

Investigation of zirconium interactions with a DOTA based theranostic hybrid nanoparticle using X-ray absorption spectroscopy.

Ilyes Mahti^{1†}, Laurence Berthon¹, Charles Truillet², Bertrand Kuhnast², Thomas Dumas¹,
Dominique Guillaumont^{1*}

¹CEA, DES, ISEC, DMRC, Univ Montpellier, Marcoule, France

²Laboratoire d'Imagerie Biomédicale Multimodale Paris Saclay CEA, INSERM, CNRS, Université Paris-Saclay
Orsay 91401, France

[†]Current affiliation: Chalmers University of Technology, Department of Chemistry and Chemical Engineering,
Nuclear Chemistry and Industrial Materials Recycling, Gothenburg, SE-412 96, Sweden

*Corresponding author: dominique.guillaumont@cea.fr

Supporting information

Structural parameters of optimized geometries

The x, y and z coordinates of the optimized geometries used to simulate the EXAFS spectra (Zr-DOTA C1 and C2) are shown in Table S1 and Table S2.

Table S1: x, y and z coordinates of the $[Zr(DOTA)(H_2O)_4]$ complex (C1).

Atom	x	y	z
Zr	-1.71405	-0.01308	0.017138
O	-1.2673	-1.1019	-1.79339
O	-1.00888	-3.2866	-1.43476
N	1.5754	-1.06156	-2.06594
C	2.844171	-1.57892	-1.59042
H	3.503701	-0.73406	-1.37431
H	3.364854	-2.17629	-2.36747
C	1.668604	0.087807	-2.95515
H	2.260071	-0.15254	-3.86421
H	0.649434	0.310577	-3.28817
C	0.726608	-2.11036	-2.616
H	1.211709	-3.08955	-2.55784
H	0.51194	-1.93157	-3.68148
C	-0.60459	-2.20678	-1.88963
O	-0.16194	-1.22053	0.686953
O	-0.81588	-2.54751	2.355736
N	2.409555	-1.74668	0.882779
C	3.454467	-0.94547	1.469211
H	4.108137	-0.60369	0.659727
H	4.111015	-1.52945	2.147197
C	2.747543	-2.45142	-0.33324
H	3.708103	-2.99699	-0.24223
H	1.982517	-3.21764	-0.49826
C	1.535637	-2.43787	1.789592
H	1.792481	-2.22106	2.83366
H	1.60137	-3.53422	1.704492
C	0.065742	-2.06278	1.623021
O	-1.4202	1.417153	-1.48684
O	-1.56444	3.5067	-0.70931
N	1.412496	2.050553	-1.40208
C	2.261178	1.367358	-2.36173
H	3.214378	1.140866	-1.87669
H	2.520533	2.025605	-3.21416
Atom	x	y	z
C	2.136237	2.832669	-0.41172
H	2.827699	3.554769	-0.8933
H	1.393807	3.440357	0.115467
C	0.368031	2.854825	-2.02556
H	0.238903	2.541596	-3.06743
H	0.606236	3.929079	-2.02532
C	-0.97275	2.62973	-1.3391
O	-0.55687	1.38818	1.065894
O	-0.79063	1.170139	3.2775
N	2.196342	1.252766	1.547067
C	2.958656	2.059816	0.620793
H	3.66594	1.402352	0.104847
H	3.583892	2.81327	1.145413
C	2.970535	0.264852	2.27424
H	3.863894	0.708732	2.760806
H	2.34086	-0.10093	3.093013
C	1.295404	1.99736	2.406658
H	1.276826	3.057829	2.127257
H	1.586927	1.95759	3.464055
C	-0.12752	1.477872	2.279073
O	-3.14912	1.769761	0.58379
H	-3.97943	1.688049	0.100587
H	-2.67351	2.557582	0.192905
O	-2.45096	-0.39042	2.113797
H	-2.00828	-1.21868	2.421035
H	-2.01821	0.328279	2.679647
O	-3.83144	-0.28427	-1.05275
H	-3.99746	-1.19495	-0.74571
H	-3.5636	-0.36391	-1.97969
O	-2.69265	-2.24782	0.201803
H	-2.14036	-2.78056	-0.46518
H	-2.42402	-2.6079	1.065419

Table S2: x, y and z coordinates of the Zr-DOTA complex (C2).

