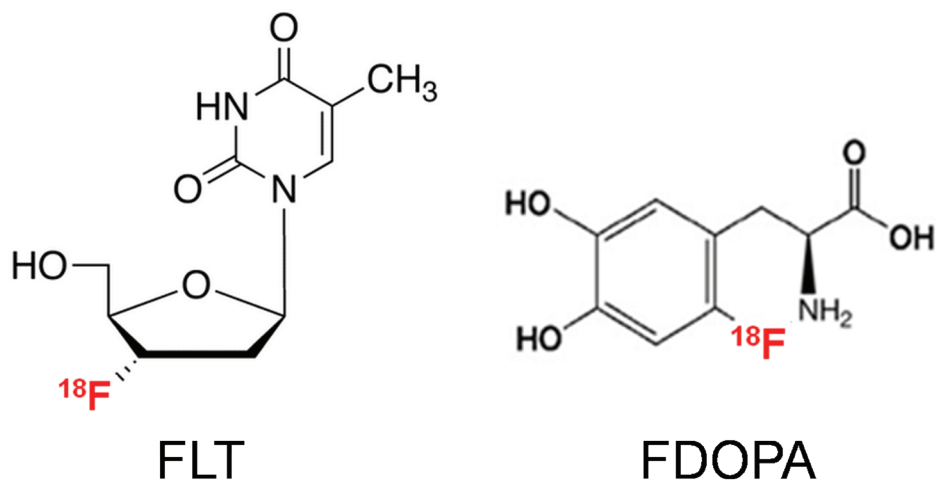
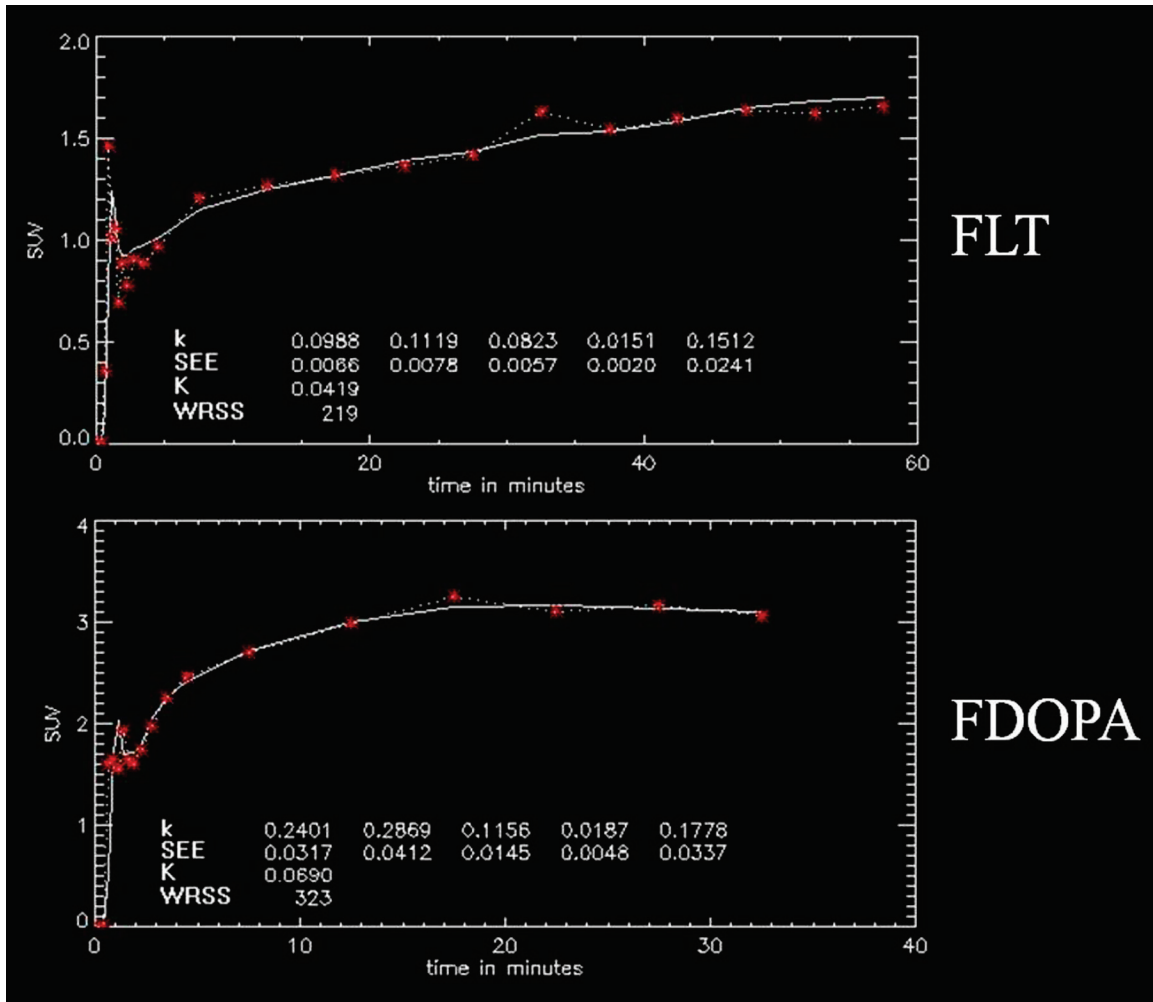


