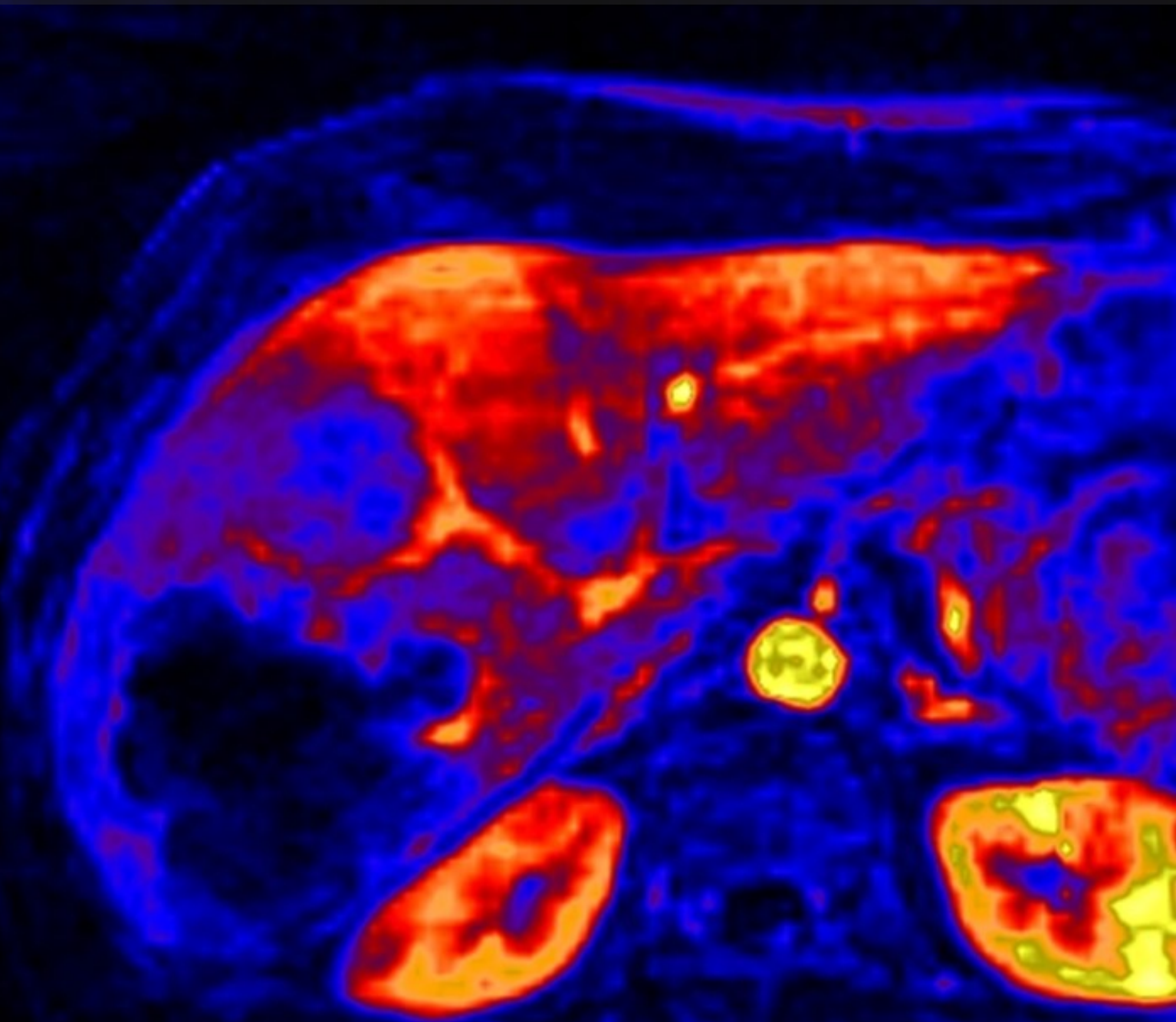


Leeds pilot study study

rifampicin (all results)

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rifampicin (all results)

by

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Two-scan results

1.1. Data summary

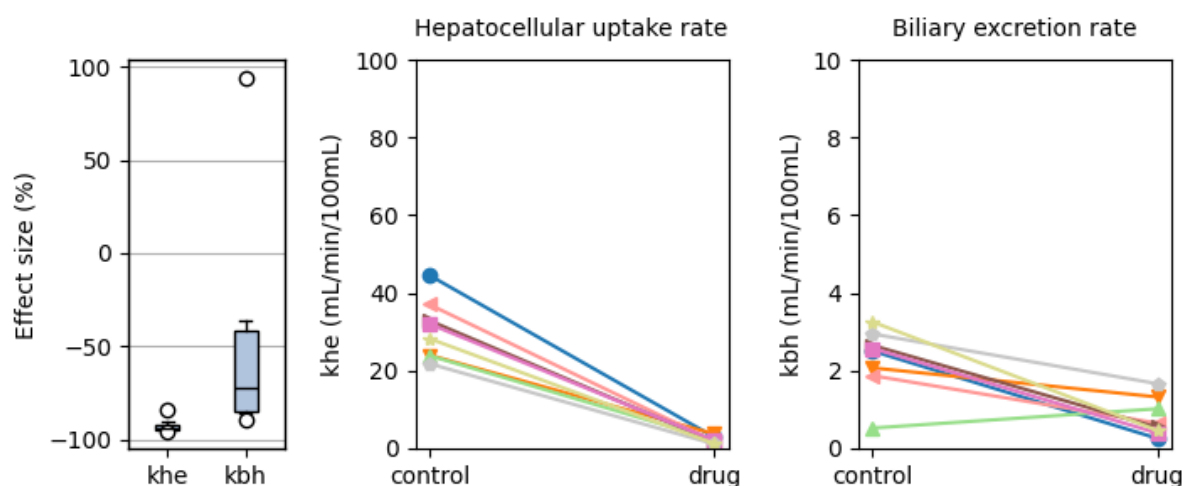


Figure 1.1: Effect size (%) on hepatocellular uptake (k_{he} , left) and biliary excretion (k_{bh} , right) of gadoxetate. The boxplot shows median, interquartile range and 95 percent range. The line plots show individual values for hepatocellular uptake (k_{he} , middle) and biliary excretion (k_{bh} , right) of gadoxetate of the control (left of plot) and treatment (right of plot). Grey lines are healthy controls with rifampicin injection.

parameter	count	mean	std	min	25%	50%	75%	max
khe effect size (%)	8.0	-92.6	3.7	-95.3	-94.7	-94.0	-92.6	-84.3
khe control (mL/min/100cm ³)	8.0	30.56	7.69	21.81	23.98	30.14	33.93	44.54
khe drug (mL/min/100cm ³)	8.0	2.17	0.86	1.16	1.69	2.0	2.46	3.76
kbh effect size (%)	8.0	-48.7	61.2	-89.7	-84.8	-72.4	-41.6	94.3
kbh control (mL/min/100cm ³)	8.0	2.3	0.84	0.52	2.02	2.54	2.72	3.25
kbh drug (mL/min/100cm ³)	8.0	0.79	0.5	0.26	0.45	0.6	1.1	1.67

Table 1.1: Effect size and absolute values of hepatocellular uptake (k_{he}) and biliary excretion (k_{bh}) of gadoxetate

1.2. Liver biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for CI (0-35min)	6e-05	441.16	984.97
AUC for CI (0-inf)	0.0012	35.49	71.93
Biliary excretion rate	0.00478	11.71	52.58
Biliary tissue excretion rate	0.00419	13.0	43.2
Extracellular dispersion	0.53091	0.4	0.55
Extracellular mean transit time	0.40589	0.46	0.44
Final biliary excretion rate	0.03153	2.69	8.5
Final hepatocellular uptake rate	0.00251	19.61	65.66
Hematocrit			
Hepatocellular mean transit time	0.06155	1.63	0.11
Hepatocellular tissue uptake rate	0.21877	0.67	3.4
Hepatocellular uptake rate	1e-05	1363.5	12220.54
Initial biliary excretion rate	0.50746	0.41	1.75
Initial hepatocellular uptake rate	3e-05	803.62	4532.55
Liver T1-MOLLI at 45min	0.0	6244.03	0.0
Liver T1-MOLLI at baseline	0.3834	0.48	0.73
Liver T1-MOLLI at scan 2	0.00215	22.19	0.06
Liver blood clearance	0.0	8478.98	1174265.47
Liver extracellular volume fraction	0.19862	0.71	0.3
RE for R1l at 20min	7e-05	364.52	993.63
RE for Sl at 20min	5e-05	479.18	1113.99

Table 1.2: Results of a pairwise comparison testing for differences in liver biomarkers between control and treatment. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for CI (0-35min)	mM*sec	148.0 (31.0)	25.8 (4.3)	-81.9 (2.7)
AUC for CI (0-inf)	mM*sec	510.0 (160.0)	111.0 (21.0)	-75.9 (4.9)
Biliary excretion rate	mL/min/100cm3	2.3 (0.58)	0.791 (0.34)	-48.7 (42.0)
Biliary tissue excretion rate	mL/min/100cm3	2.79 (0.72)	1.01 (0.44)	-44.3 (50.0)
Extracellular dispersion	%	63.6 (20.0)	70.4 (4.8)	283.0 (550.0)
Extracellular mean transit time	sec	35.8 (13.0)	43.0 (7.7)	148.0 (240.0)
Final biliary excretion rate	mL/min/100cm3	2.83 (1.2)	1.23 (0.59)	-34.7 (48.0)
Final hepatocellular uptake rate	mL/min/100cm3	29.3 (11.0)	2.56 (0.72)	-81.6 (22.0)
Hematocrit	%	45.0 (0.0)	45.0 (0.0)	0.0 (0.0)
Hepatocellular mean transit time	min	51.3 (36.0)	141.0 (62.0)	299.0 (190.0)
Hepatocellular tissue uptake rate	mL/min/100cm3	728.0 (1000.0)	10.7 (3.5)	-93.4 (6.2)
Hepatocellular uptake rate	mL/min/100cm3	30.6 (5.3)	2.17 (0.59)	-92.6 (2.5)
Initial biliary excretion rate	mL/min/100cm3	2.35 (0.76)	1.73 (1.8)	-20.7 (58.0)
Initial hepatocellular uptake rate	mL/min/100cm3	31.8 (6.3)	1.78 (0.58)	-94.2 (1.8)
Liver T1-MOLLI at 45min	sec	0.537 (0.036)	0.727 (0.041)	35.7 (5.9)
Liver T1-MOLLI at baseline	sec	0.795 (0.037)	0.805 (0.041)	1.27 (2.7)
Liver T1-MOLLI at scan 2	sec	0.669 (0.041)	0.759 (0.038)	13.8 (6.3)
Liver blood clearance	L/min	0.273 (0.032)	0.0199 (0.0044)	-92.3 (2.5)
Liver extracellular volume fraction	mL/100cm3	16.1 (7.4)	21.5 (3.3)	264.0 (420.0)
RE for R1l at 20min	%	64.0 (14.0)	8.86 (1.5)	-85.6 (1.9)
RE for Sl at 20min	%	52.9 (12.0)	6.54 (1.7)	-87.5 (1.9)

Table 1.3: Mean values along with their 95 percent confidence intervals for all liver biomarkers of the control and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

1.3. Systemic biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for Cb (0-35min)	0.01059	6.25	0.3
AUC for Cb (0-inf)	0.01062	6.23	0.16
Body extraction fraction	0.0203	3.76	9.03
Cardiac output	0.53951	0.4	0.73
Heart-lung dispersion	0.08682	1.27	0.57
Heart-lung mean transit time	0.51409	0.41	0.62
Organs blood mean transit time	0.4645	0.43	0.7
Organs extraction fraction	0.00515	11.02	5.91
Organs extravascular mean transit time	0.33616	0.51	0.45
RE for R1b at 20min	0.00821	7.63	0.2
RE for Sb at 20min	0.21085	0.68	0.24

Table 1.4: Results of a pairwise comparison testing for differences in systemic biomarkers between control and treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	28.2 (6.3)	35.2 (8.1)	26.8 (16.0)
AUC for Cb (0-inf)	mM*sec	43.4 (14.0)	67.9 (19.0)	69.4 (42.0)
Body extraction fraction	%	6.81 (2.6)	3.46 (0.77)	-41.1 (16.0)
Cardiac output	L/min	7.27 (2.1)	7.7 (1.2)	17.8 (27.0)
Heart-lung dispersion	%	43.6 (9.0)	47.4 (8.0)	10.7 (9.8)
Heart-lung mean transit time	sec	13.5 (2.5)	14.5 (2.5)	11.9 (23.0)
Organs blood mean transit time	sec	28.9 (6.7)	30.8 (7.0)	9.7 (20.0)
Organs extraction fraction	%	19.0 (3.8)	14.1 (3.2)	-25.4 (12.0)
Organs extravascular mean transit time	min	5.85 (1.5)	6.72 (1.3)	31.4 (48.0)
RE for R1b at 20min	%	16.4 (4.2)	22.9 (5.9)	45.2 (28.0)
RE for Sb at 20min	%	12.8 (5.5)	20.2 (7.4)	136.0 (130.0)

Table 1.5: Mean values along with their 95 percent confidence intervals for all systemic biomarkers at the control and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

1.4. Case notes
1.4.1. Subject LDS-002

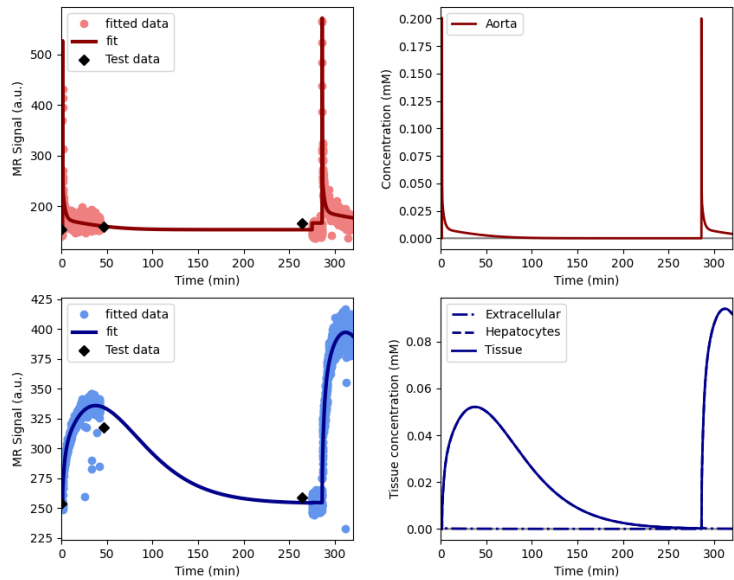


Figure 1.2: Signal-time curves for subject LDS-002 at the control visit.

