Supplemental methods: precursor syntheses

4-Amino-5-iodo-2-methoxybenzoic acid (**1**) was synthesized as described in Leysen and Van Daele US0054986618A.

N-(2-Diethylaminoethyl)-4-amino-5-iodo-2-methoxybenzamide (2)

To a solution of compound **1** (1.47 g; 5 mmoles) in THF (30 ml) was added a solution of HBTU (1.86 g; 4.90 mmoles) in DMF (10 ml) and N,N-diisopropylethylamine (1.8 ml; 10 mmoles). After a few minutes 2-diethylaminoethylamine (1.4 ml; 10 mmoles) was added and the reaction mixture stirred at room temperature. After 3 h THF was evaporated and the residue was dissolved in dichloromethane and washed with diluted aqueous NaCl solution. The organic phase was dried (Na_2SO_4) and evaporated. The semisolid residue was triturated with diethyl ether to give an off-white solid (1.33 g; 68%).

Benzo(1,3)dioxolo-5-carboxylic acid (4-(2-diethylamino-ethylcarbamoyl)-2-iodo-5-methoxy-phenyl)-amide (3)

To a solution of compound **2** (1.33 g; 5.92 mmoles) and N,N-diisopropylethylamine (1.21 ml; 6.8 mmoles) in THF (15 ml) was added a solution of piperonyloylchloride (1.1 g 5.95 mmoles) in THF (10 ml) and the reaction stirred at 70 °C for 3 h. The reaction mixture was evaporated and the residue purified in silica eluting with dichloromethane 0 to 10% of methanol to give **3** (1.66 g; 52%) as an off-white solid after trituration with diethyl ether.

Reaction of compound 3 with hexabutyldistannane in the presence of trans-dichlorbistriphenylphosphine-palladium(II)

None of numerous attempts to synthesize benzo(1,3)dioxolo-5-carboxylic acid (4-(2-diethylamino-ethylcarbamoyl)-2-tributylstannyl-5-methoxy-phenyl)-amid from compound **3** was

successful. All attempts resulted in reaction mixtures of a large number of compounds (HPLC), none of which could be isolated in a pure form.

Reaction of compound 3 with hexamethyldistannane in the presence of trans-dichlorbistriphenylphosphine-palladium(II)

Compound **3** (22 mg), hexamethyldistannane (35 µl) and trans-dichlorbistriphenylphosphine-palladium(II) (10 mg) in dioxane (2 ml) were heated at 40 °C for 1 h. Tlc on silica (10% methanol in dichloromethane) showed formation of a new compound of higher Rf than compound **3**. The new compound was purified by preparative Tlc. MS (FAB+) gave a molecular weight of 1170-1172 and an isotopic pattern corresponding to a compound containing Pd, not Sn. This would fit to a molecular composition of $C_{58}H_{56}IN_3O_5P_2Pd$ corresponding to a compound where the iodine in the 2-position of compound **3** has been substituted for an iodo-bis-triphenylphosphine-palladium group.

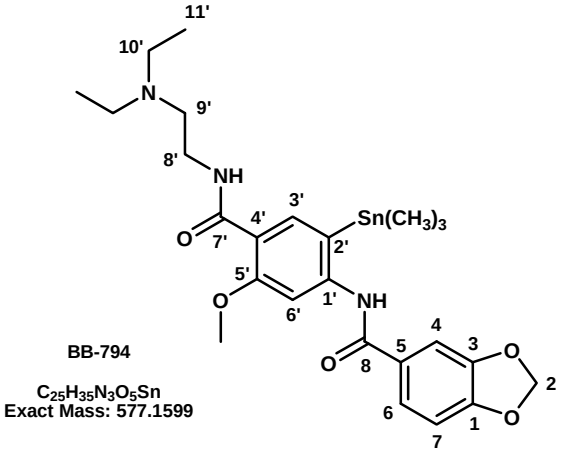
Reaction of compound 3 with hexamethyldistannane in the presence of trans-dichlorbistriphenylphosphine-palladium(II) and lithium chloride to form benzo(1,3)dioxolo-5-carboxylic acid (4-(2-diethylamino-ethylcarbamoyl)-2-trimethylstannyl-5-methoxy-phenyl)-amide (4)

