SUPPLEMENTARY MATERIAL

A Multifunctional Theranostic Nanoagent for Dual-Mode Image-Guided Synergistic HIFU-/Chemo Cancer Therapy

Nan Zhang[1, #], Xiaojun Cai [2, #], Wei Gao [1], Ronghui Wang [1], Chunyan Xu [1], Yuanzhi Yao [1], Lan Hao [1], Danli Sheng [1], Hangrong Chen [2*], Zhigang Wang [1*] , Yuanyi Zheng [1*]

[1]. Second Affiliated Hospital of Chongqing Medical University & Chongqing Key Laboratory of Ultrasound Molecular Imaging, Chongqing, 400010, China.

[2]. State Key Laboratory of High-Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences

[#] Nan Zhang and Xiaojun Cai are co-first authors who contributed equally to this study

[*] Prof. Hangrong Chen, Yuanyi Zheng and Zhigang Wang are co-corresponding authors

Address:

Second Affiliated Hospital of Chongqing Medical University & Chongqing Key Laboratory of Ultrasound Molecular Imaging, 74 Linjiang Road, 400016, Chongqing, China

TEL: 86-023-63693709

E-MAIL: zhengyuanyi@cqmu.edu.cn

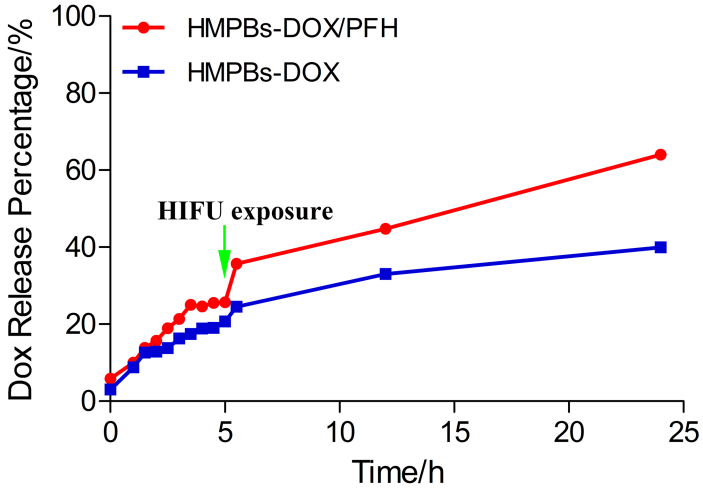

Figure S1. The DOX release curves in HMPBs-DOX/PFH group and HMPBs-DOX group with HIFU exposure. An obvious rise was exhibited in HMPBs-DOX/PFH group at 5 h for HIFU exposure.

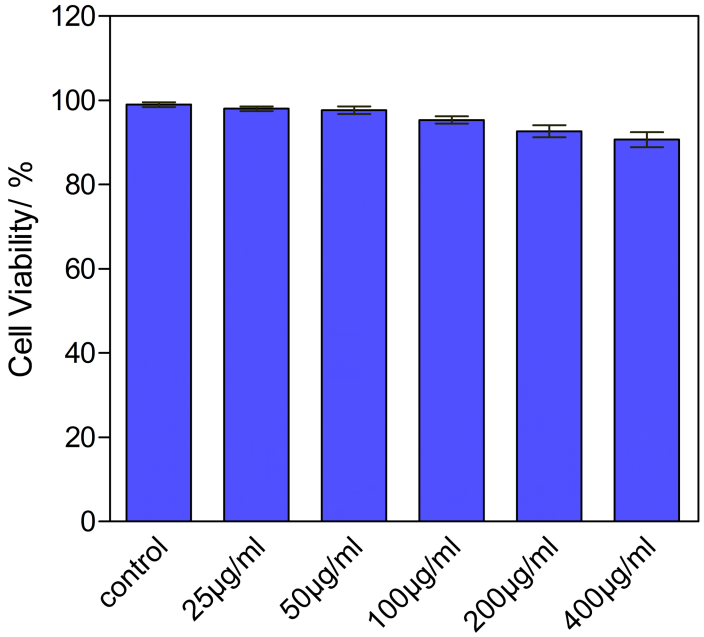

Figure S2. Cell Viability of HMPBs with different concentration.

