Supporting Information to

Internal Structure of Gd-doped polymer entrapped-perfluorocarbon nanoparticles affect ^{19}F relaxation

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Table of Content

1 Characterization of nanoparticles and nanocapsules by dynamic light scattering (DLS)

Table S1. Hydrodynamic diameter Dh and polydispersity index PDI of multicore nanoparticles determined by DLS.

	Gd_01		Gd_02	
Gd added [mg]	**D_h [nm]**	**PDI**	**D_h [nm]**	**PDI**
0	196	0.1	-	-
0.2	205	0.1	205	0.2
0.4	298	0.1	194	0.1
0.7	186	0.06	178	0.1
0.9	185	0.05	196	0.07
1.1	225	0.1	263	0.2
2.2	208	0.1	207	0.1
Prohance, 140 mg	180	0.05		

Table S2. Hydrodynamic diameter D_h and polydispersity index PDI of core-shell capsules determined by DLS.

	Gd_01		Gd_02	
Gd added [mg]	**D_h [nm]**	**PDI**	**D_h [nm]**	**PDI**
0	145	0.07	-	-
0.2	161	0.1	160	0.05
1.1	189	0.2	159	0.2
2.2	166	0.03	178	0.2
Prohance, 140 mg	155	0.07	-	-

2 Characterization of nanoparticles and nanocapsules by cryogenic SEM

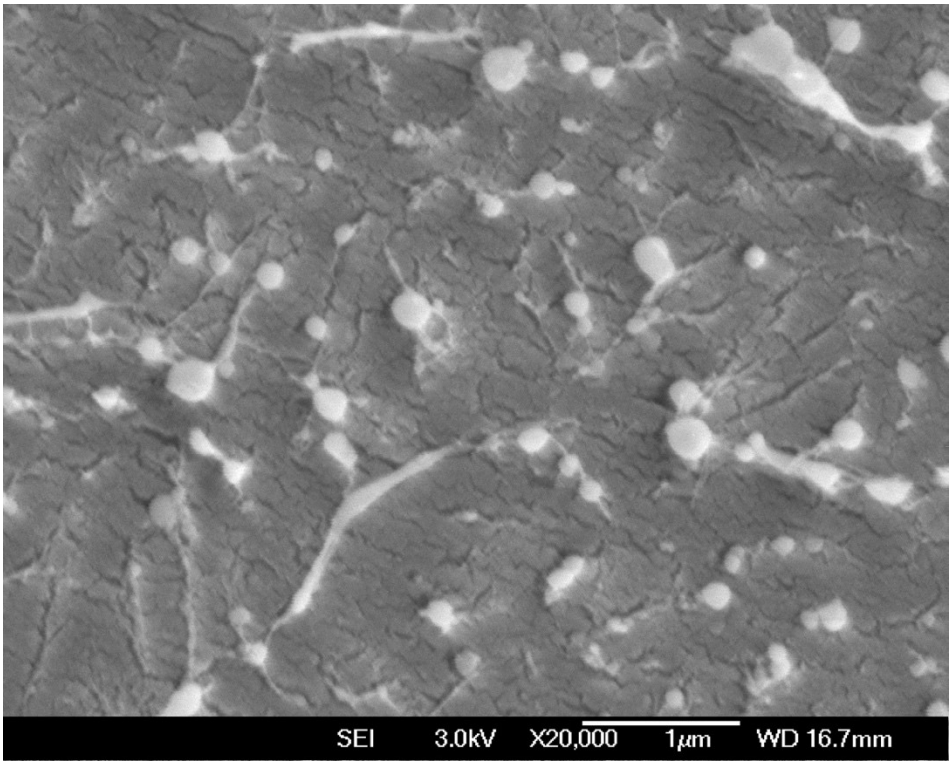

Figure S1. Cryogenic Scanning Electron Microscopy (cryoSEM) micrograph of multicore nanoparticles that were prepared using 1.1 mg Gd_01. c=10 mg mL-1, scale bar 1 µm.

