

SUPPLEMENTARY MATERIAL

Lys-urea-Aad, Lys-urea-Cmc and Lys-urea-Cms as potential pharmacophores for the design of PSMA-targeted radioligands to reduce off-target uptake in kidneys and salivary glands

Hsiou-Ting Kuo¹, Zhengxing Zhang¹, Chengcheng Zhang¹, Helen Merkens¹, Ruiyan Tan¹, Antonio A. W. L. Wong¹, Carlos F. Uribe^{2,3}, François Bénard^{1,2,3,*}, Kuo-Shyan Lin^{1,2,3,*}

¹Department of Molecular Oncology, BC Cancer, Vancouver, BC V5Z1L3, Canada

²Department of Functional Imaging, BC Cancer, Vancouver, BC V5Z4E6, Canada

³Department of Radiology, University of British Columbia, Vancouver, BC V5Z1M9, Canada

Corresponding Authors:

***François Bénard, MD**

Address: 675 West 10th Avenue, Rm 14-111, Vancouver, BC V5Z1L3, Canada

Phone: 604-675-8206

Fax: 604-675-8218

E-mail: fbenard@bccrc.ca

***Kuo-Shyan Lin, PhD**

Address: 675 West 10th Avenue, Rm 4-123, Vancouver, BC V5Z1L3, Canada

Phone: 604-675-8208

Fax: 604-675-8218

E-mail: klin@bccrc.ca

Table S1: HPLC purification conditions and MS characterizations of DOTA-conjugated PSMA-targeted ligands.

Compound name	HPLC conditions	Retention time (min)	Yield (%)	Calculated mass (m/z)	Found (m/z)
HTK03177	System A/Column A: 24% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 30 mL/min	8.2	34	[M+H] ⁺ 1124.5	[M+H] ⁺ 1124.5
HTK03187	System B/Column B: 28% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	10.4	30	[M+H] ⁺ 1108.5	[M+H] ⁺ 1108.5
HTK03170	System B/Column B: 34% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	13.1	4	[M+2H] ²⁺ 734.4	[M+2H] ²⁺ 734.6
HTK04048	System B/Column B: 35% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	11.7	53	[M+H] ⁺ 1485.7	[M+H] ⁺ 1486.0
HTK04028	System A/Column A: 28% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 30 mL/min	14.8	21	[M+H] ⁺ 1469.7	[M+H] ⁺ 1469.7

Table S2: HPLC purification conditions and MS characterizations of nonradioactive Ga- and Lu-complexed PSMA-targeted ligands.

Compound name	HPLC conditions	Retention time (min)	Yield (%)	Calculated mass (m/z)	Found (m/z)
Ga-HTK03177	System B/Column B: 32% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	7.8	56	[M+H] ⁺ 1190.4	[M+H] ⁺ 1190.3
Ga-HTK03187	System B/Column B: 29% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	13.3	53	[M+H] ⁺ 1174.4	[M+H] ⁺ 1174.3
Lu-HTK03170	System B/Column B: 34% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	15.4	95	[M+H] ⁺ 1639.7	[M+H] ⁺ 1639.7
Lu-HTK04048	System B/Column B: 35% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	13.9	70	[M+H] ⁺ 1657.6	[M+H] ⁺ 1657.9
Lu-HTK04028	System B/Column B: 35% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	11.5	29	[M+H] ⁺ 1641.6	[M+H] ⁺ 1641.8

Table S3: HPLC conditions for the purification and quality control of ⁶⁸Ga- and ¹⁷⁷Lu-labeled PSMA-targeted ligands.

Compound name	HPLC conditions		Retention time (min)
⁶⁸ Ga]Ga-HTK03177	Semi-prep	System C/Column B: 31% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	12.5
	QC	System C/Column C: 32% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 2.0 mL/min	6.0
⁶⁸ Ga]Ga-HTK03187	Semi-prep	System C/Column B: 29% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	15.5
	QC	System C/Column C: 31% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 2.0 mL/min	6.1
¹⁷⁷ Lu]Lu-HTK03170	Semi-prep	System C/Column B: 33% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	23.9
	QC	System C/Column C: 34% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 2 mL/min	8.1
¹⁷⁷ Lu]Lu-HTK04048	Semi-prep	System C/Column B: 35% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	18.4
	QC	System C/Column C: 37% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 2.0 mL/min	5.7
¹⁷⁷ Lu]Lu-HTK04028	Semi-prep	System C/Column B: 34% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 4.5 mL/min	18.7
	QC	System C/Column C: 35% CH ₃ CN and 0.1% TFA in H ₂ O; flow rate 2.0 mL/min	7.0

