pharmaceutics

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Supplementary Materials: Simplified ^{89}Zr-Labeling Protocol of Oxine (8-Hydroxyquinoline) Enabling Prolonged Tracking of Liposome-Based Nanomedicines and Cells

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Table S1. Radiolabeling yields (%) of [^{89}Zr]Zr(oxinate)$_4$ until extraction (5 min to 60 min) and in the subsequentstability samplings (2 h to 24 h): Quick kinetics until a max. 98.7% labeling yield.

Entry	Before Extraction							Stability in PBS After Extraction		
	5 min	10 min	15 min	20 min	30 min	60 min	2 h	4 h	8 h	24 h
#1	22.4	73.5	94.2	95.9	98.7	97.5	97.1	94.9	95.6	93.7
#2	45.1	61.3	84.5	91.2	94.8	94.2	91.8	92.9	92.0	88.0
#3	27.8	73.5	86.0	93.1	97.1	91.3	-	-	-	-
#4	-	-	87.6	91.5	96.3	-	-	-	-	-
AVG ± SD	31.8 ± 11.9	69.4 ± 7.0	88.1 ± 4.3	92.9 ± 2.2	96.7 ± 1.6	94.3 ± 3.1	94.5 ± 3.7	93.9 ± 1.4	93.8 ± 2.5	90.9 ± 4.0

Table S2. Radiolabeling yields (%) of [^{89}Zr]Zr(oxinate)$_4$ liposome complex until extraction (5 min to 24 h) and in the subsequent stability samplings (+ 24 h): Relatively slow oxine incorporation kinetics.

	Labeling							Stability		
Entry	5 min	10 min	15 min	20 min	30 min	60 min	6 h	18 h	24 h	+ 24 h
#1	9.8	18.0	30.0	35.0	42.0	48.2	81.6	98.1	94.6	96.2
#2	12.3	26.3	32.2	38.9	51.6	51.0	80.3	99.0	94.0	95.8
#3	8.6	15.2	26.2	26.9	34.3	66.3	78.2	95.6	97.1	98.3
#4	15.9	21.0	41.7	46.3	48.9	64.5	90.2	99.6	98.1	98.6
AVG ± SD	11.7 ± 3.2	20.1 ± 4.7	32.5 ± 6.6	36.8 ± 8.1	44.2 ± 7.7	59.2 ± 9.2	82.6 ± 5.3	98.1 ± 1.8	96.0 ± 2.0	97.2 ± 1.4

Table S3. Radiolabeling yields (%) of hiPSCs at different times of incubation and different DMSO concentrations: Quick kinetics in neutral conditions, ~50% max. labeling yield upon 30 min incubation.

		1% DMSO	2% DMSO	3% DMSO
5 min	**#1**	16.5	19.5	23.9
	#2	24.7	22.6	21.4
	AVG ± SD	20.6 ± 5.8	21.1 ± 2.2	22.7 ± 1.8
10 min	**#1**	45.3	47.6	45.5
	#2	35.8	39.0	40.1
	AVG ± SD	40.6 ± 6.7	43.3 ± 6.1	42.8 ± 3.8
15 min	**#1**	53.7	55.2	53.9
	#2	48.1	51.3	51.1
	AVG ± SD	50.9 ± 4.0	53.3 ± 2.8	52.5 ± 2.0
30 min	**#1**	48.0	48.8	51.7
	#2	47.1	52.3	54.8
	AVG ± SD	47.6 ± 0.6	50.6 ± 2.5	53.3 ± 2.2
60 min	**#1**	48.1	52.0	52.8
	#2	42.6	46.5	46.9
	AVG ± SD	45.4 ± 3.9	49.3 ± 3.9	49.9 ± 4.2
6 h	**#1**	45.0	44.0	42.0
	#2	39.0	40.0	39.0
	AVG ± SD	42.0 ± 4.2	42.0 ± 2.8	40.5 ± 2.1
24 h	**#1**	41.0	42.0	41.0
	#2	35.0	33.0	37.0

