

Supporting Information for:

**CEST MRI detectable liposomal hydrogels for multiparametric monitoring in the brain
at 3T**

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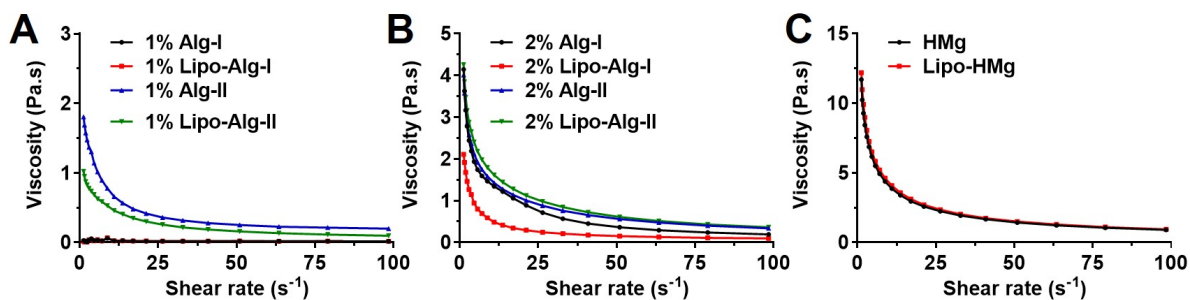


Figure S1. Injectabilities of hydrogels. (A) and (B) were viscosity measurements of 1 wt% and 2 wt% alginate hydrogels with and without liposomes under 40% and 80% crosslinking density under various shear rate; (C) was viscosity measurements of 0.75% HAMC hydrogels with and without liposomes under various shear rate.

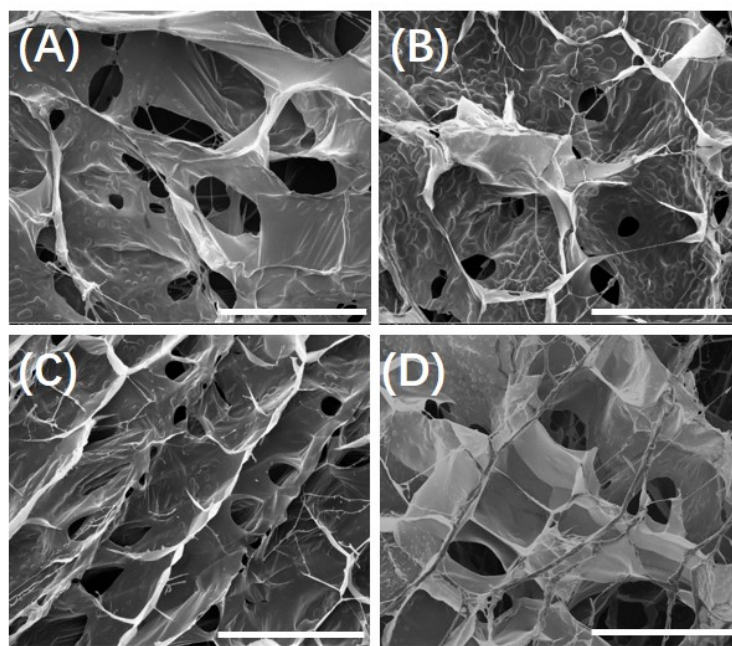


Figure S2. SEM images of the liposomal hydrogel. (A) and (B) were 1 wt% liposomal alginate hydrogel with 40% and 80 % crosslinking; (C) and (D) were 2 wt% liposomal alginate hydrogel with 40% and 80 % crosslinking. Scale bar=200 μm.

