SUPPORTING INFORMATION

Water-mediated nanostructures for enhanced MRI: impact of water dynamics on relaxometric properties of Gd-DTPA

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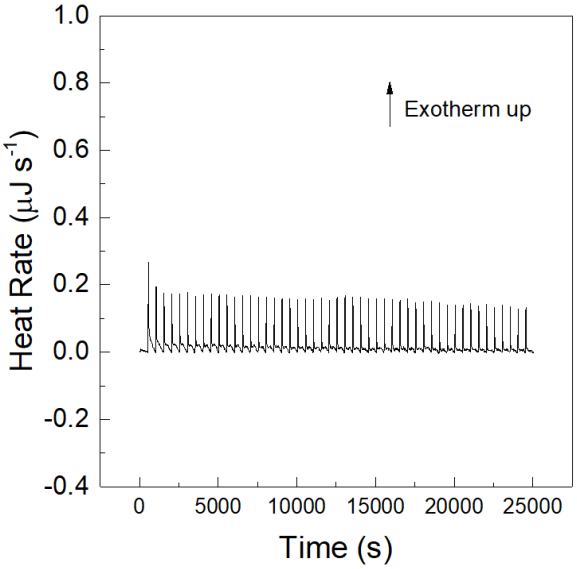

Figure S1. Titration curve of Gd-DTPA solution injected into water at 25 °C.

Table S1. Longitudinal (R1) and transverse (R2) relaxation rates for Gd-DTPA, Gd-DTPA-HA 0.5% and Gd-DTPA-HA 0.5% with DVS 4%. Relaxivities r1 and r2 are also reported.

Gd-DTPA (mM)	**HA 0.5% R1 (s^{-1})**	**HA 0.5% R2 (s^{-1})**	**HA 0.5% with 4% DVS R1 (s^{-1})**	**HA 0.5% with 4% DVS R2 (s^{-1})**	**Gd-DTPA R1 (s^{-1})**	**Gd-DTPA R2 (s^{-1})**
0.010	0.3205 ± 0.001	0.4762 ± 0.0001	0.3055 ± 0.0007	0.4827 ± 0.0001	0.3047 ± 0.0005	0.3642 ± 0.0001
0.020	0.3433 ± 0.0011	0.5155 ± 0.0001	0.3676 ± 0.0014	0.4735 ± 0.0001	0.3345 ± 0.0006	0.349 ± 0.0001
0.030	0.3887 ± 0.0009	0.5522 ± 0.0001	0.3906 ± 0.0015	0.5612 ± 0.0002	0.3683 ± 0.0006	0.3908 ± 0.0001
0.040	0.4144 ± 0.0014	0.6452 ± 0.0002	0.4545 ± 0.0021	0.5432 ± 0.0001	0.4082 ± 0.001	0.4139 ± 0.0001
0.050	0.4566 ± 0.0021	0.6609 ± 0.0003	0.5155 ± 0.0027	0.6821 ± 0.0004	0.4447 ± 0.0011	0.4463 ± 0.0001
0.060	0.495 ± 0.0025	0.7205 ± 0.0004	0.4926 ± 0.0024	0.5931 ± 0.0001	0.4589 ± 0.0013	0.4852 ± 0.0001
0.080	0.5099 ± 0.0026	0.846 ± 0.0006	0.646 ± 0.0029	0.7519 ± 0.0002	0.5176 ± 0.0121	0.5451 ± 0.0002
0.100	0.6057 ± 0.0018	0.9111 ± 0.0005	0.602 ± 0.0033	0.7576 ± 0.0002	-	0.6609 ± 0.0004
0.130	0.6789 ± 0.0032	0.9892 ± 0.0009	0.7117 ± 0.0035	0.9009 ± 0.0002	-	0.7153 ± 0.0001
0.150	0.7564 ± 0.0046	1.0694 ± 0.0008	0.8137 ± 0.0053	0.9524 ± 0.0002	-	1.0661 ± 0.0003
0.200	0.9259 ± 0.0034	1.1138 ± 0.0002	1.1136 ± 0.005	1.4201 ± 0.0004	0.8961 ± 0.004	1.9376 ± 0.0023
0.500	1.7857 ± 0.0319	2.1834 ± 0.0004	-	-	1.6949 ± 0.0287	3.2906 ± 0.0325
1	3.3898 ± 0.046	4.077 ± 0.001	-	-	3.2051 ± 0.0616	0.971 ± 0.002
Relaxivity ($mM^{-1}s^{-1}$)	r1 3.082 ± 0.29	r2 4.443 ± 0.387	r1 3.556 ± 0.487	r2 3.812 ± 0.282	r1 2.904 ± 0.286	r2 2.963 ± 0.385