Table S4: Biodistribution (mean \pm SD) and uptake ratios of ^{68}Ga -labeled PSMA-targeted tracers in LNCaP tumor-bearing mice. The mice in the blocked group were co-injected with DCFPyL (0.5 mg). Statistical analyses were conducted for the data of [^{68}Ga]Ga-HTK03177 and [^{68}Ga]Ga-HTK03187 with/without co-injection of DCFPyL(0.5 mg). *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Tissue (%ID/g)	[^{68}Ga]Ga- HTK03177		[^{68}Ga]Ga- HTK03187	
	1 h (n = 5)	1 h blocked (n = 4)	1 h (n = 5)	1 h blocked (n = 4)
Blood	0.70 \pm 0.06	0.85 \pm 0.15*	0.67 \pm 0.10	0.33 \pm 0.16**
Fat	0.09 \pm 0.04	0.20 \pm 0.16	0.07 \pm 0.02	0.06 \pm 0.04
Testes	0.25 \pm 0.07	0.36 \pm 0.14	0.15 \pm 0.03	0.15 \pm 0.01
Intestines	0.21 \pm 0.02	0.69 \pm 0.76	0.23 \pm 0.05	0.13 \pm 0.03**
Stomach	0.15 \pm 0.09	0.12 \pm 0.05	0.08 \pm 0.05	0.03 \pm 0.01*
Spleen	0.42 \pm 0.15	0.25 \pm 0.18	0.17 \pm 0.02	0.12 \pm 0.03*
Liver	0.33 \pm 0.20	0.37 \pm 0.22	0.21 \pm 0.05	0.16 \pm 0.05
Pancreas	0.14 \pm 0.01	0.54 \pm 0.54	0.12 \pm 0.02	0.07 \pm 0.02**
Adrenal glands	0.46 \pm 0.17	0.61 \pm 0.38	0.26 \pm 0.06	0.13 \pm 0.06**
Kidneys	7.76 \pm 1.00	1.73 \pm 0.36***	2.83 \pm 0.45	1.15 \pm 0.37***
Lungs	0.61 \pm 0.08	0.54 \pm 0.06	0.52 \pm 0.09	0.31 \pm 0.10**
Heart	0.21 \pm 0.01	0.23 \pm 0.04	0.19 \pm 0.04	0.10 \pm 0.05*
Tumor	24.7 \pm 6.85	0.74 \pm 0.12***	21.1 \pm 3.62	0.35 \pm 0.09***
Muscle	0.10 \pm 0.01	0.13 \pm 0.05	0.09 \pm 0.01	0.08 \pm 0.06
Bone	0.10 \pm 0.03	0.24 \pm 0.17	0.13 \pm 0.03	0.06 \pm 0.02**
Brain	0.02 \pm 0.00	0.02 \pm 0.00	0.02 \pm 0.00	0.01 \pm 0.00*
Thyroid	0.23 \pm 0.01	0.21 \pm 0.06	0.18 \pm 0.02	0.12 \pm 0.05*
Salivary glands	0.22 \pm 0.02	0.15 \pm 0.04**	0.16 \pm 0.02	0.09 \pm 0.04**
Lacrimal glands	0.12 \pm 0.06	0.15 \pm 0.10	0.09 \pm 0.03	0.06 \pm 0.03
Tumor:Blood	36.1 \pm 12.5	0.89 \pm 0.19***	32.2 \pm 8.53	1.14 \pm 0.25***
Tumor:Muscle	265 \pm 103	5.50 \pm 2.68*	249 \pm 61.2	5.34 \pm 2.25***
Tumor:Kidney	3.25 \pm 1.16	0.43 \pm 0.05**	7.67 \pm 2.10	0.31 \pm 0.08***
Tumor:Salivary gland	112 \pm 33.1	5.05 \pm 0.77***	133 \pm 14.0	4.13 \pm 0.92***
Blood:Salivary gland	3.14 \pm 0.19	6.07 \pm 2.53*	4.27 \pm 0.74	3.64 \pm 0.44

Table S5: Biodistribution (mean \pm SD) and uptake ratios of [^{177}Lu]Lu-HTK03170 in LNCaP tumor-bearing mice.

