

Supplementary tables

Table S1. Definition and units of compartments and rate constants.

Abbreviation	Definition	Unit
C_a	Arterial plasma input	
C_T	$F + NS + S$	
C_I	$F + NS$	
C_2	S	Bq • mL ⁻¹ or molar
F	Free	
NS	Nonspecific	
S	Specific	
K_1	Rate constant for transfer from arterial plasma to tissue $K_1 = F \cdot E$	mL • cm ⁻³ • min ⁻¹
F	blood flow	mL • cm ⁻³ • min ⁻¹
E	unidirectional extraction fraction $E = 1 - e^{-PS/F}$	unitless
P	permeability of the tracer across the capillary surface	cm • min ⁻¹
S	capillary surface area / g of tissue	cm ² • g ⁻¹
k_2, k_3, k_4	Rate constants for transfer between compartments	min ⁻¹

Table S2. Statistical comparison of the one- and two-tissue compartment models for analysis of [¹¹C]osimertinib data.

	AIC, 1TCM	AIC, 2TCM	F statistics	Preferred model
<u>Whole brain</u>				
Subject 1	-29	-73	p < 0.0001	2TCM
Subject 2	-8	-45	p < 0.0001	2TCM
Subject 3	-1	-106	p < 0.0001	2TCM
Subject 4	25	-116	p < 0.0001	2TCM
Subject 6	3	-121	p < 0.0001	2TCM
Subject 7	11	-84	p < 0.0001	2TCM
Subject 8	37	-56	p < 0.0001	2TCM
<u>Gray matter</u>				
Subject 1	-17	-80	p < 0.0001	2TCM
Subject 2	0	-31	p < 0.0001	2TCM
Subject 3	13	-69	p < 0.0001	2TCM
Subject 4	35	-48	p < 0.0001	2TCM
Subject 6	16	-48	p < 0.0001	2TCM
Subject 7	9	-70	p < 0.0001	2TCM
Subject 8	38	-73	p < 0.0001	2TCM
<u>White matter</u>				
Subject 1	96	101	p > 0.05	1TCM
Subject 2	105	110	p > 0.05	1TCM
Subject 3	101	106	p > 0.05	1TCM
Subject 4	91	93	p > 0.05	1TCM
Subject 6	100	108	p > 0.05	1TCM
Subject 7	99	101	p > 0.05	1TCM
Subject 8	115	118	p > 0.05	1TCM

AIC, Akaike information criterion; 1TCM, one-tissue compartment model; 2TCM, two-tissue compartment model.

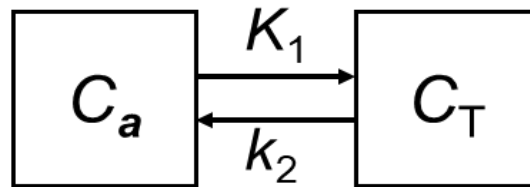
Table S3. Statistical comparison of a two-tissue compartment model with irreversible binding ($k_4=0$) and the standard two-tissue compartment model for analysis of [^{11}C]osimertinib data.

Subject no	AIC, 2TCM, irreversible	AIC, 2TCM	F statistics	Preferred model
<u>Whole brain</u>				
Subject 1	-41	-73	P<0.0001	2TCM
Subject 2	-11	-45	P<0.0001	2TCM
Subject 3	-24	-106	P<0.0001	2TCM
Subject 4	2	-116	P<0.0001	2TCM
Subject 6	-18	-121	P<0.0001	2TCM
Subject 7	-19	-84	P<0.0001	2TCM
Subject 8	3	-56	P<0.0001	2TCM
<u>Gray matter</u>				
Subject 1	-22	-80	P<0.0001	2TCM
Subject 2	-1	-31	P<0.0001	2TCM
Subject 3	0	-69	P<0.0001	2TCM
Subject 4	23	-48	P<0.0001	2TCM
Subject 6	8	-48	P<0.0001	2TCM
Subject 7	-10	-70	P<0.0001	2TCM
Subject 8	10	-73	P<0.0001	2TCM

AIC, Akaike information criterion; 2TCM, irreversible, two-tissue compartment model with irreversible binding ($k_4=0$); 2TCM, two-tissue compartment model for reversible binding.