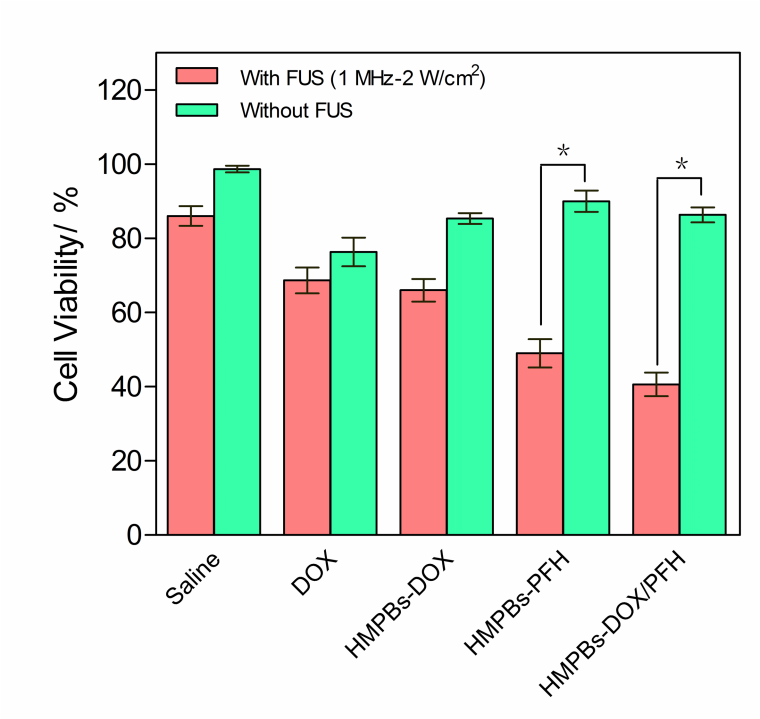

Figure S3. Viability of MB231 cells after incubated with saline, DOX, HMPBs-DOX, HMPBs-PFH, HMPBs-DOX-PFH for 18 h with and without FUS exposure by using 1 MHz transducer at 2 W/cm^2 in 60 s, respectively.

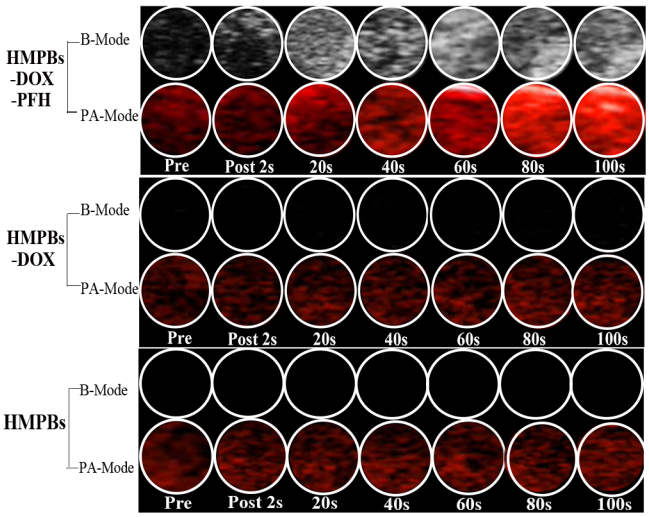

Figure S4. B-Mode and PA-Mode images of HMPBs-DOX/PFH, HMPBs-DOX and HMPBs before and after phase transition at different time-points (pre, post 2 s, 20 s, 40 s, 60 s, 80 s, 100 s). The US and PA imaging showed no distinct change between the HMPBs-DOX and HMPBs groups. It was found that as the heating time increasing, the echo intensity value of the B-mode images in the HMPBs-DOX/PFH

group rapidly increased for the initial 20 s and then stabilized after 20 s. As the heating time increased, the PA signal intensity of HMPBs-DOX/PFH group also kept increasing during the heating process, from 1.067±0.467 a.u. at the beginning to 1.590±0.315 a.u. after heating for 100 s. This enhancement was with a statistically higher amplitude than that of HMPBs group (from 0.766±0.375 a.u. to 0.794±0.361 a.u.) and HMPBs-DOX group (from 0.814±0.341 a.u. to 0.775±0.395 a.u.).

