Supporting Information

Cellular Fate and Performance of Group IV Metal Organic Framework Radioenhancers

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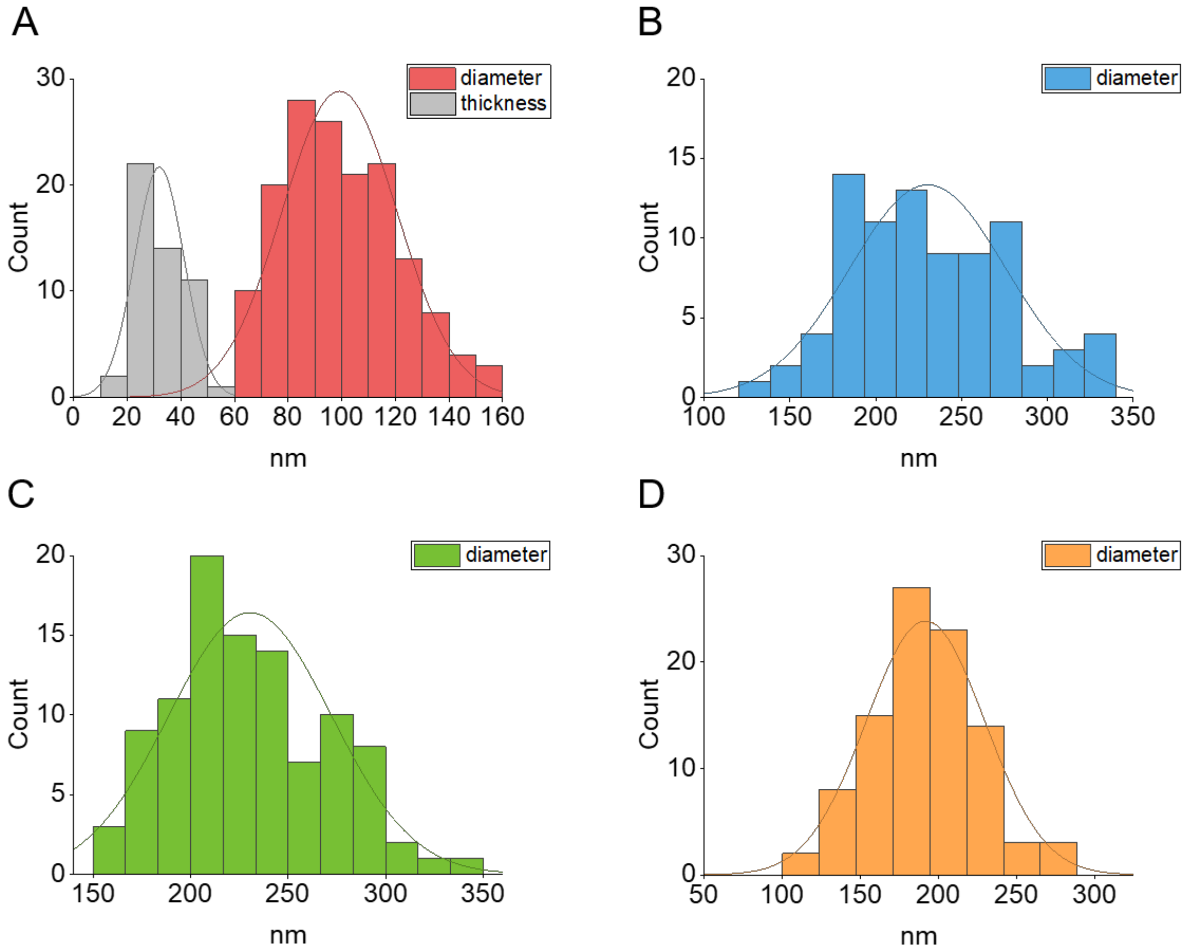


Figure S1. TEM size analysis of nanoMOFs (A) Hf-DBA, (B) Hf-TCPP, (C) Ti-MIL-125, and (D) Ti/Zr-PCN-415 plotted as histograms of at least 80 counts for diameter and 50 counts for disc thickness in case of Hf-DBA.