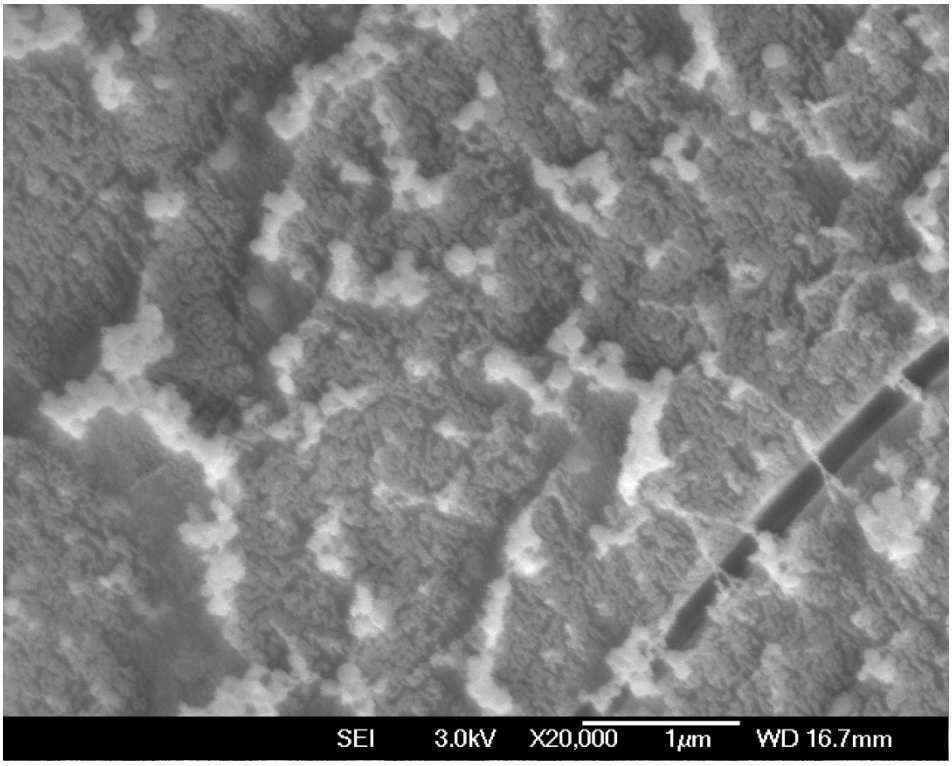

Figure S2. Cryogenic Scanning Electron Microscopy (cryoSEM) micrograph of nanocapsules that were prepared using 1.1 mg Gd_01. c=10 mg mL^{-1}, scale bar 1 µm.

3 Determination of Gd- and PFCE-content

Table S3. Multicore nanoparticles: Determination of Gd-content by ICP MS and PFCE-content by ^{19}F NMR spectroscopy (see Figure 2).

	Gd-content [µg(Gd) mg(NP)$^{-1}$]		PFCE-content [wt.-%]	
Gd added [mg]	**Gd_01**	**Gd_02**	**Gd_01**	**Gd_02**
0	0.0009		22	
0.2	0.72	1.2	29	16
0.4	0.97	1.6	15	13
0.7	1.8	2.9	11	11
0.9	2.4	3.7	11	9
1.1	2.9	5.0	8	1
2.2	7.2	12	3	2
Prohance, 140 mg	0.99		19	

Table S4. Core-shell nanocapsules: Determination of Gd-content by ICP MS and PFCE-content by ^{19}F NMR spectroscopy (see Figure 2).

	Gd-content [µg(Gd) mg(NP)$^{-1}$]		PFCE-content [wt.-%]	
Gd added [mg]	**Gd_01**	**Gd_02**	**Gd_01**	**Gd_02**
0	0.003		12	
0.2	0.97	1.9	32	34
1.1	6.8	9.2	28	33
2.2	11	8.8	30	24
Prohance, 140 mg	0.11		25	

4 Cell Viability Testing

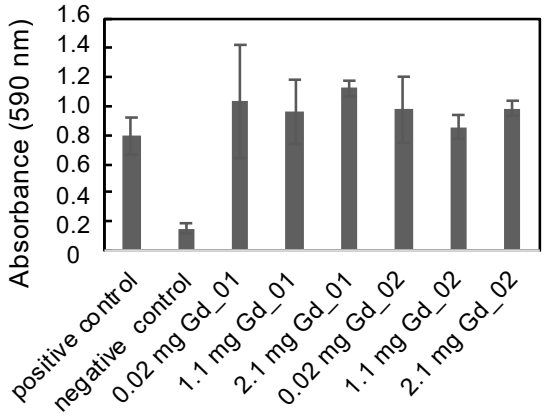

Figure S3. Viability of nanoparticles in RAW macrophages. Cells were incubated with the nanoparticles for 24 h. The cell viability was assessed by the MTT assay (absorbance at 590 nm). All labeled cells are viable and display higher absorbance than a positive control (live cells without nanoparticles. The values represent mean ± SD (n=2).