AVG ± SD	38.0 ± 4.2	37.5 ± 6.4	39.0 ± 2.8

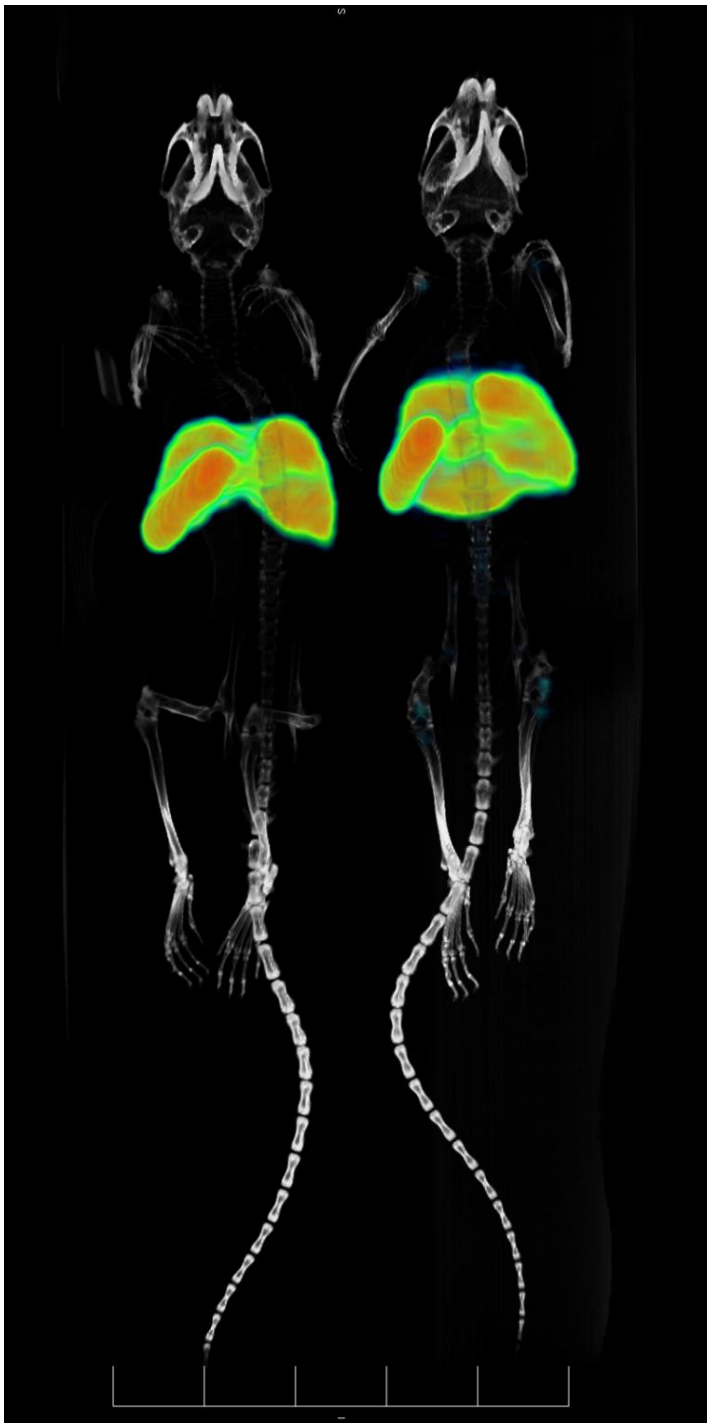

Figure S1. 3D-fused MicroPET/CT scans of [^{89}Zr]Zr(oxinate)$_4$–liposome-injected mice at 24 h post injection. High liver and spleen uptake, RES biodistribution. (Inveon DPET and CT120 small animal microPET/CT system; Siemens Healthineers, Erlangen, Germany.).