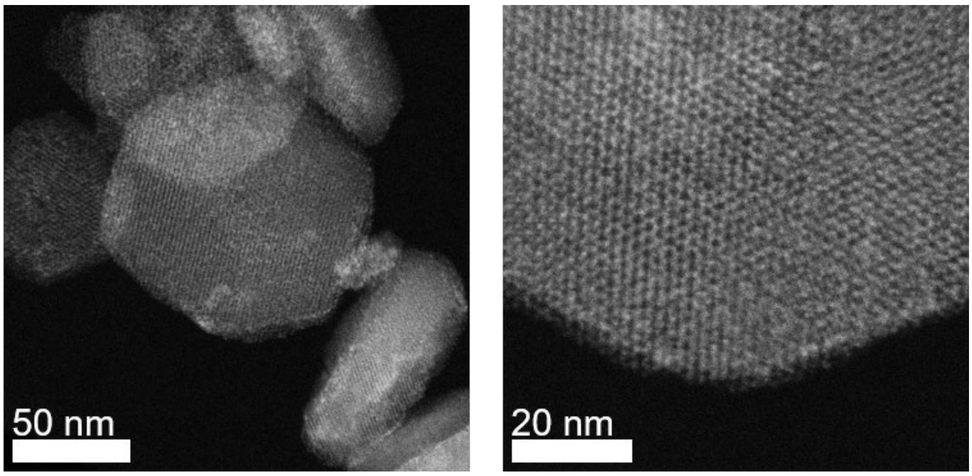


Figure S2. High resolution HAADF STEM image of as-prepared Hf-DBA nanoMOF.

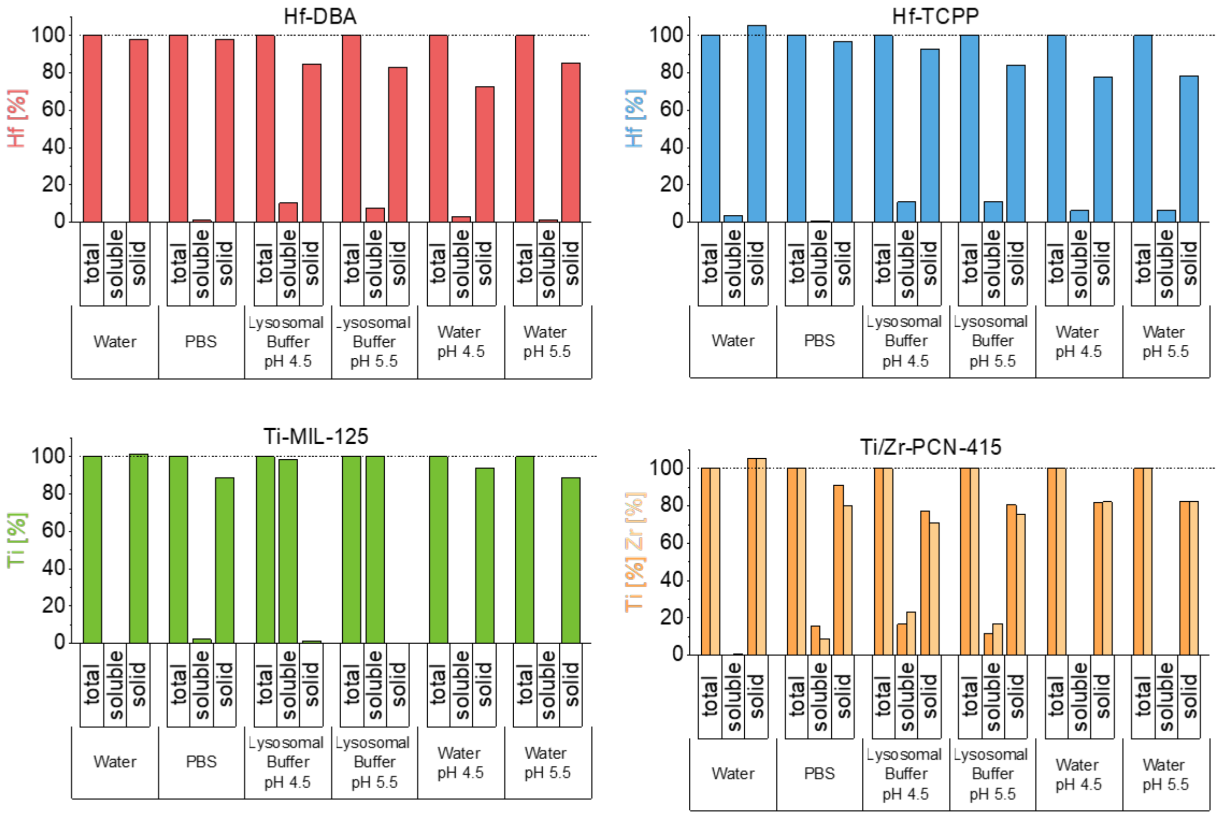


Figure S3. Stability of nanoMOFs (1 mg per mL incubation at 37°C for 24 hrs) in water, phosphate buffered saline (PBS), lysosomal buffer (pH 4.5 and 5.5) and HNO_3 acidified water (pH 4.5 and 5.5). Concentration of the corresponding metals Hf, Zr and Ti was analyzed by ICP-OES in the total fraction and the soluble and solid fractions (separated by high-speed centrifugation).