Compound **3** (54 mg), LiCl (25 mg), trans-dichlorbistriphenylphosphine-palladium(II) (4 mg) and hexamethyldistannane (25 µl) in THF (2 ml) were heated in an oil bath at 80-90 °C for about 1 h or until the solution turned brown. HPLC and Tlc showed formation of a new compound of higher Rt and Rf. The reaction mixture was cooled to room temperature and directly purified on a column (2 cm diameter) filled with Alox (1 cm) (upper layer) and silica (5 cm) (lower layer) eluting with dichloromethane 0 to 20% of methanol. The fractions containing product were

evaporated. Final purification was achieved by preparative Tlc on Alox eluting with 5% methanol in dichloromethane. The band corresponding to product was scraped out and eluted with methanol. HPLC proved the product to be ca. 97% pure. MS (ESI): Isotopic distribution and MW= 575-577 corresponded to a molecular composition of $C_{25}H_{35}N_3O_5Sn$. The structure of the isolated compound was further proved by ^{1}H and ^{13}C NMR. In this way about 10 ml of an approximately 6 mM methanolic solution of compound **4** was obtained. The solution can be stored at -80 °C for more than one year without degradation.

Supplemental methods: NMR analysis

Benzo(1,3)dioxolo-5-carboxylic acid (4-(2-diethylamino-ethylcarbamoyl)-2-trimethylstannyl-5-methoxy-phenyl)-amide (4) in CD_3OD was measured at 600.13 MHz and 0 °C (stable for 3 days). The proposed structure numbering scheme was based on its IUPAC name.



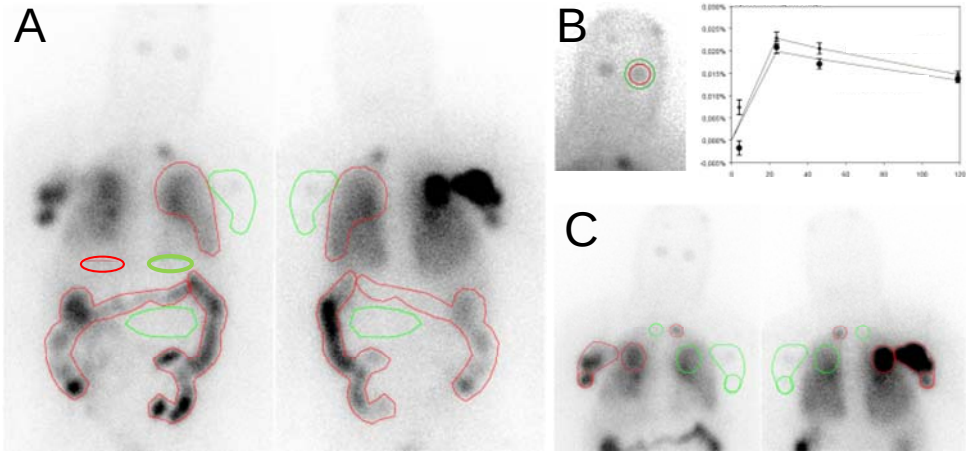
The following experiments were performed: 1D ^{1}H and ^{1}H-dec. ^{13}C and DEPT-135; 2D COSY-LR-45; $^{1}H/^{13}C$-HSQC; $^{1}H/^{13}C$-HMBC (optimized for 6 Hz coupling). All shifts are referenced to solvent signals at 3.31 ppm (^{1}H) and 49.15 ppm (^{13}C).

The ^{1}H spectrum showed what appeared to be the desired compound, a small amount of aromatic impurities and an equimolar amount of aliphatic impurities with several resonances in the range 3.4 - 3.6 / 71 - 77 ppm and a methyl group at 1.138 / 17.84 ppm. Based on 1D signal integrations and 2D NMR correlations, the following signal assignments have been made, confirming the proposed structure.