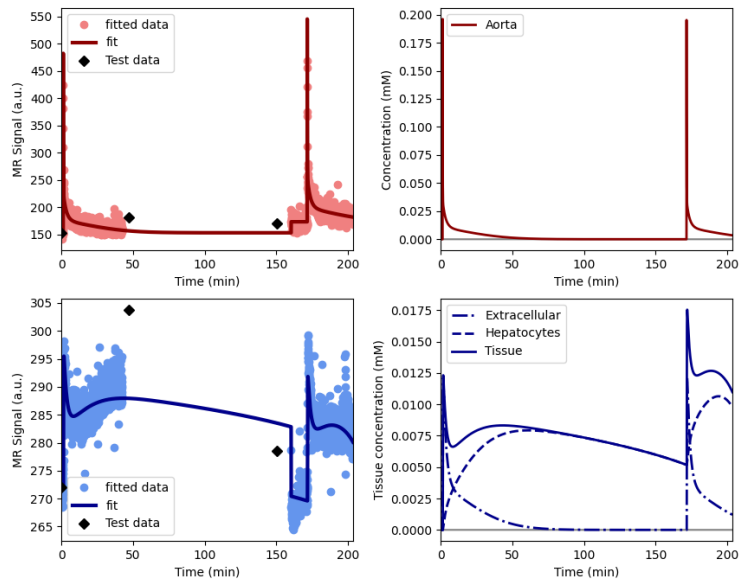


Figure 1.3: Signal-time curves for subject LDS-002 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	106.46	16.31	-84.68
AUC for Cl (0-inf)	mM*sec	346.52	80.53	-76.76
Biliary excretion rate	mL/min/100cm3	2.51	0.26	-89.68
Biliary tissue excretion rate	mL/min/100cm3	2.53	0.32	-87.46
Extracellular dispersion	%	3.06	72.17	2256.82
Extracellular mean transit time	sec	3.3	36.2	996.02
Final biliary excretion rate	mL/min/100cm3	3.26	2.7	-17.25
Final hepatocellular uptake rate	mL/min/100cm3	63.13	3.43	-94.56
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	39.51	315.12	697.6
Hepatocellular tissue uptake rate	mL/min/100cm3	4442.82	16.11	-99.64
Hepatocellular uptake rate	mL/min/100cm3	44.54	2.98	-93.32
Initial biliary excretion rate	mL/min/100cm3	2.04	0.14	-93.32
Initial hepatocellular uptake rate	mL/min/100cm3	25.95	2.52	-90.29
Liver T1-MOLLI at 45min	sec	0.58	0.72	23.26
Liver T1-MOLLI at baseline	sec	0.76	0.81	7.72
Liver T1-MOLLI at scan 2	sec	0.74	0.75	1.88
Liver blood clearance	L/min	0.3	0.02	-92.16
Liver extracellular volume fraction	mL/100cm3	1.0	18.47	1742.88
RE for R1l at 20min	%	36.16	6.15	-82.98
RE for Sl at 20min	%	29.84	4.0	-86.61

Table 1.6: Values for liver of subject LDS-002

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	17.57	17.23	-1.95
AUC for Cb (0-inf)	mM*sec	26.95	22.21	-17.6
Body extraction fraction	%	6.94	5.31	-23.5
Cardiac output	L/min	3.61	5.75	59.52
Heart-lung dispersion	%	64.21	68.67	6.95
Heart-lung mean transit time	sec	14.64	8.24	-43.74
Organs blood mean transit time	sec	32.92	25.4	-22.85
Organs extraction fraction	%	19.53	14.06	-28.03
Organs extravascular mean transit time	min	8.0	4.98	-37.75
RE for R1b at 20min	%	9.5	9.12	-3.94
RE for Sb at 20min	%	9.98	4.26	-57.37

Table 1.7: Values for aorta of subject LDS-002

1.4.2. Subject LDS-003

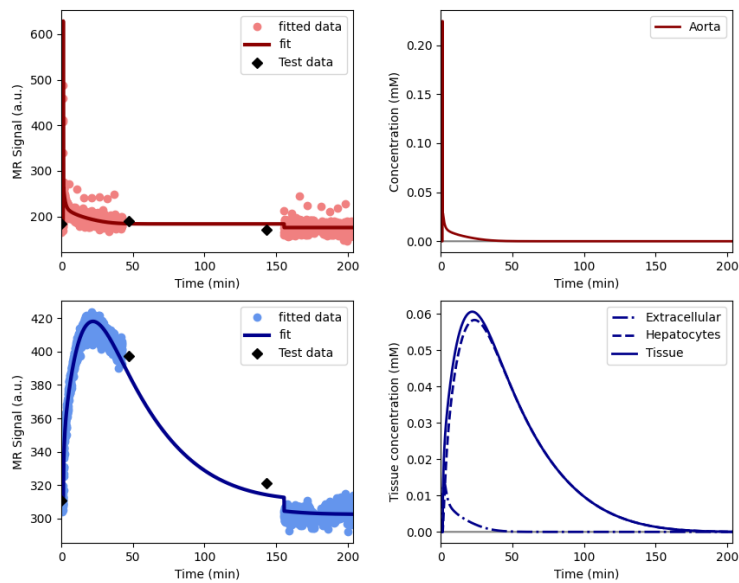


Figure 1.4: Signal-time curves for subject LDS-003 at the control visit.

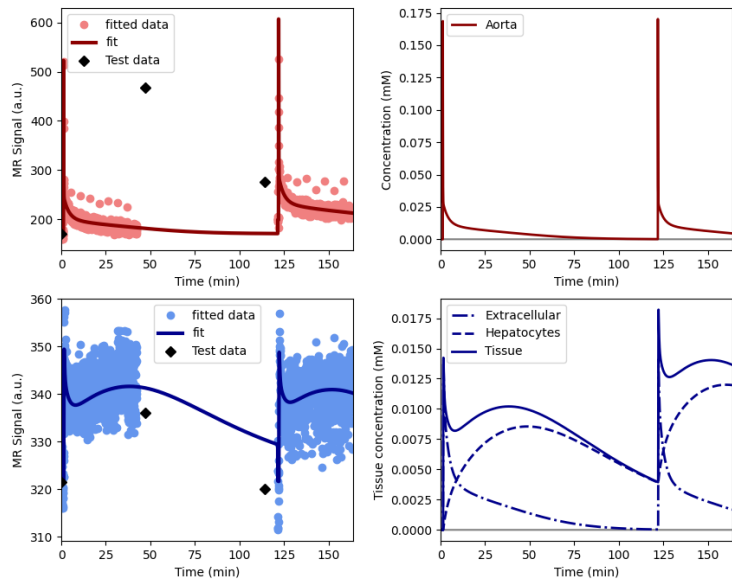


Figure 1.5: Signal-time curves for subject LDS-003 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	78.23	19.84	-74.65
AUC for Cl (0-inf)	mM*sec	219.64	72.97	-66.78
Biliary excretion rate	mL/min/100cm3	2.07	1.32	-36.09
Biliary tissue excretion rate	mL/min/100cm3	3.27	1.66	-49.29
Extracellular dispersion	%	88.4	65.13	-26.32
Extracellular mean transit time	sec	60.0	28.28	-52.86
Final biliary excretion rate	mL/min/100cm3	6.34	1.44	-77.28
Final hepatocellular uptake rate	mL/min/100cm3	4.53	4.31	-4.79
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	30.6	60.34	97.21
Hepatocellular tissue uptake rate	mL/min/100cm3	65.57	18.7	-71.48
Hepatocellular uptake rate	mL/min/100cm3	24.02	3.76	-84.34
Initial biliary excretion rate	mL/min/100cm3	1.24	1.23	-1.02
Initial hepatocellular uptake rate	mL/min/100cm3	43.5	3.21	-92.62
Liver T1-MOLLI at 45min	sec	0.53	0.69	30.25
Liver T1-MOLLI at baseline	sec	0.71	0.73	2.64
Liver T1-MOLLI at scan 2	sec	0.66	0.71	7.58
Liver blood clearance	L/min	0.21	0.03	-84.56
Liver extracellular volume fraction	mL/100cm3	36.62	20.12	-45.07
RE for R1l at 20min	%	41.64	6.71	-83.89
RE for Sl at 20min	%	36.02	4.63	-87.14

Table 1.8: Values for liver of subject LDS-003

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	12.5	20.0	60.01
AUC for Cb (0-inf)	mM*sec	13.08	32.59	149.22
Body extraction fraction	%	7.03	3.4	-51.68
Cardiac output	L/min	7.36	6.1	-17.14
Heart-lung dispersion	%	34.72	48.33	39.22
Heart-lung mean transit time	sec	10.6	13.18	24.27
Organs blood mean transit time	sec	17.46	26.82	53.61
Organs extraction fraction	%	17.55	10.81	-38.42
Organs extravascular mean transit time	min	2.31	6.37	175.4
RE for R1b at 20min	%	5.89	12.6	113.84
RE for Sb at 20min	%	28.87	4.16	-85.59

Table 1.9: Values for aorta of subject LDS-003

1.4.3. Subject LDS-004

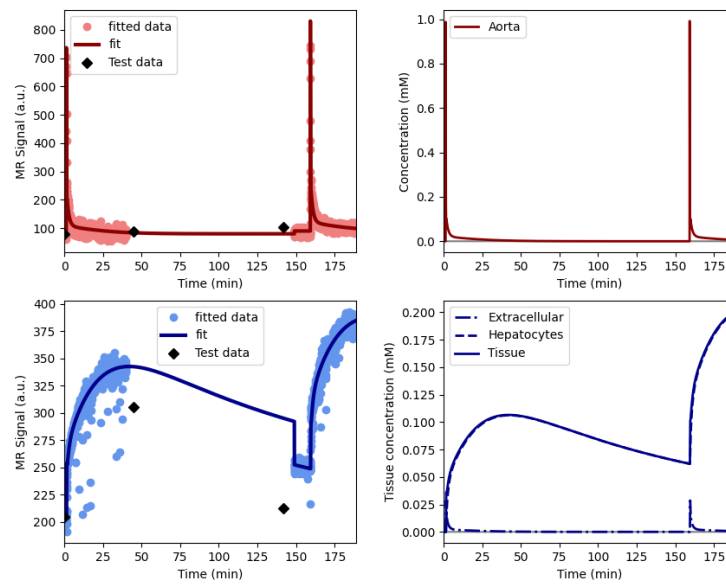


Figure 1.6: Signal-time curves for subject LDS-004 at the control visit.