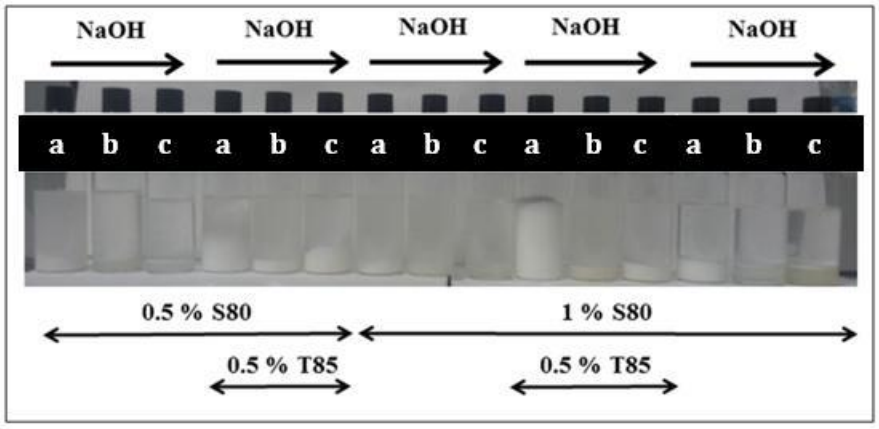

Figure S2. Photografic image of the appearance of emulsions at 25 °C by the effect of increasing concentration of surfactants and NaOH [(a) 0 M; (b) 0.1 M; (c) 0.2 M] on stability of W/O (10/90 and 20/80) emulsion after 12 h.