Tissue (%ID/g)	1 h (n = 6)	4 h (n = 6)	24 h (n = 6)	72 h (n = 6)	120 h (n = 6)
Blood	16.9 \pm 1.97	8.34 \pm 1.67	0.59 \pm 0.13	0.06 \pm 0.02	0.02 \pm 0.01
Fat	1.38 \pm 0.45	0.60 \pm 0.13	0.12 \pm 0.04	0.04 \pm 0.02	0.04 \pm 0.03
Testes	2.17 \pm 0.32	1.83 \pm 0.58	0.64 \pm 0.53	0.24 \pm 0.04	0.16 \pm 0.04
Intestines	1.19 \pm 0.25	0.61 \pm 0.17	0.18 \pm 0.07	0.14 \pm 0.11	0.05 \pm 0.06
Stomach	0.59 \pm 0.12	0.42 \pm 0.15	0.25 \pm 0.13	0.28 \pm 0.33	0.08 \pm 0.15
Spleen	1.64 \pm 0.83	0.96 \pm 0.29	0.45 \pm 0.10	0.38 \pm 0.15	0.53 \pm 0.35
Liver	2.67 \pm 0.37	1.89 \pm 0.69	0.69 \pm 0.27	0.36 \pm 0.13	0.26 \pm 0.11
Pancreas	1.41 \pm 0.31	0.74 \pm 0.18	0.12 \pm 0.03	0.04 \pm 0.01	0.02 \pm 0.02
Adrenal glands	3.34 \pm 0.45	1.78 \pm 0.45	0.50 \pm 0.16	0.27 \pm 0.11	0.23 \pm 0.18
Kidneys	13.2 \pm 1.87	9.23 \pm 2.18	5.80 \pm 1.24	2.56 \pm 0.62	1.48 \pm 0.44
Lungs	8.06 \pm 1.48	4.35 \pm 0.82	0.72 \pm 0.19	0.18 \pm 0.04	0.07 \pm 0.02
Heart	3.60 \pm 0.52	1.91 \pm 0.40	0.26 \pm 0.04	0.09 \pm 0.03	0.05 \pm 0.02
Tumor	27.2 \pm 7.55	47.6 \pm 13.5	57.2 \pm 15.3	59.3 \pm 16.0	71.9 \pm 19.4
Muscle	1.15 \pm 0.19	0.58 \pm 0.13	0.08 \pm 0.02	0.02 \pm 0.01	0.01 \pm 0.01
Bone	0.89 \pm 0.27	0.45 \pm 0.13	0.06 \pm 0.04	0.03 \pm 0.02	0.02 \pm 0.01
Brain	0.23 \pm 0.04	0.13 \pm 0.03	0.02 \pm 0.01	0.01 \pm 0.00	0.00 \pm 0.00
Thyroid	2.90 \pm 0.41	1.62 \pm 0.42	0.37 \pm 0.06	0.15 \pm 0.01	0.09 \pm 0.04
Salivary glands	2.43 \pm 0.33	1.31 \pm 0.30	0.28 \pm 0.04	0.11 \pm 0.03	0.05 \pm 0.03
Lacrimal glands	0.27 \pm 0.08	0.15 \pm 0.07	0.04 \pm 0.03	0.01 \pm 0.01	0.00 \pm 0.00
Tumor:Blood	1.58 \pm 0.26	5.81 \pm 1.58	105 \pm 57.4	1029 \pm 459	3996 \pm 2182
Tumor:Muscle	23.5 \pm 4.66	83.1 \pm 17.0	736 \pm 333	3374 \pm 1417	12778 \pm 19955
Tumor:Kidney	2.07 \pm 0.55	5.38 \pm 1.91	10.5 \pm 4.77	24.0 \pm 6.93	46.4 \pm 21.3
Tumor:Salivary gland	11.3 \pm 2.76	36.4 \pm 5.35	202 \pm 49.3	566 \pm 236	1167 \pm 531
Blood:Salivary gland	7.04 \pm 0.86	6.48 \pm 1.02	2.11 \pm 0.47	0.57 \pm 0.17	0.31 \pm 0.06

Table S6: Biodistribution (mean \pm SD) and uptake ratios of [^{177}Lu]Lu-HTK04048 in LNCaP tumor-bearing mice.

Tissue (%ID/g)	1 h (n = 7)	4 h (n = 7)	24 h (n = 7)	72 h (n = 7)	120 h (n = 8)
Blood	19.8 \pm 3.38	11.7 \pm 1.39	0.62 \pm 0.16	0.08 \pm 0.06	0.04 \pm 0.03
Fat	1.56 \pm 0.45	0.94 \pm 0.13	0.15 \pm 0.05	0.07 \pm 0.03	0.05 \pm 0.03
Testes	2.60 \pm 0.62	2.72 \pm 0.34	0.67 \pm 0.24	0.35 \pm 0.05	0.22 \pm 0.09
Intestines	1.38 \pm 0.22	1.00 \pm 0.08	0.46 \pm 0.31	0.13 \pm 0.08	0.10 \pm 0.10
Stomach	0.75 \pm 0.11	0.71 \pm 0.13	0.83 \pm 0.66	0.20 \pm 0.17	0.04 \pm 0.02
Spleen	2.57 \pm 0.48	1.96 \pm 0.39	0.64 \pm 0.10	0.54 \pm 0.14	0.55 \pm 0.27
Liver	3.94 \pm 0.69	2.28 \pm 0.46	0.77 \pm 0.52	0.25 \pm 0.02	0.18 \pm 0.07
Pancreas	1.77 \pm 0.17	1.15 \pm 0.14	0.15 \pm 0.03	0.06 \pm 0.01	0.05 \pm 0.03
Adrenal glands	4.43 \pm 1.11	2.17 \pm 0.21	0.67 \pm 0.26	0.33 \pm 0.06	0.30 \pm 0.14
Kidneys	17.4 \pm 4.32	12.5 \pm 1.35	5.68 \pm 1.28	2.19 \pm 0.21	1.43 \pm 0.48
Lungs	9.52 \pm 1.44	5.92 \pm 0.79	1.05 \pm 0.36	0.26 \pm 0.08	0.12 \pm 0.05
Heart	4.74 \pm 0.60	2.87 \pm 0.30	0.34 \pm 0.05	0.14 \pm 0.03	0.08 \pm 0.02
Tumor	16.5 \pm 5.48	39.4 \pm 22.4	65.3 \pm 19.6	64.1 \pm 15.0	65.7 \pm 19.1
Muscle	1.54 \pm 0.20	0.96 \pm 0.09	0.11 \pm 0.02	0.03 \pm 0.01	0.02 \pm 0.01
Bone	1.10 \pm 0.16	0.69 \pm 0.11	0.11 \pm 0.02	0.06 \pm 0.02	0.05 \pm 0.02
Brain	0.29 \pm 0.03	0.18 \pm 0.01	0.03 \pm 0.00	0.01 \pm 0.00	0.01 \pm 0.00
Thyroid	3.97 \pm 0.47	2.68 \pm 0.23	0.53 \pm 0.07	0.28 \pm 0.05	0.17 \pm 0.02
Salivary glands	2.92 \pm 0.36	1.91 \pm 0.20	0.39 \pm 0.08	0.18 \pm 0.03	0.13 \pm 0.03
Lacrimal glands	0.42 \pm 0.12	0.54 \pm 0.52	0.06 \pm 0.01	0.01 \pm 0.01	0.01 \pm 0.01
Tumor:Blood	0.84 \pm 0.22	3.49 \pm 2.31	113 \pm 44.5	1493 \pm 1213	4346 \pm 4168
Tumor:Muscle	10.7 \pm 2.87	42.2 \pm 27.3	594 \pm 177	2043 \pm 734	3358 \pm 2122
Tumor:Kidney	0.99 \pm 0.34	3.27 \pm 2.16	11.5 \pm 2.22	29.2 \pm 6.22	52.1 \pm 16.3
Tumor:Salivary gland	5.64 \pm 1.51	20.9 \pm 11.9	175 \pm 58.1	362 \pm 111	604 \pm 226
Blood:Salivary gland	6.78 \pm 0.76	6.12 \pm 0.58	1.61 \pm 0.40	0.43 \pm 0.28	0.22 \pm 0.13