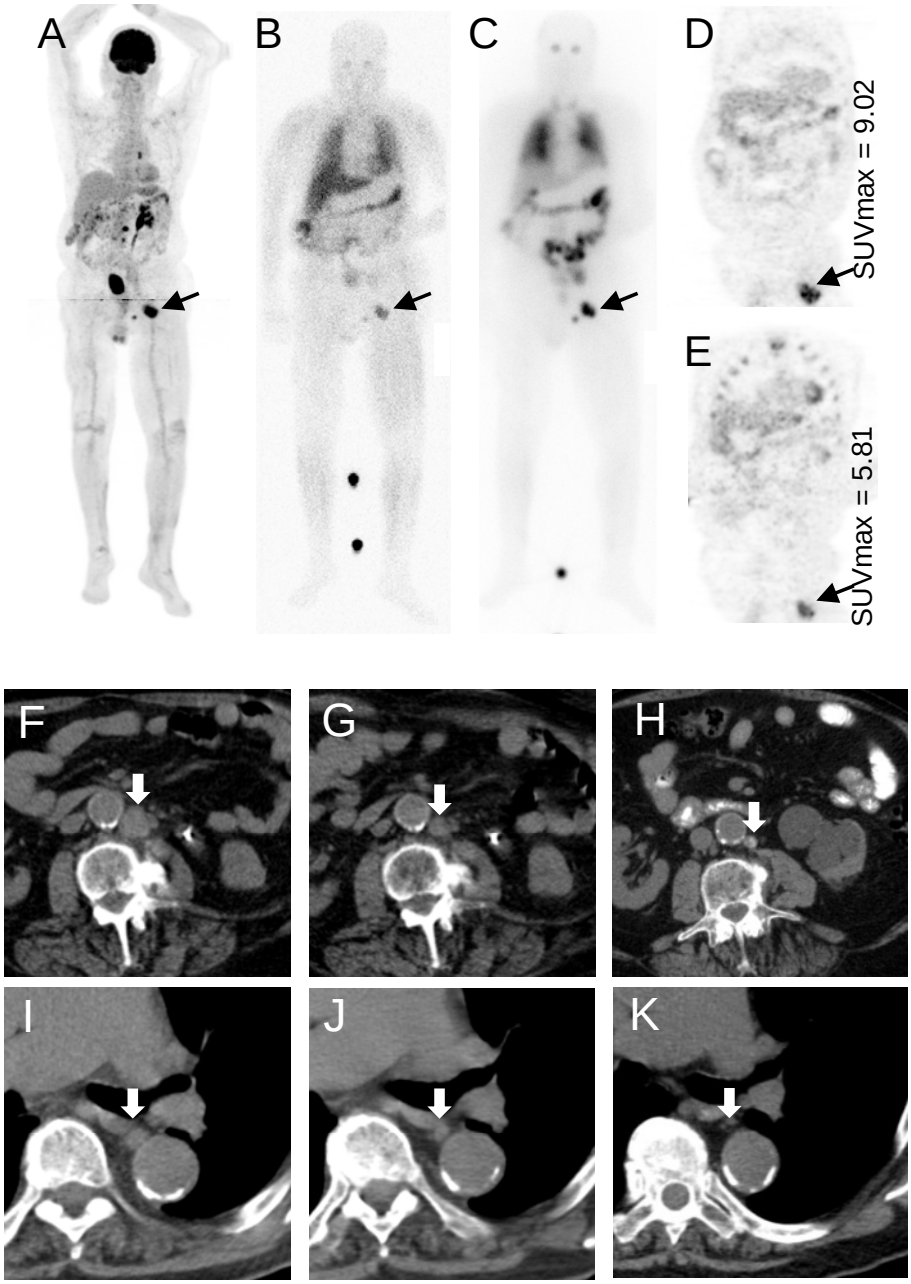
Position	^{13}C shift	^{1}H shift	Mult.	$J_{H,H}$	$J_{Sn,H}$
1	152.709				
2	103.636	6.096	s		
3	149.716				
4	108.899	7.448	d	1.8	
5	129.178				
6	124.247	7.590	dd	8.2, 1.8	
7	109.243	6.975	d	8.2	
8	168.770				
1'	149.432				
2'	132.636				
3'	140.775	8.123	s		47.2, 49.3
4'	119.968				
5'	160.220				
6'	110.457	7.048	s		13.0
7'	168.241				
5'-OCH_3	56.590	3.978	s		

2'-Sn(CH_3)$_3$	–7.881	0.232	s		53.7, 56.1
8'	38.040	3.574	t br	nd	
9'	52.497	2.836	t br	nd	
10'	48.420	2.774	q br	nd	
11'	11.504	1.156	t	7.3	

Pairs of satellite signals were observed from spin-1/2 isotopes ^{117}Sn (7.68%) and ^{119}Sn (8.59%); the ratio of their magnetic moments is 1.04619 for 119/117, which agrees well with the observed ratio of their coupling constants with ^{1}H (1.045 for $SnMe_3$ and H3'); for H6' the pair of satellites was not resolved. The Sn satellites in the ^{13}C spectrum could not be detected due to the limited S/N. The long-range correlations were completely consistent with the substitution pattern in the structure shown, and the agreement with predicted shifts can be considered good, in view of the limited accuracy of the predictions with ChemDraw.