SUPPLEMENTARY MATERIALS

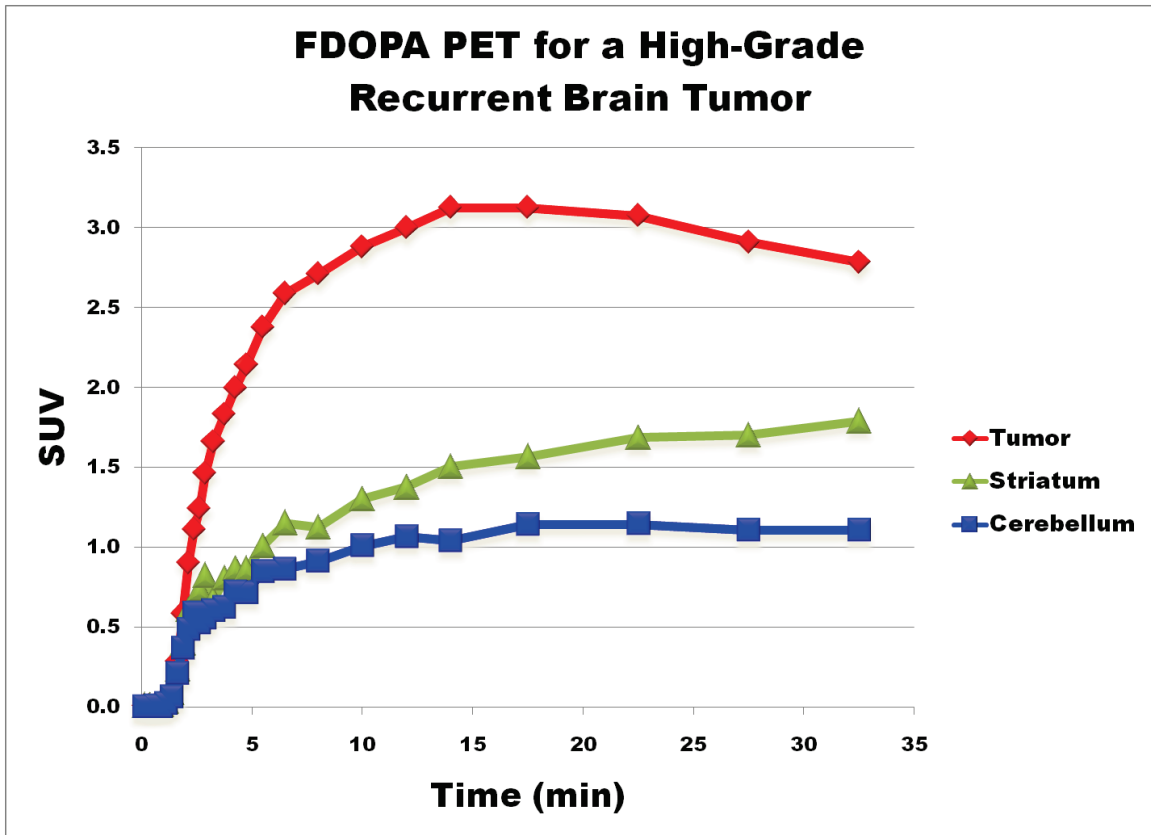
SUPPLEMENTARY FIGURES



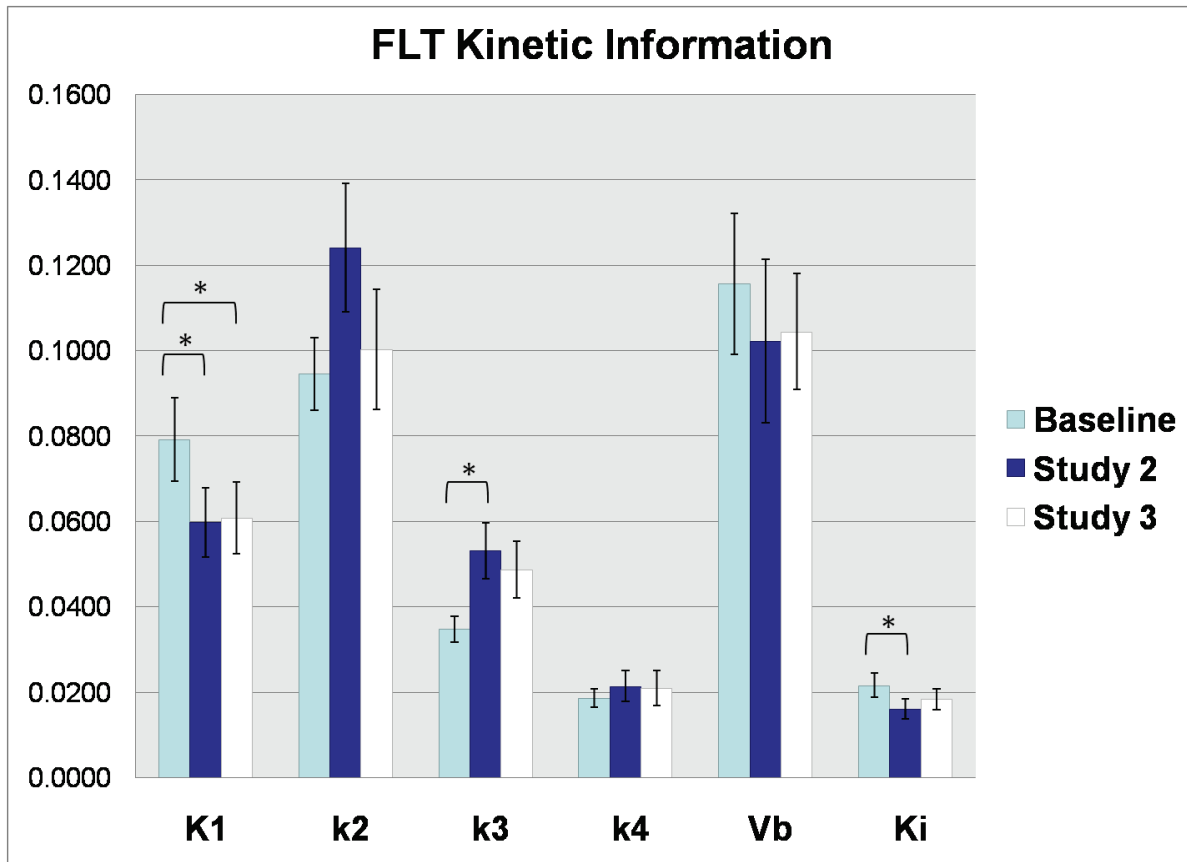
Supplementary Figure S1. Chemical structures of FLT and FDOPA. Unlabeled FLT was originally synthesized as an anti-cancer and anti-retroviral agent, and is similar in concept to azidothymidine, the first approved anti-AIDS drug [1, 2]. FLT acts as a DNA chain terminator because it lacks a 3'-hydroxyl group on the deoxyribose ring. FLT is not a substrate for thymidine phosphorylase (which is an enzyme that cleaves the sugar from the thymine base), but it is a good substrate for thymidine kinase 1 and therefore reflects metabolism by the DNA salvage pathway [1]. PET imaging with FLT was first reported by Shields *et al.* [3]. FDOPA was initially used in PET to visualize and assess the presynaptic integrity of the nigrostriatal dopamine pathway in the evaluation of patients with movement disorders such as Parkinson's disease [4, 5]. FDOPA, however, is also an amino acid analog and was shown to be taken up at the blood-brain barrier in the normal brain by neutral amino acid transporters [6]. The initial report to demonstrate the value of FDOPA PET for the detection of brain tumors came as an incidental finding in a patient undergoing evaluation for a light movement disorder of the left arm and hand [7]. The FDOPA PET scan showed that the patient not only had an asymmetric reduction in dopamine uptake in the putamen, but also a low-grade glioma in the right frontal lobe [7].



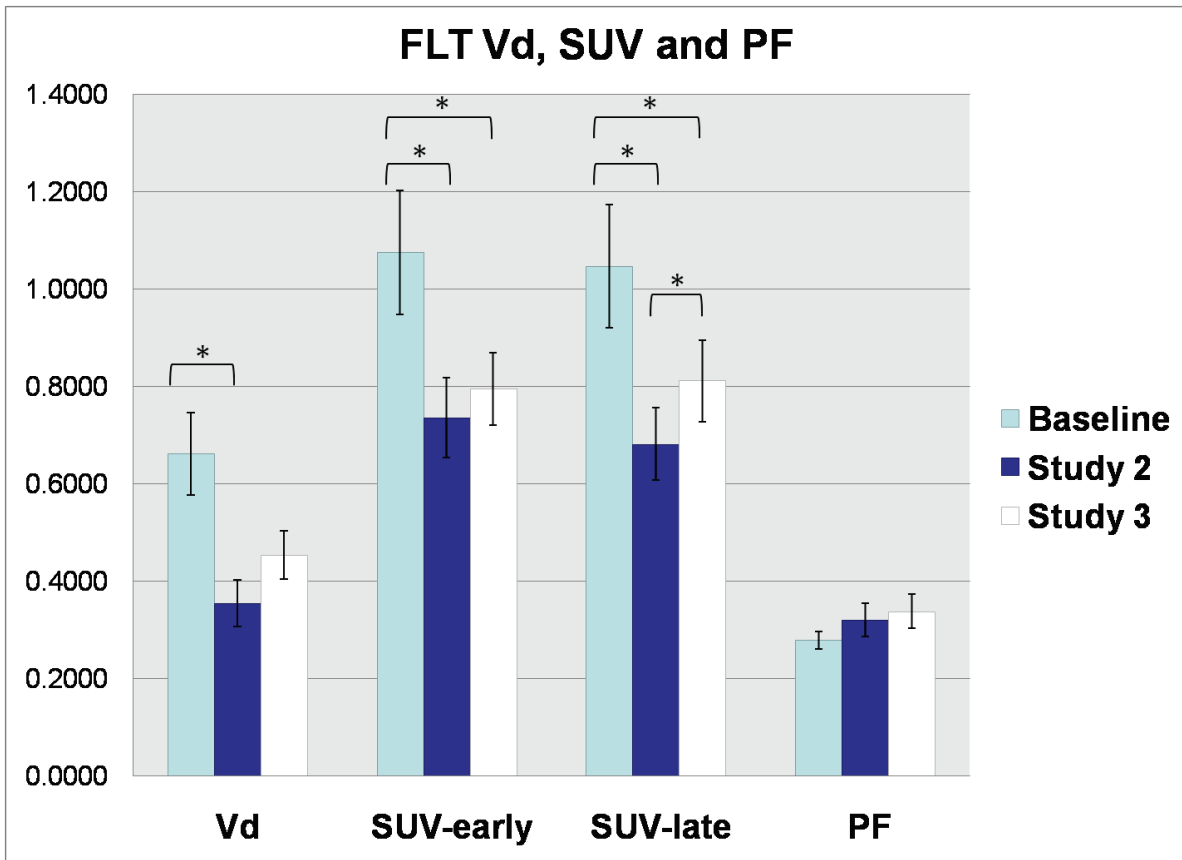
Supplementary Figure S2. Measured (dashed line and red markers) and model fitted (solid white line) tumor time-activity curves for FLT and FDOPA PET studies after the start of treatment. Tumor curves shown above are from a short-term survivor (Patient 4 in Table 1). Notice the early vascular component in the measured and fitted data.



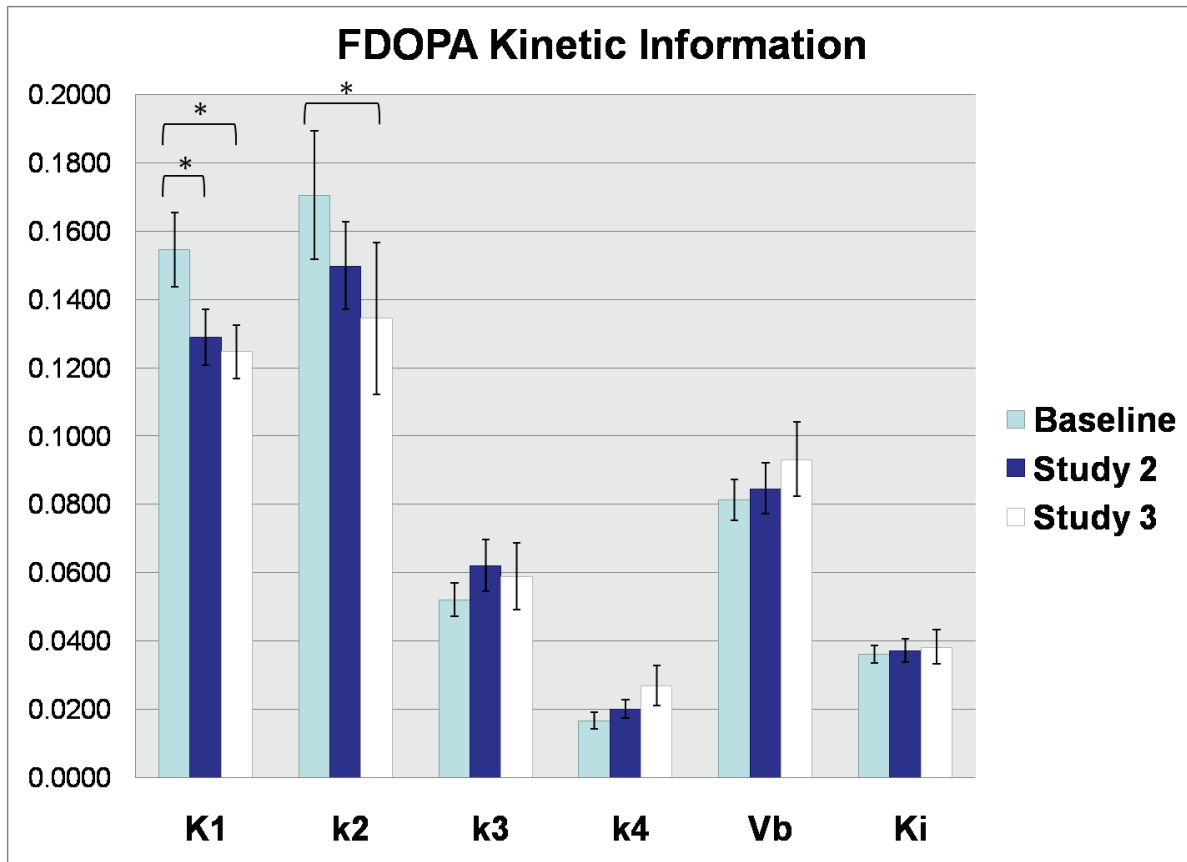
Supplementary Figure S3. Sample FDOPA time-activity curves of the tumor, striatum, and cerebellum for a recurrent brain tumor patient at baseline.