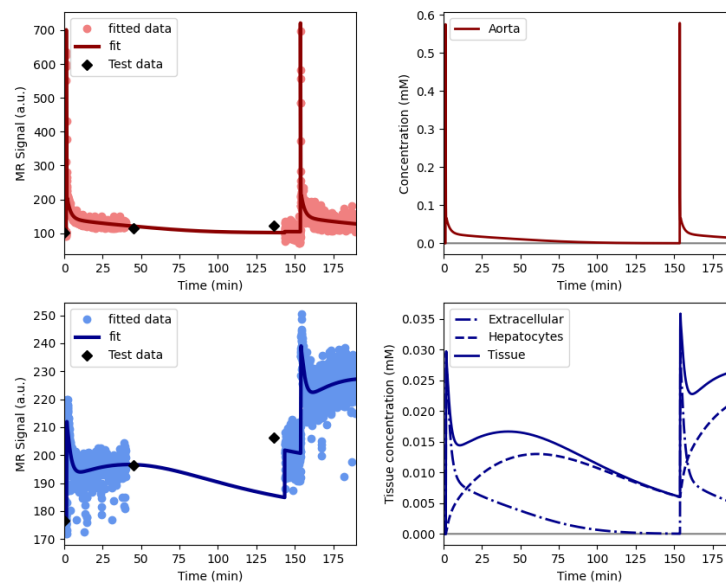


Figure 1.7: Signal-time curves for subject LDS-004 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	190.43	35.43	-81.39
AUC for Cl (0-inf)	mM*sec	945.44	140.72	-85.12
Biliary excretion rate	mL/min/100cm3	0.52	1.02	94.3
Biliary tissue excretion rate	mL/min/100cm3	0.56	1.27	127.52
Extracellular dispersion	%	56.45	80.4	42.43
Extracellular mean transit time	sec	25.54	52.6	105.91
Final biliary excretion rate	mL/min/100cm3	0.43	0.97	124.34
Final hepatocellular uptake rate	mL/min/100cm3	28.15	2.83	-89.95
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	179.44	78.87	-56.05
Hepatocellular tissue uptake rate	mL/min/100cm3	411.8	11.69	-97.16
Hepatocellular uptake rate	mL/min/100cm3	23.89	2.29	-90.43
Initial biliary excretion rate	mL/min/100cm3	0.67	1.08	61.01
Initial hepatocellular uptake rate	mL/min/100cm3	19.62	1.74	-91.12
Liver T1-MOLLI at 45min	sec	0.5	0.71	41.3
Liver T1-MOLLI at baseline	sec	0.8	0.8	-0.01
Liver T1-MOLLI at scan 2	sec	0.65	0.74	14.22
Liver blood clearance	L/min	0.21	0.02	-89.38
Liver extracellular volume fraction	mL/100cm3	5.8	19.56	237.15
RE for R1l at 20min	%	75.5	12.22	-83.82
RE for Sl at 20min	%	61.84	10.71	-82.68

Table 1.10: Values for liver of subject LDS-004

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	36.75	48.81	32.79
AUC for Cb (0-inf)	mM*sec	44.35	87.97	98.38
Body extraction fraction	%	14.91	5.11	-65.74
Cardiac output	L/min	4.13	6.0	45.14
Heart-lung dispersion	%	31.15	33.08	6.2
Heart-lung mean transit time	sec	18.76	21.1	12.47
Organs blood mean transit time	sec	26.33	36.58	38.94
Organs extraction fraction	%	30.9	22.19	-28.18
Organs extravascular mean transit time	min	5.6	5.61	0.16
RE for R1b at 20min	%	18.19	31.9	75.4
RE for Sb at 20min	%	6.02	26.78	344.97

Table 1.11: Values for aorta of subject LDS-004

1.4.4. Subject LDS-006

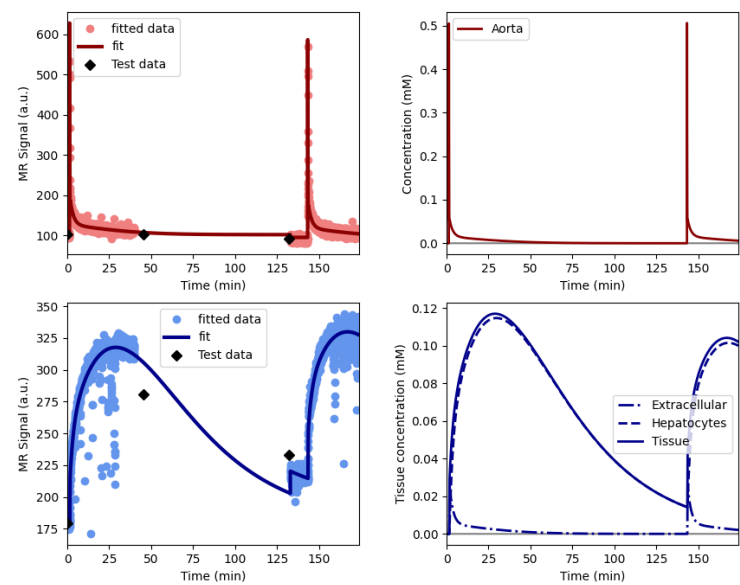


Figure 1.8: Signal-time curves for subject LDS-006 at the control visit.

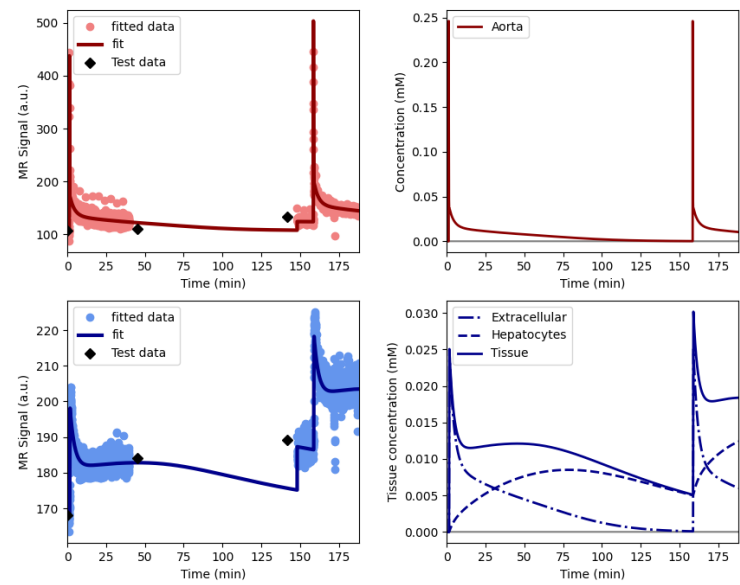


Figure 1.9: Signal-time curves for subject LDS-006 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	197.21	27.08	-86.27
AUC for Cl (0-inf)	mM*sec	623.22	109.44	-82.44
Biliary excretion rate	mL/min/100cm ³	1.87	0.65	-65.23
Biliary tissue excretion rate	mL/min/100cm ³	2.32	0.95	-58.91
Extracellular dispersion	%	71.21	66.0	-7.32
Extracellular mean transit time	sec	45.26	42.25	-6.65
Final biliary excretion rate	mL/min/100cm ³	2.0	0.84	-57.96
Final hepatocellular uptake rate	mL/min/100cm ³	33.42	2.42	-92.76
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	43.11	104.91	143.35
Hepatocellular tissue uptake rate	mL/min/100cm ³	192.09	6.02	-96.87
Hepatocellular uptake rate	mL/min/100cm ³	37.02	1.91	-94.85
Initial biliary excretion rate	mL/min/100cm ³	1.76	0.53	-69.82
Initial hepatocellular uptake rate	mL/min/100cm ³	40.62	1.4	-96.56
Liver T1-MOLLI at 45min	sec	0.5	0.75	51.37
Liver T1-MOLLI at baseline	sec	0.84	0.84	-0.39
Liver T1-MOLLI at scan 2	sec	0.68	0.79	15.44
Liver blood clearance	L/min	0.26	0.01	-94.74
Liver extracellular volume fraction	mL/100cm ³	19.27	31.7	64.5
RE for R1l at 20min	%	93.6	9.55	-89.8
RE for Sl at 20min	%	75.76	7.58	-90.0

Table 1.12: Values for liver of subject LDS-006

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	27.2	30.59	12.45
AUC for Cb (0-inf)	mM*sec	35.9	61.46	71.19
Body extraction fraction	%	8.51	2.69	-68.41
Cardiac output	L/min	4.43	8.05	81.82
Heart-lung dispersion	%	33.43	40.03	19.74
Heart-lung mean transit time	sec	16.64	15.98	-3.96
Organs blood mean transit time	sec	30.41	27.74	-8.8
Organs extraction fraction	%	20.77	12.08	-41.85
Organs extravascular mean transit time	min	6.07	6.61	8.81
RE for R1b at 20min	%	15.24	20.77	36.24
RE for Sb at 20min	%	11.98	25.11	109.67

Table 1.13: Values for aorta of subject LDS-006

1.4.5. Subject LDS-007

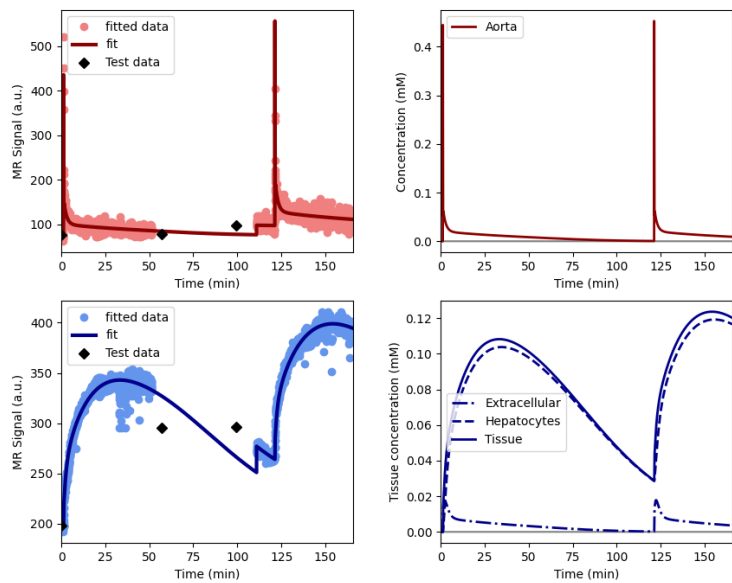


Figure 1.10: Signal-time curves for subject LDS-007 at the control visit.

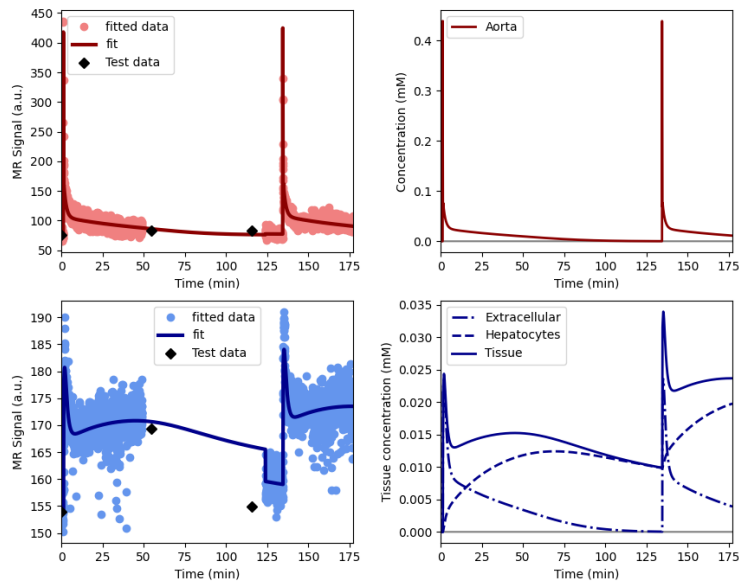


Figure 1.11: Signal-time curves for subject LDS-007 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	188.07	32.42	-82.76
AUC for Cl (0-inf)	mM*sec	656.68	143.33	-78.17
Biliary excretion rate	mL/min/100cm3	2.65	0.54	-79.5
Biliary tissue excretion rate	mL/min/100cm3	3.36	0.67	-80.06
Extracellular dispersion	%	95.11	77.13	-18.91
Extracellular mean transit time	sec	57.97	38.9	-32.89
Final biliary excretion rate	mL/min/100cm3	2.21	0.28	-87.29
Final hepatocellular uptake rate	mL/min/100cm3	29.99	1.33	-95.55
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	29.74	149.16	401.52
Hepatocellular tissue uptake rate	mL/min/100cm3	155.36	9.59	-93.83
Hepatocellular uptake rate	mL/min/100cm3	32.9	1.82	-94.48
Initial biliary excretion rate	mL/min/100cm3	3.3	8.05	143.79
Initial hepatocellular uptake rate	mL/min/100cm3	35.81	2.3	-93.58
Liver T1-MOLLI at 45min	sec	0.54	0.75	40.39
Liver T1-MOLLI at baseline	sec	0.86	0.84	-1.75
Liver T1-MOLLI at scan 2	sec	0.6	0.8	33.05
Liver blood clearance	L/min	0.31	0.02	-93.48
Liver extracellular volume fraction	mL/100cm3	21.18	18.95	-10.52
RE for R1l at 20min	%	85.37	11.7	-86.3
RE for Sl at 20min	%	72.97	9.46	-87.03

Table 1.14: Values for liver of subject LDS-007

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	36.41	44.72	22.82
AUC for Cb (0-inf)	mM*sec	67.07	78.46	16.98
Body extraction fraction	%	3.2	3.07	-4.21
Cardiac output	L/min	9.39	8.41	-10.42
Heart-lung dispersion	%	32.6	36.54	12.07
Heart-lung mean transit time	sec	12.14	12.95	6.65
Organs blood mean transit time	sec	19.12	15.42	-19.37
Organs extraction fraction	%	19.82	19.4	-2.12
Organs extravascular mean transit time	min	4.57	4.08	-10.7
RE for R1b at 20min	%	24.78	29.39	18.63
RE for Sb at 20min	%	19.07	34.27	79.65

Table 1.15: Values for aorta of subject LDS-007

1.4.6. Subject LDS-008

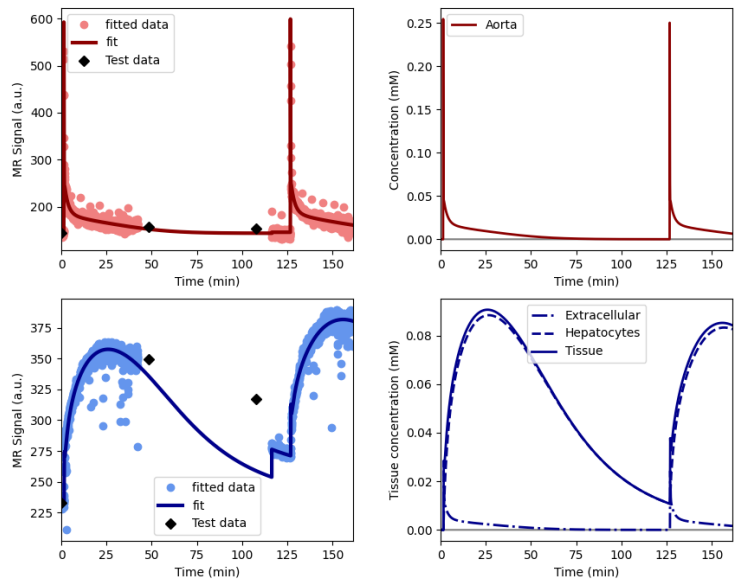


Figure 1.12: Signal-time curves for subject LDS-008 at the control visit.

