Supplemental Data: Equations and Parameters

Model equations

The following equations describe the transport of labeled and unlabeled antibody to the antigen sites, its binding, degradation, and radioactive decay. The variables are defined in Table A. Index i refers to all organs except for liver (L) and plasma (P); the asterisk labels the radiolabeled species.

$$\frac{d}{dt} AgAb_i = k_{nonl} \cdot Ab_i - k_{off} \cdot AgAb_i - \lambda_{db} \cdot AgAb_i + \lambda_{phy} \cdot AgAb^*_i$$

$$\frac{d}{dt} AgAb^*_i = k_{nonl} \cdot Ab^*_i - k_{off} \cdot AgAb^*_i - \lambda_{db} \cdot AgAb^*_i - \lambda_{phy} \cdot AgAb^*_i$$

$$\frac{d}{dt} Ab_i = -k_{nonl} \cdot Ab_i + k_{off} \cdot AgAb_i + \frac{F_i}{V_P} \cdot Ab_P - \frac{F_i}{V_i} \cdot Ab_i + \lambda_{phy} \cdot Ab^*_i$$

$$\frac{d}{dt} Ab^*_i = -k_{nonl} \cdot Ab^*_i + k_{off} \cdot AgAb^*_i + \frac{F_i}{V_P} \cdot Ab^*_P - \frac{F_i}{V_i} \cdot Ab^*_i - \lambda_{phy} \cdot Ab^*_i$$

$$\frac{d}{dt} Ab_L = -k_{nonl} \cdot Ab_L + k_{off} \cdot AgAb_L + \frac{F_L}{V_P} \cdot Ab_P + \frac{F_{GI}}{V_{GI}} \cdot Ab_{GI} + \frac{F_S}{V_S} \cdot Ab_S - \frac{F_L + F_{GI} + F_S}{V_L} \cdot Ab_L + \lambda_{phy} \cdot Ab^*_i$$

$$\frac{d}{dt} Ab^*_L = -k_{nonl} \cdot Ab^*_L + k_{off} \cdot AgAb^*_L + \frac{F_L}{V_P} \cdot Ab^*_P + \frac{F_{GI}}{V_{GI}} \cdot Ab^*_{GI} + \frac{F_S}{V_S} \cdot Ab^*_S - \frac{F_L + F_{GI} + F_S}{V_L} \cdot Ab^*_L - \lambda_{phy} \cdot Ab^*_i$$

$$\frac{d}{dt} Ab_P = -\sum_i \frac{F_i}{V_P} \cdot Ab_P + \frac{F_L + F_{GI} + F_S}{V_L} \cdot Ab_L + \frac{F_{Ly}}{V_{Ly}} \cdot Ab_{Ly} + \frac{F_{RM}}{V_{RM}} \cdot Ab_{RM} - \lambda_{du} \cdot Ab_P + \lambda_{phy} \cdot Ab^*_P$$

$$\frac{d}{dt} Ab^*_P = -\sum_i \frac{F_i}{V_P} \cdot Ab^*_P + \frac{F_L + F_{GI} + F_S}{V_L} \cdot Ab^*_L + \frac{F_{Ly}}{V_{Ly}} \cdot Ab^*_{Ly} + \frac{F_{RM}}{V_{RM}} \cdot Ab^*_{RM} - \lambda_{du} \cdot Ab^*_P - \lambda_{phy} \cdot Ab^*_P$$

with $k_{nonl} = \frac{k_{on} \cdot (Ag_i - AgAb^*_i - AgAb_i)}{V_i}$

The following submodel for degraded antibody (^{111}In-DTPA and ^{111}In-low molecular weight biodistribution) was adopted from Eger et al. *(1).* The variables are defined in Table A.

$$\frac{d}{dt}Ex = \lambda_{du} \cdot Ab_P - \lambda_{clex} \cdot Ex + \lambda_{phy} \cdot Ex^*$$

$$\frac{d}{dt}Ex^* = \lambda_{du} \cdot Ab_P^* - \lambda_{clex} \cdot Ex^* - \lambda_{phy} \cdot Ex^*$$

$$\frac{d}{dt}Meta_P = \lambda_{clex} \cdot Ex - \lambda_{cl} \cdot Meta_P - \lambda_{Metaex1} \cdot Meta_P + \lambda_{Metaex2} \cdot Meta_{ex1} + \lambda_{db} \cdot \sum_i AgAb_i + \lambda_{phy} \cdot Meta_P^*$$

$$\frac{d}{dt}Meta_P^* = \lambda_{clex} \cdot Ex^* - \lambda_{cl} \cdot Meta_P^* - \lambda_{Metaex1} \cdot Meta_P^* + \lambda_{Metaex2} \cdot Meta_{ex1}^* + \lambda_{db} \cdot \sum_i AgAb_i^* - \lambda_{phy} \cdot Meta_P^*$$

$$\frac{d}{dt}Meta_{ex1} = \lambda_{Metaex1} \cdot Meta_P - \left(\lambda_{Metaex2} + \lambda_{Metaex3}\right) \cdot Meta_{ex1} + \lambda_{Metaex4} \cdot Meta_{ex2} + \lambda_{phy} \cdot Meta_{ex1}^*$$