5 Measurements of the Relaxation Rates by ^{19}F NMR spectroscopy

Table S5. Relaxation times and rates of multicore nanoparticles with Gd_01 (see Figure 3).

Gd_01 [µg(Gd) mg(NP)$^{-1}$]	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**
0.72	0.91	1.1	0.63	1.6
0.97	0.75	1.3	0.065	16
1.8	0.59	1.7	0.017	59
2.4	0.60	1.7	0.035	29
2.9	0.68	1.5	0.0061	164
7.2	0.26	3.9	0.0044	230
Prohance 0.99	0.90	1.1	0.65	1.5
No Gd; 0.0009	0.93	1.1	0.69	1.4

Table S6. Relaxation times and rates of multicore nanoparticles with Gd_02 (see Figure 3).

Gd_02 [µg(Gd) mg(NP)$^{-1}$]	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**
1.2	0.91	1.1	0.62	1.6
1.6	0.67	1.5	0.030	33
2.9	0.38	2.6	0.0041	244
3.7	0.40	2.5	0.0060	167
5.0	0.40	2.5	0.0034	298
12	0.12	8.5	0.0025	408
Prohance 0.99	0.90	1.1	0.65	1.5
No Gd; 0.0009	0.93	1.1	0.69	1.4

Table S7. Relaxation times and rates of core-shell nanocapsules with Gd_01 (see Figure 3).

Gd_01 [µg(Gd) mg(NP)$^{-1}$]	T_1 [s]	R_1 [s^{-1}]	T_2 [s]	R_2 [s^{-1}]
0.97	0.84	1.2	0.20	5.0
6.8	0.84	1.2	0.074	13
11	0.80	1.2	0.049	20
Prohance 0.11	0.90	1.1	0.47	2.1
No Gd; 0.003	0.86	1.2	0.37	2.7

Table S8. Relaxation times and rates of core-shell nanocapsules with Gd_02 (see Figure 3).

Gd_02 [µg(Gd) mg(NP)$^{-1}$]	T_1 [s]	R_1 [s^{-1}]	T_2 [s]	R_2 [s^{-1}]
1.9	0.86	1.2	0.12	8.2
9.2	0.82	1.2	0.047	21
8.8	0.83	1.2	0.030	34
Prohance 0.11	0.90	1.1	0.47	2.1
No Gd; 0.003	0.86	1.2	0.37	2.7