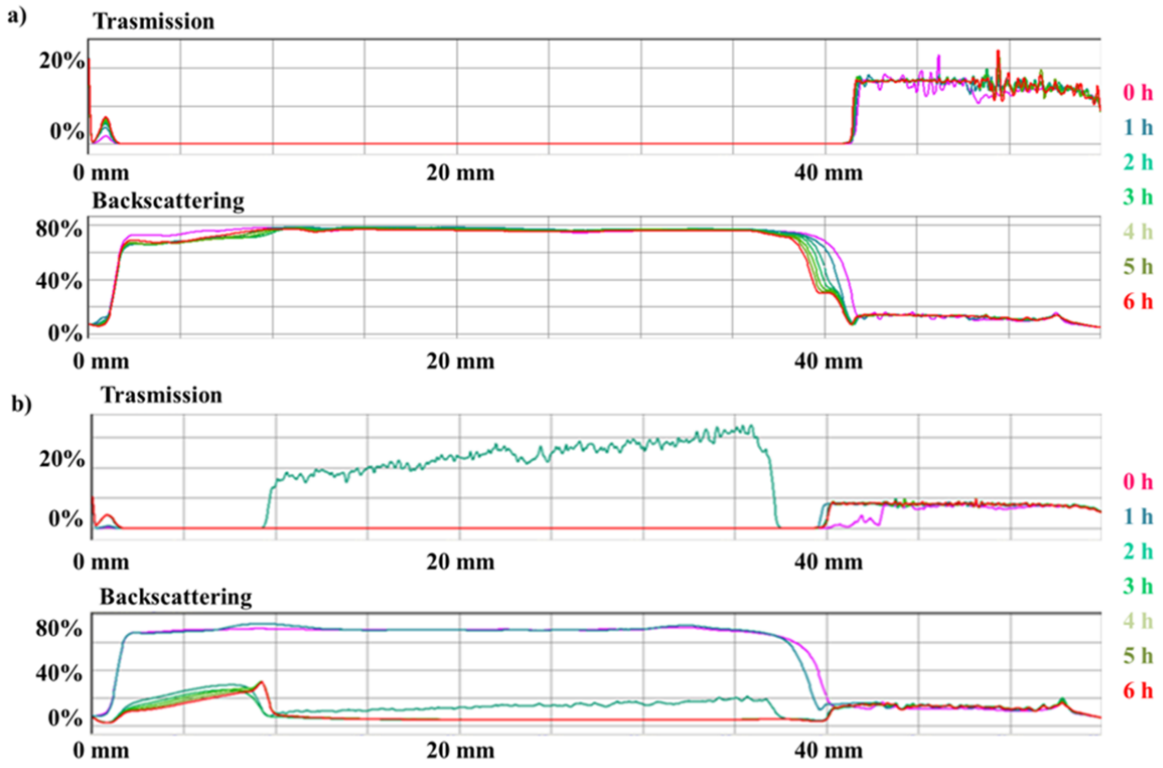

Figure S3. Trasmission and backscattering spectra of W/O (10/90) emulsion (total volume, 20 ml; 5000 rpm, 10 min) with 1% w/v of S80 without (a) and with (b) 0.2 M NaOH.

Table S2. Experimental conditions for production of HA-NPs.

Pd / Pc [a]	HA [b] [% w/v]	NaOH [M]	DVS [c] [% v/v]	Span-80 [% w/v]
10 / 90	0.1	0 0.1 0.2	0.045	1
	0.25	0 0.1 0.2		
	0.5	0 0.1 0.2		

[a] Pd is the volume of the disperse phase, Pc is the volume of the continuous phase; [b] Hyaluronic Acid; [c] Divinyl Sulfone

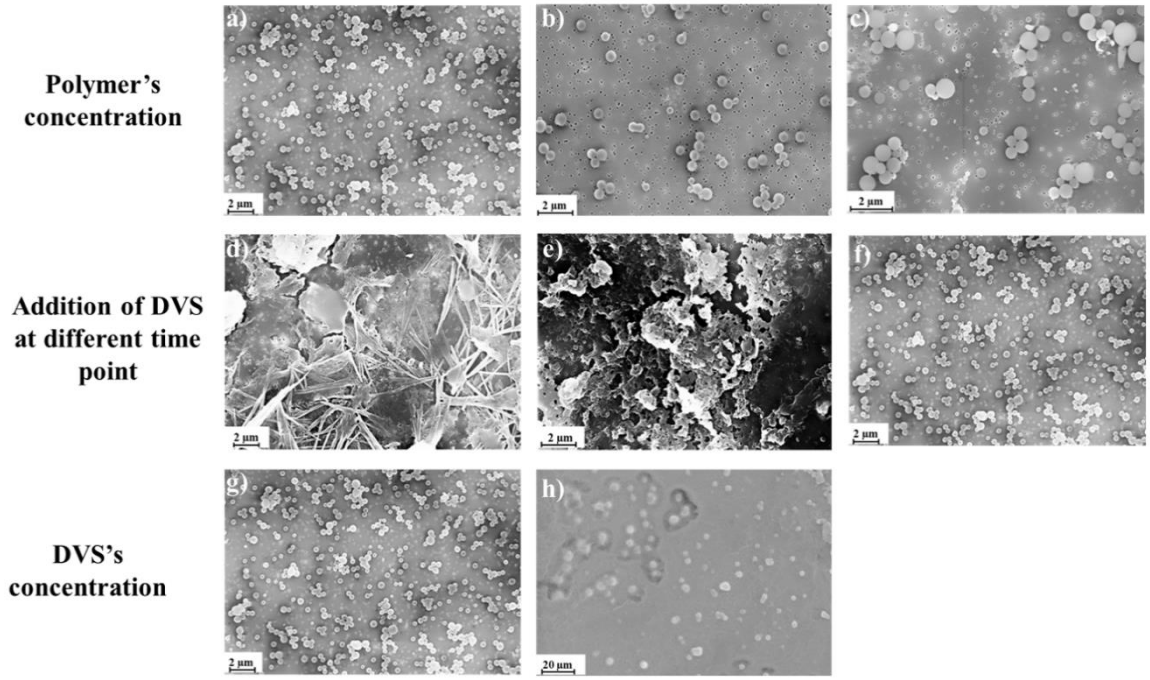

Figure S4. Optimization of HA NPs synthesis. SEM images of crosslinked nanoparticles (0.5% w/v HA; 18 µL (0.045% v/v) of DVS; 40 mL of W/O (10/90) emulsion; 5000 rpm, 10 min, RT, using high-shear homogenizer) under various conditions: **HA's concentration**, (a) 0,5% w/v; (b) 0,25% w/v and (c) 0,1% w/v. **Start of reaction**, (d) during, (e) end and (f) after homogenization. **DVS's concentration**: (g) 18 µL and (h) 200 µL (0.5% v/v).