Table S7: Biodistribution (mean \pm SD) and uptake ratios of [^{177}Lu]Lu-HTK04028 in LNCaP tumor-bearing mice.

Tissue (%ID/g)	1 h (n = 5)	4 h (n = 5)	24 h (n = 5)	72 h (n = 5)	120 h (n = 6)
Blood	17.7 \pm 2.10	12.2 \pm 1.66	0.82 \pm 0.11	0.05 \pm 0.01	0.02 \pm 0.00
Fat	1.26 \pm 0.21	0.89 \pm 0.24	0.14 \pm 0.02	0.06 \pm 0.02	0.03 \pm 0.01
Testes	2.26 \pm 0.46	2.66 \pm 0.41	0.55 \pm 0.05	0.31 \pm 0.05	0.22 \pm 0.01
Intestines	1.23 \pm 0.24	1.04 \pm 0.12	0.23 \pm 0.05	0.07 \pm 0.03	0.08 \pm 0.05
Stomach	0.51 \pm 0.18	0.45 \pm 0.06	0.31 \pm 0.10	0.07 \pm 0.07	0.10 \pm 0.10
Spleen	1.53 \pm 0.23	1.44 \pm 0.31	0.48 \pm 0.14	0.49 \pm 0.16	0.54 \pm 0.15
Liver	2.93 \pm 0.51	2.29 \pm 0.55	0.54 \pm 0.09	0.22 \pm 0.02	0.16 \pm 0.02
Pancreas	1.53 \pm 0.22	1.24 \pm 0.04	0.15 \pm 0.02	0.05 \pm 0.01	0.03 \pm 0.00
Adrenal glands	3.25 \pm 0.34	2.18 \pm 0.33	0.73 \pm 0.13	0.48 \pm 0.17	0.33 \pm 0.05
Kidneys	8.30 \pm 1.58	9.21 \pm 2.76	4.32 \pm 0.58	1.77 \pm 0.25	1.16 \pm 0.13
Lungs	7.88 \pm 1.77	5.79 \pm 0.44	1.08 \pm 0.72	0.18 \pm 0.02	0.09 \pm 0.01
Heart	4.15 \pm 0.31	2.67 \pm 0.31	0.36 \pm 0.03	0.12 \pm 0.03	0.07 \pm 0.01
Tumor	19.0 \pm 5.86	42.6 \pm 11.6	30.2 \pm 2.74	26.1 \pm 7.29	28.4 \pm 5.11
Muscle	1.32 \pm 0.19	0.83 \pm 0.09	0.11 \pm 0.02	0.03 \pm 0.01	0.02 \pm 0.00
Bone	0.99 \pm 0.21	0.63 \pm 0.10	0.11 \pm 0.02	0.05 \pm 0.02	0.04 \pm 0.02
Brain	0.26 \pm 0.03	0.19 \pm 0.02	0.02 \pm 0.00	0.01 \pm 0.00	0.00 \pm 0.00
Thyroid	3.30 \pm 0.42	2.30 \pm 0.30	0.52 \pm 0.08	0.24 \pm 0.04	0.13 \pm 0.02
Salivary glands	2.55 \pm 0.21	1.75 \pm 0.25	0.45 \pm 0.10	0.19 \pm 0.05	0.11 \pm 0.03
Lacrimal glands	0.51 \pm 0.23	0.39 \pm 0.19	0.05 \pm 0.04	0.01 \pm 0.01	0.00 \pm 0.00
Tumor:Blood	1.11 \pm 0.45	3.60 \pm 1.24	37.2 \pm 4.22	550 \pm 108	1714 \pm 320
Tumor:Muscle	14.5 \pm 4.46	52.2 \pm 17.4	275 \pm 35.3	886 \pm 181	1825 \pm 415
Tumor:Kidney	2.39 \pm 0.99	4.89 \pm 1.58	7.06 \pm 0.86	14.6 \pm 2.72	24.9 \pm 5.16
Tumor:Salivary gland	7.60 \pm 2.89	24.5 \pm 5.95	69.3 \pm 15.8	144 \pm 35.6	284 \pm 87.9
Blood:Salivary gland	6.93 \pm 0.33	7.09 \pm 1.45	1.88 \pm 0.42	0.26 \pm 0.06	0.17 \pm 0.04

