SUPPLEMENTARY MATERIAL

Table S1 Patient characteristics and PET parameters.

Patient	Sex	TNM	Histology	Primary and metastases	[18F]D4-FCH Dynamic SUV 5 min mean	max	Scan SUV 30 min mean	max	SUV 60 min mean	max	[18F[D4-FCH Static Scan SUV 60 min mean	max	[18F[FDG Static Scan SUV 60 min mean	max
1	F	T4N0M1c	Adenocarcinoma	Primary tumor	4.51	7.88	4.76	8.42	4.77	8.46	4.73	8.64	No FDG	
				Satellite nodule							7.18	13.72		
				Scapular Met							7.17	10.64		
				Scalp Met							6.73	10.56		
				Liver Met							3.36	8.36		
2	F	T4N2M1b	Squamous	Primary tumor	3.58	8.57	4.23	9.10	4.28	9.51	6.06	10.13	No FDG	
				Hilar node							7.17	9.75		
				Liver Met							8.83	12.7		
3	M	T2aN0M0	Squamous	Primary tumor	2.28	2.65	2.64	3.01	2.80	3.17	2.95	6.14	7.46	11.95
				Paratracheal node*							3.42	5.11	2.38	2.82
				Hilar node*							3.01	4.32	2.04	2.19
4	F	T1bN1M0	Squamous	Primary tumor	2.96	4.32	3.11	4.29	3.20	4.53	3.46	5.41	7.10	10.77
				Hilar node¥							2.41	3.13	4.48	6.12
5	M	T4N1M0	Squamous	Primary tumor	5.36	7.98	5.26	7.43	5.29	7.79	5.47	9.15	8.02	14.10
6	M	T2bN0M1b	Squamous	Primary tumor	3.68	7.46	3.20	6.14	3.18	6.09	3.12	3.20	9.55	12.2
				L2 vertebral met									3.12	5.40
7	F	T1bN1M0	Squamous	Primary tumor	2.85	5.32	2.59	3.87	2.54	3.83	2.24	3.18	4.96	6.89
				Hilar node¥							2.64	3.46	3.10	3.83
8	F	T3N2M0	Adenocarcinoma	Primary tumor	6.11	12.48	6.70	14.30	6.93	16.19	4.26	8.61	No FDG	
				PT node							3.07	3.83		
9	M	T1bN0M0	Adenocarcinoma	Primary tumor	3.34	4.76	3.34	5.03	3.39	5.15	2.79	3.68	5.43	7.36
10	M	T4N3M1a	Adenocarcinoma	Primary tumor	3.53	6.70	2.51	5.05	2.13	4.68	3.00	3.80	No FDG	
				Hilar node							3.11	3.98		

#	Sex	Stage	Histology	Lesion										
				Hilar node							2.51	3.17		
				LUL tumor mass	3.01	7.10	2.61	3.80	2.47	3.97	2.29	3.10		
				PT node							2.66	3.73		
				Hilar node (2)							2.21	2.62		
				Hilar node (2)							2.82	3.30		
11	M	**T3N1M0**	Squamous	Primary tumor 1	3.86	5.11	4.06	5.69	4.24	6.19	3.65	4.84	5.11	6.94
				Primary tumor 2	4.23	7.04	4.68	7.43	4.84	8.15	4.82	6.99	11.93	22.64
12	F	**T3N2M1b**	Adenocarcinoma	Primary tumor (mix of pleural fluid)	2.61	2.61	2.23	2.23	2.08	2.08	1.94	2.87	3.70	5.63
13	F	**T3N1M1b**	Adenocarcinoma	Primary tumor (chest wall)	4.18	4.62	3.54	4.17	3.23	4.57	2.77	4.45	5.53	10.01
				Hilar node							3.22	4.77	4.87	10.53
				Hilar node							3.66	4.36	4.00	5.12
14	F	**T4N2M1a**	Squamous	Primary tumor	3.09	4.64	2.80	4.03	2.65	3.97	2.87	3.48	7.29	12.82
				Hilar node							2.12	2.89	2.16	2.95
				Ant rib met							3.73	4.22	6.10	10.54
				LUL tumor	1.49	3.40	1.56	2.25	1.55	2.35	2.19	2.69	4.28	5.25
15	M	**T3N2M1b**	Squamous	Primary tumor	2.41	5.38	3.28	6.33	3.41	6.39	3.54	7.59	4.11	7.58
				Hilar node							3.37	4.22	3.28	4.80
				Post Rib met							3.05	5.23	4.03	6.07
				Ant rib met							3.22	4.21	3.57	5.48
				Subcarinal node							2.55	4.45	5.33	8.90
16	M	**T4N2M0**	Adenocarcinoma	Primary tumor	2.61	5.83	2.90	5.22	2.96	6.16	2.60	3.84	7.06	12.28
				Hilar node							2.70	3.33	5.71	6.38
				Hilar node							1.86	2.33	7.24	10.56
				RLL tumor	3.67	7.53	4.39	7.59	4.16	7.10	3.86	5.47	9.46	14.91
				PT node							2.65	4.11	7.16	10.11
				PT node							3.34	4.48	8.18	13.64
17	F	**T3N2M1b**	Adenocarcinoma	Primary tumor	4.37	8.13	4.34	6.94	4.37	7.01	3.43	5.75	**No FDG**	
				PT node							3.26	4.54		
				Subcarinal node							2.24	2.73		

