pH-responsive doxorubicin-loaded magnetosomes for magnetic

resonance-guided focused ultrasound real-time monitoring and

ablation of breast cancer

Na Tang,^{‡a,b} Yi Zhu,^{‡b} Ziwei Lu,^{‡c} Jiali Deng,^{d,b} Jiajing Guo,^b Xinyi Ding,^b Jingyi Wang,^{d,b} Rong Cao,^b An Chen,^b Zhongyi Huang,^e Hongwei Lu*^f, and Zhongling Wang*^b

^a Shanghai Key Laboratory of Molecular Imaging, Shanghai University of Medicine and Health Sciences, Shanghai 201318, China.

^b.Department of Radiology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200080, China. E-mail: zlwang138136@126.com

^{c.}Department of Radiology, the First Affiliated Hospital of Soochow University, Suzhou, Jiangsu 215006, China.

^d School of Health Science and Engineering, University of Shanghai for Science and Technology, Shanghai, 200093, China.

^{e.}Department of Neurology, School of Medicine, New York University, New York, 10016, American.

^{f.}Department of Biomedical Engineering, College of Engineering, Shantou University, Shantou, 515063, China. E-mail: hwlu@stu.edu.cn

[‡]These authors contributed equally to this work.



Fig. S1 Molecular weight of SKDEEWHKNNFPLSP, measured with Maldi-Tof-Ms.



Fig. S2 Non-invasive, in situ tumor monitoring of SPIO accumulation from the STPS nanoparticles by MRI. (a-c) T_2 -weighted images, T_2 map (a), T_2 SNR (b) and R_2 values (c) of the tumors of the nude rat with breast cancer before injection, 6 and 12 hours after the STPS nanoparticles. Measure the mean T_2 signal intensity of per tumor. Subsequently, calculating the relative signal-to-noise ratio (SNR = Smean/Standard deviation of noise (NSD) (Standard deviation of the background signal)). Regions of interest (ROIs) are set to about 20-30 mm² in each tumor. (d) Prussian blue staining revealed the tumor deposition of STPS. All values are presented in mean \pm s.d. (n = 3).



Fig. S3 (a-b) Representative ex vivo fluorescence imaging (a) and quantitative analysis (b) of the heart, liver, spleen, lung, kidney and tumor of the mice injected with the STPSD after 24 h.



Fig. S4 H&E staining of tissue slices of the main organs taken from mice 24 h after different treatment.

Time (h)	STPS		STPSD	
	$T_2 SNR$	<i>R</i> ₂ (S ⁻¹)	T_2 SNR	<i>R</i> ₂ (S ⁻¹)
0	55.46 [±] 2.39	10.18 [±] 0.77	58.69 [±] 3.43	10.00 [±] 0.86
6	27.93 [±] 2.04	15.12 [±] 1.09	30.17 [±] 2.48	13.66 [±] 1.04
12	19.93±1.89	20.00 [±] 1.41	21.55 [±] 2.59	18.03 [±] 1.64

Table.S1 The T_2 SNR, R_2 values of STPS and STPSD nanoparticles.

 T_2 SNR and R_2 of tumors were measured before and after injection of STPS and STPSD nanoparticles (1 mg/mL) (Timing: 0, 6, 12 h; n = 3) by tail vein injection (200 μ L/mL, 200 μ L). Data are represented by mean ± s.d. (n = 3).

Groups/parameter	Negative	Positive control	STPS	STPSD
	control			
Power (w)	53.37 [±] 3.13	70.21 [±] 3.38	53.44 [±] 2.26	52.42 [±] 2.73
Treatment time (s)	22.27 [±] 1.48	21.94 [±] 1.73	22.16 [±] 1.63	22.39 [±] 0.96
Temperature (°C)	53.22 [±] 2.34	67.91 [±] 3.49	71.54 [±] 3.18	72.45 [±] 2.90

Table.S2 Power, treatment time and temperature of the four groups.

Numbers in the table are illustrated by mean \pm s.d. (n = 3).