Supplementary figures

One-tissue compartment model



Two-tissue compartment model

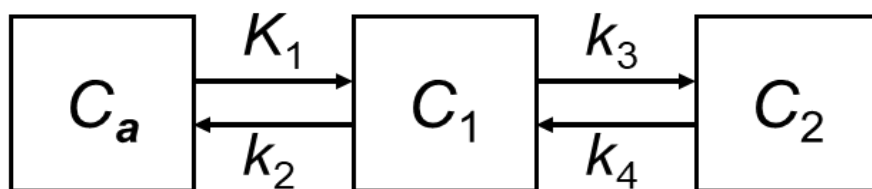


Figure S1. Representation of one-tissue and two-tissue compartment models. For definitions and units, see Table S1.

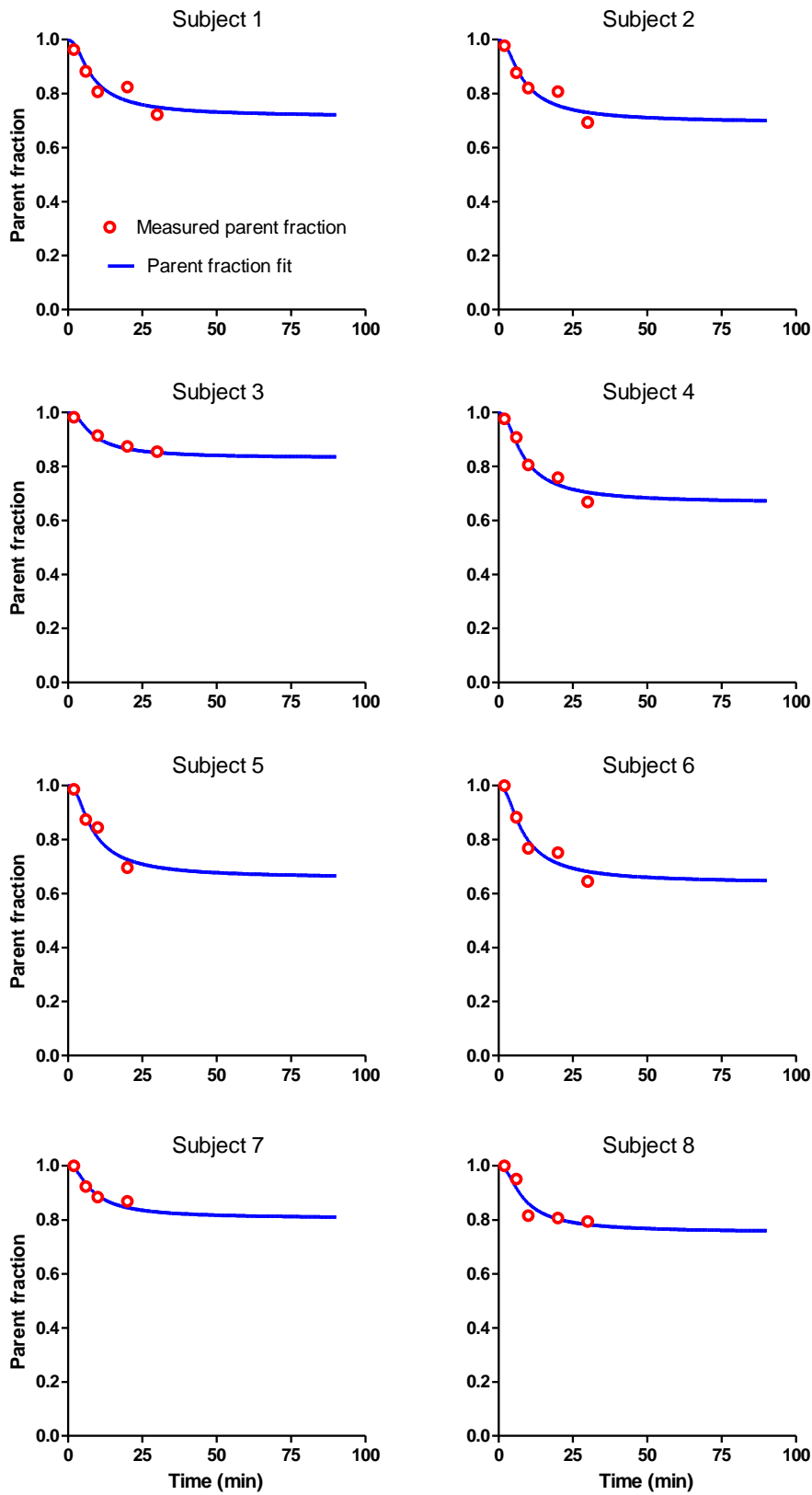


Figure S2. Population fit of the fraction of parent radioligand in plasma using Hills-Richard mixed model.