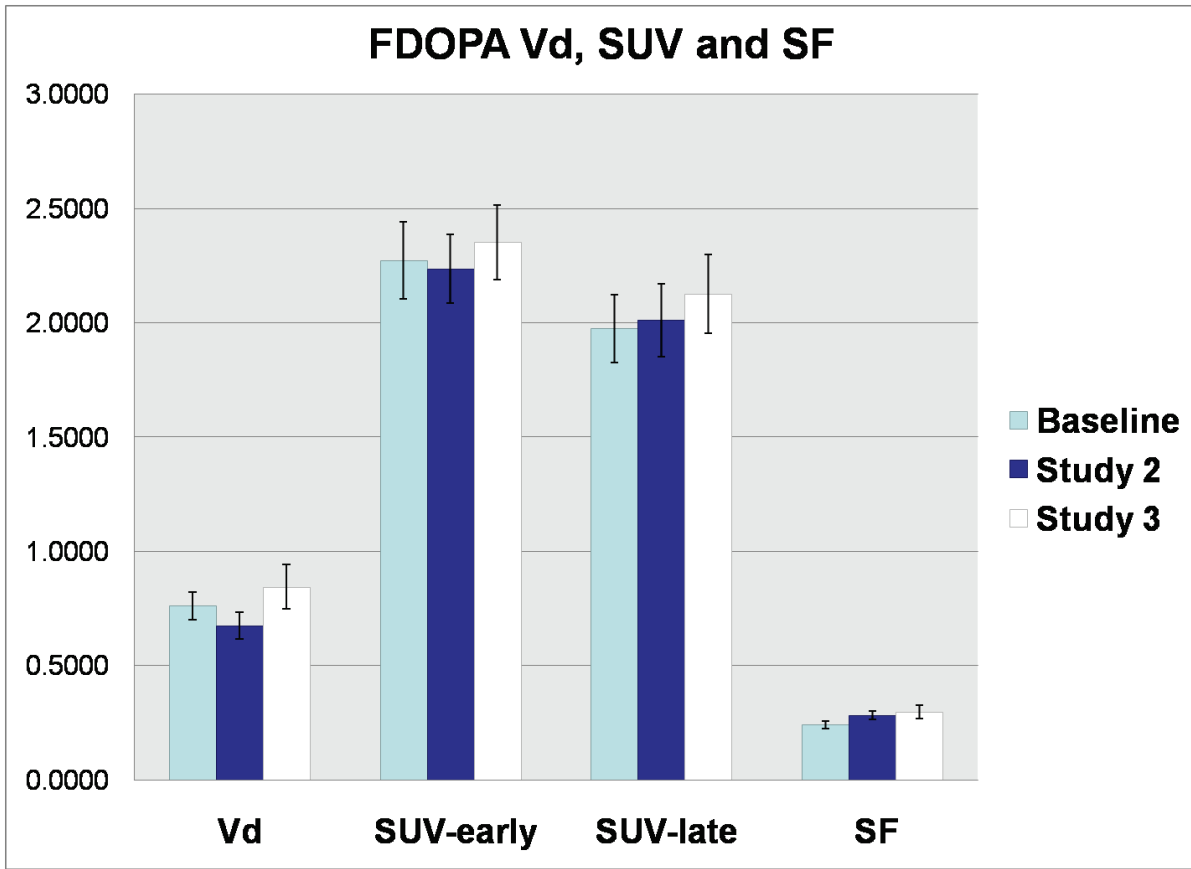
Supplementary Figure S4. Bar graphs showing the sample mean \pm SEM for the various FLT kinetic microparameters and the FLT influx rate constant K_i at each of the three study time points (i.e., at baseline and after 2 and 6 weeks from the start of treatment). Asterisks and hanging bars indicate where significant paired sample differences were found between time points using the Wilcoxon signed-rank test. If the Bonferroni method was applied to correct for multiple comparisons, then the paired sample differences for K_1 between baseline and study 3 would no longer be significant, while the other starred differences shown above would remain significant.



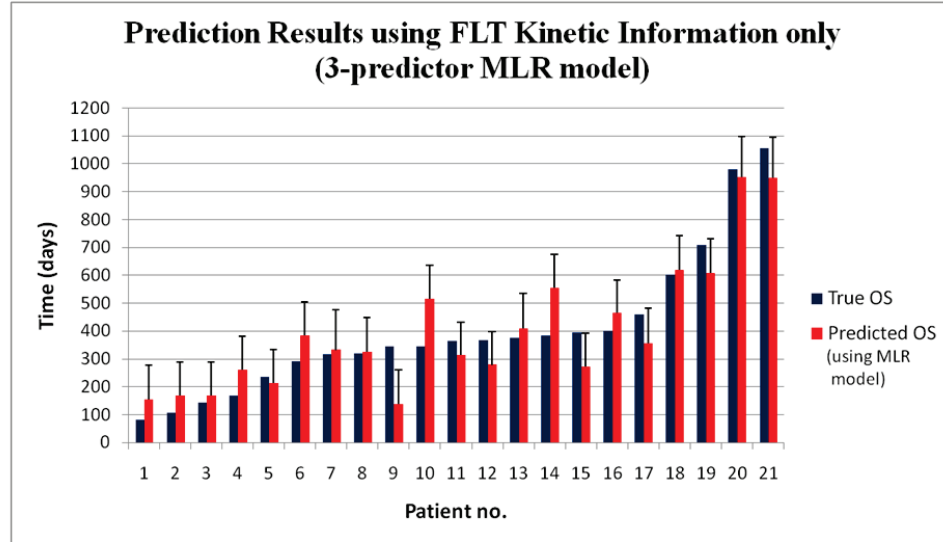
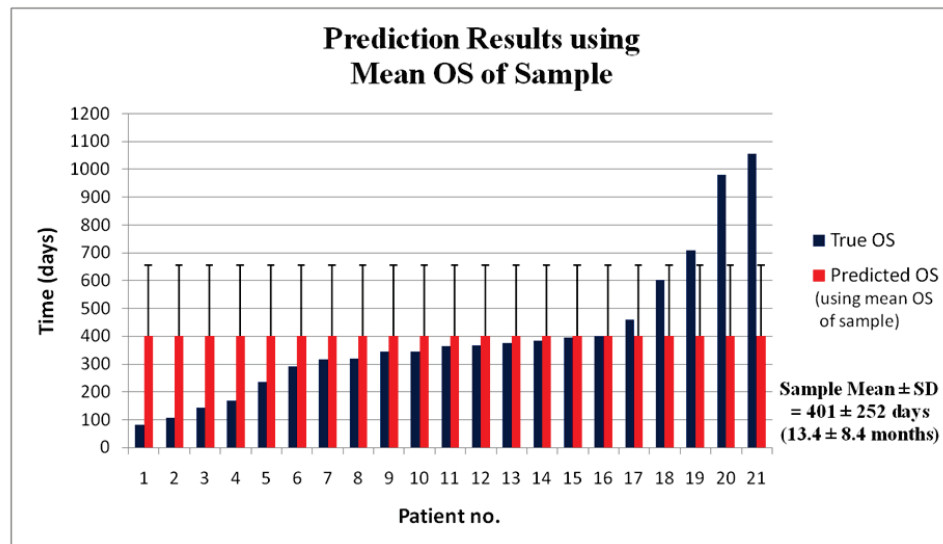
Supplementary Figure S5. Bar graphs showing the sample mean \pm SEM for FLT V_d , SUV (early and late), and PF at each of the three study time points (i.e., at baseline and after 2 and 6 weeks from the start of treatment). SUV is a unitless parameter. Asterisks and hanging bars indicate where significant paired sample differences were found between time points using the Wilcoxon signed-rank test. If the Bonferroni method was applied to correct for multiple comparisons, then the paired sample differences for SUV_{late} between baseline and study 3 would no longer be significant, while the other starred differences shown above would remain significant.



Supplementary Figure S6. Bar graphs showing the sample mean \pm SEM for the various FDOPA kinetic microparameters and the FDOPA influx rate constant K_i at each of the three study time points (i.e., at baseline and after 2 and 6 weeks from the start of treatment). Asterisks and hanging bars indicate where significant paired sample differences were found between time points using the Wilcoxon signed-rank test. If the Bonferroni method was applied to correct for multiple comparisons, then the starred differences shown above would remain significant even at the new adjusted P -value.



Supplementary Figure S7. Bar graphs showing the sample mean \pm SEM for FDOPA V_d , SUV (early and late), and SF at each of the three study time points (i.e., at baseline and after 2 and 6 weeks from the start of treatment). SF is a dimensionless parameter. No significant paired sample differences were found between time points using the Wilcoxon signed-rank test.

A**B**

Supplementary Figure S8. (A) Bar graphs showing the true OS and model predicted OS when using only FLT kinetic information in selecting the best three-predictor MLR model. Error bars denote 1 SD. **(B)** Bar graphs showing the true OS of each patient and the mean OS of the sample. If the mean OS of the sample was used for predicting each patient's OS, then every patient would have a predicted OS of 401 ± 252 days (13.2 ± 8.3 months); with 1 SD, this prediction is anywhere from 4.9-21.5 months. Error bars denote 1 SD.

SUPPLEMENTARY TABLES

Supplementary Table S1. Percent change in FLT and FDOPA kinetic parameters (Baseline → 2 weeks).

Patient No.	FLT								FDOPA							
	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔPF	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔSF
1	128	143	59	-52	-63	69	7	-26	-30	29	-1	-95	-48	-43	-43	-20
2	69	202	58	-37	17	2	-36	-40	-43	-68	-17	1800	33	19	44	111
3	-20	67	-9	-13	7	-46	-41	-33	-11	5	-31	-59	-18	-36	-6	-27
4	3	324	236	32	-48	-12	-74	-14	26	76	67	31	36	21	-28	-4
5	-34	-11	-44	1	61	-53	-16	-29	-10	-26	-34	-30	-17	-16	27	-7
6	-78	-52	103	-12	-37	-52	-76	120	-42	-53	-71	-50	-2	-61	37	-32
7	-50	-47	-42	137	2	-46	-8	8	-33	27	246	143	-32	39	-60	108
8	-28	135	208	-42	-43	-10	-71	25	-33	-51	4	-13	21	13	9	67
9	-49	15	-25	-60	-81	-60	-47	-23	-2	-6	-24	-27	-10	-17	10	-15
10	-41	137	406	103	1	-8	-82	56	-17	61	30	4	11	-30	-46	-15
11	61	90	16	19	-52	10	-5	-32	-37	-20	-4	-59	-48	-27	-25	14
12	-23	24	24	33	-42	-22	-38	0	-14	-42	21	503	-36	52	26	76
13	-18	45	39	-12	-45	-21	-43	-3	48	1	1	29	6	48	47	0
14	-53	-40	-7	56	90	-37	-32	34	-17	-37	49	460	37	52	2	83
15	-18	89	-9	26	29	-56	-52	-47	-29	21	151	407	69	18	-53	68
16	-28	25	55	-3	-48	-18	-47	15	-8	-3	-6	-18	21	-10	-5	-2
17	-16	7	19	-65	-37	-8	-23	9	-29	-8	9	-6	30	-18	-25	14
18	-9	101	305	174	1247	55	-62	70	7	-12	-23	-74	6	-3	26	-9
19	-16	6	84	32	-13	19	-35	42	-8	27	153	256	94	64	-36	78
20	-76	-63	-13	35	45	-57	-51	80	18	32	124	129	96	69	-25	43
21	-72	-75	92	330	244	-22	-59	177	2	-3	-19	53	-40	-12	9	-14
Median	-23	25	39	19	-13	-21	-43	8	-14	-3	1	4	6	-3	-5	0
Mean ± SD	-18 ± 50	53 ± 98	74 ± 119	32 ± 92	59 ± 281	-18 ± 35	-42 ± 24	19 ± 57	-12 ± 23	-2 ± 37	30 ± 78	161 ± 416	10 ± 42	6 ± 38	-5 ± 33	25 ± 47

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Supplementary Table S2. Percent change in FLT and FDOPA kinetic parameters (Baseline → 6 weeks).