6 NMR Spectra of nanoparticles and nanocapsules with different gadolinium content

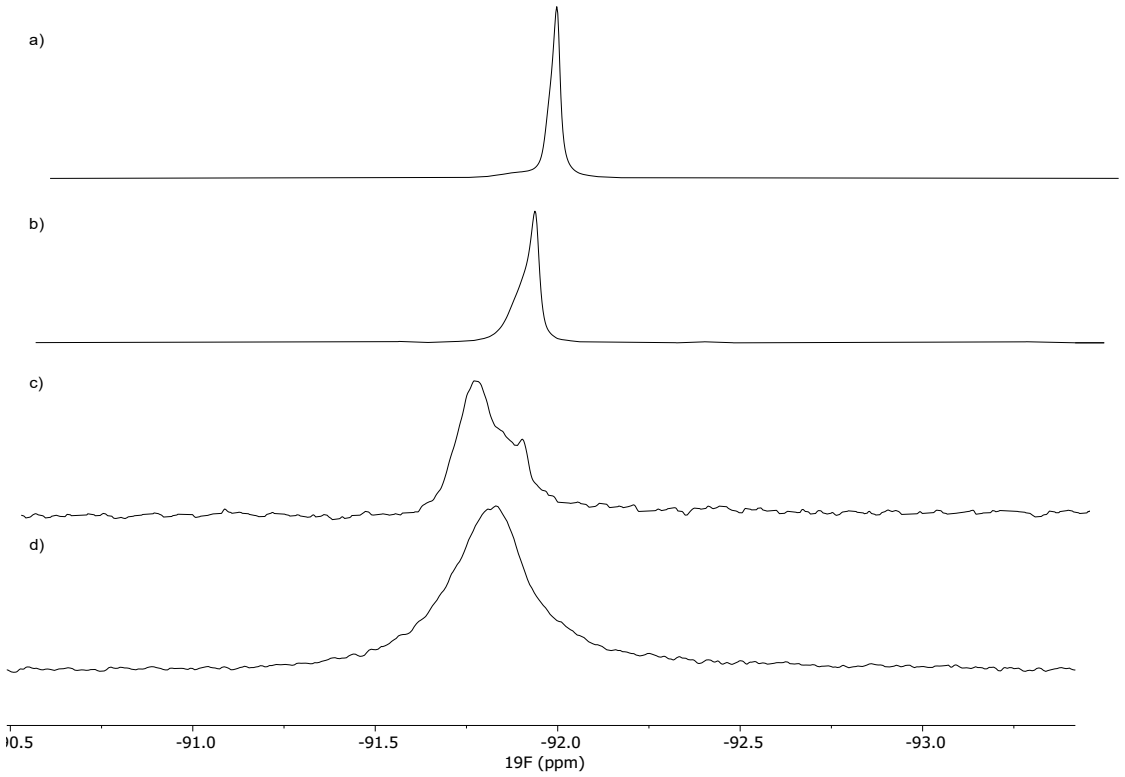

Figure S4. Stacked ^{19}F NMR spectra of PFCE-loaded nanoparticles: (a) Gd-free h (b) Prohance, (c) 5 mg BK21 or (d) 10 mg BK21.

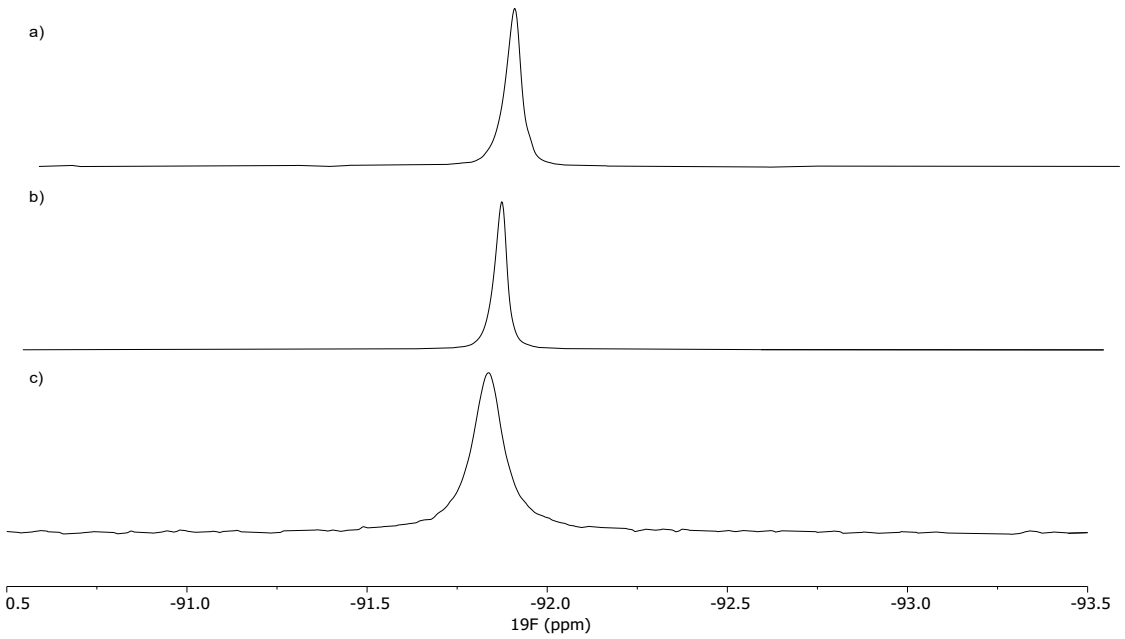

Figure S5. Stacked ^{19}F spectra of PFCE-loaded nanocapsules: (a) Gd-free, (b) Prohance, and (c) 10 mg BK21. Nanocapsules in D_2O, c = 10 mg mL^{-1}, 378 MHz.