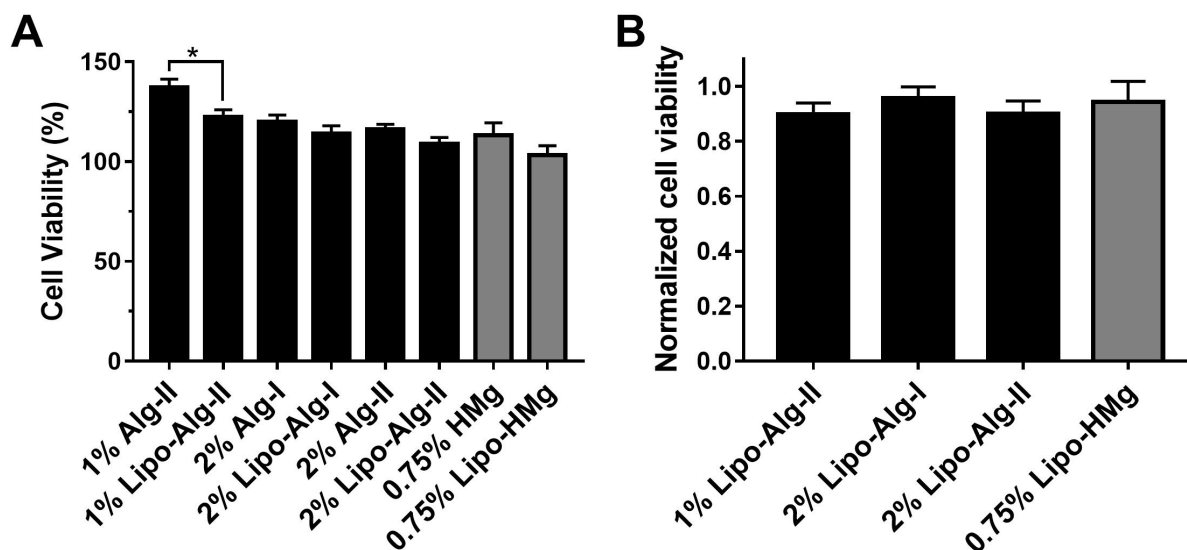


Figure S3. Cell viability of hydrogels without and with liposomes in (A) percentage; and (B) in normalized cell viability with reference to hydrogels without liposomes ($n = 8$) two days in culture, where 1% and 2% were the alginate concentration; Ag-I and Ag-II were the alginate hydrogel with 40% or 80% crosslinking density; HMg was the abbreviation of HAMC hydrogel; Lipo represented the liposome-containing hydrogel.

Table S1. The CEST contrast (%) at 5.0 and -3.4 ppm in different BA-Liposome concentration under 0.8 μ T.

Lipid Conc. (mg/mL)	Liposome Conc. (particles/mL)	CEST (%)	
		-3.4 ppm	5.0 ppm
0	0	0	0
25	1.01×10^{16}	5.94	20.76
50	1.54×10^{16}	10.30	25.75
75	1.70×10^{16}	13.20	26.66

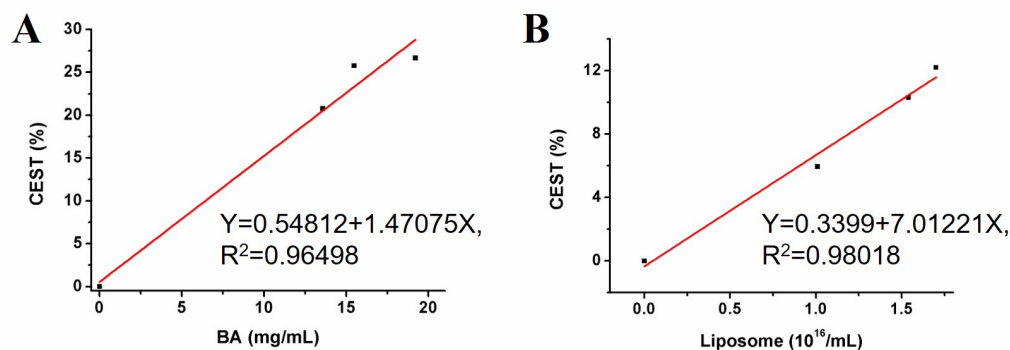


Figure S4. The linear fitting of CEST contrast at 5.0 ppm (A) and -3.4 ppm (A) by using the data listed in **Table S-1**.

Table S2. Physicochemical properties of Gemcitabine loaded liposomes.

Lipid Conc. (mg/mL)	Size (nm)	PDI	Z-potential (mV)	Gem Conc. (mg/mL)	Encapsulation Efficiency (%)
25	218.2±3.9	0.127±0.032	-0.79±0.81	14.87±1.27	50.80±0.79

Data represent mean ± S.D. (n ≥ 3).

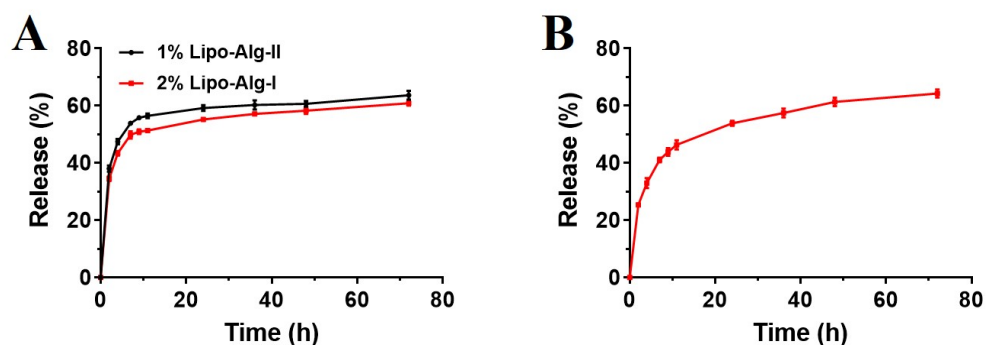


Figure S5. Drug cumulative release from liposomal hydrogel. **A** BA release profile from the liposomal hydrogel of 1% Lipo-Alg-II and 2% Lipo-Alg-I, which showed equivalent mechanical properties. **B** Gemcibine (Gem) release profile from its liposomal hydrogel of 2% Lipo-Alg-I. Data was presented as mean ± SD (n=3).