Patient No.	FLT								FDOPA							
	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔPF	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔSF
1	21	-7	-28	-45	-52	1	41	-16	30	170	16	3	-43	-37	-46	-52
2	123	35	-6	-26	26	70	80	-24	-5	-32	112	2109	25	124	6	137
3	-52	3	119	8	45	-30	-68	46	-23	-25	-67	-44	-11	-60	21	-48
4	-26	72	127	26	15	-13	-62	18	-7	9	130	269	84	47	-36	58
5	-46	-27	-10	24	22	-38	-32	15	-18	-58	-63	174	11	-25	102	-9
6	-53	-66	-34	-63	-68	-28	8	54	-17	-37	16	35	63	27	10	53
7	-63	-43	-55	17	-60	-69	-31	-17	-57	-35	67	98	-11	-15	-49	101
8	-40	73	426	122	49	40	-73	135	-42	-80	-71	-76	-59	-26	157	28
9	-42	-60	-84	-53	-45	-68	98	-44	-20	7	69	83	4	8	-36	35
10	-33	99	269	108	-2	-3	-74	45	-38	-47	-43	51	71	-35	15	6
11	65	26	-15	-15	-26	22	44	-27	-11	22	75	20	-13	15	-34	30
12	-48	-21	53	9	-11	-15	-45	63	-24	-59	-44	124	-2	-3	73	28
13	-4	131	264	34	-37	25	-66	31	31	-61	-93	11	127	-64	417	-73
14	4	-35	-18	-1	23	22	49	19	-12	-59	205	1316	135	175	-10	213
15	-35	-23	-18	-20	-22	-31	-16	5	-37	-24	7	181	11	-18	-23	30
16	21	65	-14	-62	-46	-26	-14	-39	9	1	-23	-77	13	-11	16	-19
17	-29	72	179	-47	187	8	-62	50	-56	-50	-4	-40	2	-30	-26	60
18	49	20	187	226	949	186	-1	90	2	-5	38	33	-14	31	-5	29
19	16	39	-21	34	8	-24	-4	-35	-15	37	239	209	45	78	-48	109
20	-55	-4	13	28	-19	-48	-55	14	25	-9	2	-50	-58	34	32	8
21	-66	-82	120	400	8	2	-53	207	-25	-36	-60	72	-8	-50	26	-33
Median	-33	3	-6	9	-2	-13	-31	18	-17	-32	7	51	4	-11	6	29
Mean ± SD	-14 ± 49	13 ± 58	69 ± 133	34 ± 108	45 ± 214	-1 ± 55	-16 ± 52	28 ± 61	-15 ± 25	-18 ± 53	24 ± 90	214 ± 522	18 ± 53	8 ± 60	27 ± 103	33 ± 67

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Supplementary Table S3. Percent change in FLT and FDOPA kinetic parameters (2 weeks → 6 weeks).

Patient No.	FLT								FDOPA							
	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔPF	ΔK_1	Δk_2	Δk_3	Δk_4	ΔV_b	ΔK_i	ΔV_d	ΔSF
1	-47	-62	-55	16	28	-40	32	-47	85	110	18	1900	8	11	-6	-40
2	32	-55	-40	16	8	67	180	32	67	116	157	16	-6	88	-27	12
3	-40	-38	141	24	36	31	-46	-40	-14	-29	-52	38	9	-38	29	-28
4	-28	-59	-32	-4	120	-1	47	-28	-26	-38	38	182	36	21	-12	64
5	-18	-18	63	23	-25	33	-19	-18	-9	-43	-44	291	33	-11	59	-2
6	114	-30	-67	-58	-50	51	358	114	43	35	302	171	66	224	-20	126
7	-25	7	-24	-51	-61	-43	-25	-25	-37	-49	-52	-19	31	-38	27	-3
8	-17	-26	71	283	162	57	-9	-17	-15	-58	-72	-72	-66	-34	137	-23
9	13	-65	-78	16	185	-18	274	13	-18	15	124	151	16	30	-42	59
10	13	-16	-27	2	-3	5	45	13	-26	-67	-56	45	54	-7	111	25
11	3	-33	-27	-28	55	11	52	3	40	52	82	191	68	58	-13	13
12	-33	-37	23	-18	51	9	-11	-33	-12	-29	-54	-63	54	-36	38	-27
13	17	59	162	52	14	58	-40	17	-12	-61	-93	-14	114	-76	252	-73
14	120	7	-11	-37	-35	95	121	120	5	-36	104	153	72	81	-12	71
15	-21	-59	-10	-37	-39	58	76	-21	-10	-37	-57	-45	-35	-30	62	-23
16	69	32	-44	-61	5	-11	61	69	19	4	-19	-72	-6	-1	22	-17
17	-15	61	134	49	354	16	-50	-15	-38	-45	-12	-37	-21	-14	-1	40
18	65	-40	-29	19	-22	84	159	65	-5	8	80	420	-19	35	-25	42
19	39	31	-57	1	24	-36	48	39	-7	8	34	-13	-25	9	-18	18
20	91	158	30	-5	-44	20	-7	91	6	-31	-55	-78	-79	-20	75	-25
21	20	-27	15	16	-69	31	15	20	-27	-34	-51	12	53	-43	16	-23
Median	13	-27	-24	2	8	20	45	13	-10	-31	-19	16	16	-7	16	-2
Mean ± SD	17 ± 50	-10 ± 54	7 ± 70	10 ± 70	33 ± 101	23 ± 40	60 ± 107	17 ± 50	0 ± 33	-10 ± 52	15 ± 97	150 ± 422	17 ± 48	10 ± 65	31 ± 69	9 ± 46

Supplementary Table S4. FLT kinetic parameters at the baseline study.

Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	PF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.0224	0.0571	0.0307	0.0316	0.1720	0.0078	0.2549	0.3497	0.0078	0.0270	0.0267	0.0341	0.0391
2	0.0391	0.0541	0.0209	0.0193	0.0803	0.0109	0.5214	0.2787	0.0017	0.0033	0.0017	0.0054	0.0082
3	0.0656	0.0431	0.0297	0.0163	0.0748	0.0268	0.9014	0.4080	0.0036	0.0061	0.0057	0.0033	0.0198
4	0.1341	0.0650	0.0362	0.0120	0.1312	0.0479	1.3254	0.3577	0.0133	0.0135	0.0058	0.0044	0.0378
5	0.0792	0.0724	0.0353	0.0137	0.0599	0.0260	0.7355	0.3278	0.0042	0.0038	0.0048	0.0026	0.0132
6	0.0707	0.1120	0.0445	0.0399	0.1659	0.0201	0.4521	0.2843	0.0089	0.0277	0.0096	0.0106	0.0210
7	0.1731	0.1221	0.0377	0.0078	0.1174	0.0408	1.0830	0.2359	0.0122	0.0133	0.0057	0.0014	0.0221
8	0.0532	0.0864	0.0145	0.0129	0.0719	0.0077	0.5276	0.1437	0.0039	0.0148	0.0043	0.0147	0.0140
9	0.0569	0.0660	0.0519	0.0367	0.2577	0.0250	0.4825	0.4402	0.0094	0.0191	0.0142	0.0143	0.0480
10	0.0744	0.0293	0.0143	0.0122	0.0787	0.0244	1.7034	0.3280	0.0042	0.0037	0.0015	0.0039	0.0270
11	0.0510	0.0997	0.0364	0.0109	0.0745	0.0136	0.3746	0.2675	0.0042	0.0119	0.0047	0.0021	0.0116
12	0.1528	0.1650	0.0418	0.0180	0.1248	0.0308	0.7389	0.2021	0.0126	0.0201	0.0033	0.0036	0.0216
13	0.1103	0.0642	0.0357	0.0236	0.1551	0.0394	1.1041	0.3574	0.0027	0.0025	0.0015	0.0014	0.0114
14	0.0478	0.1146	0.0444	0.0117	0.0363	0.0134	0.3007	0.2792	0.0036	0.0137	0.0025	0.0019	0.0074
15	0.0864	0.1139	0.0223	0.0121	0.0967	0.0141	0.6346	0.1637	0.0085	0.0130	0.0022	0.0050	0.0228
16	0.1522	0.1542	0.0692	0.0394	0.3422	0.0472	0.6813	0.3098	0.0108	0.0177	0.0055	0.0075	0.0275
17	0.1222	0.1441	0.0215	0.0144	0.1110	0.0158	0.7379	0.1298	0.0092	0.0137	0.0015	0.0032	0.0147
18	0.0314	0.0556	0.0127	0.0050	0.0081	0.0058	0.4595	0.1859	0.0017	0.0059	0.0016	0.4303	0.0135
19	0.0356	0.1078	0.0452	0.0204	0.0902	0.0105	0.2325	0.2954	0.0057	0.0208	0.0082	0.0257	0.0159
20	0.0715	0.1250	0.0363	0.0127	0.0450	0.0161	0.4430	0.2250	0.0043	0.0099	0.0021	0.0036	0.0052
21	0.0327	0.1325	0.0477	0.0197	0.1336	0.0087	0.1817	0.2647	0.0072	0.0271	0.0113	0.0072	0.0206
Median	0.0707	0.0997	0.0362	0.0144	0.0967	0.0161	0.5276	0.2792	0.0057	0.0135	0.0047	0.0044	0.0198
Mean ± SD	0.0792 ± 0.0447	0.0945 ± 0.0387	0.0347 ± 0.0139	0.0186 ± 0.0102	0.1156 ± 0.0756	0.0216 ± 0.0132	0.6608 ± 0.3853	0.2778 ± 0.0835	0.0067 ± 0.0037	0.0137 ± 0.0079	0.0059 ± 0.0059	0.0279 ± 0.0926	0.0201 ± 0.0110

* SEE = standard error of the estimate.