Table S8: Radiation dose (mGy/MBq) of [¹⁷⁷Lu]Lu-HTK03170, [¹⁷⁷Lu]Lu-HTK03149 and [¹⁷⁷Lu]Lu-PSMA-617 calculated from unit density sphere models for the LNCaP tumors.

Sphere/Tumor volume (mL)	[¹⁷⁷ Lu]Lu-HTK03170	[¹⁷⁷ Lu]Lu-HTK03149*	[¹⁷⁷ Lu]Lu-PSMA-617*
0.01	5.02E+05	7.53E+04	3.07E+04
0.1	5.25E+04	7.87E+03	3.21E+03
0.5	1.07E+04	1.60E+03	6.51E+02
1	5.38E+03	8.06E+02	3.28E+02
2	2.70E+03	4.05E+02	1.65E+02
4	1.36E+03	2.03E+02	8.28E+01
6	9.06E+02	1.36E+02	5.53E+01
8	6.80E+02	1.02E+02	4.15E+01
10	5.45E+02	8.17E+01	3.33E+01
20	2.74E+02	4.10E+01	1.67E+01
40	1.37E+02	2.06E+01	8.38E+00
60	9.17E+01	1.37E+01	5.60E+00
80	6.90E+01	1.03E+01	4.21E+00
100	5.52E+01	8.28E+00	3.37E+00
300	1.86E+01	2.79E+00	1.13E+00
400	1.40E+01	2.10E+00	8.54E-01
500	1.12E+01	1.68E+00	6.85E-01
600	9.37E+00	1.40E+00	5.72E-01
1000	5.66E+00	8.48E-01	3.45E-01
2000	2.87E+00	4.29E-01	1.75E-01
3000	1.92E+00	2.88E-01	1.17E-01
4000	1.45E+00	2.17E-01	8.86E-02
5000	1.17E+00	1.75E-01	7.12E-02
6000	9.76E-01	1.46E-01	5.96E-02

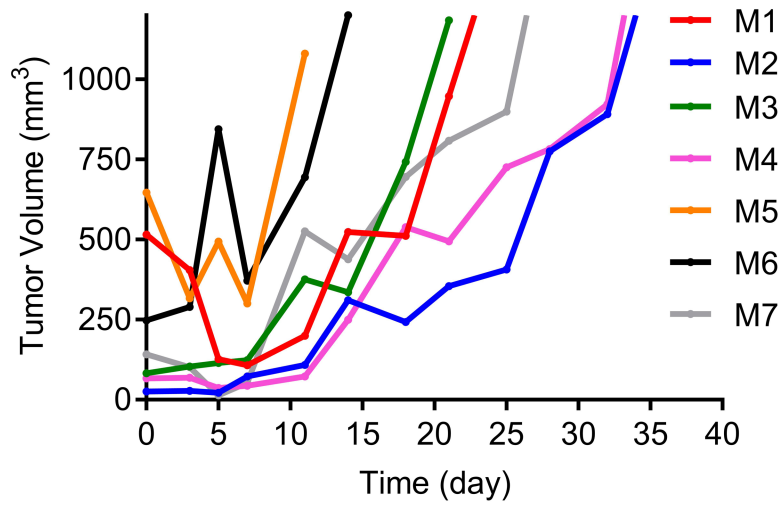
*The calculated dosimetry data of [¹⁷⁷Lu]Lu-HTK03149 and [¹⁷⁷Lu]Lu-PSMA-617 has been previously reported in Kuo H-T, et al. *Theranostics* 2022; 12: 6179-6188.

Table S9: Radiation doses (mGy/MBq) of [¹⁷⁷Lu]Lu-HTK03170, [¹⁷⁷Lu]Lu-HTK03149 and [¹⁷⁷Lu]Lu-PSMA-617 calculated for the major organs of 25-g mice using the OLINDA software.