* Node found to be negative at surgery

¥ Node found to be positive at surgery

M Male

F Female

PT Paratracheal lymph node

Met Metastasis

(TNM lung cancer staging AJCC 7TH Edition)

Table S2 Histogram analysis of parametric Ki_SA, K1_SA, Ki_P and Vt maps. Kurtosis, Skewness and Ratio (Skewness/Kurtosis) have been evaluated in tumor and healthy lung, for each patient. Last column shows CHKa expression in NSCLC. Last three rows show average (± sd) in n=10 healthy lung, n=3 lesions which showed negative CHKa expression, n=7 lesions which showed positive CHKa expression.

		Ki SA			K1 SA			Ki P			Vt			
		skewness	kurtosis	ratio	skewness	kurtosis	ratio	skewness	kurtosis	ratio	skewness	kurtosis	ratio	
Pt 3	*tum*	0.66	3.18	0.21	0.56	7.33	0.08	0.08	2.82	0.03	36.70	1566.00	0.02	**CHKa+**
	lung	0.64	2.85	0.22	0.44	2.16	0.20	1.05	3.61	0.30	26.65	911.23	0.03	
Pt 4	*tum*	4.07	25.39	0.16	1.41	4.41	0.32	1.05	3.61	0.29	19.08	385.51	0.05	**CHKa+**
	lung	-0.31	3.05	-0.10	0.41	2.78	0.15	-0.08	3.47	-0.02	13.37	231.13	0.06	
Pt 5	*tum*	10.56	149.13	0.07	3.03	14.68	0.21	-0.22	2.41	-0.09	30.02	1002.00	0.03	**CHKa+**
	lung	1.32	6.05	0.22	3.60	0.96	3.75	0.56	3.50	0.16	38.21	1656.00	0.02	
Pt 6	*tum*	1.22	5.59	0.22	2.19	18.34	0.12	0.50	3.18	0.16	24.83	661.36	0.04	**CHKa+**
	lung	1.26	5.99	0.21	1.05	3.18	0.33	1.15	4.34	0.26	19.92	579.28	0.03	
Pt 7	*tum*	5.07	31.99	0.16	2.88	13.90	0.21	-0.41	2.39	-0.17	16.55	344.84	0.05	**CHKa+**
	lung	3.58	25.22	0.14	2.54	17.05	0.15	2.07	7.17	0.29	35.30	1386.00	0.03	
Pt 8	*tum*	45.96	2175.00	0.02	2.85	29.19	0.10	0.77	5.05	0.15	56.56	3378.00	0.02	**CHKa+**
	lung	-0.08	3.28	-0.02	3.89	1.01	3.87	-0.55	3.23	-0.17	33.89	1355.00	0.03	
Pt 9	*tum*	0.46	2.28	0.20	1.13	3.78	0.30	0.20	2.30	0.09	4.04	24.77	0.16	**CHKa+**
	lung	4.33	24.21	0.18	1.67	5.69	0.29	0.51	1.50	0.34	3.55	17.94	0.20	
Pt 10	*tum*	0.03	1.98	0.01	0.74	2.54	0.29	0.05	2.72	0.01	10.46	130.21	0.08	**CHKa-**
	lung	0.91	3.69	0.25	1.67	5.22	0.32	0.42	2.44	0.17	29.12	861.07	0.03	
Pt 12	*tum*	0.58	2.66	0.22	-0.72	2.63	-0.27	-0.23	2.29	-0.10	7.59	76.27	0.10	**CHKa-**
	lung	0.30	2.14	0.14	3.75	18.16	0.21	0.19	2.73	0.07	0.38	8.78	0.04	
Pt 2	*tum*	1.12	4.08	0.27	1.26	4.19	0.30	0.18	1.77	0.10	45.46	2279.00	0.02	**CHKa-**
	lung	1.93	15.19	0.13	1.42	5.78	0.25	1.37	6.82	0.20	20.84	545.00	0.04	
Average ± SD	Lung [n = 10]	1.39 ± 1.52	9.17 ± 9.01	0.14 ± 0.11	2.05 ± 0.33	6.20 ± 6.27	0.95 ± 1.51	0.67 ± 0.76	3.88 ± 1.81	0.16 ± 0.16	22.13 ± 13.08	755.14 ± 582.63	0.05 ± 0.05	
	Tum_CHKa- [n = 3]	0.58 ± 0.55	2.91 ± 1.07	0.17 ± 0.14	0.43 ± 1.02	3.12 ± 0.93	0.11 ± 0.33	-0.01 ± 0.21	2.26 ± 0.47	0.01 ± 0.10	21.17 ± 21.08	828.50 ± 1256.46	0.07 ± 0.04	
	Tum_CHKa+ [n = 7]	9.71 ± 16.37	341.79 ± 810.02	0.15 ± 0.08	2.01 ± 0.98	13.06 ± 8.99	0.19 ± 0.10	0.28 ± 0.53	3.11 ± 0.98	0.06 ± 0.16	26.83 ± 16.74	1051.78 ± 1142.30	0.05 ± 0.05	