Supplementary Table S5. FLT kinetic parameters at 2 weeks after the start of therapy.

Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	PF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.0510	0.1388	0.0487	0.0151	0.0645	0.0132	0.2722	0.2597	0.0067	0.0268	0.0096	0.0041	0.0137
2	0.0660	0.1634	0.0331	0.0122	0.0938	0.0111	0.3358	0.1684	0.0066	0.0202	0.0042	0.0033	0.0175
3	0.0528	0.0718	0.0270	0.0142	0.0797	0.0144	0.5344	0.2733	0.0045	0.0078	0.0051	0.0040	0.0190
4	0.1378	0.2753	0.1216	0.0158	0.0686	0.0422	0.3473	0.3064	0.0144	0.0353	0.0366	0.0037	0.0279
5	0.0519	0.0644	0.0196	0.0138	0.0967	0.0121	0.6188	0.2333	0.0041	0.0083	0.0041	0.0044	0.0167
6	0.0154	0.0541	0.0902	0.0353	0.1051	0.0096	0.1068	0.6251	0.0048	0.0366	0.0583	0.0236	0.0235
7	0.0867	0.0647	0.0220	0.0185	0.1198	0.0220	1.0003	0.2537	0.0035	0.0037	0.0015	0.0017	0.0098
8	0.0384	0.2028	0.0446	0.0075	0.0410	0.0069	0.1554	0.1803	0.0059	0.0334	0.0104	0.0059	0.0118
9	0.0293	0.0758	0.0390	0.0147	0.0494	0.0099	0.2551	0.3397	0.0031	0.0166	0.0056	0.0095	0.0112
10	0.0439	0.0693	0.0724	0.0248	0.0793	0.0224	0.3098	0.5109	0.0074	0.0200	0.0191	0.0077	0.0252
11	0.0821	0.1892	0.0421	0.0130	0.0359	0.0149	0.3549	0.1820	0.0061	0.0178	0.0035	0.0015	0.0060
12	0.1182	0.2050	0.0520	0.0240	0.0730	0.0239	0.4599	0.2023	0.0156	0.0374	0.0074	0.0028	0.0226
13	0.0903	0.0934	0.0495	0.0208	0.0852	0.0313	0.6319	0.3464	0.0031	0.0045	0.0029	0.0017	0.0091
14	0.0225	0.0693	0.0412	0.0183	0.0690	0.0084	0.2035	0.3729	0.0040	0.0268	0.0129	0.0106	0.0159
15	0.0712	0.2153	0.0204	0.0153	0.1252	0.0062	0.3023	0.0866	0.0100	0.0307	0.0025	0.0052	0.0189
16	0.1089	0.1930	0.1071	0.0384	0.1767	0.0389	0.3630	0.3569	0.0071	0.0176	0.0105	0.0038	0.0196
17	0.1028	0.1545	0.0256	0.0051	0.0702	0.0146	0.5707	0.1421	0.0089	0.0171	0.0027	0.0255	0.0168
18	0.0285	0.1116	0.0514	0.0137	0.1091	0.0090	0.1750	0.3153	0.0085	0.0439	0.0172	0.0078	0.0200
19	0.0298	0.1148	0.0832	0.0269	0.0787	0.0125	0.1506	0.4202	0.0051	0.0319	0.0124	0.0137	0.0130
20	0.0169	0.0464	0.0317	0.0171	0.0653	0.0069	0.2166	0.4059	0.0021	0.0113	0.0089	0.0044	0.0100
21	0.0092	0.0331	0.0915	0.0847	0.4592	0.0068	0.0741	0.7343	0.0047	0.0230	0.1250	0.1348	0.0583
Median	0.0519	0.1116	0.0446	0.0158	0.0793	0.0125	0.3098	0.3064	0.0059	0.0202	0.0089	0.0044	0.0168
Mean ± SD	0.0597 ± 0.0371	0.1241 ± 0.0686	0.0530 ± 0.0298	0.0214 ± 0.0166	0.1022 ± 0.0877	0.0161 ± 0.0104	0.3542 ± 0.2204	0.3198 ± 0.1586	0.0065 ± 0.0035	0.0224 ± 0.0116	0.0172 ± 0.0280	0.0133 ± 0.0286	0.0184 ± 0.0108

* SEE = standard error of the estimate.

Supplementary Table S6. FLT kinetic parameters at 6 weeks after the start of therapy.

Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	PF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.0270	0.0532	0.0221	0.0175	0.0827	0.0079	0.3591	0.2935	0.0021	0.0062	0.0047	0.0035	0.0146
2	0.0872	0.0730	0.0197	0.0142	0.1014	0.0185	0.9406	0.2125	0.0044	0.0047	0.0021	1.0482	0.0184
3	0.0317	0.0442	0.0650	0.0176	0.1081	0.0188	0.2900	0.5952	0.0027	0.0059	0.0115	0.0057	0.0183
4	0.0988	0.1119	0.0823	0.0151	0.1512	0.0419	0.5089	0.4238	0.0066	0.0078	0.0057	0.0020	0.0241
5	0.0428	0.0531	0.0319	0.0170	0.0729	0.0161	0.5031	0.3753	0.0043	0.0063	0.0101	0.0056	0.0237
6	0.0329	0.0377	0.0295	0.0147	0.0526	0.0145	0.4895	0.4390	0.0027	0.0048	0.0068	0.0062	0.0129
7	0.0648	0.0695	0.0168	0.0091	0.0473	0.0126	0.7515	0.1947	0.0048	0.0105	0.0042	0.0017	0.0100
8	0.0320	0.1496	0.0762	0.0287	0.1073	0.0108	0.1415	0.3375	0.0079	0.0492	0.0210	0.0120	0.0252
9	0.0331	0.0262	0.0085	0.0171	0.1407	0.0081	0.9530	0.2450	0.0021	0.0027	0.0019	0.0534	0.0230
10	0.0497	0.0582	0.0528	0.0254	0.0769	0.0236	0.4481	0.4757	0.0053	0.0109	0.0083	0.0113	0.0213
11	0.0844	0.1261	0.0308	0.0093	0.0555	0.0166	0.5378	0.1963	0.0056	0.0130	0.0040	0.0012	0.0109
12	0.0789	0.1296	0.0639	0.0196	0.1105	0.0261	0.4077	0.3302	0.0027	0.0053	0.0024	0.0008	0.0059
13	0.1057	0.1486	0.1299	0.0316	0.0971	0.0493	0.3794	0.4664	0.0089	0.0274	0.0119	0.0056	0.0139
14	0.0496	0.0740	0.0366	0.0116	0.0447	0.0164	0.4489	0.3309	0.0042	0.0081	0.0052	0.0038	0.0105
15	0.0565	0.0879	0.0183	0.0097	0.0758	0.0098	0.5324	0.1723	0.0065	0.0133	0.0034	0.0182	0.0200
16	0.1839	0.2548	0.0596	0.0148	0.1858	0.0348	0.5848	0.1896	0.0120	0.0276	0.0085	0.0020	0.0216
17	0.0873	0.2480	0.0599	0.0076	0.3185	0.0170	0.2836	0.1945	0.0101	0.0222	0.0065	0.9195	0.0273
18	0.0469	0.0668	0.0365	0.0163	0.0850	0.0166	0.4532	0.3533	0.0066	0.0164	0.0057	0.0075	0.0169
19	0.0413	0.1499	0.0359	0.0273	0.0977	0.0080	0.2226	0.1932	0.0050	0.0231	0.0069	0.0073	0.0134
20	0.0323	0.1196	0.0411	0.0163	0.0364	0.0083	0.2011	0.2558	0.0041	0.0183	0.0128	0.0036	0.0109
21	0.0110	0.0242	0.1051	0.0985	0.1446	0.0089	0.0850	0.8128	0.0025	0.0150	0.0732	0.0677	0.0383
Median	0.0496	0.0740	0.0366	0.0163	0.0971	0.0164	0.4489	0.3302	0.0048	0.0109	0.0065	0.0057	0.0183
Mean ± SD	0.0608 ± 0.0386	0.1003 ± 0.0645	0.0487 ± 0.0308	0.0209 ± 0.0189	0.1044 ± 0.0623	0.0183 ± 0.0114	0.4534 ± 0.2275	0.3375 ± 0.1599	0.0053 ± 0.0027	0.0142 ± 0.0110	0.0103 ± 0.0151	0.1041 ± 0.2937	0.0181 ± 0.0075

* SEE = standard error of the estimate.

Supplementary Table S7. FDOPA kinetic parameters at the baseline study.