Atom	x	y	z
Zr	0	0	0.441503
O	0	1.93399	1.349734
O	-1.93399	0	1.349734
O	1.93399	0	1.349734
O	0	-1.93399	1.349734
N	1.368946	1.549646	-0.94191
N	-1.54965	1.368946	-0.94191
N	-1.36895	-1.54965	-0.94191
N	1.549646	-1.36895	-0.94191
C	0.886184	2.861147	1.14135
C	-0.88618	-2.86115	1.14135
C	-2.86115	0.886184	1.14135
C	2.861147	-0.88618	1.14135
C	1.833109	2.612346	-0.02239
C	2.612346	-1.83311	-0.02239
C	-1.83311	-2.61235	-0.02239
C	-2.61235	1.833109	-0.02239
C	0.538707	2.132093	-2.02518
C	-2.13209	0.538707	-2.02518
C	2.132093	-0.53871	-2.02518
C	-0.53871	-2.13209	-2.02518
C	2.526841	0.836186	-1.5347
C	-0.83619	2.526841	-1.5347
C	0.836186	-2.52684	-1.5347
C	-2.52684	-0.83619	-1.5347
H	-0.45857	-1.39754	-2.82975
H	1.39754	-0.45857	-2.82975
H	0.458569	1.39754	-2.82975
H	-1.39754	0.458569	-2.82975
H	-3.30651	-0.758	-0.77468
H	3.306511	0.757995	-0.77468
H	-0.758	3.306511	-0.77468
H	0.757995	-3.30651	-0.77468
H	2.779302	2.30228	0.428093
H	-2.7793	-2.30228	0.428093
H	2.30228	-2.7793	0.428093
H	-2.30228	2.779302	0.428093
H	3.549783	-2.01776	-0.55867
H	2.017759	3.549783	-0.55867
H	-3.54978	2.017759	-0.55867
H	-2.01776	-3.54978	-0.55867
O	1.00568	3.872197	1.822459
O	-3.8722	1.00568	1.822459
O	3.872197	-1.00568	1.822459
O	-1.00568	-3.8722	1.822459
H	1.040462	3.009734	-2.45352
H	-3.00973	1.040462	-2.45352
H	-1.04046	-3.00973	-2.45352
H	3.009734	-1.04046	-2.45352
H	-1.41462	2.951423	-2.36517
H	2.951423	1.414617	-2.36517
H	1.414617	-2.95142	-2.36517
H	-2.95142	-1.41462	-2.36517

Influence of DOTAGA, M:L ratio and carbonates on Zr AGuIX interactions

Figure S1 and Figure S2 show the XANES and EXAFS spectra obtained for Zr-DOTAGA, Zr-B (Zr:DOTA ratio of 1 : 6) and Zr-C (no carbonates added in the synthesis) compared with the spectra of Zr-AGuIX (presence of carbonate and Zr:DOTA ratio of 1 : 2). Due to concentration problems, only the XANES spectra of Zr-DOTAGA is viable to study. The composition of the samples is shown in Table S3. First, the XANES spectrum of Zr-DOTAGA solution is very similar to the Zr-DOTA complex one. It seems that there is the same chemical environment around Zr in both structures. Decreasing the Zr:DOTA ratio does not affect the coordination mode of Zr at the nanoparticle. The XAS spectra of Zr-AGuIX and Zr-B are identical. In the absence of carbonate, the spectra are only slightly modified compared with those of Zr-AGuIX. The presence of carbonates seems to have little to no influence on the coordination mode of zirconium at the nanoparticle. The coordination number turns out to be the same, 6, given the shape of the XANES spectrum.

Table S3: Compositions of the samples, Concentrations are in mol·L⁻¹.

	Zr-DOTA	Zr-DOTAGA	Zr-AGuIX	Zr-B	Zr-C
[DOTA]	5.10 ⁻³	<5	1.4.10 ^{-3*}	4.2.10 ⁻³	1.4
[AGuIX]	-	-	7.10 ⁻²	-	70
[Zr]	5.10 ⁻³	<5	7.10 ⁻⁴	7.10 ⁻⁴	0.7
[Na ₂ CO ₃]	-	-	7.10 ⁻²	7.10 ⁻²	-
[HEPES]	-	-	4.3.10 ⁻¹	4.3.10 ⁻¹	430
pH	5.7	-	7	7	6.7

* The [DOTA] in the Zr-AGuIX sample is evaluated considering that free DOTA accounts for 2% of the total AGuIX content.