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Table S3 Comparison of simplified parameters to K_i_P, K_1_SA, K_i_SA, V_t_L and K_i_CM. Results of the linear regression analysis.

N=62	Simplified parameter	K_i_P			K_1_SA			K_i_SA			V_t_L			K_i_CM		
		slope	intercept	R^2	slope	intercept	R^2	slope	intercept	R^2	slope	intercept	R^2	slope	intercept	R^2
[18F]D4-FCH	**SUV$_{5mean}$**	0.02	-0.02	0.50	0.06	-0.01	0.20	-4E-07	5E-06	5E-03	0.05	0.03	0.09	3.27	-3.36	0.47
	SUV$_{60mean}$	0.02	-0.02	0.53	0.09	-0.10	0.46	2E-07	6E-06	1E-03	0.07	-0.10	0.21	3.23	-3.46	0.49
	SUV$_{5max}$	3E-04	0.04	5E-04	-3E-04	0.16	4E-03	1E-07	1E-05	0.09	-6E-04	0.13	0.01	6E-03	5.40	1E-03
	SUV$_{60max}$	1E-03	0.03	0.13	1E-03	0.13	0.02	-1E-07	9E-06	0.04	7E-04	0.09	1E-03	0.18	3.13	0.16
	SUV$_{AUC\_5mean}$	0.04	-0.01	0.39	0.08	0.05	0.10	2E-06	1E-05	0.04	0.04	0.05	0.02	0.02	5.23	4E-03
	SUV$_{AUC\_60mean}$	4E-04	-0.02	0.52	1E-03	-0.10	0.45	-1E-07	5E-06	0.03	1E-03	-0.10	0.20	0.05	-3.60	0.49
	SUV$_{AUC\_5max}$	2E-04	0.04	0.01	-6E-04	0.16	3E-03	1E-08	5E-06	0.01	-1E-03	0.12	0.01	3E-03	3.06	0.14
	SUV$_{AUC\_60max}$	2E-05	0.03	0.12	3E-04	0.13	0.02	-1E-09	8E-06	0.02	5E-06	0.10	4E-04	3E-03	3.06	0.14