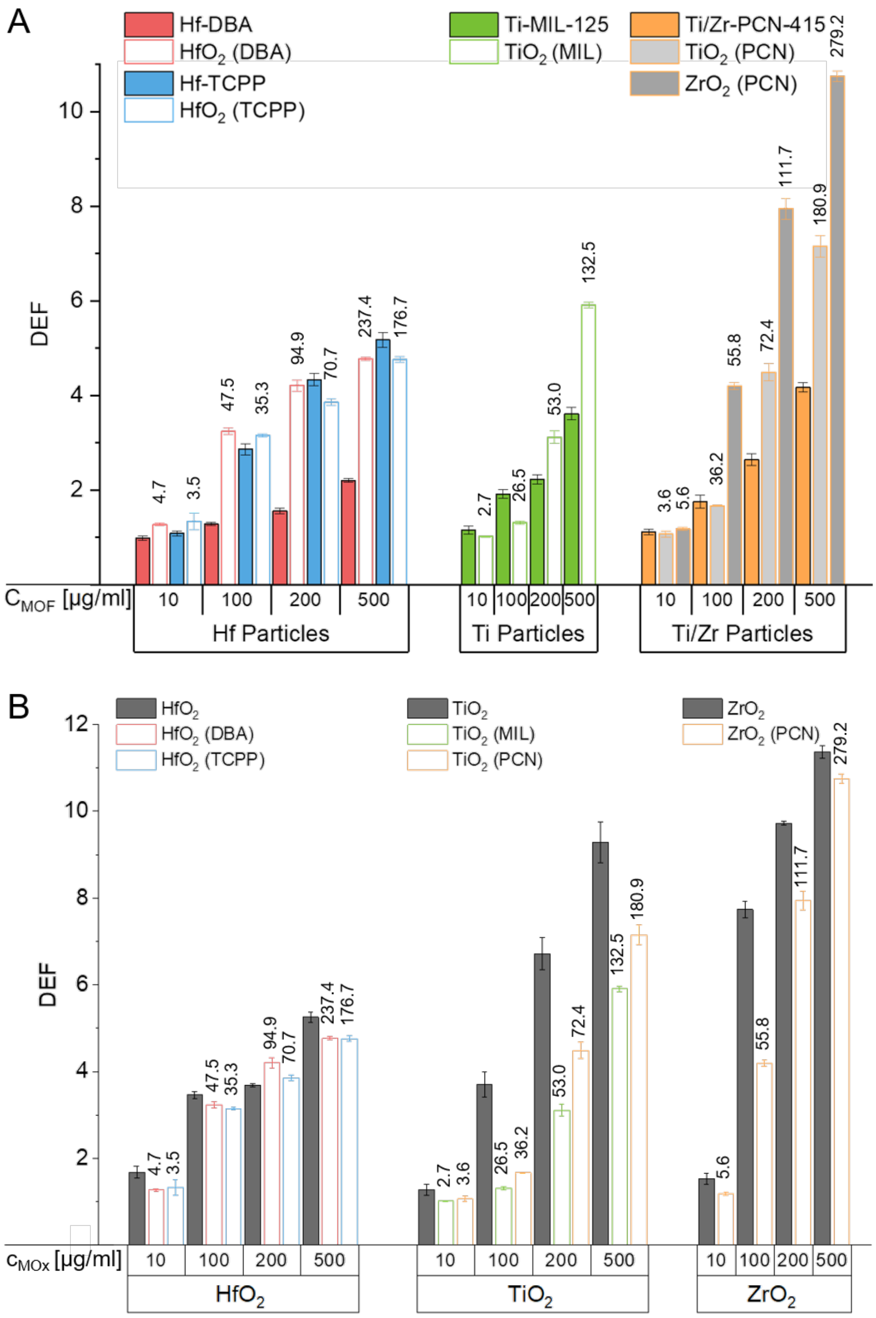
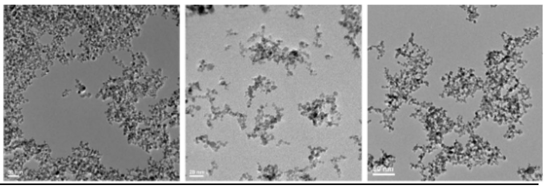