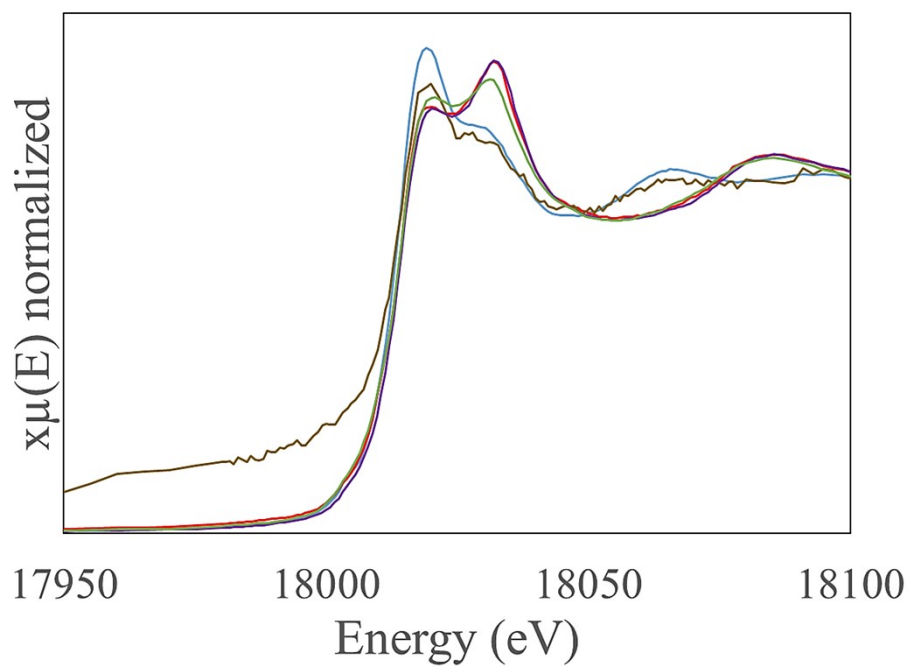


Figure S1: K-edge XANES spectra of Zr-DOTA complex (blue), Zr-DOTAGA complex (brown), Zr-AGuIX (red), Zr-AGuIX B (purple) and Zr AGuIX C (green) solutions.

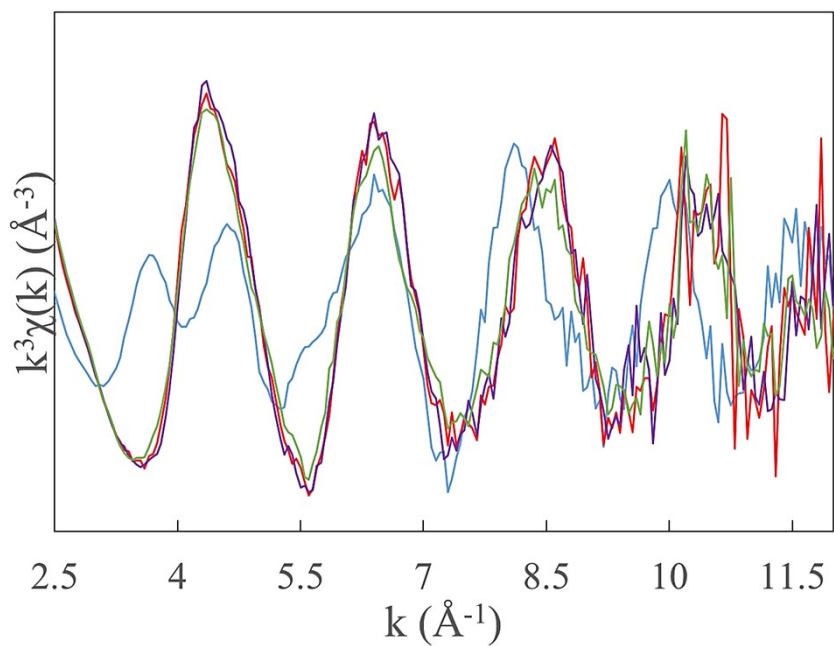


Figure S2: K-edge EXAFS spectra of Zr-DOTA complex (blue), Zr-AGuIX (red), Zr-AGuIX B (purple) and Zr AGuIX C (green) solutions.