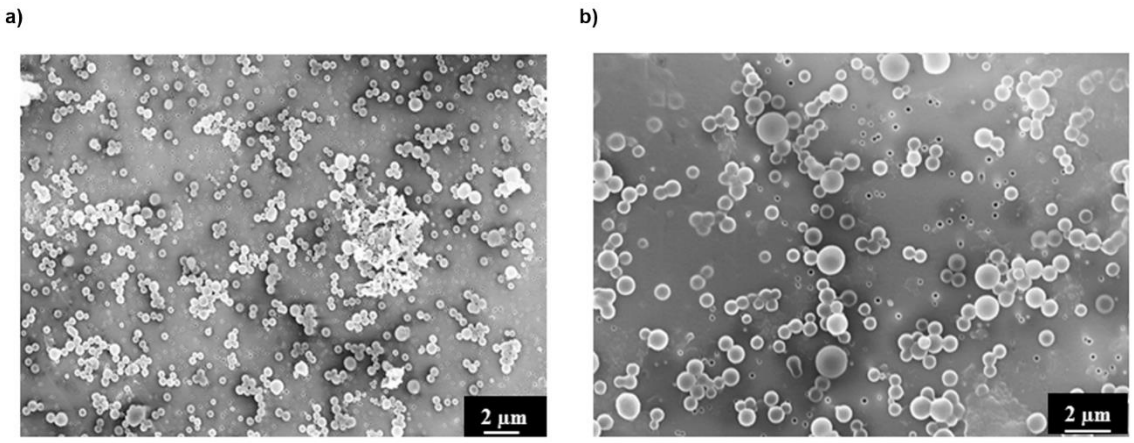

Figure S5. SEM images of crosslinked HA nanoparticles (0.5% w/v of HA; 1% w/v of S80; 0.045% v/v of DVS) without **(a)** and with (**b)** contrast agent.

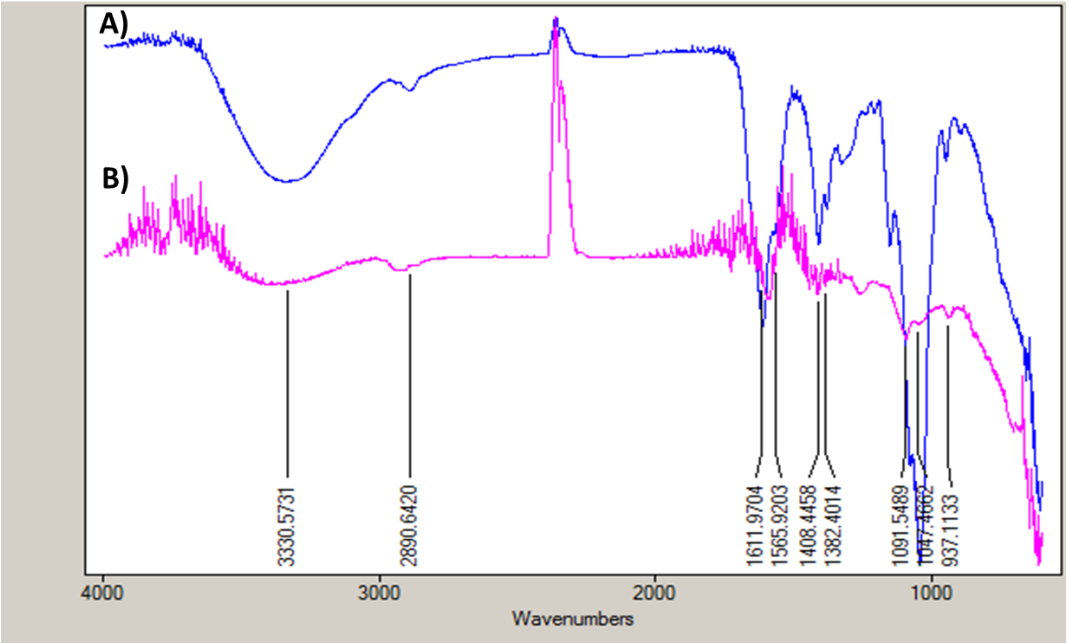

Figure S6. FTIR spectra of A) HA NPs and B) HA NPs encapsulating Gd-DTPA.