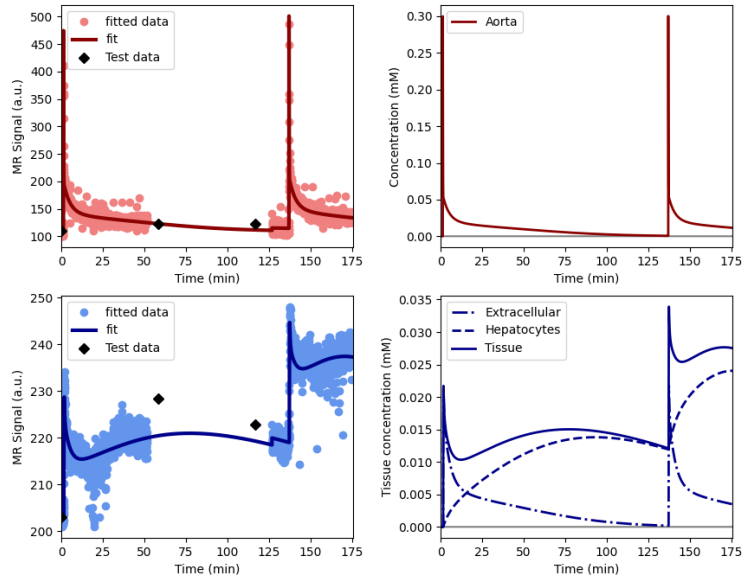


Figure 1.13: Signal-time curves for subject LDS-008 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	162.37	26.62	-83.61
AUC for Cl (0-inf)	mM*sec	434.22	148.42	-65.82
Biliary excretion rate	mL/min/100cm ³	2.57	0.4	-84.52
Biliary tissue excretion rate	mL/min/100cm ³	2.98	0.48	-83.98
Extracellular dispersion	%	47.35	59.27	25.16
Extracellular mean transit time	sec	18.81	32.12	70.74
Final biliary excretion rate	mL/min/100cm ³	1.96	1.17	-40.01
Final hepatocellular uptake rate	mL/min/100cm ³	24.48	2.93	-88.02
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	33.57	209.55	524.19
Hepatocellular tissue uptake rate	mL/min/100cm ³	234.37	12.63	-94.61
Hepatocellular uptake rate	mL/min/100cm ³	32.03	2.09	-93.47
Initial biliary excretion rate	mL/min/100cm ³	3.76	0.24	-93.62
Initial hepatocellular uptake rate	mL/min/100cm ³	39.58	1.25	-96.83
Liver T1-MOLLI at 45min	sec	0.46	0.62	33.65
Liver T1-MOLLI at baseline	sec	0.74	0.71	-5.07
Liver T1-MOLLI at scan 2	sec	0.57	0.66	14.25
Liver blood clearance	L/min	0.33	0.02	-94.41
Liver extracellular volume fraction	mL/100cm ³	13.67	16.57	21.26
RE for R1l at 20min	%	65.15	7.66	-88.24
RE for Sl at 20min	%	54.36	4.54	-91.65

Table 1.16: Values for liver of subject LDS-008

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	28.29	41.15	45.48
AUC for Cb (0-inf)	mM*sec	39.76	79.9	100.97
Body extraction fraction	%	4.76	2.62	-44.98
Cardiac output	L/min	10.74	9.5	-11.52
Heart-lung dispersion	%	42.41	43.94	3.63
Heart-lung mean transit time	sec	16.26	14.68	-9.76
Organs blood mean transit time	sec	22.62	26.04	15.11
Organs extraction fraction	%	15.52	9.01	-41.93
Organs extravascular mean transit time	min	4.63	8.88	91.6
RE for R1b at 20min	%	18.35	25.19	37.31
RE for Sb at 20min	%	12.39	21.0	69.58

Table 1.17: Values for aorta of subject LDS-008

1.4.7. Subject LDS-009

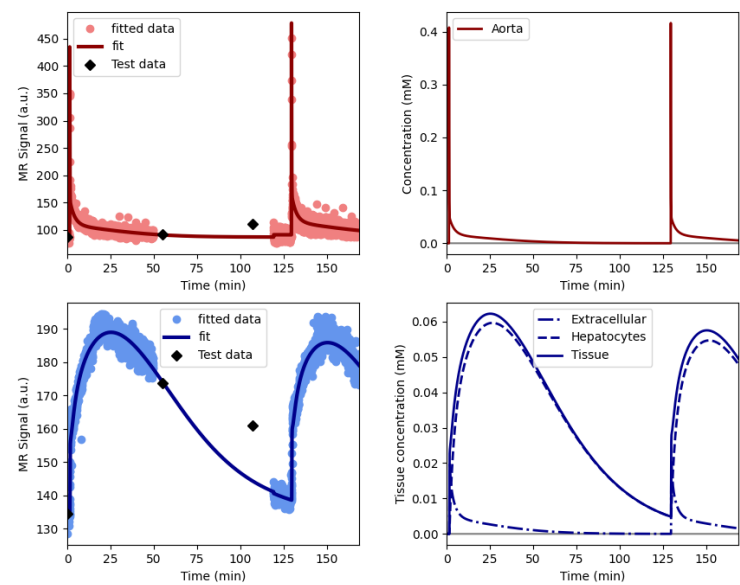


Figure 1.14: Signal-time curves for subject LDS-009 at the control visit.

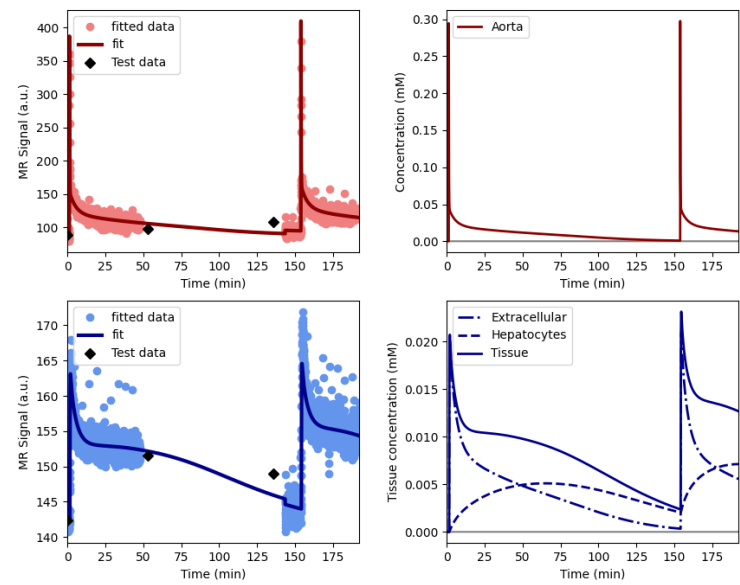


Figure 1.15: Signal-time curves for subject LDS-009 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	108.62	24.35	-77.58
AUC for Cl (0-inf)	mM*sec	287.46	79.4	-72.38
Biliary excretion rate	mL/min/100cm3	2.95	1.67	-43.44
Biliary tissue excretion rate	mL/min/100cm3	3.5	2.15	-38.52
Extracellular dispersion	%	72.72	69.86	-3.93
Extracellular mean transit time	sec	36.25	58.18	60.5
Final biliary excretion rate	mL/min/100cm3	3.15	2.18	-30.84
Final hepatocellular uptake rate	mL/min/100cm3	20.68	1.5	-92.75
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	28.56	46.46	62.66
Hepatocellular tissue uptake rate	mL/min/100cm3	137.29	5.13	-96.26
Hepatocellular uptake rate	mL/min/100cm3	21.81	1.16	-94.68
Initial biliary excretion rate	mL/min/100cm3	2.76	1.35	-51.23
Initial hepatocellular uptake rate	mL/min/100cm3	22.94	0.82	-96.42
Liver T1-MOLLI at 45min	sec	0.62	0.82	31.46
Liver T1-MOLLI at baseline	sec	0.85	0.88	4.05
Liver T1-MOLLI at scan 2	sec	0.73	0.83	14.19
Liver blood clearance	L/min	0.26	0.01	-94.61
Liver extracellular volume fraction	mL/100cm3	15.88	22.62	42.38
RE for R1l at 20min	%	51.21	9.04	-82.34
RE for Sl at 20min	%	40.87	5.56	-86.39

Table 1.18: Values for liver of subject LDS-009

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	29.52	42.86	45.19
AUC for Cb (0-inf)	mM*sec	41.79	95.13	127.65
Body extraction fraction	%	5.7	2.62	-54.06
Cardiac output	L/min	11.39	10.38	-8.83
Heart-lung dispersion	%	51.72	55.63	7.57
Heart-lung mean transit time	sec	9.42	14.8	57.1
Organs blood mean transit time	sec	35.44	45.45	28.25
Organs extraction fraction	%	13.83	10.21	-26.13
Organs extravascular mean transit time	min	6.65	8.03	20.9
RE for R1b at 20min	%	17.91	31.62	76.54
RE for Sb at 20min	%	3.78	22.02	483.11

Table 1.19: Values for aorta of subject LDS-009

1.4.8. Subject LDS-010

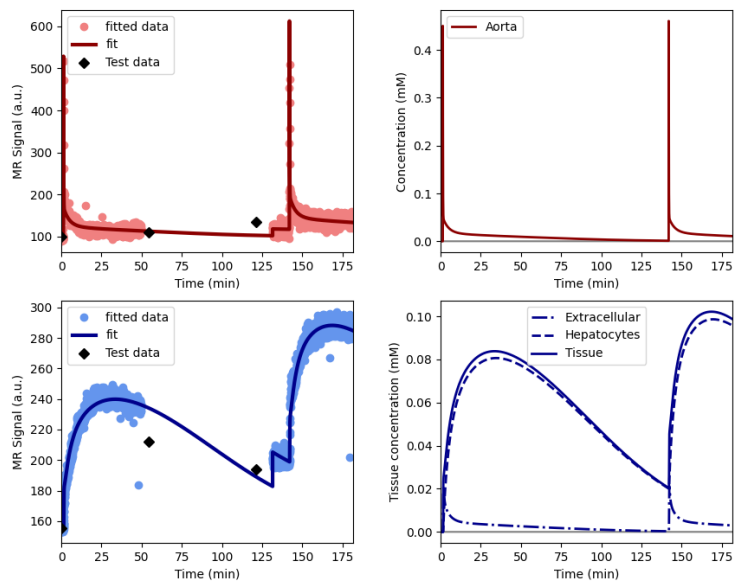


Figure 1.16: Signal-time curves for subject LDS-010 at the control visit.