A

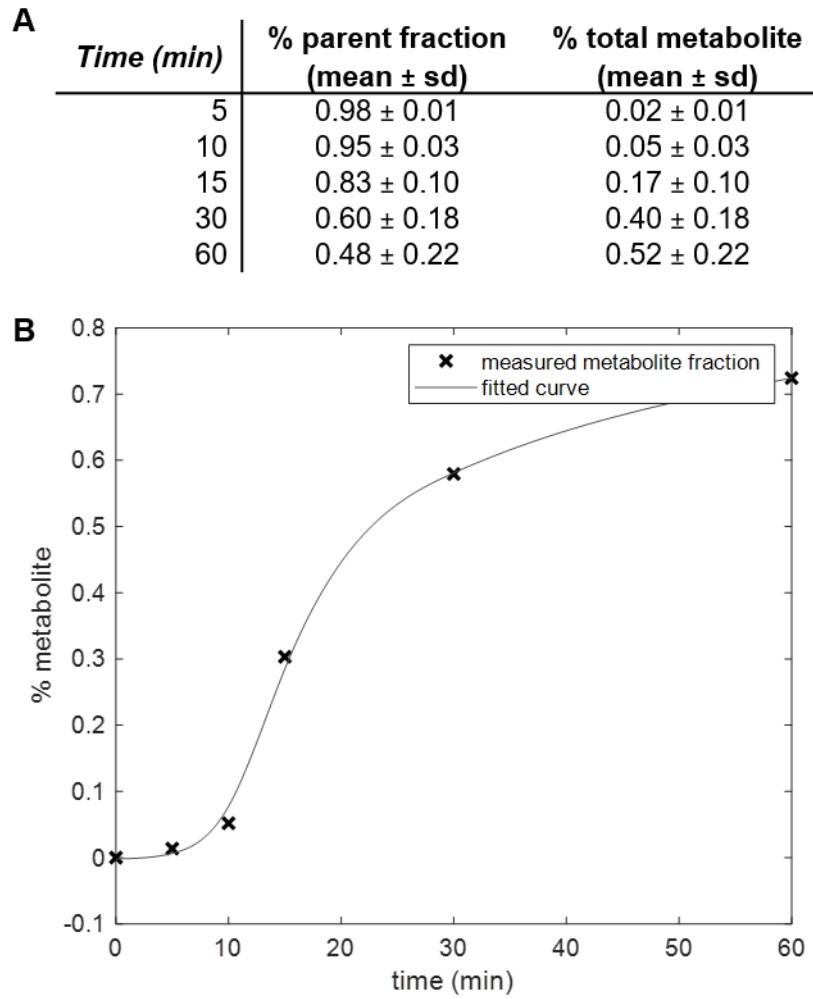| Time (min)	% parent fraction (mean ± sd)	% total metabolite (mean ± sd)
5	0.98 ± 0.01	0.02 ± 0.01
10	0.95 ± 0.03	0.05 ± 0.03
15	0.83 ± 0.10	0.17 ± 0.10
30	0.60 ± 0.18	0.40 ± 0.18
60	0.48 ± 0.22	0.52 ± 0.22

