Supplementary Information for:

Synthesis and biological evaluation of RGD peptides with the ^{99m}Tc/^{188}Re chelated iminodiacetate core: Highly enhanced uptake and excretion kinetics of theranostics against tumor angiogenesis

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Synthesis of ^{99m}Tc-IDA-D-[c(RADfK)]$_2$ and $^{185/187}$Re-IDA-D-[c(RADfK)]$_2$

The cyclic pentapeptides, i.e., cyclic-Arg(Pbf)-Gly-Asp(O^{t}Bu)-D-Phe-Lys-NH_2 and cyclic-Arg(Pbf)-Ala-Asp(O^{t}Bu)-D-Phe-Lys-NH_2 (for ^{99m}Tc-IDA-D-[c(RADfK)]$_2$) were prepared using solid support coupling protocol according to previously described methods.[21,27] The ^{99m}Tc-IDA-D-[c(RADfK)]$_2$ (t_R = 18.6 min by HPLC conditon A), $^{185/187}$Re-IDA-D-[c(RADfK)]$_2$ [t_R = 19.2 min by HPLC conditon A, MS (ESI) *m*/*z* 1448.7 $(M+H)^+$] and IDA-D-[c(RADfK)]$_2$ [MS (ESI) *m*/*z* 1448.7 $(M+H)^+$] were prepared by according to same procedure of ^{99m}Tc-IDA-D-[c(RGDfK)]$_2$, $^{185/187}$Re-IDA-D-[c(RGDfK)]$_2$ and IDA-D-[c(RGDfK)]$_2$, respectively.

Table 1. HPLC data of $^{185/187}$Re or ^{99m}Tc-IDA-RGD Analogs (1-6)

[a]HPLC condition A

- semi-Preparative column (Agilent, Eclipse XDB-C18 column, 5 μ, 9.4 × 250 mm)
- UV detector (Thermo, SectraSystem UV3000 set at 214 nm) with a gamma-ray detector (Bioscan, Flow-Count fitted with a NaI(Tl) detector)
- Eluant: 0 min (20% CH_3CN/H_2O/0.1% TFA); 5 min (20% CH_3CN/H_2O/0.1% TFA); 40 min (60% CH_3CN/H_2O/0.1% TFA)
- Flow rate: 2 mL/min

[b]HPLC condition B

- Analytical column (YMC, YMC-triart-C18 column, 5 μ, 4.6 × 250 mm)
- UV detector (Thermo, SectraSystem UV2000 set at 214 nm)
- Eluant: 0 min (20% CH_3CN/H_2O/0.1% TFA); 5 min (20% CH_3CN/H_2O/0.1% TFA); 20 min (80% CH_3CN/H_2O/0.1% TFA)
- Flow rate: 0.7 mL/min

Compound	t_R (min)[a]	t_R (min)[b]	*k'*
1	21.8	15.1	1.90
2	22.1	15.5	1.98
3	19.2	14.8	1.85
4	20.6	15.1	1.90
5	21.4	15.4	1.96
6	18.4	14.7	1.83

Table 2. Extraction efficiency of the organ homogenates and the blood samples 30 min and 120 min postinjection.

	Extraction Efficiency [%][a]	
	30 min	120 min
blood	47.8	55.9
urine	97.1	93.2
tumor	93.2	87.3
liver	86.5	62.3
kidney	95.5	88.6

[a]Amount of activity of soluble fractions, which was eluted form the C-18 Sep-Pak cartridge using acetonitrile.