Kinetics value [MBq-h/MBq]				Organ doses [mGy/MBq]			
Source organ	[¹⁷⁷ Lu]Lu-HTK03170	[¹⁷⁷ Lu]Lu-HTK03149*	[¹⁷⁷ Lu]Lu-PSMA-617*	Target organ	[¹⁷⁷ Lu]Lu-HTK03170	[¹⁷⁷ Lu]Lu-HTK03149*	[¹⁷⁷ Lu]Lu-PSMA-617*
Brain	2.55E-02	2.23E-03	6.64E-03	Brain	1.98E+01	2.35E+00	1.79E+00
Large intestine contents	1.12E-01	9.24E-02	8.80E-03	Large intestine	3.27E+01	1.59E+01	2.42E+00
Small intestine	3.35E-01	2.76E-01	2.63E-02	Small intestine	3.21E+01	1.57E+01	2.08E+00
Stomach	1.32E-02	8.07E-03	2.34E-04	Stomach wall	4.00E+01	1.57E+01	1.51E+00
Heart	7.94E-02	1.94E-02	3.28E-03	Heart	4.55E+01	9.38E+00	1.90E+00
Kidneys	1.33E+00	2.41E-01	8.23E-01	Kidneys	3.74E+02	6.72E+01	2.23E+02
Liver	1.24E+00	3.91E-01	6.38E-02	Liver	7.50E+01	2.09E+01	3.84E+00
Lungs	6.60E-02	1.72E-02	4.85E-03	Lungs	6.90E+01	1.62E+01	4.46E+00
Pancreas	4.12E-02	1.79E-02	4.76E-03	Pancreas	3.01E+01	7.72E+00	3.60E+00
Cortical bone	1.91E-01	7.60E-02	8.28E-03	Skeleton	2.93E+01	7.45E+00	1.25E+00
Spleen	1.04E-01	2.30E-02	1.41E-02	Spleen	9.14E+01	1.89E+01	1.15E+01
Testes	9.21E-02	1.29E-02	4.23E-03	Testes	6.22E+01	8.72E+00	3.04E+00
Thyroid	5.15E-03	2.03E-03	4.01E-04	Thyroid	4.31E+01	1.29E+01	2.78E+00
Urinary bladder	1.11E+00	8.14E-01	8.04E-01	Urinary bladder wall	8.08E+02	5.84E+02	5.76E+02
Remainder of the body	4.23E+00	5.31E-01	1.68E-01	Remainder of the body	3.18E+01	8.95E+00	6.89E+00

*The calculated dosimetry data of [¹⁷⁷Lu]Lu-HTK03149 and [¹⁷⁷Lu]Lu-PSMA-617 has been previously reported in Kuo H-T, et al. Theranostics 2022; 12: 6179-6188.

(A)



(B)

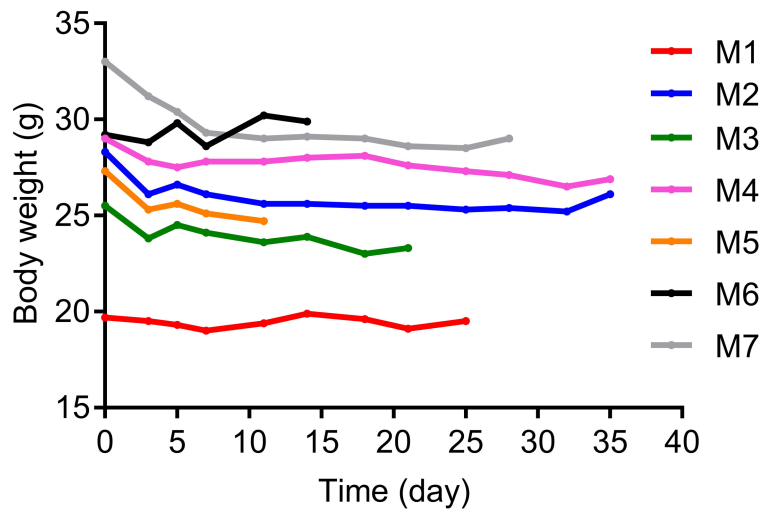
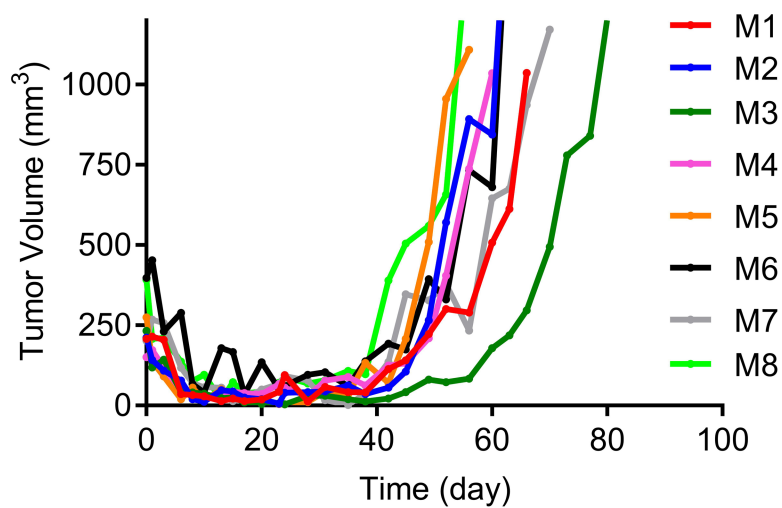


Figure S1: Changes of (A) tumor volume and (B) body weight over time after mice were treated with PBS.