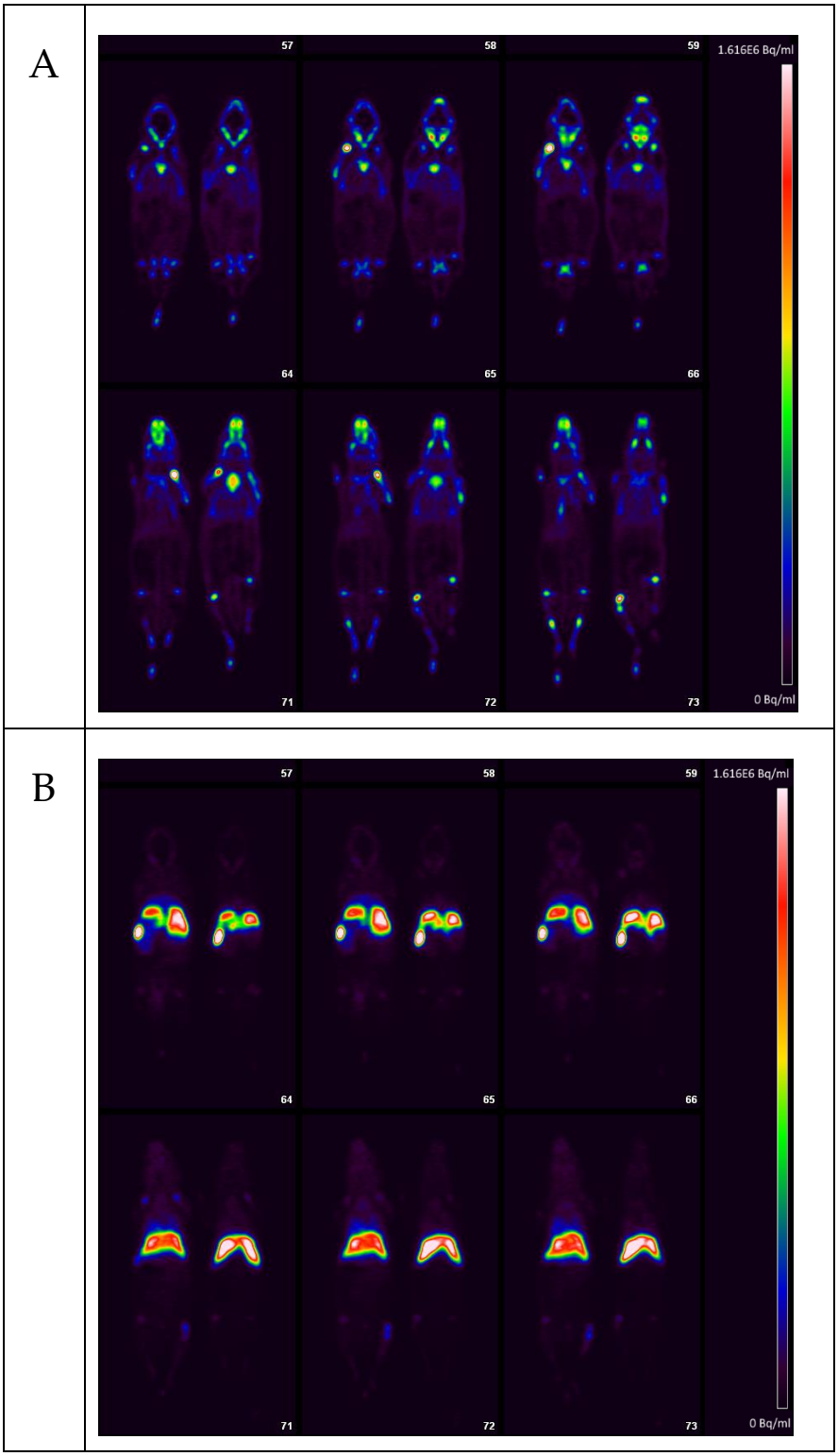

Figure S2. Representative PET slices of the ^{89}Zr control group (A), and the [^{89}Zr]Zr(oxinate)$_4$–liposome-complex-injected group (B) 24 h after IV injection. High liver and spleen uptake vs. bone uptake in the control group. (Inveon DPET and CT120 small animal microPET/CT system; Siemens Healthineers, Erlangen, Germany.).

SOP Name:	mansettings.nano		
File Name:	AP_NuclMed.dts	**Dispersant Name:**	PBS
Record Number:	9	**Dispersant RI:**	1.330
Material RI:	1.45	**Viscosity (cP):**	0.8924
Material Absorbtion:	0.001	**Measurement Date and Time:**	Montag, 11. Februar 2019 15
Temperature (°C):	25.0	**Duration Used (s):**	80
Count Rate (kcps):	155.9	**Measurement Position (mm):**	1.05
Cell Description:	Disposable sizing cuvette	**Attenuator:**	6

			Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm):	89.12	**Peak 1:**	91.51	96.8	29.09
PdI:	0.209	**Peak 2:**	4933	3.2	646.5
Intercept:	0.972	**Peak 3:**	0.000	0.0	0.000
Result quality :	Good				