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Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	SF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.1440	0.1801	0.0397	0.0097	0.0883	0.0260	0.6550	0.1806	0.0186	0.0301	0.0055	0.0040	0.0280
2	0.1884	0.4193	0.0740	0.0011	0.0562	0.0283	0.3820	0.1500	0.0189	0.0314	0.0080	0.0693	0.0188
3	0.1682	0.0794	0.0300	0.0264	0.1146	0.0462	1.5371	0.2742	0.0060	0.0059	0.0025	0.5300	0.0111
4	0.1913	0.1630	0.0692	0.0143	0.1312	0.0570	0.8238	0.2980	0.0152	0.0250	0.0064	0.0030	0.0217
5	0.1006	0.1211	0.0588	0.0216	0.0849	0.0329	0.5594	0.3268	0.0131	0.0348	0.0146	0.0050	0.0218
6	0.1623	0.1610	0.0501	0.0179	0.0505	0.0386	0.7690	0.2373	0.0177	0.0286	0.0062	0.0099	0.0242
7	0.2059	0.1558	0.0343	0.0129	0.0865	0.0372	1.0831	0.1804	0.0323	0.0400	0.0071	0.0058	0.0461
8	0.2160	0.3544	0.1118	0.0360	0.0805	0.0518	0.4633	0.2398	0.0213	0.0419	0.0113	0.0079	0.0206
9	0.1671	0.1943	0.0776	0.0230	0.1083	0.0477	0.6147	0.2854	0.0149	0.0225	0.0055	0.0051	0.0257
10	0.1114	0.0826	0.0278	0.0146	0.0602	0.0280	1.0101	0.2518	0.0070	0.0082	0.0048	0.0058	0.0179
11	0.1737	0.1592	0.0513	0.0192	0.1247	0.0423	0.8249	0.2437	0.0107	0.0155	0.0039	0.0034	0.0135
12	0.1683	0.2274	0.0458	0.0058	0.0962	0.0282	0.6158	0.1676	0.0134	0.0197	0.0043	0.0258	0.0208
13	0.0686	0.1020	0.0752	0.0178	0.0414	0.0291	0.3871	0.4244	0.0080	0.0281	0.0148	0.0044	0.0107
14	0.1703	0.1169	0.0321	0.0088	0.0837	0.0367	1.1430	0.2154	0.0086	0.0103	0.0028	0.6135	0.0142
15	0.1937	0.1629	0.0462	0.0054	0.0610	0.0428	0.9265	0.2209	0.0063	0.0059	0.0029	0.0010	0.0105
16	0.1454	0.1607	0.0635	0.0407	0.1026	0.0412	0.6487	0.2832	0.0104	0.0160	0.0088	0.0121	0.0227
17	0.2680	0.2663	0.0706	0.0324	0.1005	0.0562	0.7955	0.2096	0.0329	0.0360	0.0135	0.0096	0.0392
18	0.0971	0.0996	0.0402	0.0235	0.0918	0.0279	0.6946	0.2876	0.0075	0.0135	0.0069	0.0148	0.0147
19	0.0978	0.0968	0.0135	0.0045	0.0435	0.0119	0.8864	0.1224	0.0073	0.0131	0.0036	0.4709	0.0135
20	0.1150	0.1374	0.0509	0.0068	0.0455	0.0311	0.6105	0.2703	0.0146	0.0359	0.0101	0.0029	0.0177
21	0.0922	0.1395	0.0297	0.0053	0.0536	0.0162	0.5446	0.1755	0.0078	0.0192	0.0030	0.5951	0.0088
Median	0.1671	0.1592	0.0501	0.0146	0.0849	0.0367	0.6946	0.2398	0.0131	0.0225	0.0062	0.0079	0.0188
Mean ± SD	0.1545 ± 0.0494	0.1705 ± 0.0860	0.0520 ± 0.0226	0.0166 ± 0.0110	0.0812 ± 0.0274	0.0361 ± 0.0120	0.7607 ± 0.2756	0.2402 ± 0.0684	0.0139 ± 0.0077	0.0229 ± 0.0114	0.0070 ± 0.0039	0.1143 ± 0.2197	0.0201 ± 0.0093

* SEE = standard error of the estimate.

Supplementary Table S8. FDOPA kinetic parameters at 2 weeks after the start of therapy.

Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	SF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.1015	0.2318	0.0393	0.0005	0.0463	0.0147	0.3744	0.1450	0.0107	0.0267	0.0035	0.0286	0.0130
2	0.1065	0.1322	0.0612	0.0209	0.0746	0.0337	0.5507	0.3164	0.0103	0.0174	0.0100	0.0053	0.0216
3	0.1494	0.0830	0.0206	0.0107	0.0935	0.0297	1.4417	0.1988	0.0082	0.0119	0.0060	0.0040	0.0153
4	0.2401	0.2869	0.1156	0.0187	0.1778	0.0690	0.5965	0.2872	0.0317	0.0412	0.0145	0.0048	0.0337
5	0.0909	0.0893	0.0388	0.0151	0.0707	0.0275	0.7100	0.3029	0.0094	0.0281	0.0153	0.0090	0.0126
6	0.0944	0.0752	0.0144	0.0089	0.0495	0.0151	1.0545	0.1607	0.0036	0.0044	0.0024	0.4948	0.0101
7	0.1382	0.1981	0.1186	0.0313	0.0590	0.0517	0.4364	0.3745	0.0097	0.0291	0.0151	0.0053	0.0088
8	0.1458	0.1741	0.1160	0.0315	0.0971	0.0583	0.5027	0.3999	0.0165	0.0347	0.0126	0.0155	0.0183
9	0.1632	0.1822	0.0586	0.0168	0.0973	0.0397	0.6775	0.2434	0.0125	0.0209	0.0038	0.0045	0.0188
10	0.0924	0.1329	0.0360	0.0152	0.0669	0.0197	0.5471	0.2131	0.0026	0.0059	0.0019	0.0262	0.0065
11	0.1102	0.1279	0.0494	0.0079	0.0643	0.0307	0.6220	0.2786	0.0066	0.0143	0.0048	0.1239	0.0131
12	0.1451	0.1319	0.0554	0.0350	0.0612	0.0429	0.7745	0.2958	0.0085	0.0151	0.0029	0.0081	0.0068
13	0.1018	0.1031	0.0759	0.0229	0.0438	0.0432	0.5687	0.4240	0.0037	0.0087	0.0040	0.0060	0.0039
14	0.1420	0.0736	0.0479	0.0493	0.1144	0.0559	1.1687	0.3942	0.0111	0.0127	0.0156	0.0141	0.0356
15	0.1366	0.1970	0.1161	0.0274	0.1031	0.0506	0.4364	0.3708	0.0125	0.0358	0.0090	0.0104	0.0183
16	0.1336	0.1559	0.0600	0.0333	0.1237	0.0371	0.6186	0.2779	0.0161	0.0338	0.0157	0.0158	0.0261
17	0.1911	0.2443	0.0771	0.0306	0.1302	0.0459	0.5947	0.2399	0.0120	0.0182	0.0129	0.0091	0.0183
18	0.1036	0.0878	0.0309	0.0060	0.0971	0.0270	0.8731	0.2603	0.0086	0.0166	0.0089	0.0012	0.0203
19	0.0896	0.1231	0.0342	0.0160	0.0842	0.0195	0.5695	0.2174	0.0070	0.0137	0.0051	0.0042	0.0139
20	0.1358	0.1811	0.1142	0.0156	0.0891	0.0525	0.4600	0.3867	0.0089	0.0183	0.0069	0.0033	0.0128
21	0.0943	0.1347	0.0240	0.0081	0.0321	0.0143	0.5940	0.1512	0.0039	0.0092	0.0021	0.3059	0.0046
Median	0.1336	0.1329	0.0554	0.0168	0.0842	0.0371	0.5947	0.2786	0.0094	0.0174	0.0069	0.0090	0.0139
Mean ± SD	0.1289 ± 0.0377	0.1498 ± 0.0590	0.0621 ± 0.0349	0.0201 ± 0.0120	0.0846 ± 0.0342	0.0371 ± 0.0159	0.6748 ± 0.2632	0.2828 ± 0.0855	0.0102 ± 0.0062	0.0198 ± 0.0105	0.0082 ± 0.0051	0.0524 ± 0.1222	0.0158 ± 0.0085

* SEE = standard error of the estimate.

Supplementary Table S9. FDOPA kinetic parameters at 6 weeks after the start of therapy.

Patient No.	K ₁	k ₂	k ₃	k ₄	V _b	K _i	V _d	SF	SEE-K ₁	SEE-k ₂	SEE-k ₃	SEE-k ₄	SEE-V _b
1	0.1875	0.4863	0.0462	0.0100	0.0501	0.0163	0.3522	0.0868	0.0358	0.0937	0.0053	0.0047	0.0225
2	0.1782	0.2850	0.1570	0.0243	0.0702	0.0633	0.4031	0.3552	0.0151	0.0238	0.0148	0.0026	0.0188
3	0.1288	0.0593	0.0099	0.0148	0.1019	0.0185	1.8595	0.1431	0.0087	0.0067	0.0040	1.0581	0.0288
4	0.1773	0.1783	0.1594	0.0527	0.2415	0.0837	0.5250	0.4720	0.0214	0.0294	0.0294	0.0245	0.0376
5	0.0826	0.0512	0.0217	0.0591	0.0942	0.0246	1.1324	0.2977	0.0056	0.0068	0.0063	6.2455	0.0165
6	0.1348	0.1015	0.0579	0.0241	0.0824	0.0489	0.8457	0.3632	0.0103	0.0126	0.0072	0.0085	0.0300
7	0.0877	0.1008	0.0573	0.0255	0.0772	0.0318	0.5545	0.3624	0.0054	0.0124	0.0060	0.0058	0.0111
8	0.1244	0.0723	0.0320	0.0087	0.0328	0.0382	1.1922	0.3068	0.0101	0.0122	0.0040	0.0398	0.0217
9	0.1340	0.2087	0.1312	0.0421	0.1127	0.0517	0.3942	0.3860	0.0128	0.0324	0.0091	0.0099	0.0162
10	0.0687	0.0436	0.0158	0.0221	0.1032	0.0183	1.1568	0.2660	0.0063	0.0091	0.0063	0.0885	0.0210
11	0.1539	0.1943	0.0898	0.0230	0.1079	0.0486	0.5416	0.3161	0.0063	0.0142	0.0101	0.0031	0.0127
12	0.1271	0.0937	0.0256	0.0130	0.0944	0.0273	1.0659	0.2146	0.0082	0.0107	0.0039	0.0065	0.0218
13	0.0898	0.0397	0.0052	0.0198	0.0938	0.0104	2.0001	0.1158	0.0052	0.0039	0.0873	1.6339	0.0225
14	0.1498	0.0474	0.0979	0.1246	0.1966	0.1009	1.0311	0.6738	0.0109	0.0130	0.0322	0.0349	0.0322
15	0.1226	0.1233	0.0496	0.0152	0.0675	0.0352	0.7090	0.2869	0.0082	0.0221	0.0251	0.0088	0.0149
16	0.1592	0.1629	0.0486	0.0094	0.1163	0.0366	0.7528	0.2298	0.0155	0.0263	0.0054	0.0058	0.0234
17	0.1179	0.1336	0.0676	0.0193	0.1027	0.0396	0.5861	0.3360	0.0097	0.0173	0.0067	0.0071	0.0211
18	0.0986	0.0945	0.0555	0.0312	0.0789	0.0365	0.6574	0.3700	0.0051	0.0085	0.0074	0.0045	0.0108
19	0.0829	0.1327	0.0457	0.0139	0.0631	0.0212	0.4644	0.2562	0.0079	0.0216	0.0059	1.2961	0.0138
20	0.1433	0.1257	0.0518	0.0034	0.0190	0.0418	0.8071	0.2918	0.0141	0.0185	0.0068	0.3991	0.0288
21	0.0693	0.0889	0.0118	0.0091	0.0491	0.0081	0.6876	0.1172	0.0036	0.0044	0.0022	1.0289	0.0077
Median	0.1271	0.1015	0.0496	0.0198	0.0938	0.0365	0.7090	0.2977	0.0087	0.0130	0.0067	0.0099	0.0211
Mean ± SD	0.1247 ± 0.0359	0.1345 ± 0.1018	0.0589 ± 0.0451	0.0269 ± 0.0265	0.0931 ± 0.0499	0.0382 ± 0.0231	0.8437 ± 0.4454	0.2975 ± 0.1317	0.0108 ± 0.0072	0.0190 ± 0.0189	0.0136 ± 0.0189	0.5675 ± 1.3954	0.0207 ± 0.0077

* SEE = standard error of the estimate.