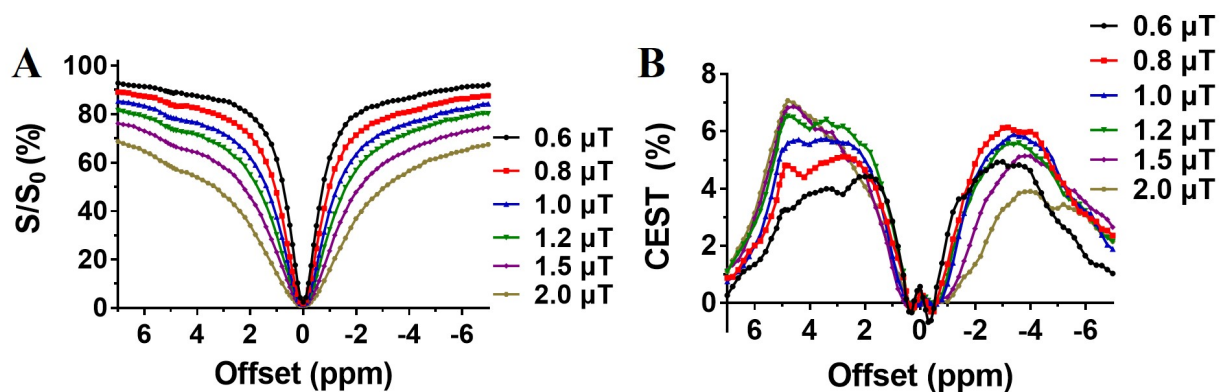


Figure S6. B_1 optimization for *in vivo* measurements. **A** and **B** were the Z-spectra and corresponding CEST contrasts of liposomal hydrogel 4 hours after transplantation under various B_1 fields. Under $0.8 \mu\text{T}$, it gave out the highest NOE contrast at -3.4 ppm . While under $1.2 \mu\text{T}$, it produced good CEST contrast with clear peaks at 5.0 ppm . Thus, $0.8 \mu\text{T}$ and $1.2 \mu\text{T}$ were selected for *in vivo* monitoring of CEST contrast at -3.4 and 5.0 ppm , respectively.

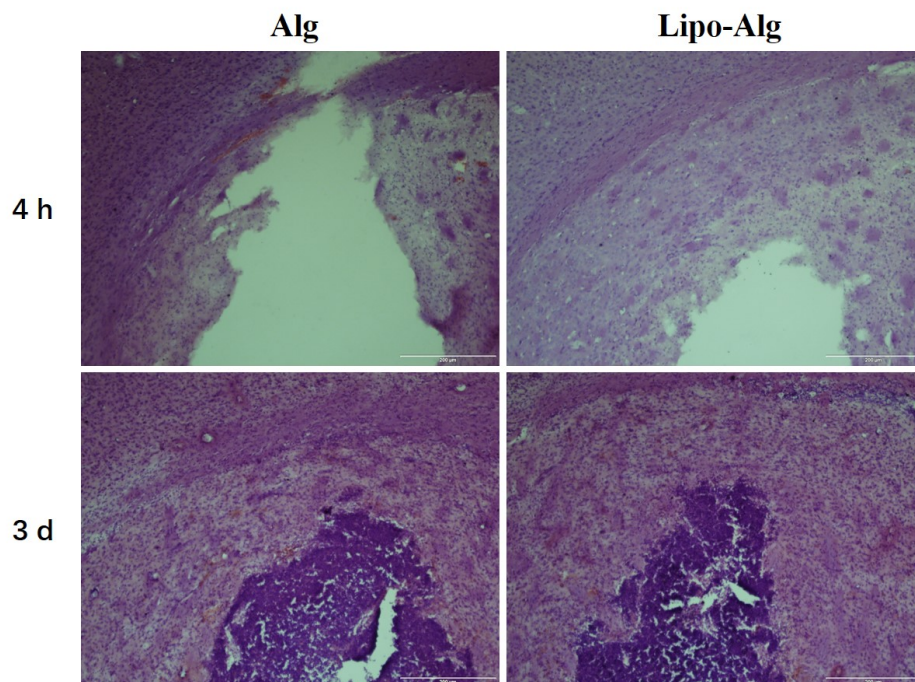


Figure S7. Histological assessment 4 hours and 3 days after hydrogel implantation using H&E staining, in which the scaffold appeared purple. Scale bar = $200 \mu\text{m}$.