(A)



(B)

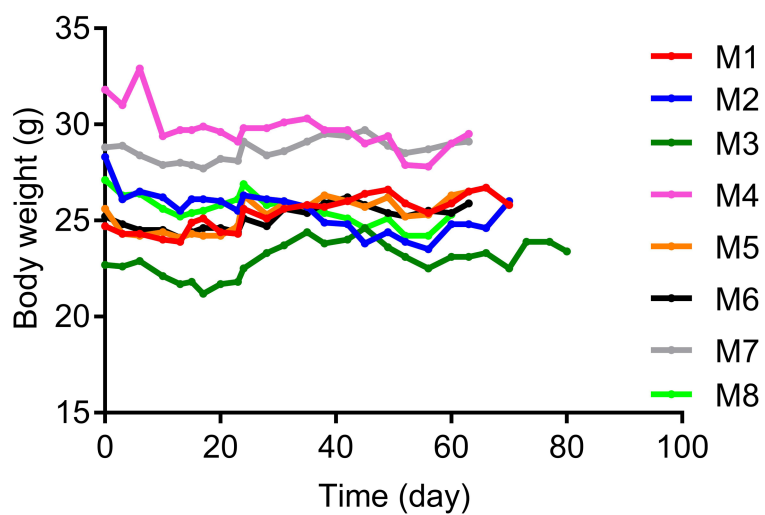
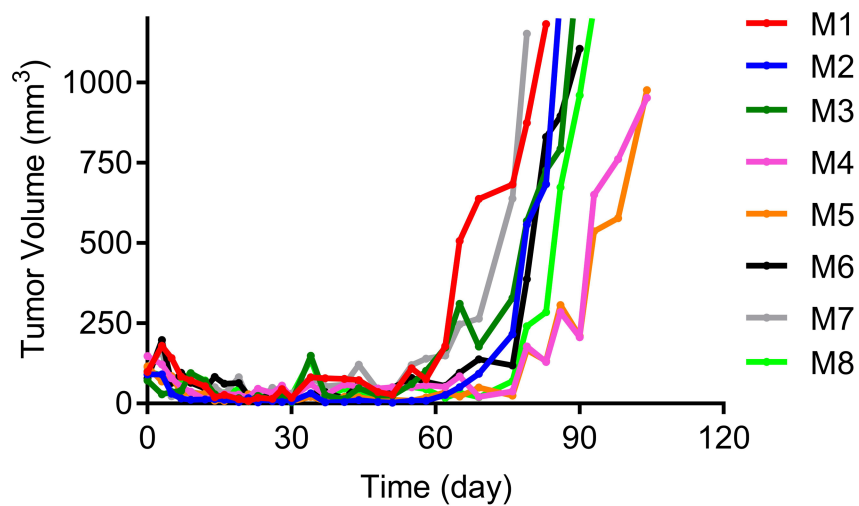


Figure S2: Changes of (A) tumor volume and (B) body weight over time after mice were treated with 37 MBq of [¹⁷⁷Lu]Lu-PSMA-617.

(A)



(B)

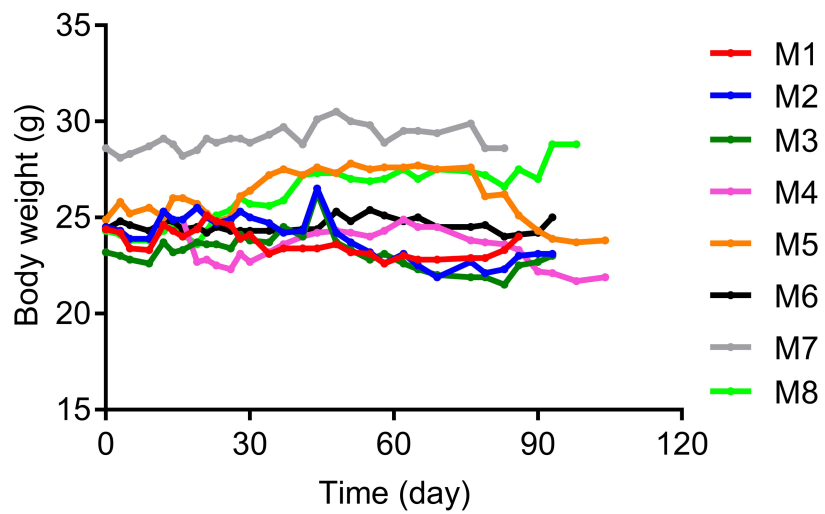
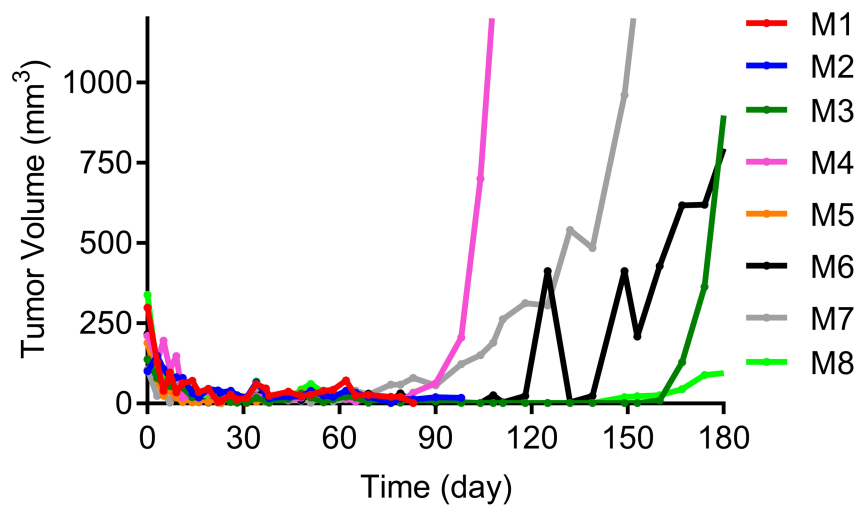


Figure S3: Changes of (A) tumor volume and (B) body weight over time after mice were treated with 9.3 MBq of [¹⁷⁷Lu]Lu-HTK03170.

