

Supporting Information for:

Preclinical Evaluation of [^{155/161}Tb]Tb-Crown-TATE — A Novel SPECT Imaging Theranostic Agent Targeting Neuroendocrine Tumours

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Synthesis and Characterisation

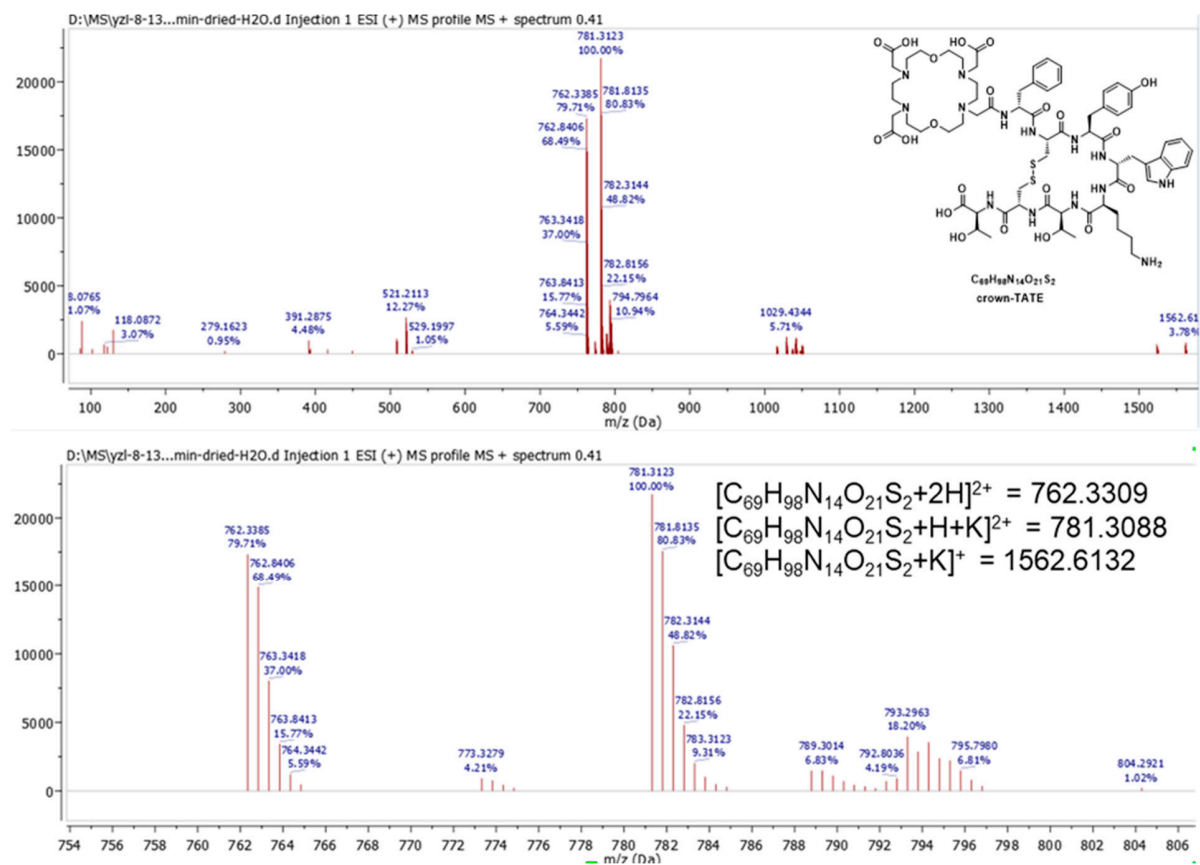


Figure S1. High-resolution electrospray ionisation mass spectrometry characterisation of crown-TATE.