Figure S4. Dose enhancement factors (DEF) calculated based on reactive oxygen species generation for the different nanoMOFs as a (A) function of nanoMOF mass concentration and benchmarking against the corresponding equi-molar dosed metal oxides in buffer (cell-free) conditions. Dose enhancement factors for (B) absolute masses of HfO_2, TiO_2 and ZrO_2 against the corresponding equi-molar dosed metal oxides in buffer conditions. Absolut mass of equi-molar dosed oxide nanoparticle given in µg per mL above the respective bars.



Nanoparticle	TiO_2	ZrO_2	HfO_2
SSA [m_2/g]	235	161	89
d_{TEM} [nm]	5	5	5
D_{DLS} [nm]	142	158	158

Figure S5. Oxide nanoparticle characterization data for the flame spray pyrolysis synthesized metal oxide nanoparticle batches from Gerken et al.[42] with specific surface area (SSA) measurement and TEM and DLS size analysis.

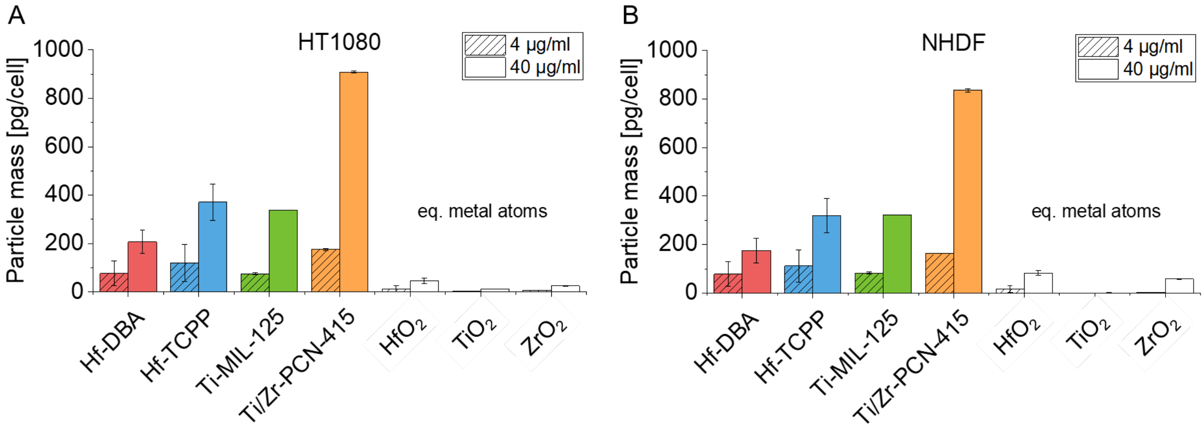


Figure S6. Particle mass in HT1080 (A) and NHDF cells (B) after 24h cellular exposure to nanoMOFs and corresponding oxide nanoparticles at different sub-toxic concentrations analyzed with ICP-OES.