$$\frac{d}{dt}Meta_{ex1}^* = \lambda_{Metaex1} \cdot Meta_P^* - \left(\lambda_{Metaex2} + \lambda_{Metaex3}\right) \cdot Meta_{ex1}^* + \lambda_{Metaex4} \cdot Meta_{ex2}^* - \lambda_{phy} \cdot Meta_{ex1}^*$$

$$\frac{d}{dt}Meta_{ex2} = \lambda_{Metaex3} \cdot Meta_{ex1} - \lambda_{Metaex4} \cdot Meta_{ex2} + \lambda_{phy} \cdot Meta_{ex2}^*$$

$$\frac{d}{dt}Meta_{ex2}^* = \lambda_{Metaex3} \cdot Meta_{ex1}^* - \lambda_{Metaex4} \cdot Meta_{ex2}^* - \lambda_{phy} \cdot Meta_{ex2}^*$$

Blood volume according to standard formula

The blood volumes estimated by fitting the data to the model were compared to values determined as follows *(2)* (BW = body weight in kg).

males

$$V = 0.041\,\mathrm{l/kg} \cdot \mathrm{BW} + 1.53\,\mathrm{l}$$

females

$$V = 0.047\,\mathrm{l/kg} \cdot \mathrm{BW} + 0.86\,\mathrm{l}$$

TABLE A. Parameter definitions

	Variable	Value	Unit	Source
k_{on}	association rate	estimated	$l \cdot mol^{-1} \cdot min^{-1}$	
K_D	dissociation constant	estimated	$nmol \cdot l^{-1}$	
k_{off}	dissociation rate	$k_{off} = k_{on} \cdot K_D$	min^{-1}	
k_{nonl}	nonlinear association term	see definition above	min^{-1}	
F	total plasma flow	=V·1.23*	$ml \cdot min^{-1}$	
F_L	liver arterial	0.065·F	$ml \cdot min^{-1}$	*(3)*
F_S	spleen	0.03 Bayes SD 0.02 †	$ml \cdot min^{-1}$	*(3)*
F_{GI}	GI-tract	0.16·F	$ml \cdot min^{-1}$	*(3)*
F_{RM}	red marrow	0.03 Bayes SD 0.03 †	$ml \cdot min^{-1}$	*(3)*
F_{Ly}	lymph nodes	0.017·F	$ml \cdot min^{-1}$	*(3)*
V	total plasma volume	estimated	ml	
V_L	liver	0.1·V	ml	*(3)*
V_S	spleen	0.014·V	ml	*(3)*
V_{GI}	GI-tract	0.076·V	ml	*(3)*
V_{RM}	red marrow	0.04·V	ml	*(3)*
V_{Ly}	lymph nodes	0.002·V	ml	*(3)*
V_P	total plasma minus organs	V· (1-0.232)	ml	
Ag_i	antigens of organ i	estimated	mol	
$AgAb_i$	bound antibody of organ i		mol	
Ab_i	unbound antibody of organ i			
Ex	degraded antibody in e.v. ‡ delay compartment		mol	*(1)*
$Meta_P$	degraded antibody in plasma		mol	*(4)*

$Meta_{ex1}$	degraded antibody in e.v.1 ‡		mol	*(4)*
$Meta_{ex2}$	degraded antibody in e.v.2 ‡		mol	*(4)*
λ_{phy}	physical decay ^{111}In	$1.72 \cdot 10^{-4}$	min^{-1}	
λ_{db}	degradation of bound antibody	estimated	min^{-1}	
λ_{du}	degradation of unbound antibody	$3.9 \cdot 10^{-4}$	min^{-1}	*(1)*
λ_{clex}	clearance from e.v.‡ delay space	$3.9 \cdot 10^{-5}$	min^{-1}	*(1)*
$\lambda_{Metaex1}$	vascular to e.v. 1	0.39	min^{-1}	*(4)*
$\lambda_{Metaex2}$	e.v. 1 to vascular	0.17	min^{-1}	*(4)*
$\lambda_{Metaex3}$	e.v. 1 to e.v. 2	0.018	min^{-1}	*(4)*
$\lambda_{Metaex4}$	e.v. 2 to e.v. 1	0.013	min^{-1}	*(4)*
λ_{cl}	clearance from body	0.047	min^{-1}	*(4)*

* For the average normal adult (blood) F = 6500 ml/min and V = 5300 ml. Therefore, a factor of 1.23 was assigned to account for the changes in total blood flow due to volume changes.

† standard deviation and mean value from Leggett et al. *(3)*

‡ e.v., extra vascular

References

1. Eger RR, Covell DG, Carrasquillo JA et al. Kinetic model for the biodistribution of an ^{111}In-labeled monoclonal antibody in humans. *Cancer Res.* 1987;47:3328-3336.
2. Silbernagl S, Despopoulos A. Taschenatlas der Physiologie. Stuttgart: Thieme; 2003.
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4. Houston AS, Sampson WF, Macleod MA. A compartmental model for the distribution of ^{113m}In-DTPA and ^{99m}Tc-(Sn)DTPA in man following intravenous injection. *Int J Nucl Med Biol.* 1979;6:85-95.