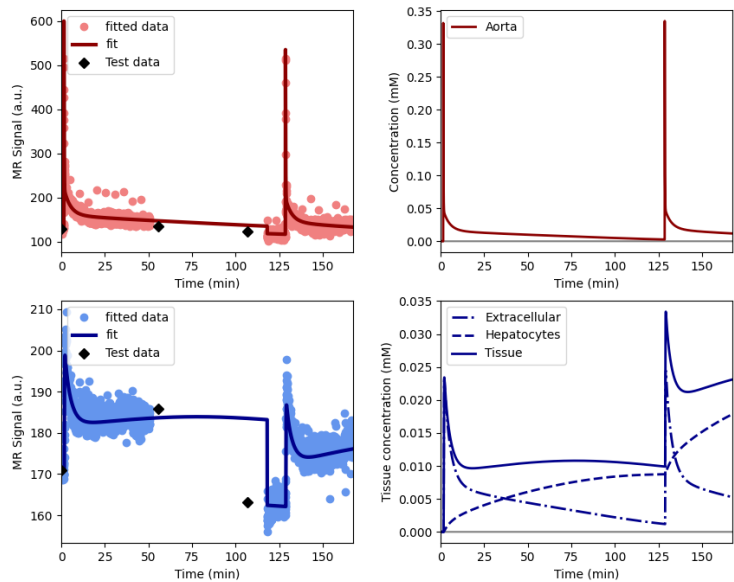


Figure 1.17: Signal-time curves for subject LDS-010 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	151.8	24.05	-84.16
AUC for Cl (0-inf)	mM*sec	562.83	114.55	-79.65
Biliary excretion rate	mL/min/100cm ³	3.25	0.47	-85.68
Biliary tissue excretion rate	mL/min/100cm ³	3.84	0.62	-83.97
Extracellular dispersion	%	74.61	73.61	-1.33
Extracellular mean transit time	sec	39.06	55.14	41.16
Final biliary excretion rate	mL/min/100cm ³	3.25	0.29	-91.21
Final hepatocellular uptake rate	mL/min/100cm ³	30.09	1.68	-94.41
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	26.05	162.54	523.91
Hepatocellular tissue uptake rate	mL/min/100cm ³	185.6	5.47	-97.05
Hepatocellular uptake rate	mL/min/100cm ³	28.26	1.32	-95.31
Initial biliary excretion rate	mL/min/100cm ³	3.26	1.27	-61.05
Initial hepatocellular uptake rate	mL/min/100cm ³	26.43	0.97	-96.34
Liver T1-MOLLI at 45min	sec	0.56	0.75	34.2
Liver T1-MOLLI at baseline	sec	0.81	0.83	2.99
Liver T1-MOLLI at scan 2	sec	0.72	0.79	9.82
Liver blood clearance	L/min	0.3	0.01	-95.17
Liver extracellular volume fraction	mL/100cm ³	15.23	24.24	59.18
RE for R1l at 20min	%	63.37	7.86	-87.6
RE for Sl at 20min	%	51.68	5.85	-88.68

Table 1.20: Values for liver of subject LDS-010

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	37.21	36.32	-2.4
AUC for Cb (0-inf)	mM*sec	78.64	85.48	8.71
Body extraction fraction	%	3.46	2.91	-16.06
Cardiac output	L/min	7.12	7.41	4.07
Heart-lung dispersion	%	58.77	53.09	-9.66
Heart-lung mean transit time	sec	9.73	14.78	51.87
Organs blood mean transit time	sec	46.75	43.36	-7.26
Organs extraction fraction	%	14.24	14.72	3.39
Organs extravascular mean transit time	min	8.96	9.22	2.89
RE for R1b at 20min	%	21.07	22.66	7.51
RE for Sb at 20min	%	10.06	24.15	140.13

Table 1.21: Values for aorta of subject LDS-010

2

One-scan results

2.1. Data summary

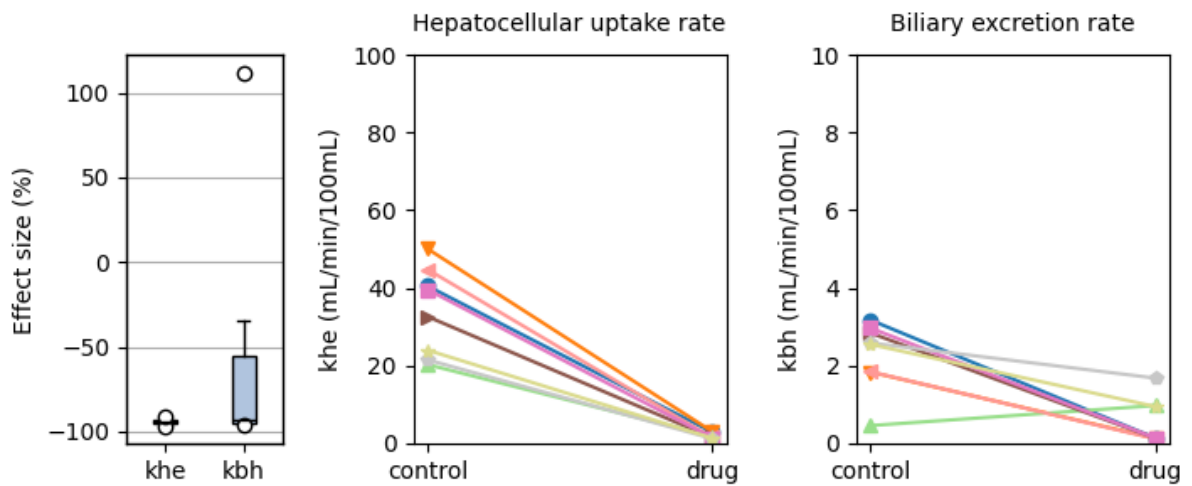


Figure 2.1: Effect size (%) on hepatocellular uptake (k_{he} , left) and biliary excretion (k_{bh} , right) of gadoxetate. The boxplot shows median, interquartile range and 95 percent range. The line plots show individual values for hepatocellular uptake (k_{he} , middle) and biliary excretion (k_{bh} , right) of gadoxetate of the control (left of plot) and treatment (right of plot). Grey lines are healthy controls with rifampicin injection.

	parameter	count	mean	std	min	25%	50%	75%	max
	khe effect size (%)	8.0	-94.2	1.8	-96.6	-95.5	-94.1	-93.5	-90.9
	khe control (mL/min/100cm3)	8.0	34.18	11.3	20.3	23.39	36.12	41.59	50.09
	khe drug (mL/min/100cm3)	8.0	1.9	0.72	1.27	1.49	1.54	2.12	3.12
	kbh effect size (%)	8.0	-57.3	71.8	-95.6	-95.2	-93.2	-55.8	111.9
	kbh control (mL/min/100cm3)	8.0	2.28	0.88	0.46	1.84	2.57	2.87	3.17
	kbh drug (mL/min/100cm3)	8.0	0.53	0.6	0.12	0.14	0.14	0.96	1.68

Table 2.1: Effect size and absolute values of hepatocellular uptake (k_{he}) and biliary excretion (k_{bh}) of gadoxetate

2.2. Liver biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for CI (0-35min)	4e-05	620.98	1594.2
AUC for CI (0-inf)	0.00064	59.19	112.63
Biliary excretion rate	0.00391	13.73	67.42
Biliary tissue excretion rate	0.00517	11.0	61.67
Extracellular dispersion	0.01065	6.22	5.19
Extracellular mean transit time	0.75483	0.35	1.24
Hematocrit			
Hepatocellular mean transit time	0.01471	4.83	0.04
Hepatocellular tissue uptake rate	0.00146	30.38	95.89
Hepatocellular uptake rate	7e-05	382.28	1501.73
Liver T1-MOLLI at 45min	0.0	6244.03	0.0
Liver T1-MOLLI at baseline	0.3834	0.48	0.73
Liver blood clearance	2e-05	883.28	6278.37
Liver extracellular volume fraction	0.03233	2.64	0.2
RE for R1l at 20min	8e-05	318.1	822.36
RE for Sl at 20min	8e-05	336.87	910.99

Table 2.2: Results of a pairwise comparison testing for differences in liver biomarkers between control and treatment. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for CI (0-35min)	mM*sec	148.0 (30.0)	23.9 (4.0)	-83.4 (1.8)
AUC for CI (0-inf)	mM*sec	589.0 (170.0)	134.0 (27.0)	-75.1 (6.0)
Biliary excretion rate	mL/min/100cm3	2.28 (0.61)	0.534 (0.41)	-57.3 (50.0)
Biliary tissue excretion rate	mL/min/100cm3	2.68 (0.7)	0.665 (0.51)	-52.6 (56.0)
Extracellular dispersion	%	78.3 (9.5)	67.8 (6.1)	-12.4 (6.5)
Extracellular mean transit time	sec	47.4 (11.0)	45.7 (8.8)	4.76 (30.0)
Hematocrit	%	45.0 (0.0)	45.0 (0.0)	0.0 (0.0)
Hepatocellular mean transit time	min	54.7 (40.0)	402.0 (190.0)	1090.0 (640.0)
Hepatocellular tissue uptake rate	mL/min/100cm3	276.0 (100.0)	10.1 (3.1)	-96.0 (1.0)
Hepatocellular uptake rate	mL/min/100cm3	34.2 (7.8)	1.9 (0.5)	-94.2 (1.3)
Liver T1-MOLLI at 45min	sec	0.537 (0.036)	0.727 (0.041)	35.7 (5.9)
Liver T1-MOLLI at baseline	sec	0.795 (0.037)	0.805 (0.041)	1.27 (2.7)
Liver blood clearance	L/min	0.304 (0.058)	0.0176 (0.0037)	-93.8 (1.6)
Liver extracellular volume fraction	mL/100cm3	14.4 (5.0)	19.6 (3.0)	63.5 (55.0)
RE for R1l at 20min	%	63.6 (14.0)	8.82 (1.5)	-85.6 (1.9)
RE for Sl at 20min	%	52.9 (12.0)	7.45 (1.6)	-85.3 (3.2)

Table 2.3: Mean values along with their 95 percent confidence intervals for all liver biomarkers of the control and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

2.3. Systemic biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for Cb (0-35min)	0.00893	7.14	0.31
AUC for Cb (0-inf)	0.11098	1.06	0.24
Body extraction fraction	0.12832	0.96	5.49
Cardiac output	0.28611	0.56	0.57
Heart-lung dispersion	0.80805	0.34	1.27
Heart-lung mean transit time	0.24649	0.62	0.38
Organs blood mean transit time	0.81701	0.34	1.19
Organs extraction fraction	0.03284	2.6	4.09
Organs extravascular mean transit time	0.96181	0.34	1.02
RE for R1b at 20min	0.00804	7.75	0.2
RE for Sb at 20min	0.25609	0.6	0.23

Table 2.4: Results of a pairwise comparison testing for differences in systemic biomarkers between control and treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	27.0 (6.7)	34.3 (8.6)	28.7 (15.0)
AUC for Cb (0-inf)	mM*sec	48.9 (14.0)	73.8 (27.0)	64.1 (55.0)
Body extraction fraction	%	6.55 (2.9)	3.58 (0.96)	20.1 (130.0)
Cardiac output	L/min	6.4 (1.7)	6.99 (0.88)	16.3 (17.0)
Heart-lung dispersion	%	46.8 (6.3)	45.4 (8.6)	0.468 (25.0)
Heart-lung mean transit time	sec	14.1 (2.6)	15.9 (2.2)	19.9 (25.0)
Organs blood mean transit time	sec	33.4 (5.4)	32.2 (11.0)	-2.86 (29.0)
Organs extraction fraction	%	21.0 (5.4)	16.3 (2.7)	-18.1 (13.0)
Organs extravascular mean transit time	min	7.82 (1.9)	7.77 (2.8)	-1.96 (26.0)
RE for R1b at 20min	%	15.2 (3.8)	21.6 (5.8)	46.6 (29.0)
RE for Sb at 20min	%	14.2 (5.2)	21.3 (6.7)	208.0 (330.0)

Table 2.5: Mean values along with their 95 percent confidence intervals for all systemic biomarkers at the control and and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

2.4. Case notes
2.4.1. Subject LDS-002

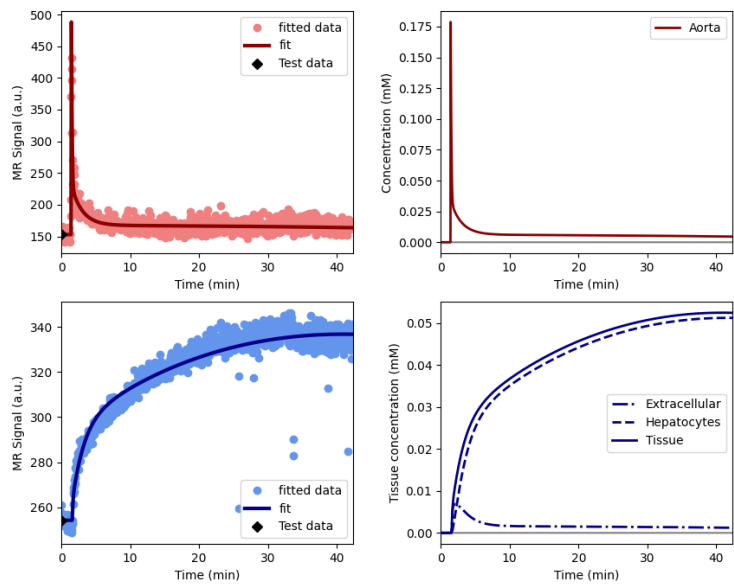


Figure 2.2: Signal-time curves for subject LDS-002 at the control visit.