7 Quantification of MRI signal

Table S9. Signal-to-Noise ratio (SNR) of ^{19}F and ^{1}H MRI signals, 11.7 T (see Figure 4).

Gd [µg(Gd) mg(NP)$^{-1}$]	PFCE [wt.-%]	^{19}F SNR	^{1}H SNR
Water-ctrl: 0	0	1.0	16
No-Gd NPs: 0	27	7.4	17
0.7	29	8.4	29
1.0	15	2.9	33
1.8	11	1.0	38
2.4	11	1.5	49

8 Relaxation rates/times measurement of nanoparticles in acidic environment

Table S10. Relaxation times and rates of multicore nanoparticles loaded with Gd_01 at different pH (see Figure 5).

	Gd_01				No Gd			
pH	T_1 [s]	R_1 [s^{-1}]	T_2 [s]	R_2 [s^{-1}]	T_1 [s]	R_1 [s^{-1}]	T_2 [s]	R_2 [s^{-1}]
2	0.79	1.26	0.25	4	0.81	1.23	0.4	2.5
3	0.73	1.37	0.16	6.25	0.80	1.25	0.4	2.5
5.5	0.68	1.47	0.04	27.8	0.80	1.25	0.45	2

7	0.65	1.54	0.017	58.8	0.82	1.23	0.45	2.2

Table S11. Relaxation times and rates of multicore nanoparticles loaded with Gd_02 at different pH.

	Gd_02				No Gd			
pH	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**
2	0.77	1.3	0.3	3.3	0.81	1.23	0.4	2.5
3	0.77	1.3	0.22	4.5	0.80	1.25	0.4	2.5
5.5	0.53	1.88	0.017	58.8	0.80	1.25	0.5	2
7	0.57	1.75	0.019	52.6	0.81	1.23	0.45	2.2

Table S12. Relaxation times and rates of core-shell nanocapsules loaded with Gd_01 at different pH.

	Gd_01				No Gd			
pH	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**
2	0.74	1.35	0.062	16.13	0.78	1.28	0.28	3.6
3	0.74	1.35	0.063	15.87	0.79	1.26	0.28	3.6
5.5	0.73	1.37	0.061	16.39	0.78	1.28	0.29	3.4
7	0.73	1.37	0.061	16.39	0.77	1.3	0.27	3.7

Table S13. Relaxation times and rates of core-shell nanocapsules loaded with Gd_02 at different pH.

	Gd_02				No Gd			
pH	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**	**T_1 [s]**	**R_1 [s^{-1}]**	**T_2 [s]**	**R_2 [s^{-1}]**
2	0.73	1.37	0.062	16.13	0.78	1.28	0.28	3.6
3	0.74	1.35	0.061	16.39	0.79	1.26	0.28	3.6
5.5	0.72	1.39	0.061	16.39	0.78	1.28	0.29	3.4
7	0.72	1.39	0.062	16.13	0.77	1.3	0.27	3.7

9 ^{19}F NMR Spectra of multicore nanoparticles when dissolved in basic environment