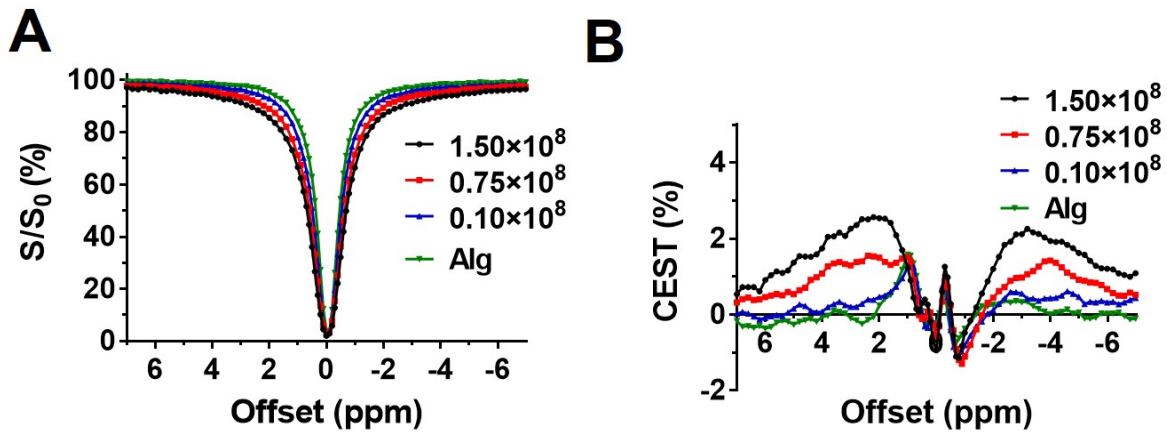


Figure S8. CEST contrast of U87 cell dispersed in alginate hydrogel with various cell density. **A** Z-spectra and **B** the corresponding CEST contrast by Lorentz fitting.

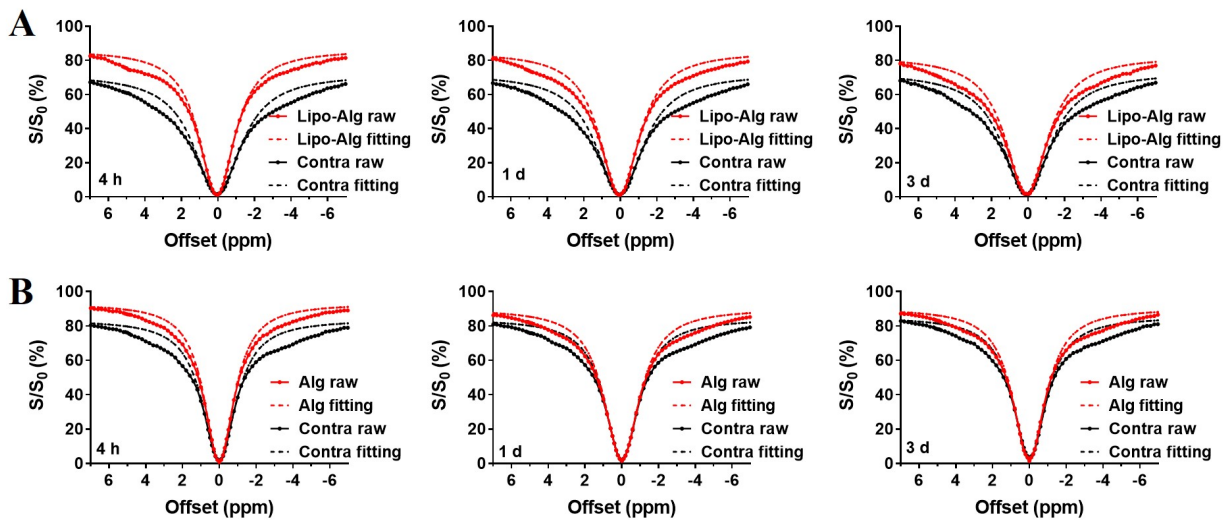


Figure S9. The *in vivo* representative longitudinal Z-spectra raw data and Lorentzian fitting results using the Z-spectra between -0.8 ppm to 0.8 ppm and 6~7 ppm. **(A)** and **(B)** were respectively for Lipo-Alg under 1.2 μ T and Alg hydrogel 0.8 μ T at different time points.