(A)



(B)

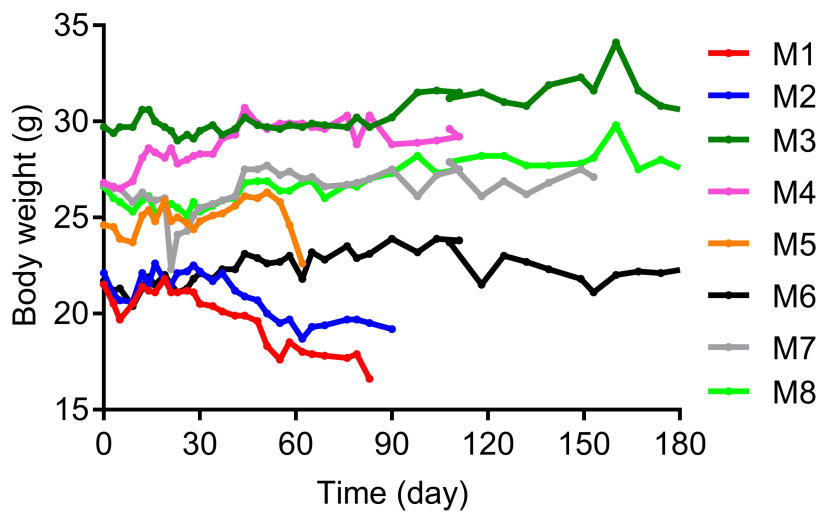
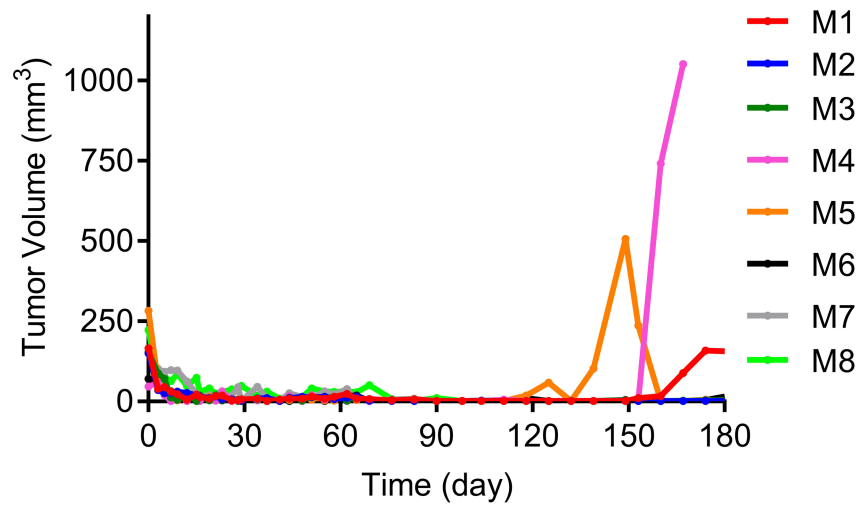


Figure S4: Changes of (A) tumor volume and (B) body weight over time after mice were treated with 18.5 MBq of [¹⁷⁷Lu]Lu-HTK03170.

(A)



(B)

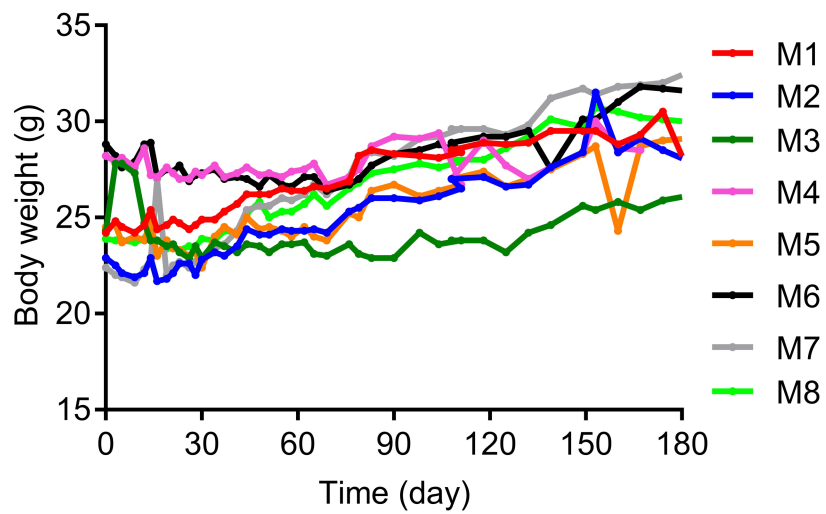


Figure S5: Changes of (A) tumor volume and (B) body weight over time after mice were treated with 37 MBq of [¹⁷⁷Lu]Lu-HTK03170.