Supplementary Table S10. Standardized uptake values of FLT at each of the three study time points.

Patient No.	FLT SUV-early			FLT SUV-late		
	Baseline	2 wks	6 wks	Baseline	2 wks	6 wks
1	0.44	0.64	0.37	0.44	0.61	0.37
2	0.53	0.62	1.22	0.56	0.47	1.05
3	0.75	0.50	0.51	0.85	0.45	0.58
4	1.64	0.85	1.29	1.91	1.15	1.64
5	0.72	0.51	0.50	0.85	0.51	0.55
6	0.82	0.44	0.69	0.67	0.44	0.78
7	2.56	1.79	1.23	2.57	1.58	1.07
8	0.78	0.29	0.44	0.66	0.33	0.42
9	1.33	0.50	0.74	1.30	0.46	0.76
10	1.38	0.65	0.77	1.41	0.68	0.85
11	0.86	0.84	1.44	0.79	0.78	1.48
12	1.72	0.96	0.94	1.57	0.84	0.99
13	1.71	1.35	1.18	1.74	1.25	1.40
14	1.06	0.62	0.61	0.90	0.53	0.61
15	0.74	0.70	0.67	0.68	0.51	0.55
16	1.37	1.02	1.08	1.19	0.90	1.07
17	1.41	1.30	1.00	1.13	1.08	1.07
18	0.18	0.48	0.65	0.31	0.49	0.64
19	0.44	0.27	0.40	0.40	0.26	0.29
20	1.63	0.55	0.65	1.52	0.57	0.53
21	0.51	0.56	0.30	0.52	0.41	0.33
Median	0.86	0.62	0.69	0.85	0.53	0.76
Mean ± SD	1.07 ± 0.58	0.74 ± 0.37	0.79 ± 0.34	1.05 ± 0.58	0.68 ± 0.34	0.81 ± 0.38

Supplementary Table S11. FDOPA standardized uptake values at each of the three study time points.

Patient No.	FDOPA SUV-early			FDOPA SUV-late		
	Baseline	2 wks	6 wks	Baseline	2 wks	6 wks
1	1.85	1.38	1.05	1.46	1.25	0.82
2	1.44	1.81	2.03	1.39	1.64	2.14
3	2.43	2.11	2.27	2.28	1.78	1.72
4	3.16	3.12	3.43	3.13	3.11	3.38
5	1.15	1.34	1.69	1.04	1.15	1.51
6	2.38	1.83	2.85	2.03	1.44	2.64
7	3.51	2.25	2.00	2.84	2.16	1.85
8	2.12	2.50	1.85	1.85	2.34	1.68
9	2.46	2.30	2.83	2.33	2.02	2.48
10	2.34	1.50	1.95	1.93	1.20	1.69
11	3.07	2.73	2.69	2.45	2.38	2.47
12	2.46	2.76	2.89	2.03	2.36	2.35
13	1.76	2.35	2.16	1.77	2.25	1.83
14	2.70	3.09	2.99	2.28	2.80	2.97
15	2.17	2.03	1.99	2.01	1.96	1.87
16	1.58	1.82	2.37	1.23	1.52	2.07
17	4.03	3.05	3.13	3.30	2.57	2.80
18	2.02	2.73	2.57	1.74	2.42	2.29
19	0.89	1.20	1.22	0.64	1.00	1.05
20	2.64	3.68	4.05	2.50	3.81	4.06
21	1.55	1.35	1.37	1.21	1.03	0.98
Median	2.34	2.25	2.27	2.01	2.02	2.07
Mean ± SD	2.27 ± 0.77	2.24 ± 0.69	2.35 ± 0.75	1.97 ± 0.68	2.01 ± 0.73	2.13 ± 0.79

Supplementary Table S12. FDOPA tumor-to-striatum standardized uptake value ratios (early and late) at each of the three study time points.

Patient No.	FDOPA Tumor-to-Striatum SUV Ratios (early)			FDOPA Tumor-to-Striatum SUV Ratios (late)		
	Baseline	2 wks	6 wks	Baseline	2 wks	6 wks
1	1.38	0.76	0.60	1.02	0.67	0.47
2	0.92	1.04	1.68	0.89	0.97	1.61
3	1.41	1.90	1.98	1.25	1.53	1.38
4	1.49	1.45	1.34	1.33	1.39	1.29
5	1.02	1.12	1.26	0.90	0.93	1.06
6	1.36	1.18	1.57	1.01	0.90	1.34
7	1.29	1.32	1.13	0.98	1.20	0.97
8	1.16	1.46	1.20	0.96	1.30	1.09
9	1.17	1.14	1.07	1.09	0.95	0.97
10	1.05	0.94	1.00	0.82	0.73	0.86
11	2.29	1.73	1.53	1.77	1.46	1.35
12	1.82	1.59	1.85	1.47	1.34	1.41
13	0.97	1.52	1.22	0.93	1.38	0.96
14	1.27	1.29	1.35	1.05	1.15	1.28
15	1.39	1.07	1.00	1.20	0.97	0.86
16	2.00	1.87	2.18	1.51	1.51	1.79
17	1.63	1.38	1.49	1.32	1.18	1.36
18	1.09	1.14	1.11	0.90	0.96	0.99
19	1.65	0.86	1.06	1.17	0.65	0.90
20	1.32	1.32	1.19	1.22	1.31	1.10
21	1.02	0.95	0.96	0.79	0.69	0.67
Median	1.32	1.29	1.22	1.05	1.15	1.09
Mean ± SD	1.37 ± 0.35	1.29 ± 0.32	1.32 ± 0.38	1.12 ± 0.25	1.10 ± 0.29	1.13 ± 0.31

Supplementary Table S13. Parameter estimates from MLR model using information from FDOPA only (absolute values and changes).

Multiple Linear Regression Model for Predicting Overall Survival (MLR-2)		
Predictor Variable	Parameter Estimates	P-value
FDOPA k_3 absolute value at S1	-7993.19	0.0042
FDOPA V_d absolute value at S1	-662.05	0.0049
FDOPA K_1 ratio (S3/S2)	-380.15	0.0135
Intercept	+1702.61	<.0001

* $R^2 = 0.50$, adjusted- $R^2 = 0.41$, root MSE = 194 days, and the average variance inflation factors were $\cong 1.5$.

S1 = Baseline FDOPA PET, S2 = FDOPA PET at 2 weeks after start of treatment, S3 = FDOPA PET at 6 weeks after start of treatment.

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Supplementary Table S14. Parameter estimates from MLR model using information from FLT and FDOPA combined (absolute values and changes).

Multiple Linear Regression Model for Predicting Overall Survival (MLR-3)		
Predictor Variable	Parameter Estimates	P-value
FLT k_4 ratio (S3/S1)	+158.66	<.0001
FLT k_2 ratio (S3/S2)	+314.86	<.0001
FDOPA tumor-to-striatum SUV_{late} ratio (S2/S1)	-450.85	<.0001
Intercept	+354.23	<.01

* $R^2 = 0.86$, adjusted- $R^2 = 0.83$, root MSE = 104 days, and the average variance inflation factors were $\cong 1$.

S1 = Baseline PET, S2 = PET at 2 weeks after start of treatment, S3 = PET at 6 weeks after start of treatment.

APPENDIX

Since FDOPA does not cross the red blood cell membrane and is confined to the plasma component when it is in blood (Appendix Figure A1), we had to somehow convert the total ^{18}F activity concentration in whole blood (which we measured from the dynamic PET images) to the total FDOPA activity concentration in plasma. To do this, we used the following formula:

$$C_{wb}(t) = (1 - Hct) \times C_{FDOPA}(t)_p + f_{OMFD}(t) \times [C_{FDOPA}(t) + C_{OMFD}(t) + C_{METS}(t)]_p + (1 - Hct) \times f_{METS}(t) \times [C_{FDOPA}(t) + C_{OMFD}(t) + C_{METS}(t)]_p$$

where

$$(C_{F-18\ total})_{plasma} = [C_{FDOPA}(t) + C_{OMFD}(t) + C_{METS}(t)]_p.$$

In order to solve the above equation, we need to find a relationship between the total ^{18}F activity in plasma and the total ^{18}F activity in whole blood. This can be done using the following formula:

$$\frac{(C_{F-18\ total})_{plasma}}{(C_{F-18\ total})_{wb}} = \frac{[C_{FDOPA}(t) + C_{OMFD}(t) + C_{METS}(t)]_p}{(1 - Hct) \times [C_{FDOPA}(t) + C_{METS}(t)]_p + C_{OMFD}(t)_p}$$

which can be reduced in terms of the fractional plasma radioactivity using the following mathematical trick:

$$\frac{(C_{F-18 \text{ total}})_{\text{plasma}}}{(C_{F-18 \text{ total}})_{\text{wb}}} = \frac{[C_{FDOPA}(t) + C_{OMFD}(t) + C_{METS}(t)]_p}{(1 - Hct) \times [C_{FDOPA}(t) + C_{METS}(t)]_p + C_{OMFD}(t)_p} \cdot \frac{1}{\frac{(C_{F-18 \text{ total}})_{\text{plasma}}}{1}}{\frac{1}{(C_{F-18 \text{ total}})_{\text{plasma}}}}$$

$$\frac{(C_{F-18 \text{ total}})_{\text{plasma}}}{(C_{F-18 \text{ total}})_{\text{wb}}} = \frac{[f_{FDOPA}(t) + f_{OMFD}(t) + f_{METS}(t)]_p}{(1 - Hct) \times [f_{FDOPA}(t) + f_{METS}(t)]_p + f_{OMFD}(t)_p}$$

This can be further reduced to:

$$\frac{(C_{F-18 \text{ total}})_{\text{plasma}}}{(C_{F-18 \text{ total}})_{\text{wb}}} = \frac{1}{(1 - Hct) \times [1 - f_{OMFD}(t)_p] + f_{OMFD}(t)_p}$$

using the fact that $[f_{FDOPA}(t) + f_{OMFD}(t) + f_{METS}(t)]_p = 1$.