Radiochemistry Studies

Radio-TLCs

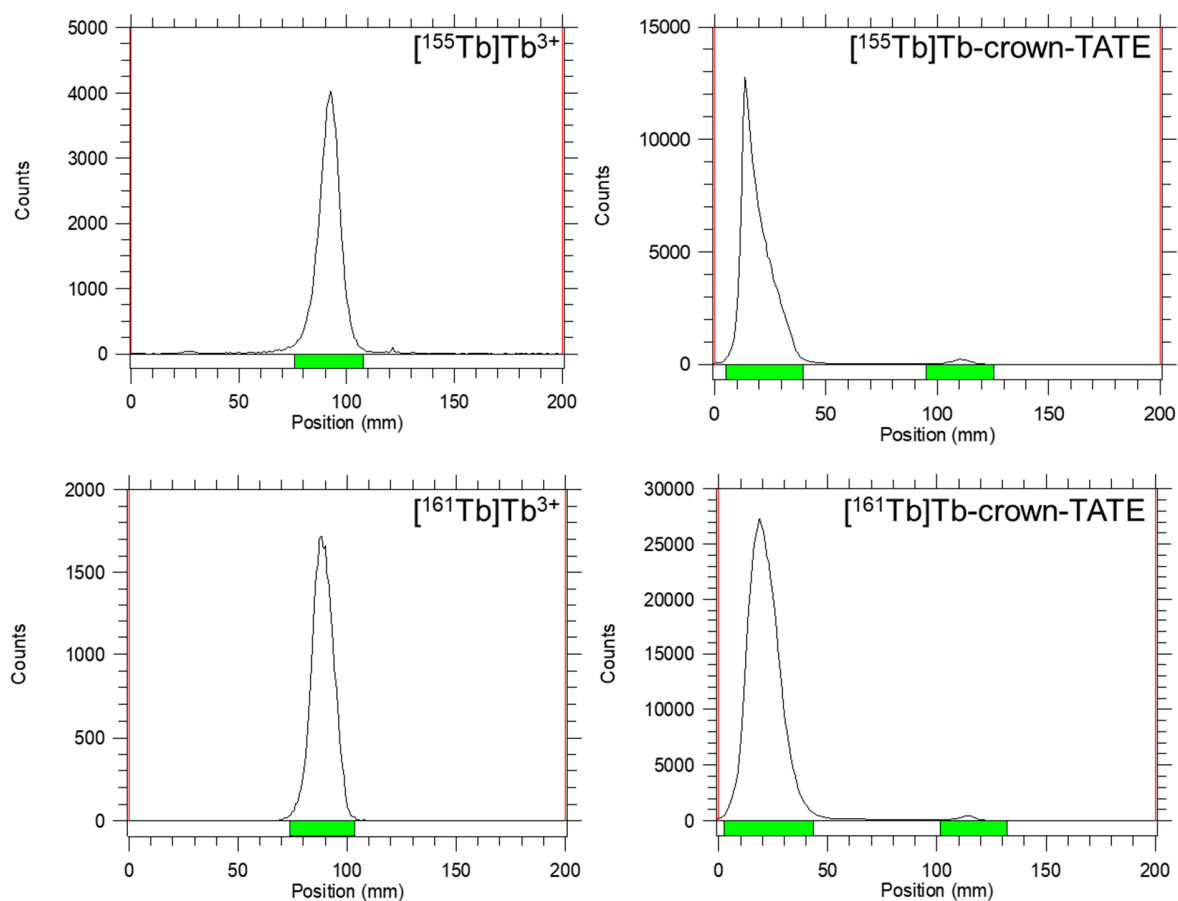


Figure S2. Representative radio-TLC traces for ^{155}Tb and ^{161}Tb – labelled crown-TATE and negative control reactions. Measured using SG-paper iTLC plates with EDTA (50 mM, pH 5.5) as eluent.