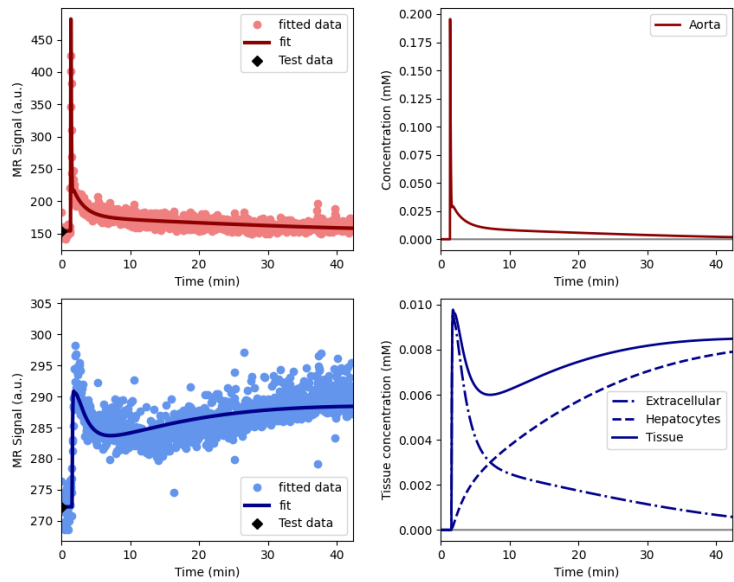


Figure 2.3: Signal-time curves for subject LDS-002 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for CI (0-35min)	mM*sec	86.94	15.27	-82.44
AUC for CI (0-inf)	mM*sec	556.81	91.28	-83.61
Biliary excretion rate	mL/min/100cm3	3.17	0.14	-95.6
Biliary tissue excretion rate	mL/min/100cm3	3.71	0.17	-95.51
Extracellular dispersion	%	83.64	70.3	-15.95
Extracellular mean transit time	sec	55.79	40.23	-27.89
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	26.97	600.0	2124.95
Hepatocellular tissue uptake rate	mL/min/100cm3	280.61	18.06	-93.56
Hepatocellular uptake rate	mL/min/100cm3	40.52	2.95	-92.73
Liver T1-MOLLI at 45min	sec	0.58	0.72	23.26
Liver T1-MOLLI at baseline	sec	0.76	0.81	7.72
Liver blood clearance	L/min	0.28	0.02	-91.46
Liver extracellular volume fraction	mL/100cm3	14.44	16.32	13.0
RE for R1l at 20min	%	34.57	6.08	-82.41
RE for Sl at 20min	%	28.34	6.65	-76.52

Table 2.6: Values for liver of subject LDS-002

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	15.3	15.89	3.83
AUC for Cb (0-inf)	mM*sec	56.18	20.68	-63.18
Body extraction fraction	%	1.02	6.08	494.28
Cardiac output	L/min	4.49	5.38	19.77
Heart-lung dispersion	%	47.75	38.38	-19.61
Heart-lung mean transit time	sec	17.72	15.92	-10.19
Organs blood mean transit time	sec	27.11	21.3	-21.44
Organs extraction fraction	%	32.8	18.92	-42.31
Organs extravascular mean transit time	min	7.11	4.4	-38.15
RE for R1b at 20min	%	9.66	8.55	-11.41
RE for Sb at 20min	%	9.91	12.87	29.85

Table 2.7: Values for aorta of subject LDS-002

2.4.2. Subject LDS-003

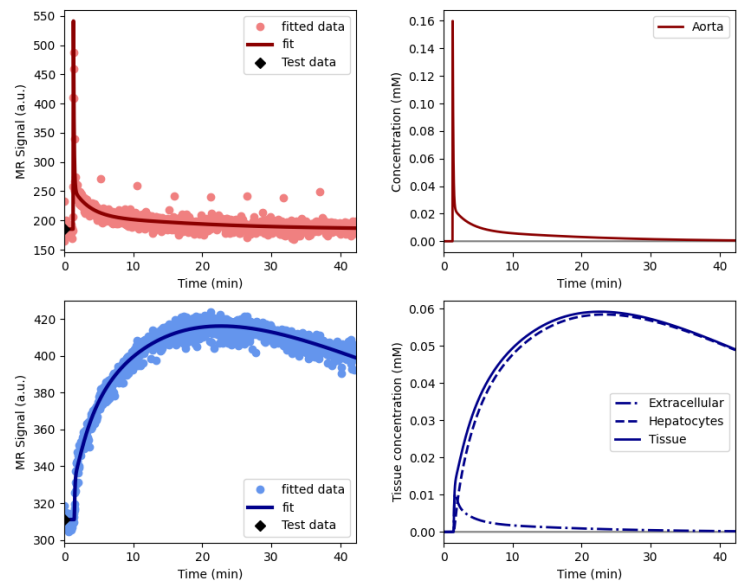


Figure 2.4: Signal-time curves for subject LDS-003 at the control visit.

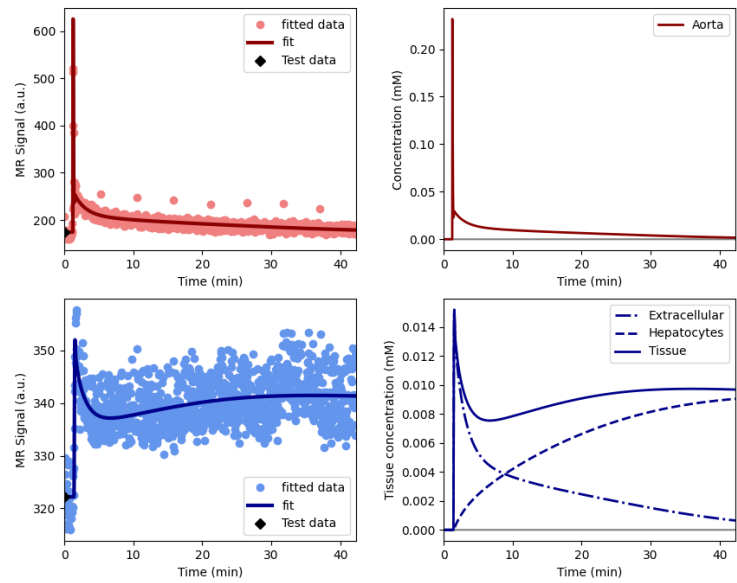


Figure 2.5: Signal-time curves for subject LDS-003 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	106.17	18.51	-82.57
AUC for Cl (0-inf)	mM*sec	269.18	100.99	-62.48
Biliary excretion rate	mL/min/100cm3	1.84	0.13	-92.79
Biliary tissue excretion rate	mL/min/100cm3	2.18	0.17	-92.37
Extracellular dispersion	%	69.34	61.76	-10.94
Extracellular mean transit time	sec	30.84	26.71	-13.41
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	45.8	600.0	1210.11
Hepatocellular tissue uptake rate	mL/min/100cm3	314.9	15.21	-95.17
Hepatocellular uptake rate	mL/min/100cm3	50.09	3.12	-93.77
Liver T1-MOLLI at 45min	sec	0.53	0.69	30.25
Liver T1-MOLLI at baseline	sec	0.71	0.73	2.64
Liver blood clearance	L/min	0.44	0.03	-93.85
Liver extracellular volume fraction	mL/100cm3	15.91	20.53	29.06
RE for R1l at 20min	%	41.11	6.54	-84.1
RE for Sl at 20min	%	36.02	4.72	-86.91

Table 2.8: Values for liver of subject LDS-003

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	10.72	17.15	59.94
AUC for Cb (0-inf)	mM*sec	11.9	21.04	76.73
Body extraction fraction	%	9.55	4.28	-55.17
Cardiac output	L/min	5.94	7.5	26.36
Heart-lung dispersion	%	55.66	30.93	-44.44
Heart-lung mean transit time	sec	12.51	10.65	-14.94
Organs blood mean transit time	sec	33.48	18.38	-45.11
Organs extraction fraction	%	13.11	13.13	0.09
Organs extravascular mean transit time	min	5.4	3.44	-36.34
RE for R1b at 20min	%	4.83	10.41	115.66
RE for Sb at 20min	%	28.87	4.52	-84.34

Table 2.9: Values for aorta of subject LDS-003

2.4.3. Subject LDS-004

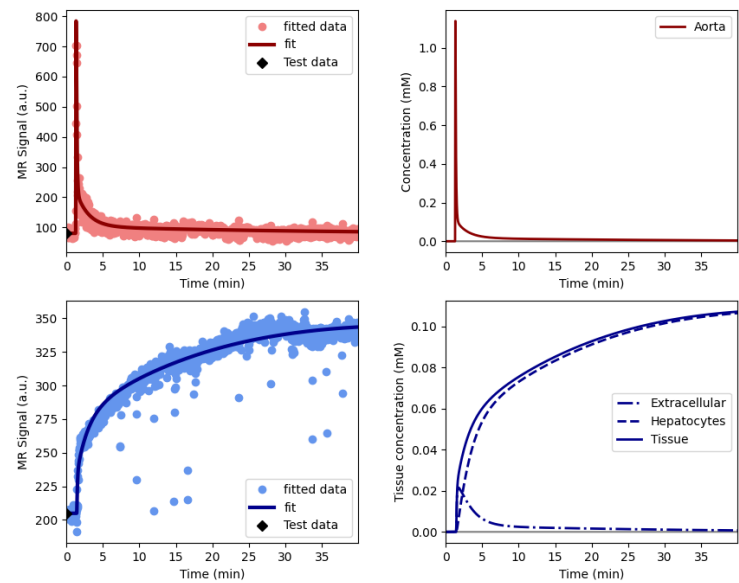


Figure 2.6: Signal-time curves for subject LDS-004 at the control visit.

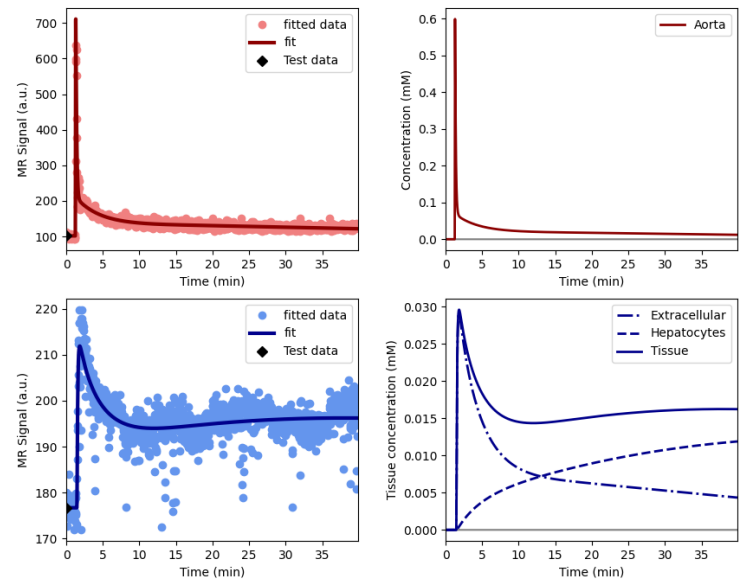


Figure 2.7: Signal-time curves for subject LDS-004 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	179.43	33.46	-81.35
AUC for Cl (0-inf)	mM*sec	1049.0	184.62	-82.4
Biliary excretion rate	mL/min/100cm ³	0.46	0.97	111.93
Biliary tissue excretion rate	mL/min/100cm ³	0.51	1.21	137.35
Extracellular dispersion	%	86.8	79.93	-7.91
Extracellular mean transit time	sec	60.0	60.0	0.0
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	196.41	82.75	-57.87
Hepatocellular tissue uptake rate	mL/min/100cm ³	209.03	9.52	-95.45
Hepatocellular uptake rate	mL/min/100cm ³	20.3	1.84	-90.92
Liver T1-MOLLI at 45min	sec	0.5	0.71	41.3
Liver T1-MOLLI at baseline	sec	0.8	0.8	-0.01
Liver blood clearance	L/min	0.18	0.02	-89.92
Liver extracellular volume fraction	mL/100cm ³	9.71	19.38	99.53
RE for R1l at 20min	%	75.89	12.14	-84.0
RE for Sl at 20min	%	63.38	11.68	-81.56

Table 2.10: Values for liver of subject LDS-004

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	35.72	48.68	36.28
AUC for Cb (0-inf)	mM*sec	47.24	128.49	172.03
Body extraction fraction	%	14.89	3.08	-79.29
Cardiac output	L/min	3.88	5.56	43.13
Heart-lung dispersion	%	64.14	51.83	-19.19
Heart-lung mean transit time	sec	8.27	14.54	75.82
Organs blood mean transit time	sec	39.85	52.71	32.28
Organs extraction fraction	%	30.2	21.29	-29.52
Organs extravascular mean transit time	min	7.98	9.42	18.17
RE for R1b at 20min	%	16.96	30.79	81.54
RE for Sb at 20min	%	14.55	30.96	112.8

Table 2.11: Values for aorta of subject LDS-004

2.4.4. Subject LDS-006

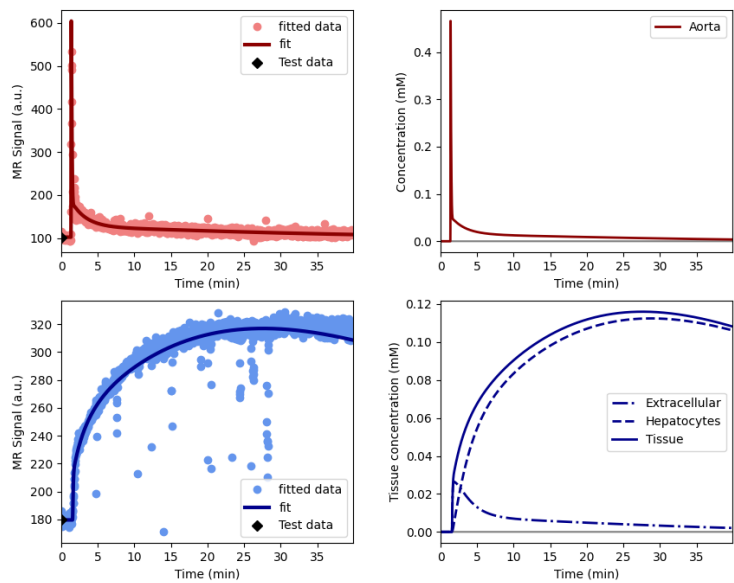


Figure 2.8: Signal-time curves for subject LDS-006 at the control visit.