Since we now found a relationship between the total ^{18}F activity in plasma and the total ^{18}F activity in whole blood, we can solve our initial equation which sought to find a relationship between the total ^{18}F activity concentration in whole blood and the total FDOPA activity concentration in plasma.

Thus,

$$C_{FDOPA}(t)_p = C_{\text{wb}}(t) \times \frac{(1 - \mu(t) \cdot [f_{OMFD}(t) + (1 - Hct) \cdot f_{METS}(t)]_p)}{(1 - Hct)}$$

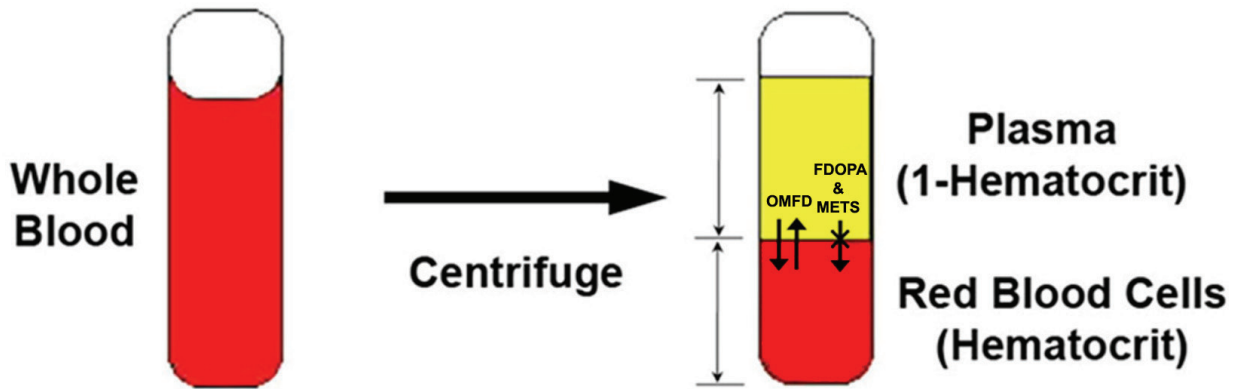
where

$$\frac{(C_{F-18 \text{ total}})_{\text{plasma}}}{(C_{F-18 \text{ total}})_{\text{whole blood}}} = \mu(t).$$

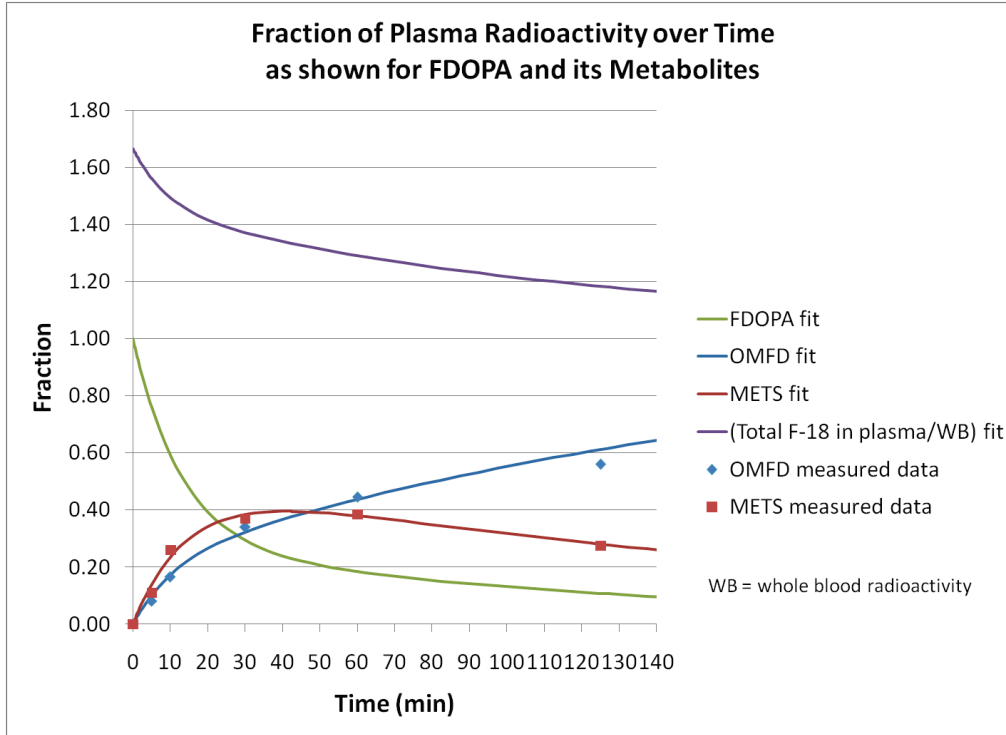
At very short t , $\frac{(C_{F-18\ total})_{plasma}}{(C_{F-18\ total})_{wb}} \cong \frac{1}{1-Hct}$ since $f_{FDOPA}(t)_p$ is 1 and $f_{OMFD}(t)_p$ and

$f_{METS}(t)_p$ are 0 (i.e., OMFD and METS have not formed yet). At very long t ,

$$\frac{(C_{F-18\ total})_{plasma}}{(C_{F-18\ total})_{wb}} \cong 1.$$



Appendix Figure A1. FDOPA does not cross the red blood cell membrane and is confined to the plasma space when it is in blood. OMFD, on the other hand, can cross the red blood cell membrane bidirectionally.



Appendix Figure A2. Fitted exponential curves to the measured fractions of plasma radioactivity for OMFD and METS. The measured data was taken from the publication of Huang *et al.* [8]. The equations for the fitted exponential curves are shown below:

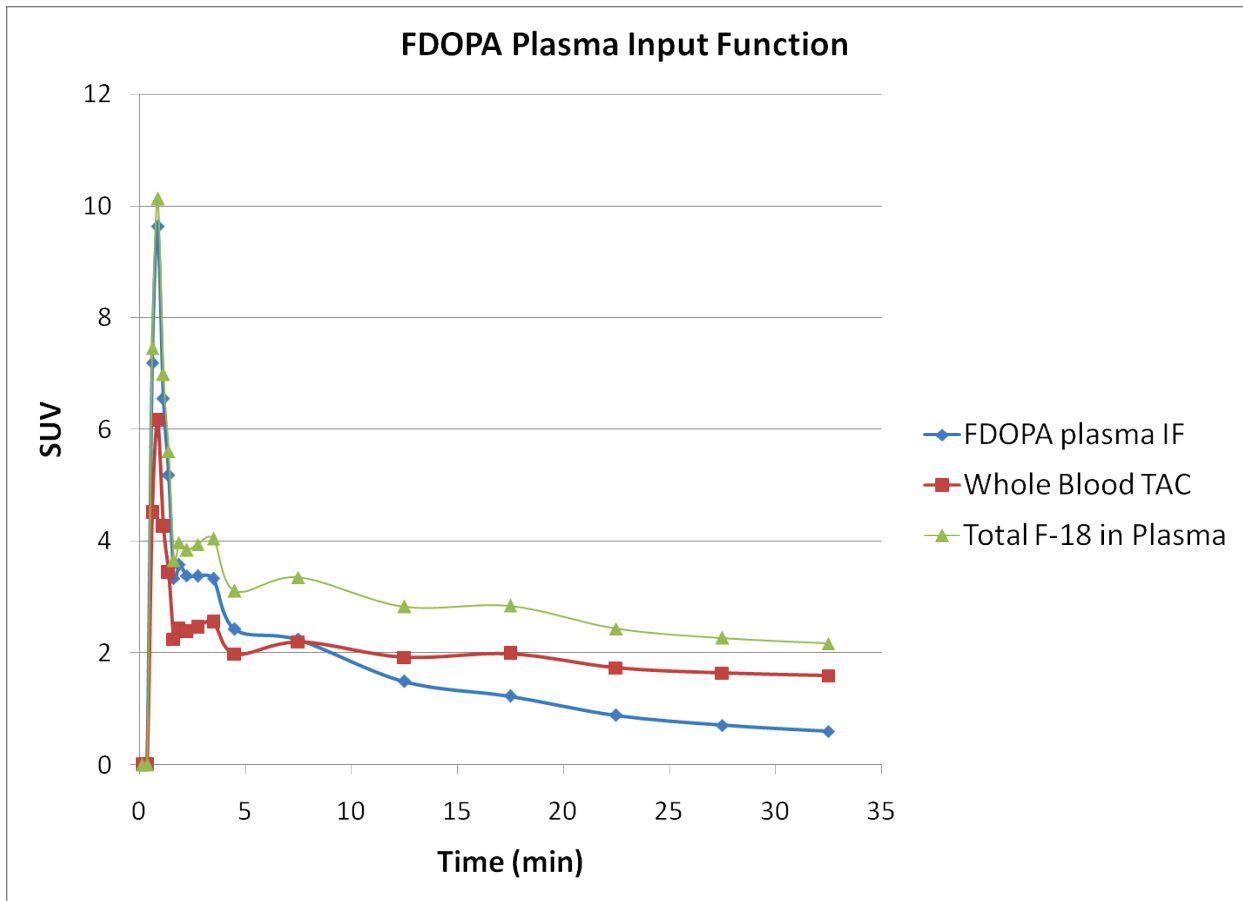
$$f_{METS}(t)_p = 0.52 \times (e^{-0.004997t} - e^{-0.06892t})$$

$$f_{OMFD}(t)_p = 0.80 \times (1 - e^{-0.005337t}) + 0.20 \times (1 - e^{-0.09695t})$$

The decaying exponential curve (shown in green) represents the fraction of plasma radioactivity over time for FDOPA and was derived using the following relationship:

$$f_{FDOPA}(t)_p = 1 - [f_{OMFD}(t) + f_{METS}(t)]_p$$

The top descending purple curve is the total ^{18}F activity in plasma divided by the total ^{18}F activity in whole blood [i.e., $\mu(t)$].



Appendix Figure A3. FDOPA plasma input function (shown in blue) after corrections for metabolites, hematocrit, and partial volume effects. Shown in red is the whole blood time-activity curve after partial volume correction only. Shown in green is the total ^{18}F radioactivity in plasma.

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