B

Figure S1 Parent and metabolite fractions measured by HPLC. A) Summary of the fraction of parent tracer and metabolite (mean ± standard deviation) measured by HPLC for each patient (*N = 11*). B) Typical fit of the metabolite fraction data for D4 choline.
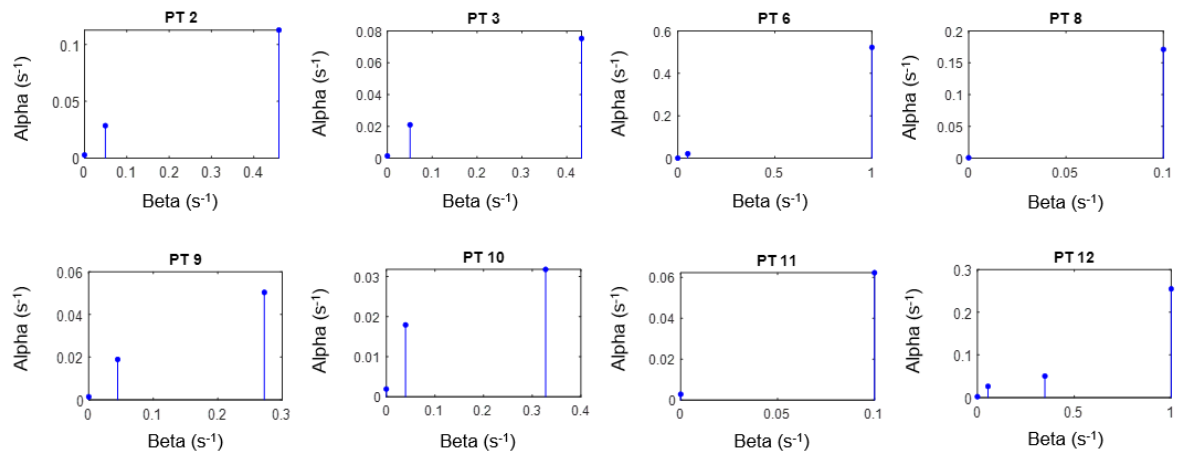
Figure S2 Spectral Analysis results. The panel shows the spectra of 8 patients where an irreversible kinetic component was found (in 0). The x axis represents the amplitude of the kinetic components while the position in the spectrum (y axis) reflects the nature of the exchanges between different compartments.
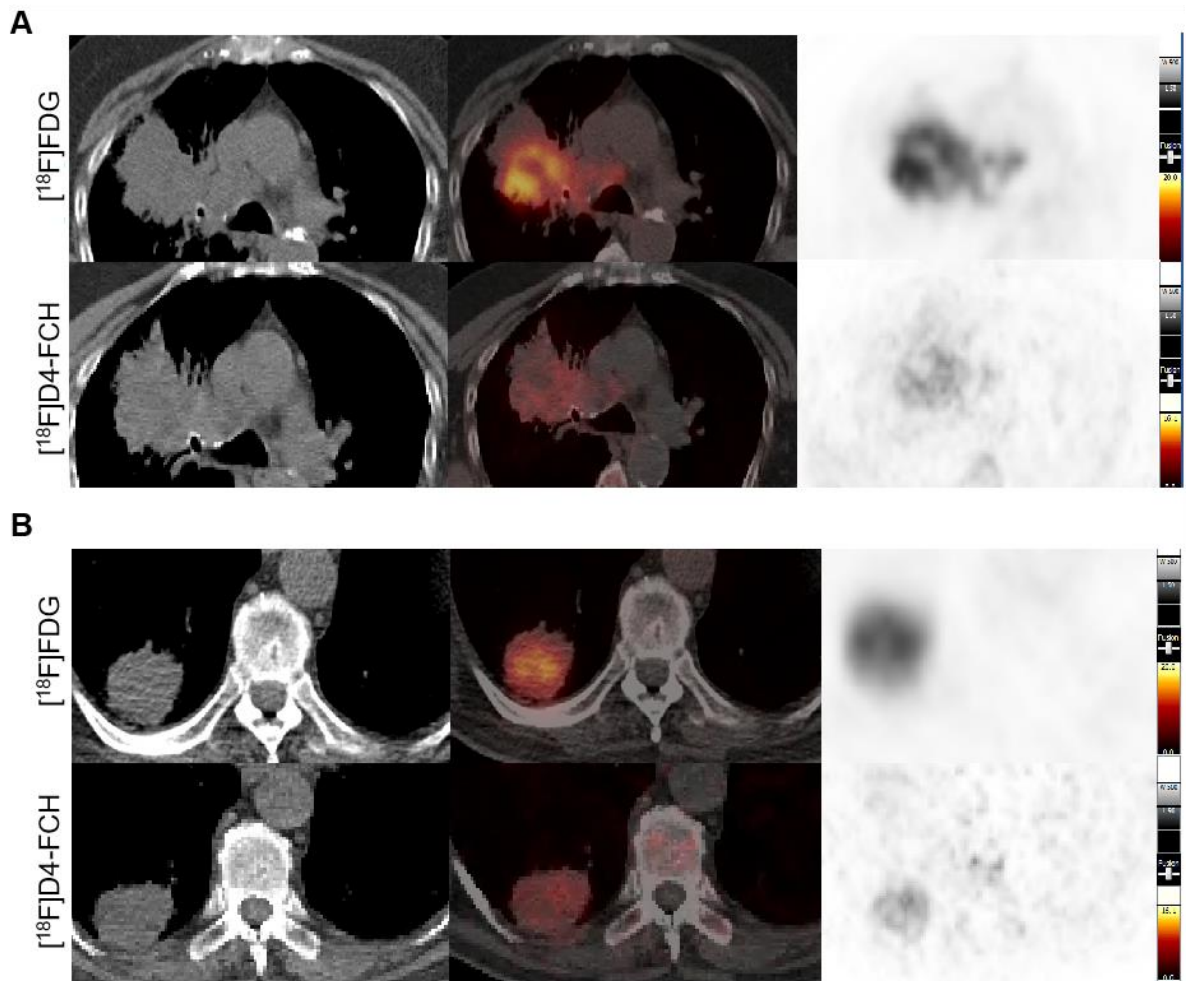
Figure S3 Display of [18F]D4-FCH and [18F]FDG images at different intensities to illustrate tumoral heterogeneity. Panel **A** and **B** show uptake of [18F]FDG and [18F]D4-FCH in tumors of patient's 16 and 9, respectively. Because, sufficient tumor variations in radiotracer localization was not visualized at SUV 0-10 (often used clinically for display) the highest display is set to 20 in the case of [18F]FDG images and 16 for [18F]D4-FCH images. There are visually non-overlapping and more heterogeneous intensity localization in [18F]D4-FCH derived images even at this display level.