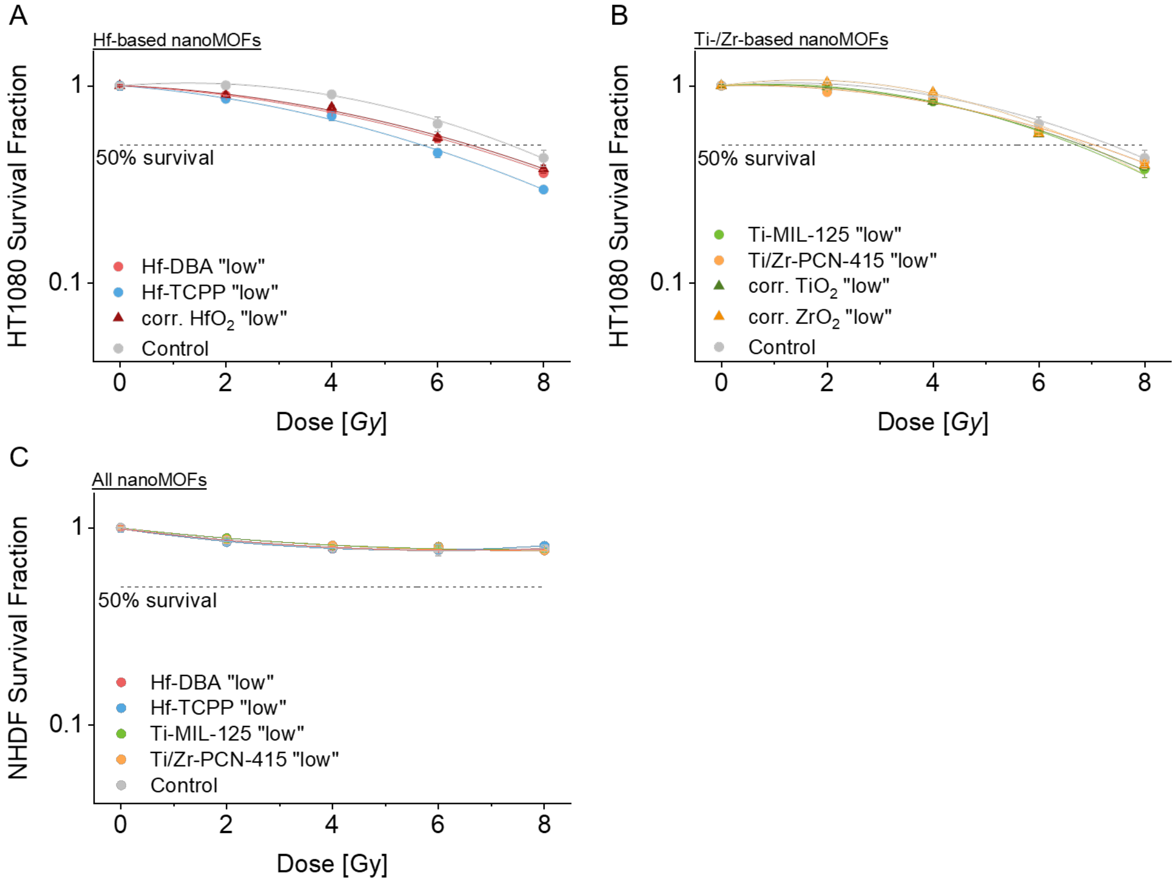


Figure S7. Radioenhancement effects in HT1080 for (A) Hf-based nanoMOFs with equi-dosed HfO_2 and (B) Ti-/Zr-based nano-MOFs with equi-dosed TiO_2 and ZiO_2, (equimolar dose of oxide nanoparticles). Radioenhancement effects in NHDF cells (C) for all nanoMOFs. Treatment doses at 4 µg per mL.

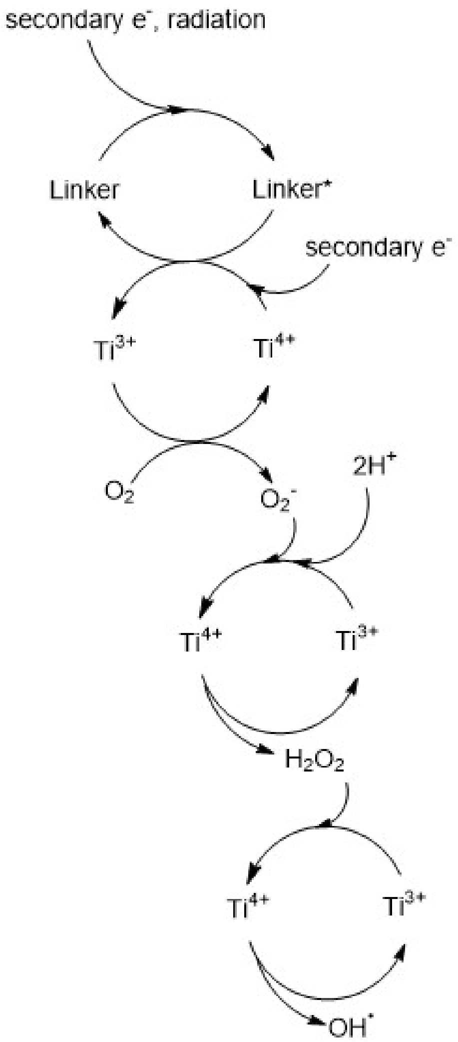


Figure S8. Possible catalytic cycle for a linker-mediated metal reduction. Adapted in parts from Liu et al.[45]

Table S1. Dynamic lights scattering data for nanoMOFs dispersed in water (d_{H2O}), ethanol (d_{EtOH}) and cell culture media (d_{Medium}).