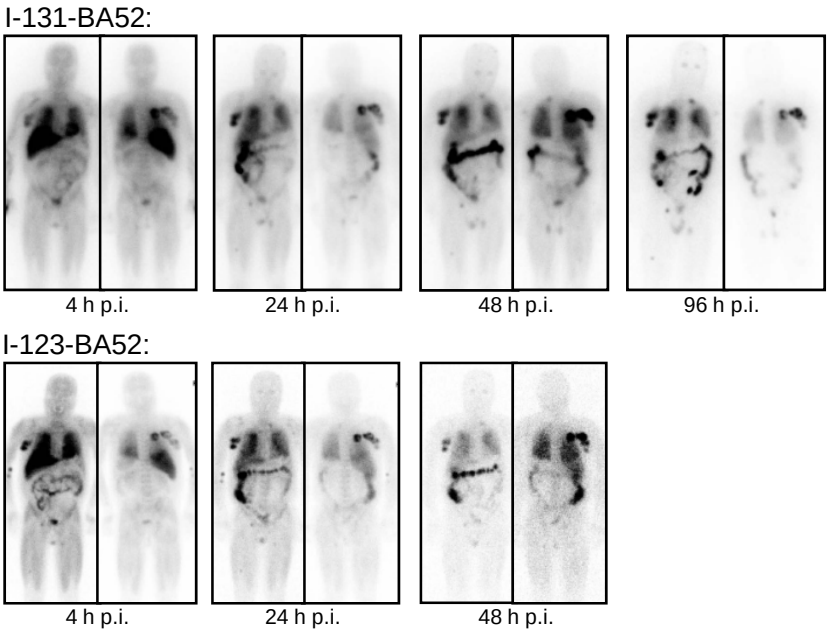


Supplemental Figure 1: Regions of interest (ROIs) of normal organs and metastases used for dosimetric estimations. a) Normal organs in anterior (left) and posterior (right) planar scans. b) On the left: Eye (red ROI) and background correction (green ROI minus red ROI as described in the text); On the right: time activity curve to determine the effective half-live. c) ROI around metastases (red) and mirrored to the contralateral side for background correction (green) both in anterior and posterior conjugate view (left/right).



Supplemental Figure 2: (A) Presenting a 59 year old patient with a malignant melanoma of the left lower extremity causing LK-metastasis inguinal and paraortal up to the mediastinum. FDG-PET/CT (A) presenting the high glucose uptake in the metastases. The pre-therapeutic whole-body scan with ^{123}I-BA52 (B) demonstrates high uptake, predicting suitability for endoradiotherapy which was conducted with 5.7 GBq ^{131}I-BA52 (C). Initially, the

endoradiotherapy resulted in a decrease of tumoral FDG-consumption (SUVmax 9.02 (D); prior, and SUVmax 5.81 after therapy (E)). (B) Finally, this patient survived 3 years after treatment. In serially performed follow-up imaging the paraaortal lymph node metastasis in the abdomen presented with shrinkage from pre-therapeutic staging (F), to follow-up at 6 weeks after treatment (G) and even continued even until 3 years after therapy (H). The paraaortal thoracic lymph node metastasis from pre-therapeutic staging (I) demonstrated shrinkage at the 6 week re-staging (J) and was long lasting until 3 years (K) after treatment. The sum diameter of target lesions decreased by 32% - partial remission according to RECIST criteria and was long lasting. The first new lesions occurred after 2.5 years in the peritoneum (data not shown).



Supplemental Figure 3: Comparison of serial I-131-BA52 imaging until 96 h p.i. (top row) and I-123-BA52 imaging until 48 h p.i.(lower row). No relevant differences in the calculated biological organ half-lives and therefore dosimetry estimations were observed.