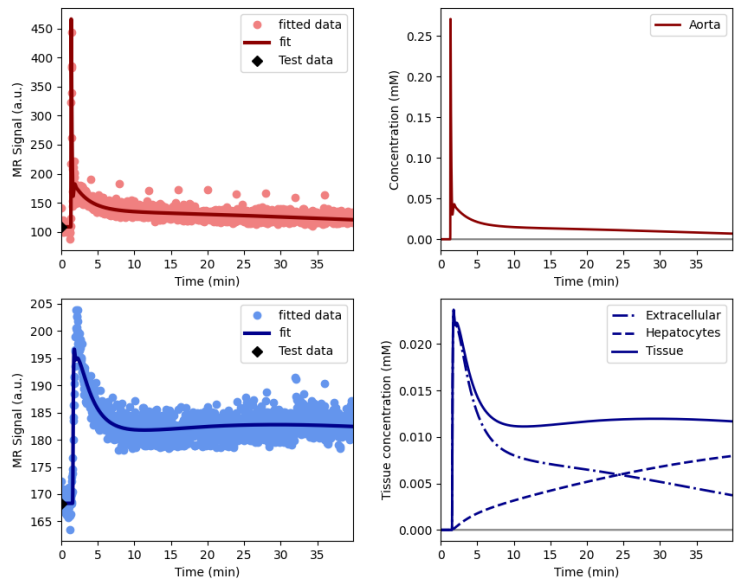


Figure 2.9: Signal-time curves for subject LDS-006 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	206.52	25.55	-87.63
AUC for Cl (0-inf)	mM*sec	630.61	144.19	-77.13
Biliary excretion rate	mL/min/100cm ³	1.84	0.12	-93.57
Biliary tissue excretion rate	mL/min/100cm ³	2.6	0.17	-93.59
Extracellular dispersion	%	79.06	67.86	-14.16
Extracellular mean transit time	sec	59.62	43.49	-27.05
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	38.48	600.0	1459.43
Hepatocellular tissue uptake rate	mL/min/100cm ³	154.18	5.33	-96.54
Hepatocellular uptake rate	mL/min/100cm ³	44.78	1.54	-96.56
Liver T1-MOLLI at 45min	sec	0.5	0.75	51.37
Liver T1-MOLLI at baseline	sec	0.84	0.84	-0.39
Liver blood clearance	L/min	0.31	0.01	-96.49
Liver extracellular volume fraction	mL/100cm ³	29.05	28.87	-0.61
RE for R1l at 20min	%	93.67	9.65	-89.7
RE for Sl at 20min	%	75.73	7.26	-90.42

Table 2.12: Values for liver of subject LDS-006

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	25.91	30.55	17.91
AUC for Cb (0-inf)	mM*sec	36.3	60.35	66.24
Body extraction fraction	%	7.72	2.99	-61.28
Cardiac output	L/min	4.83	7.41	53.42
Heart-lung dispersion	%	37.22	32.16	-13.6
Heart-lung mean transit time	sec	14.96	19.76	32.1
Organs blood mean transit time	sec	35.42	20.48	-42.2
Organs extraction fraction	%	22.38	16.62	-25.76
Organs extravascular mean transit time	min	5.47	5.35	-2.03
RE for R1b at 20min	%	15.37	21.02	36.8
RE for Sb at 20min	%	11.88	26.22	120.62

Table 2.13: Values for aorta of subject LDS-006

2.4.5. Subject LDS-007

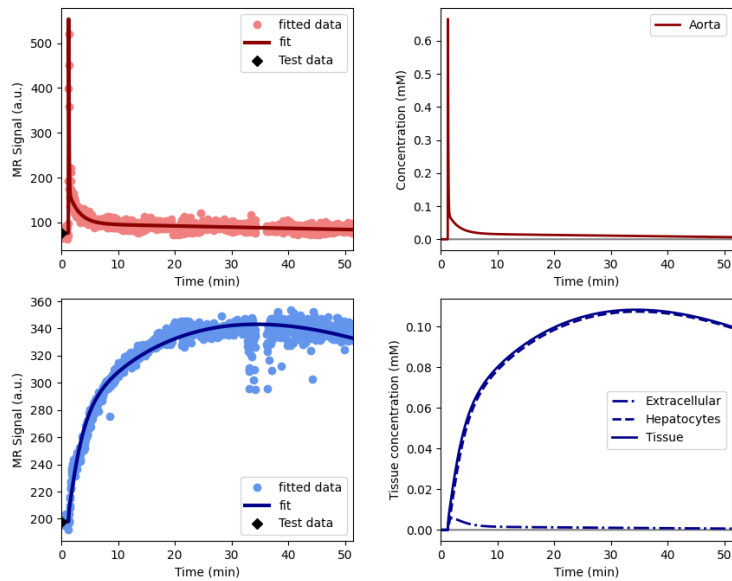


Figure 2.10: Signal-time curves for subject LDS-007 at the control visit.

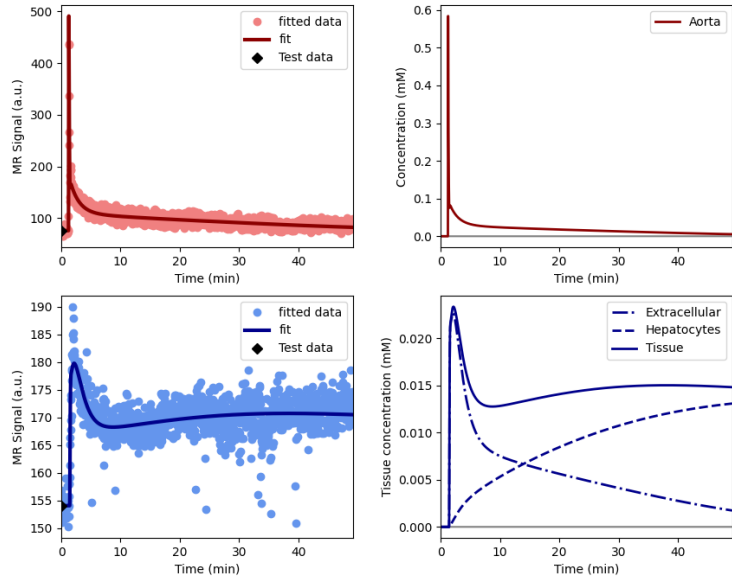


Figure 2.11: Signal-time curves for subject LDS-007 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	184.07	29.77	-83.83
AUC for Cl (0-inf)	mM*sec	744.41	160.34	-78.46
Biliary excretion rate	mL/min/100cm ³	2.84	0.14	-95.13
Biliary tissue excretion rate	mL/min/100cm ³	3.0	0.17	-94.44
Extracellular dispersion	%	100.0	77.21	-22.79
Extracellular mean transit time	sec	60.0	50.92	-15.12
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	33.37	600.0	1698.2
Hepatocellular tissue uptake rate	mL/min/100cm ³	622.09	9.11	-98.54
Hepatocellular uptake rate	mL/min/100cm ³	32.65	1.55	-95.26
Liver T1-MOLLI at 45min	sec	0.54	0.75	40.39
Liver T1-MOLLI at baseline	sec	0.86	0.84	-1.75
Liver blood clearance	L/min	0.31	0.02	-94.39
Liver extracellular volume fraction	mL/100cm ³	5.25	17.0	223.89
RE for R1l at 20min	%	84.86	11.7	-86.21
RE for Sl at 20min	%	72.82	9.46	-87.0

Table 2.14: Values for liver of subject LDS-007

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	36.07	46.28	28.3
AUC for Cb (0-inf)	mM*sec	70.85	66.41	-6.27
Body extraction fraction	%	4.92	4.98	1.26
Cardiac output	L/min	5.67	6.15	8.5
Heart-lung dispersion	%	45.72	35.34	-22.7
Heart-lung mean transit time	sec	9.91	14.13	42.59
Organs blood mean transit time	sec	31.97	20.75	-35.09
Organs extraction fraction	%	24.89	20.73	-16.71
Organs extravascular mean transit time	min	6.95	3.96	-42.98
RE for R1b at 20min	%	22.29	28.87	29.48
RE for Sb at 20min	%	2.31	34.27	1382.32

Table 2.15: Values for aorta of subject LDS-007

2.4.6. Subject LDS-008

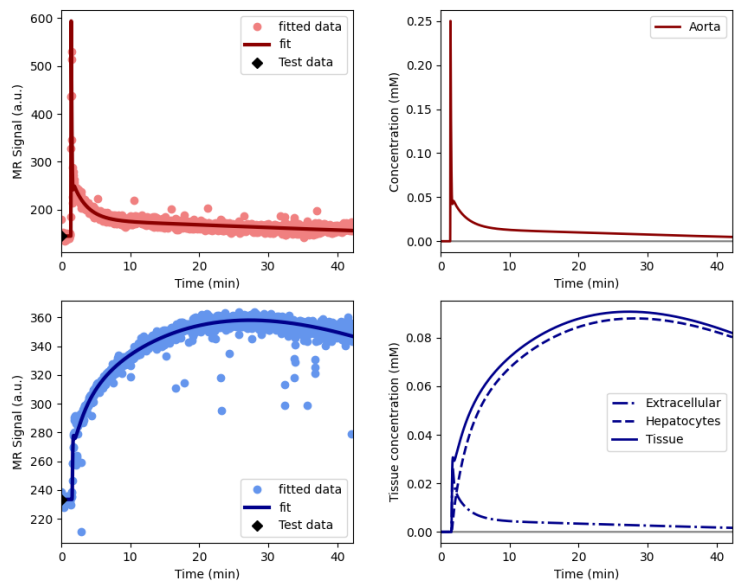


Figure 2.12: Signal-time curves for subject LDS-008 at the control visit.

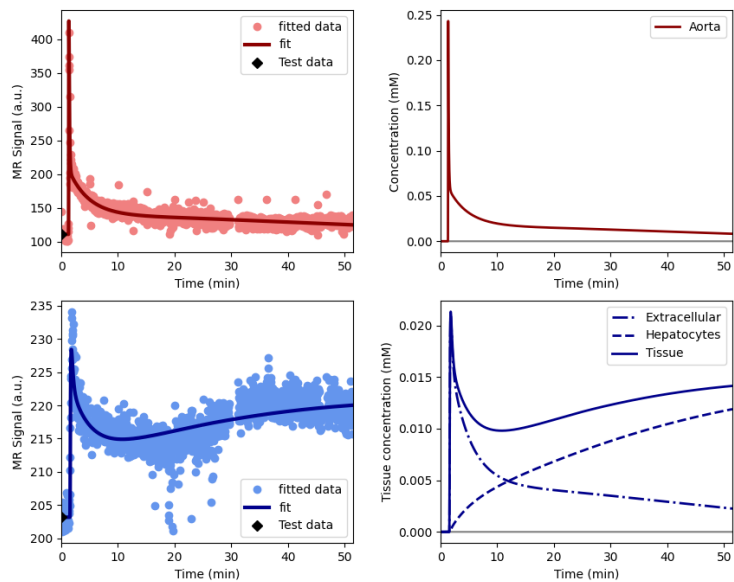


Figure 2.13: Signal-time curves for subject LDS-008 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	162.18	23.44	-85.55
AUC for Cl (0-inf)	mM*sec	490.56	181.57	-62.99
Biliary excretion rate	mL/min/100cm ³	2.97	0.14	-95.22
Biliary tissue excretion rate	mL/min/100cm ³	3.64	0.17	-95.42
Extracellular dispersion	%	55.53	52.27	-5.88
Extracellular mean transit time	sec	23.52	30.12	28.09
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	27.46	600.0	2085.21
Hepatocellular tissue uptake rate	mL/min/100cm ³	213.23	10.19	-95.22
Hepatocellular uptake rate	mL/min/100cm ³	39.59	1.51	-96.17
Liver T1-MOLLI at 45min	sec	0.46	0.62	33.65
Liver T1-MOLLI at baseline	sec	0.74	0.71	-5.07
Liver blood clearance	L/min	0.41	0.01	-96.73
Liver extracellular volume fraction	mL/100cm ³	18.57	14.87	-19.91
RE for R1l at 20min	%	64.79	7.65	-88.2
RE for Sl at 20min	%	52.32	5.61	-89.29

Table 2.16: Values for liver of subject LDS-008

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	26.77	39.64	48.12
AUC for Cb (0-inf)	mM*sec	44.3	91.71	107.03
Body extraction fraction	%	4.33	2.3	-46.95
Cardiac output	L/min	10.55	8.83	-16.28
Heart-lung dispersion	%	38.73	58.41	50.79
Heart-lung mean transit time	sec	18.39	15.41	-16.19
Organs blood mean transit time	sec	19.79	26.02	31.48
Organs extraction fraction	%	17.4	11.52	-33.8
Organs extravascular mean transit time	min	6.0	9.77	62.72
RE for R1b at 20min	%	17.24	24.06	39.59
RE for Sb at 20min	%	13.54	21.65	59.91

Table 2.17: Values for aorta of subject LDS-008

2.4.7. Subject LDS-009

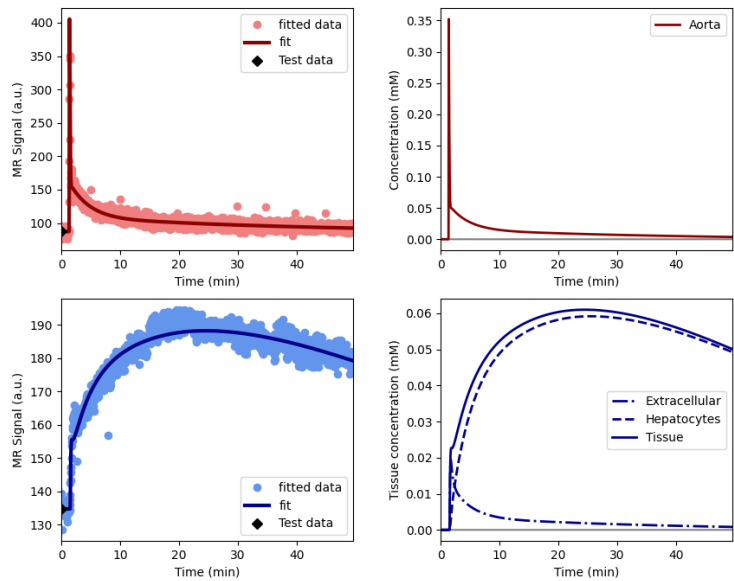


Figure 2.14: Signal-time curves for subject LDS-009 at the control visit.