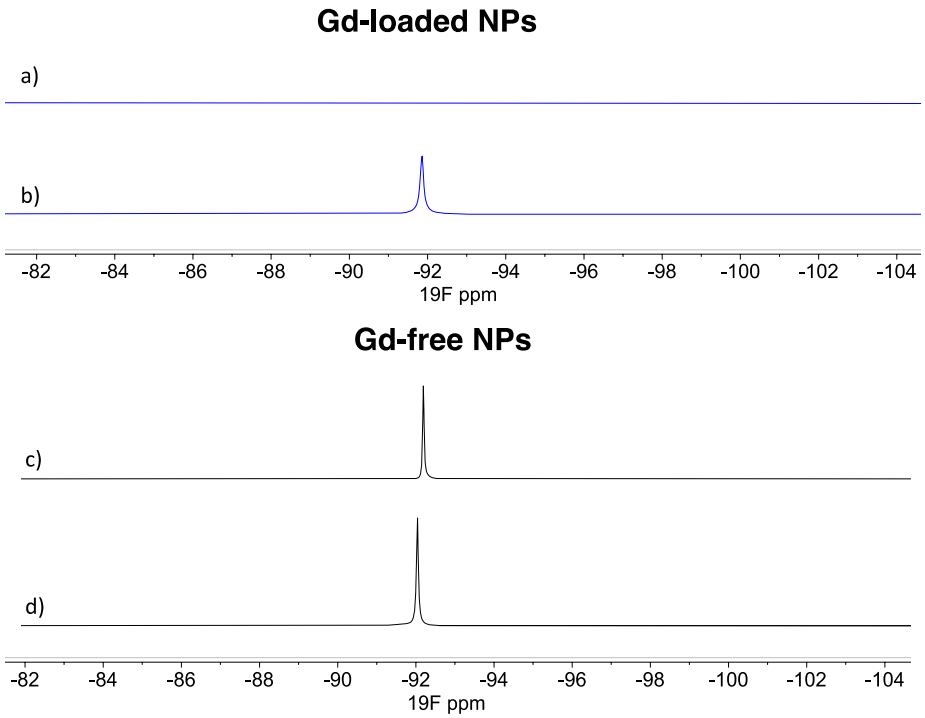

Figure S6. Stacked ^{19}F spectra of gadolinium-loaded and Gd_free multicore nanoparticles when dissolved in: (b and d) neutral (pH 7), and (a and c) basic environment (pH 14). Multicore Nanoparticles: c =10 mg mL^{-1}, 378 MHz.

10 ^{1}H NMR Spectra of multicore nanoparticles loaded with Gd_01

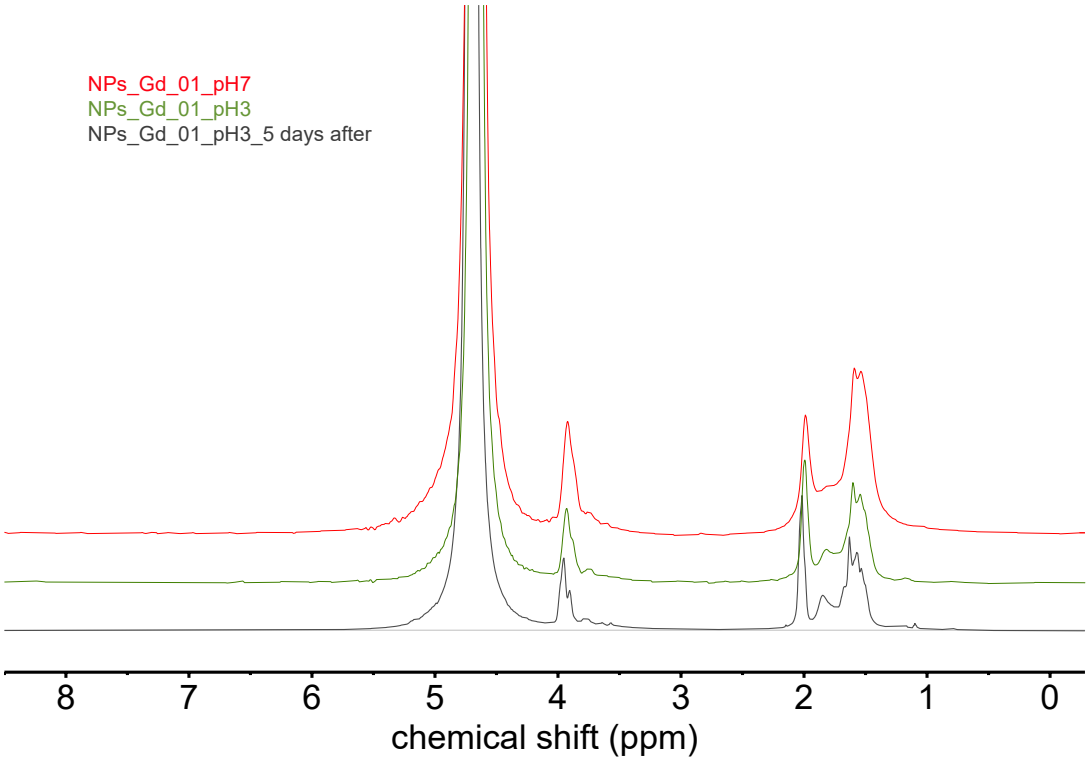

Figure S7. ^{1}H spectral line profile of multicore nanoparticles loaded with Gd_02 at pH 7 and 3, immediately after solubilization and five days after (a) to study the stability in acidic environment. Multicore nanoaprticles in in D2O (pH 7) and acidic solvent (pH 3), 700 MHz, c = 10 mg mL^{-1}.