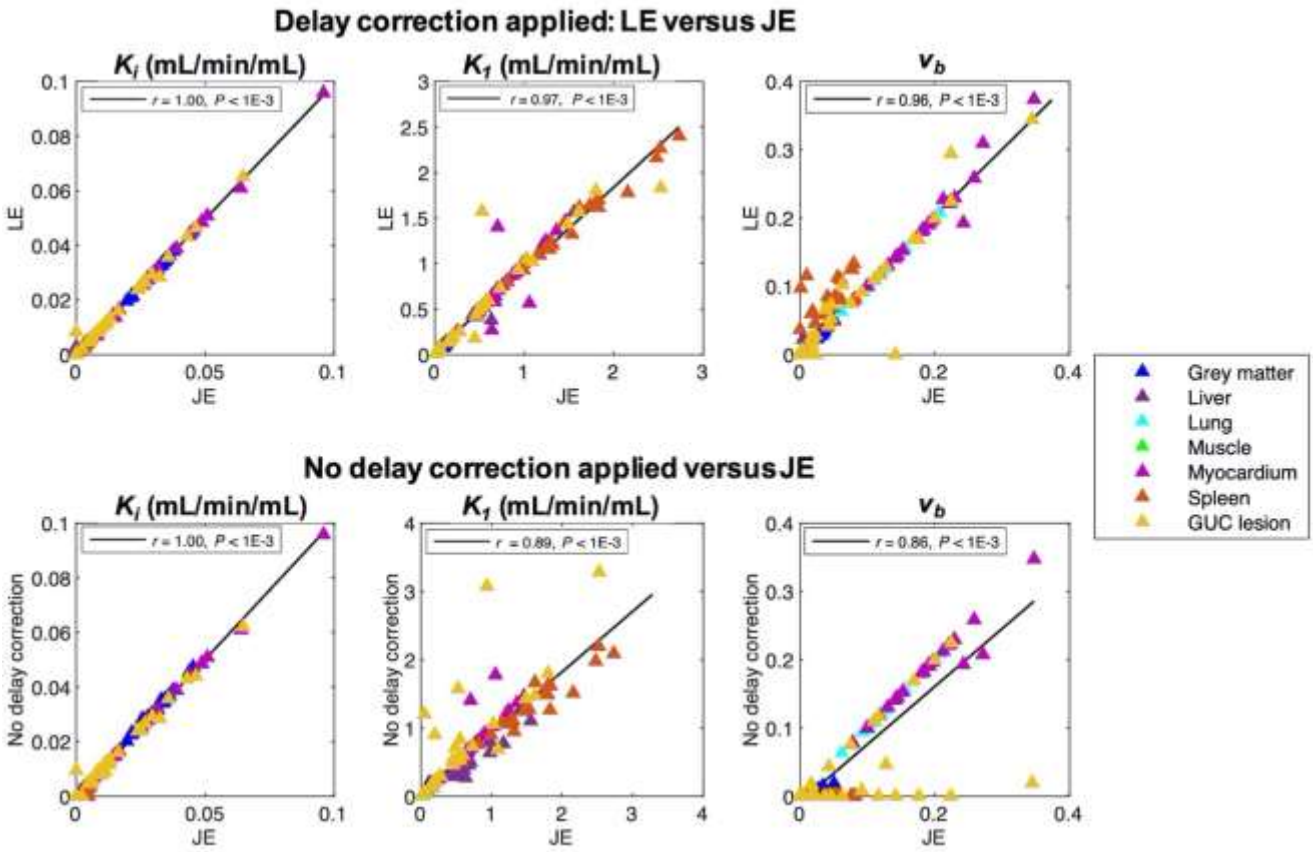
SUPPLEMENTAL FIGURE 1: Time activity curves (TACs) for simulations (A), example LE (B) and CFD (C) delay estimates. In the left panel, a delay of 19.2 seconds was used to shift the IF and generate the ground truth TAC (—). In this example noisy realization (•), the scaling factor of the standard deviation S_c is equal to 0.1. The TACs were then re-binned to reflect different frame lengths. Shown here are 2 (—) and 10 (—) second frames, with example LE (B, ●) and CFD (C, ▼) delay estimates for the 10-second frames. For the LE delay estimation in (B), a 10% LE trigger threshold was selected to mark the time at which the signal amplitude passes the trigger value, which is recorded as the arrival time. For the CFD method in (C), the following three steps were performed: (i) TACs were shifted in time by 2 seconds for shorter framing, or 1 frame when the frame length was greater than 2 seconds (C, Ct_{shift}). (ii) Attenuated and inverted versions of the TAC (attenuated to between 2.5 and 50% of the peak activity) (C, Ct_{inv}) were added to the shifted TAC. (iii) The zero-crossing point, or the timepoint at which the TAC sign changes from negative to positive marks the arrival time (C, ▼).