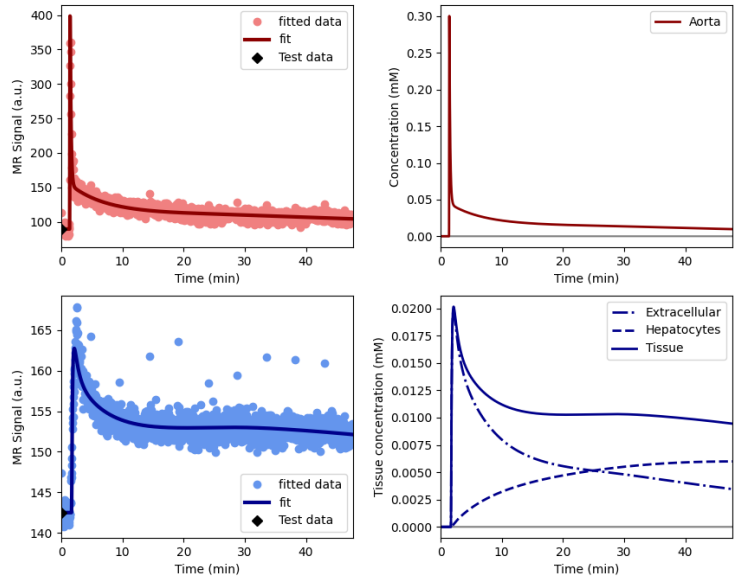


Figure 2.15: Signal-time curves for subject LDS-009 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for CI (0-35min)	mM*sec	111.34	22.83	-79.49
AUC for CI (0-inf)	mM*sec	334.27	96.52	-71.13
Biliary excretion rate	mL/min/100cm3	2.58	1.68	-34.99
Biliary tissue excretion rate	mL/min/100cm3	2.94	2.08	-29.26
Extracellular dispersion	%	67.51	69.92	3.57
Extracellular mean transit time	sec	29.47	60.0	103.62
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	33.98	48.04	41.37
Hepatocellular tissue uptake rate	mL/min/100cm3	177.1	6.58	-96.29
Hepatocellular uptake rate	mL/min/100cm3	21.53	1.27	-94.11
Liver T1-MOLLI at 45min	sec	0.62	0.82	31.46
Liver T1-MOLLI at baseline	sec	0.85	0.88	4.05
Liver blood clearance	L/min	0.26	0.02	-94.04
Liver extracellular volume fraction	mL/100cm3	12.15	19.26	58.5
RE for R1l at 20min	%	50.45	8.86	-82.43
RE for Sl at 20min	%	43.1	5.58	-87.05

Table 2.18: Values for liver of subject LDS-009

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	29.61	41.43	39.9
AUC for Cb (0-inf)	mM*sec	45.31	112.02	147.2
Body extraction fraction	%	6.2	2.22	-64.17
Cardiac output	L/min	9.6	8.37	-12.74
Heart-lung dispersion	%	40.85	60.71	48.59
Heart-lung mean transit time	sec	17.89	16.92	-5.43
Organs blood mean transit time	sec	34.37	57.58	67.53
Organs extraction fraction	%	13.17	11.94	-9.35
Organs extravascular mean transit time	min	10.35	13.3	28.59
RE for R1b at 20min	%	16.54	28.68	73.43
RE for Sb at 20min	%	16.15	21.8	34.98

Table 2.19: Values for aorta of subject LDS-009

2.4.8. Subject LDS-010

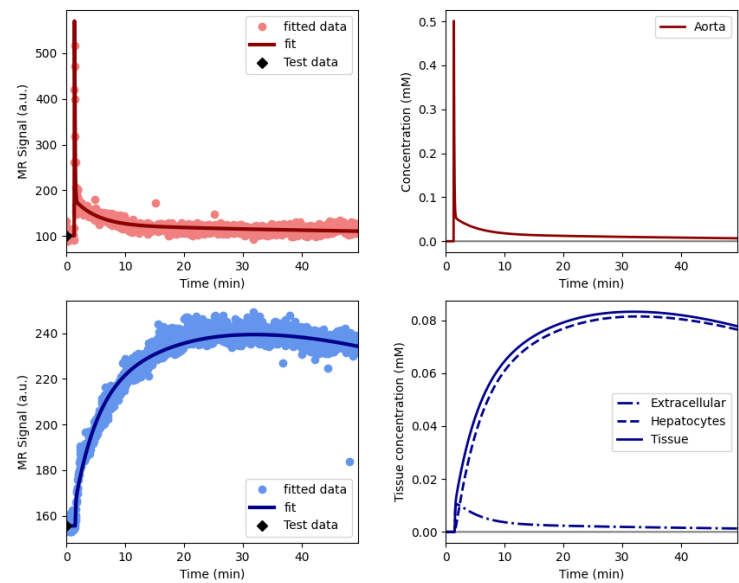


Figure 2.16: Signal-time curves for subject LDS-010 at the control visit.

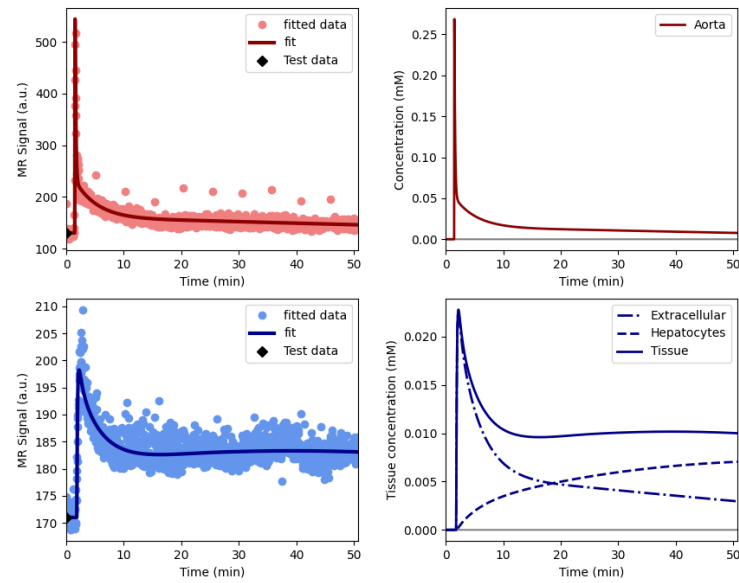


Figure 2.17: Signal-time curves for subject LDS-010 at the treatment visit.

Biomarker	Units	control	drug	change (%)
AUC for Cl (0-35min)	mM*sec	144.72	22.12	-84.72
AUC for Cl (0-inf)	mM*sec	638.81	109.25	-82.9
Biliary excretion rate	mL/min/100cm3	2.55	0.95	-62.72
Biliary tissue excretion rate	mL/min/100cm3	2.84	1.2	-57.68
Extracellular dispersion	%	84.16	62.87	-25.3
Extracellular mean transit time	sec	59.93	53.84	-10.17
Hematocrit	%	45.0	45.0	0.0
Hepatocellular mean transit time	min	35.26	83.32	136.32
Hepatocellular tissue uptake rate	mL/min/100cm3	235.27	6.8	-97.11
Hepatocellular uptake rate	mL/min/100cm3	24.01	1.42	-94.09
Liver T1-MOLLI at 45min	sec	0.56	0.75	34.2
Liver T1-MOLLI at baseline	sec	0.81	0.83	2.99
Liver blood clearance	L/min	0.26	0.02	-93.9
Liver extracellular volume fraction	mL/100cm3	10.2	20.88	104.64
RE for R1l at 20min	%	63.27	7.94	-87.45
RE for Sl at 20min	%	51.77	8.63	-83.33

Table 2.20: Values for liver of subject LDS-010

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	36.26	34.49	-4.88
AUC for Cb (0-inf)	mM*sec	79.49	89.72	12.87
Body extraction fraction	%	3.74	2.71	-27.61
Cardiac output	L/min	6.2	6.7	8.04
Heart-lung dispersion	%	44.69	55.38	23.91
Heart-lung mean transit time	sec	13.02	20.22	55.23
Organs blood mean transit time	sec	45.48	40.77	-10.37
Organs extraction fraction	%	14.23	15.97	12.2
Organs extravascular mean transit time	min	13.29	12.53	-5.7
RE for R1b at 20min	%	18.78	20.29	8.05
RE for Sb at 20min	%	16.7	17.76	6.33

Table 2.21: Values for aorta of subject LDS-010

3

Secondary results

3.1. Diurnal variation

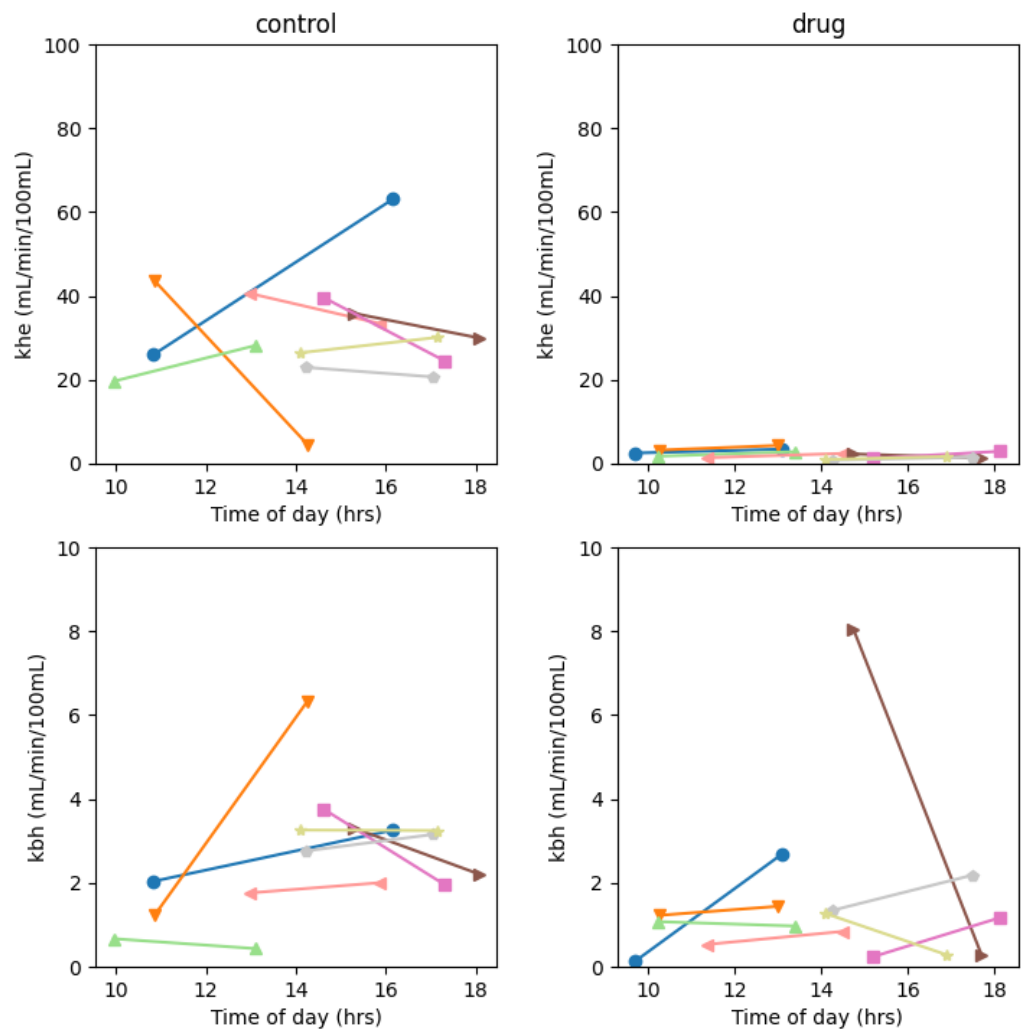


Figure 3.1: Intra-day changes in hepatocellular uptake (k_{he} , top row) and biliary excretion (k_{bh} , bottom row) of gadoxetate at for the control (left column) and treatment (right column). Full lines connect values taken in the same subject at the same day.