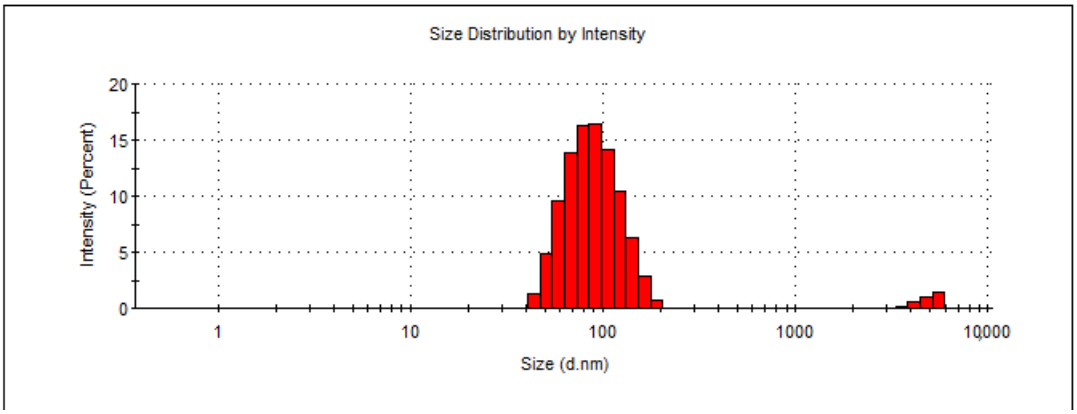

Figure S3. Particle size distribution of TargoSphere® [by Malvern Zetasizer Nano ZS dynamic light scattering (DLS) device.] (Translation: "Montag" = "Monday").

Table S4. 24 h ex vivo biodistribution results of [^{89}Zr]Zr(oxinate)$_4$–liposome-injected animals, and the ^{89}Zr control group (I.D./g organ percentages): High liver and spleen uptake vs. bone uptake in the control group.

	I.D./g organ %								
	[^{89}Zr]Zr(oxinate)$_4$–Liposome						**^{89}Zr Control**		
Animal No.	1	2	3	4	5	**AVG ± SD**	6	7	**AVG ± SD**
Liver	29.31	23.68	30.07	26.67	25.62	**27.07 ± 2.64**	1.30	1.15	**1.22 ± 0.11**
Spleen	75.43	61.28	65.31	88.78	63.90	**70.94 ± 11.33**	1.42	1.39	**1.40 ± 0.02**
Lung	7.49	4.98	11.35	7.02	3.18	**6.80 ± 3.07**	1.33	1.38	**1.36 ± 0.03**
Kidney	27.81	5.67	4.30	4.55	1.54	**8.77 ± 10.75**	1.24	1.23	**1.24 ± 0.01**
Lymph Node	2.21	2.88	6.59	1.17	1.89	**2.95 ± 2.13**	1.48	1.92	**1.70 ± 0.32**
Salivary Gland	1.53	1.24	1.98	1.40	0.78	**1.39 ± 0.43**	1.30	1.23	**1.26 ± 0.04**
Blood	1.79	1.69	1.46	1.15	0.51	**1.32 ± 0.51**	1.44	1.57	**1.51 ± 0.09**
Urine	0.34	0.24	1.50	1.34	1.02	**0.89 ± 0.58**	0.68	0.58	**0.63 ± 0.07**

Table S5. 24 h ex vivo biodistribution results of [^{89}Zr]Zr(oxinate)$_4$–liposome-injected animals, and the ^{89}Zr control group (I.D./whole organ percentages): High liver and spleen uptake vs. bone uptake in the control group.

	I.D./whole organ %								
	[^{89}Zr]Zr(oxinate)$_4$–Liposome						**^{89}Zr Control**		
Animal No.	1*	2*	3**	4**	5**	**AVG ± SD**	6**	7**	**AVG ± SD**
Liver	34.06	27.51	33.86	28.91	25.98	**30.06 ± 3.70**	1.92	1.66	**1.79 ± 0.19**
Spleen	4.55	3.68	7.18	6.03	5.41	**5.37 ± 1.35**	0.11	0.10	**0.11 ± 0.01**
Lung	-	-	2.17	1.84	0.56	**1.52 ± 0.85**	0.28	0.22	**0.25 ± 0.04**

Kidney	9.68	1.97	1.80	1.93	0.60	**3.20 ± 3.67**	0.57	0.53	**0.55 ± 0.03**
Salivary Gland	-	-	0.16	0.06	0.07	**0.09 ± 0.05**	0.10	0.11	**0.10 ± 0.01**
Blood*	2.61	2.47	2.13	1.68	0.75	**1.93 ± 0.75**	0.65	1.34	**0.99 ± 0.49**

* Extrapolated from I.D./g organ values and from calculated organ weights (using empiric body weight percentage). ** Calculated by real whole-organ activities and whole-organ weights, except for the blood values.