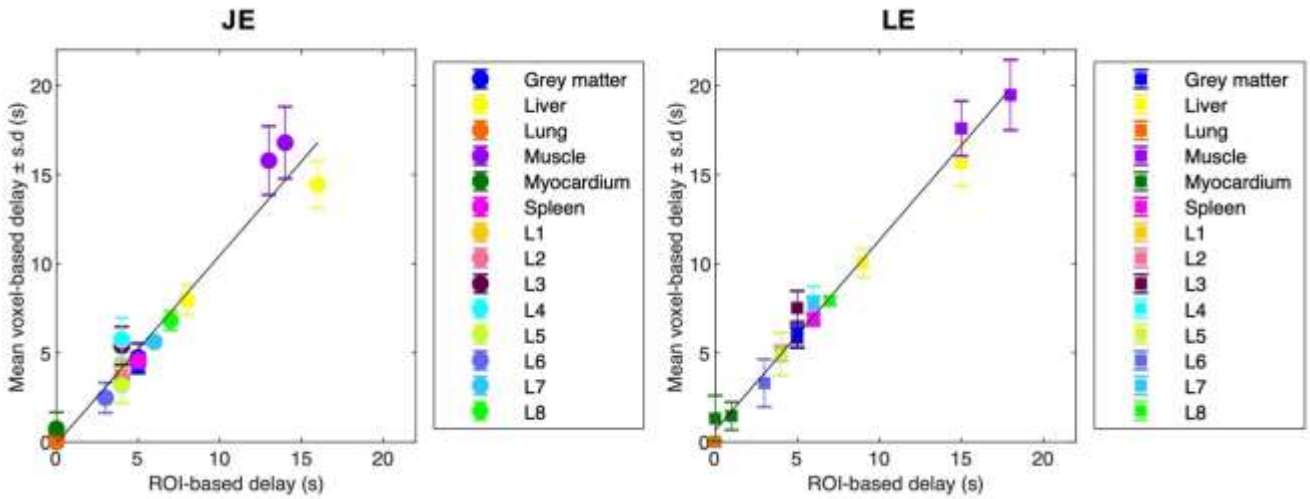
SUPPLEMENTAL FIGURE 2: Cross sectional delay maps with overlay of regions of interest (ROIs) from a number of GUC patient tissues selected for parametric kinetic analysis. As noted in the text, an additional vascular ROI was delineated in order to assess the impact of delay correction within the blood pool. The descending aorta, as shown above, reflects a positive delay value with respect to the left ventricle.



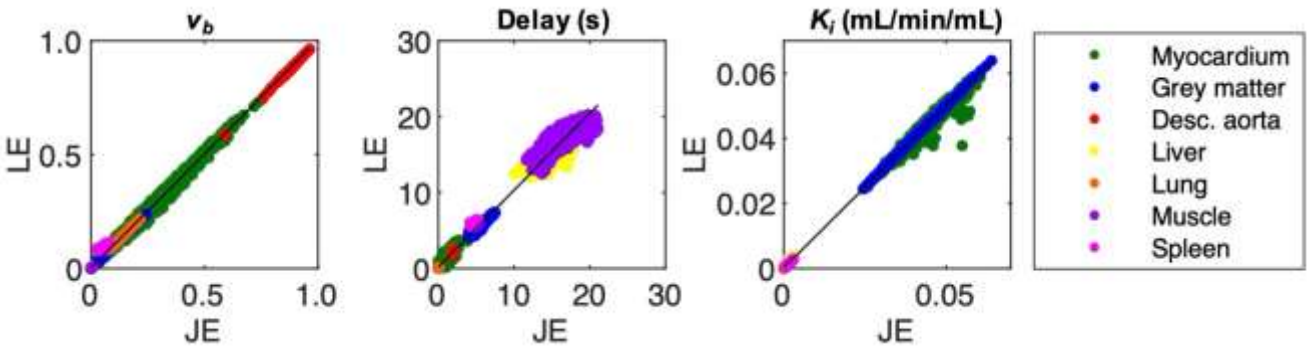
SUPPLEMENTAL FIGURE 3: TACs in a number of healthy subject and GUC patient tissues. As noted in the caption for Fig. 1, a single lesion is shown per GUC patient for ease of visualization.



SUPPLEMENTAL FIGURE 4: Parameter estimates as compared to JE. Linear fits were performed on pooled ROI-based results. *Top:* LE estimates for K_i (r=1.00, P<1E-3, slope: 0.99), K_1 (r=0.97, P<1E-3, slope: 0.91), and v_b (r=0.96, P<1E-3, slope: 0.98), were in strong agreement with JE. *Bottom:* Without delay correction, K_i results were not affected (r=1.00, P<1E-3, slope: 1.02). However, estimates for K_1 (r = 0.89, P<1E-3, slope: 0.89) and v_b (r=0.86, P<1E-3, slope: 0.85) were poorer in some tissues when delay correction was not applied, notably in the spleen and GUC lesions.



SUPPLEMENTAL FIGURE 5: Average parametric delay estimates as compared to ROI-based estimates. *Left:* JE estimates for delay (r=0.97, P<1E-3, slope: 1.05), were in strong agreement with ROI-based TAC results. *Right:* LE estimates for delay (r=0.99, P<1E-3, slope: 1.06) were also in strong agreement with ROI-based TAC results. To generate this figure, parametric delay values were averaged across all voxels per tissue. Delay estimates for both representative subjects were included.



SUPPLEMENTAL FIGURE 6: Parametric LE versus JE results for a representative healthy subject. LE delay was in agreement with JE results (r=0.99, P<1E-3, slope: 1.01), but demonstrated a spread of delay values in the liver and muscle for both methods. LE estimates of v_b (r=1.00, P<1E-3, slope: 1.00) and K_i (r=1.00, P<1E-3, slope: 0.99) were in agreement with JE results.