Preclinical Studies

SPECT Biodistribution Studies

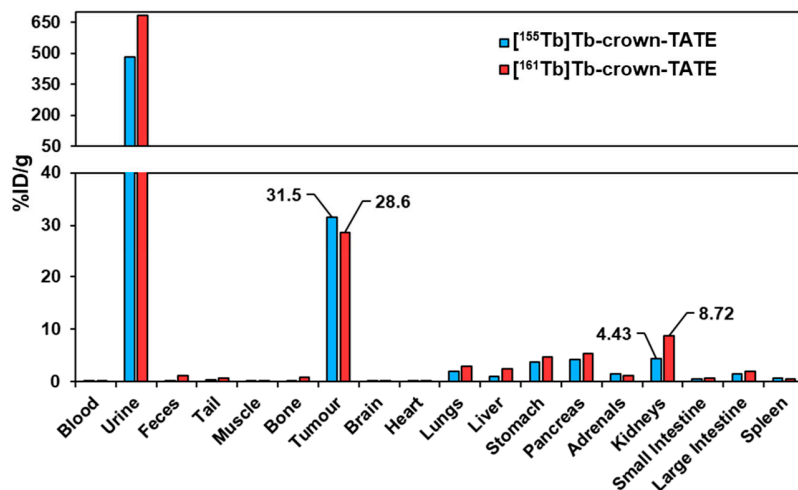


Figure S3. Biodistribution results for imaging mice bearing AR42J tumour xenografts at 2.5 h post-administration of $[^{155}\text{Tb}]$ Tb-crown-TATE (13.8 MBq, 0.71 nmol) and $[^{161}\text{Tb}]$ Tb-crown-TATE (7.95 MBq, 0.70 nmol).

Table S1. Biodistribution results for imaging mice bearing AR42J tumours xenografts at 2.5 h post administration of $[^{155}\text{Tb}]$ Tb-crown-TATE (13.8 MBq, 0.71 nmol) and $[^{161}\text{Tb}]$ Tb-crown-TATE (7.95 MBq, 0.70 nmol).

Organ	$[^{155}\text{Tb}]$ Tb-crown-TATE	$[^{161}\text{Tb}]$ Tb-crown-TATE
	%ID/g	%ID/g
Blood	0.07	0.21
Urine	482.5	683.1
Feces	0.22	1.23
Tail	0.32	0.68
Muscle	0.02	0.04
Bone	0.28	0.83
Tumour	31.51	28.58
Brain	0.02	0.02
Heart	0.10	0.21
Lungs	1.97	2.91
Liver	0.98	2.39
Stomach	3.74	4.78
Pancreas	4.31	5.39
Adrenals	1.42	1.22
Kidneys	4.43	8.72
Small Intestine	0.50	0.75
Large Intestine	1.43	1.99
Spleen	0.70	0.44
Tumour-to-Blood	465	134
Tumour-to-Muscle	1534	650
Tumour-to-Bone	114	34.3
Tumour-to-Kidney	7.12	3.28