MOF	d_{H2O}	PDI_{H2O}	d_{EtOH}	PDI_{EtOH}	d_{Medium}	PDI_{Medium}
Hf-DBA	103.4 (±28) nm	0.166 (±0.01)	147.0 (±17.7) nm	0.204 (±0.03)	623.2 (±70) nm	0.248 (±0.02)
Hf-TCPP	228.3 (±34) nm	0.164 (±0.03)	229.4 (±51.0) nm	0.234 (±0.03)	360.8 (±98) nm	0.181 (±0.01)
Ti-MIL-125	824.7 (±132) nm	0.252 (±0.04)	217.3 (±13.3) nm	0.175 (±0.01)	707.2 (±92) nm	0.281 (±0.01)
Ti/Zr-PCN-415	779.3 (±102) nm	0.181 (±0.06)	247.1 (±48.5) nm	0.205 (±0.03)	506.4 (±19) nm	0.307 (±0.05)

Table S2. Inductively coupled plasma spectroscopy (ICP-OES) analysis of nanoMOFs.

MOF	Metal per mass [%]	Theoretical total metal per mass [%]	Metal per mass [mol/mg]
Hf-DBA	36.90	38.89	2.07×10^{-6}
Hf-TCPP	28.19	24.53	1.58×10^{-6}
Ti-MIL-125	17.72	23.16	3.70×10^{-6}
Ti/Zr-PCN-415	21.85 (Ti: 14.73 Zr: 7.11)	19.18	3.86×10^{-6}

Table S3. Carbon hydrogen nitrogen (CHN) analysis of nanoMOFs including recovery [%] compared to theoretical values using metal data from ICP-OES (Table S2).

MOF	theoretical Formula	% calculated					% measured CHN-Analyzer		
		C	H	N	O	Metal	C	H	N
Hf-DBA	$C_{180}H_{149}N_9O_{58}Hf_{12}$	39.25	2.73	2.29	16.85	38.89	40.22	3.58	2.26
Hf-TCPP	$C_{192}H_{124}N_{16}O_{40}Hf_6$	52.82	2.86	5.13	14.66	24.53	43.02	3.56	4.28
Ti-MIL-125	$C_{48}H_{34}N_6O_{36}Ti_8$	34.86	2.07	5.08	34.83	23.16	31.74	2.70	0.67
Ti/Zr-PCN-415	$C_{144}H_{96}O_{108}Ti_{10}Zr_4$	39.33	2.20	0.00	39.29	19.18	34.18	5.03	5.18

	Theoretical ratio		measured ratio CHN-Analyzer		% recovery
	C/N	C/H	C/N	C/H	CHN_{CHN}+ICP_{Metal}+$theoretical_O$
Hf-DBA	17.15	14.39	17.84	11.23	99.80
Hf-TCPP	10.29	18.45	10.05	12.08	93.71
Ti-MIL-125	6.86	16.82	6.60	6.80	87.66
Ti/Zr-PCN-415	-	17.87		11.74	105.51

Table S4. Dose enhancement factor (DEFs) at 8Gy radiation, dose modifying ratio (DMR) at 50% survival and the 50% lethal dose (LD) for all used nanoMOFs and concentrations with corresponding oxide nanoparticle in HT1080 cells.

HT1080 MOFs	Hf-DBA 40 µg per mL	Hf-DBA 4 µg per mL	Hf-TCPP 4 µg per mL	Ti-MIL-125 40 µg per mL	Ti-MIL-125 4 µg per mL	Ti/Zr-PCN-415 40 µg per mL	Ti/Zr-PCN-415 4 µg per mL
DEF_{8Gy}	1.28	1.10	1.29	3.88	1.09	2.30	1.03
$DMR_{50\%}$	1.36	1.14	1.37	3.84	0.96	2.20	0.91
LD_{50} [a)]	5.40 Gy	6.48 Gy	5.38 Gy	1.67 Gy	6.71 Gy	2.91 Gy	7.05 Gy

Oxide NP	corr. HfO_2 to 40 µg per mL	corr. HfO_2 to 4 µg per mL		corr. TiO_2 to 40 µg per mL	corr. TiO_2 to 4 µg per mL	corr. ZrO_2 to 40 µg per mL	corr. ZrO_2 to 4 µg per mL
DEF_{8Gy}	1.07	1.08		1.34	1.07	1.08	1.08
$DMR_{50\%}$	1.09	1.11		1.19	0.94	0.93	0.93
LD_{50}*	6.75 Gy	6.62 Gy		5.39 Gy	6.82 Gy	6.91 Gy	6.90 Gy

[a)]Control LD_{50} 7.37 Gy