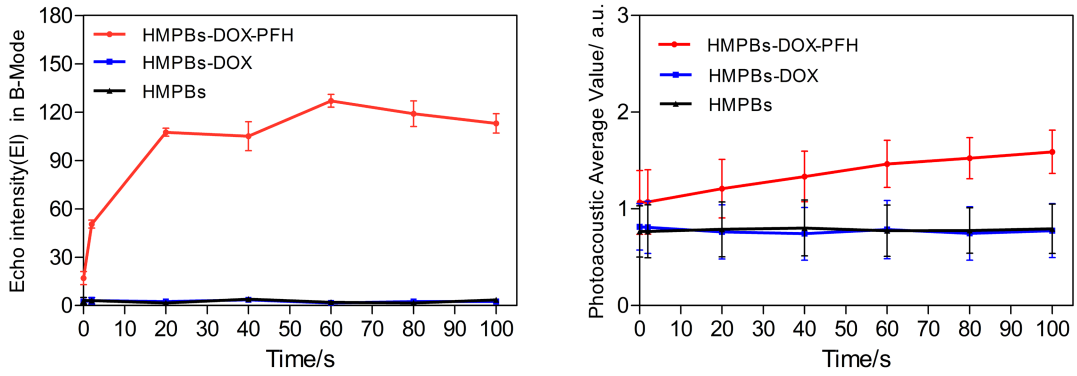

Figure S5. Echo Intensity (EI) in B-Mode and PA signal intensity before and after HIFU exposure at different time points. Echo intensity value of B-mode in HMPBs-DOX/PFH group rapidly increased from 17±5.657 to 113±8.485. PA signal intensity in HMPBs-DOX/PFH group apparently increased from 1.067±0.467 a.u. to 1.590±0.315 a.u..

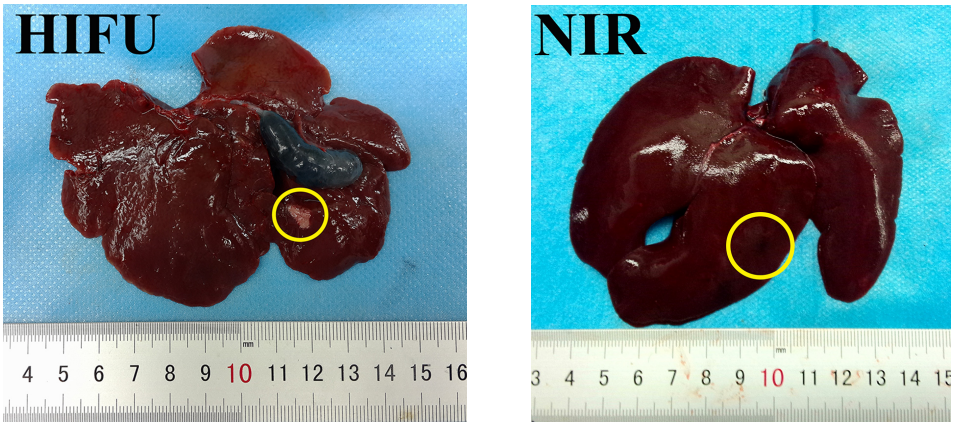

Figure S6. Digital photos of ablated rabbit livers exposed to HIFU at 120 W for 5 s (left) and exposed to NIR (right) under the same power of exposure after injection of 0.2 mL HMPBs-DOX/PFH, respectively.