Full Biodistribution Studies

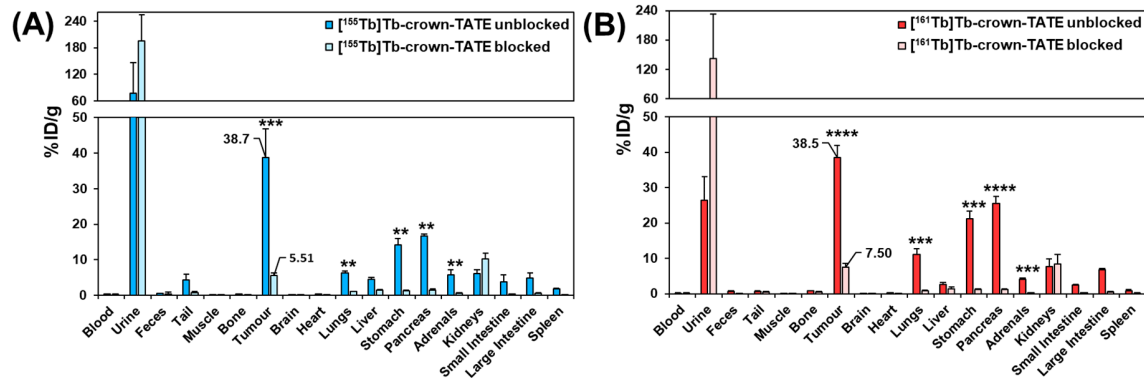


Figure S4. Biodistribution results in male NRG mice bearing AR42J tumour xenografts at 2 h p.i. of: (A) [^{155}Tb]Tb-crown-TATE (~175 kBq, 93 pmol/animal) (n=4) (unblocked) and [^{155}Tb]Tb-crown-TATE (~175 kBq, 93 pmol/animal) (blocked with DOTATOC (23 nmol/animal)) (n=3); (B) [^{161}Tb]Tb-crown-TATE (~850 kBq, 76 pmol/animal) (unblocked) (n=4) and [^{161}Tb]Tb-crown-TATE (~850 kBq, 76 pmol) (blocked with DOTATOC (23 nmol/animal)) (n=3). (** = $p < 0.01$, *** = $p < 0.001$, **** = $p < 0.0001$).

Table S2. Full biodistribution results for [^{155}Tb]Tb-crown-TATE (~175 kBq, 93 pmol/animal) (n=4) (unblocked); [^{155}Tb]Tb-crown-TATE (~175 kBq, 93 pmol/animal) (blocked with DOTATOC (23 nmol/animal)) (n=3); [^{161}Tb]Tb-crown-TATE (~850 kBq, 76 pmol/animal) (unblocked) (n=4); and [^{161}Tb]Tb-crown-TATE (~850 kBq, 76 pmol) (blocked with DOTATOC (23 nmol/animal)) (n=3) in male NRG mice bearing AR42J tumour xenografts at 2 h p.i.

Organ	[^{155}Tb]Tb-crown-TATE blocked		[^{155}Tb]Tb-crown-TATE unblocked		[^{161}Tb]Tb-crown-TATE blocked		[^{161}Tb]Tb-crown-TATE unblocked	
	%ID/g	Error	%ID/g	Error	%ID/g	Error	%ID/g	Error
Blood	0.25	0.08	0.28	0.15	0.14	0.07	0.17	0.02
Urine	196	58.0	78.0	68.5	142	91.1	26.5	6.5
Feces	0.41	0.55	0.54	0.02	0.09	0.03	0.63	0.13
Tail	0.72	0.31	4.31	1.54	0.46	0.14	0.70	0.09
Muscle	0.04	0.01	0.08	0.03	0.03	0.01	0.04	0.01
Bone	0.13	0.03	0.34	0.06	0.47	0.10	0.73	0.09
Tumour	5.51	0.73	38.7	8.02	7.50	1.08	38.5	3.45
Brain	0.02	0.01	0.04	0.01	0.01	0.00	0.02	0.00
Heart	0.13	0.02	0.32	0.07	0.12	0.04	0.24	0.02
Lungs	1.13	0.03	6.27	0.59	0.89	0.14	11.1	1.62
Liver	1.40	0.29	4.48	0.49	1.43	0.42	2.63	0.59
Stomach	1.31	0.17	14.2	1.88	1.23	0.18	21.2	2.12
Pancreas	1.50	0.26	19.7	4.30	1.20	0.21	25.5	1.96
Adrenals	0.53	0.18	5.79	1.41	0.21	0.05	4.04	0.44
Kidneys	10.2	1.65	6.13	0.99	8.44	2.68	7.71	2.11
Small Intestine	0.38	0.04	3.85	1.84	0.24	0.09	2.43	0.23
Large Intestine	0.60	0.06	4.84	1.42	0.48	0.08	6.75	0.40
Spleen	0.19	0.06	1.73	0.33	0.16	0.08	0.86	0.29
Tumour-to-Blood	21.8	-	139	-	52.9	-	226	-
Tumour-to-Muscle	136	-	488	-	236	-	1021	-
Tumour-to-Bone	42.2	-	113	-	16.0	-	52.4	-
Tumour-to-Kidney	0.54	-	6.32	-	0.89	-	4.99	-