**Supplementary Information**

**Berberine Nanoparticles for Promising Sonodynamic Therapy on HeLa Xenograft Tumor**

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Part 1. SEM morphology study of BBR and BBRNPs

Figure S1. (A-1) to (A-3) present BBR crystals in natural buffer with irregular microstructure, (B-1) to (B-2) present BBRNPs monodispersed nanostructure.

Part 2. Viscera morphology after excess BBRNPs injection

Figure S2. Images of viscera morphology after BBR excess dosage intravenous injection.

Part 3. Tumour ultrasound contrast imaging
Figure S3. Ultrasound contrast imaging of tumor blood vessels. 1-7 indicate different mice No. at each group. (N = 7, means ± SD, * P < 0.05, vs control group. Ctrl: control group, BBR: BBR group, US: ultrasound group, SDT: BBR mediated SDT group.)

Part 4. Data analysis of ultrasound contrast imaging

Figure S4. (A) Representative images of ultrasound examination and microbubble imaging. Left peak shows an example of contrast mean power vs time to peak after microbubbles intravenous injection. Right figures show ultrasonography and power Doppler images after microbubbles injection. Red arrow pointed to the maximum contrast mean power of M(B) Time of maximum microbubble accumulation according to the value of contrast mean power. (N = 7, means ± SD, * P < 0.05, vs control group. Ctrl: control group, BBR: BBR group, US: ultrasound group, SDT: BBR mediated SDT group.)

Part 5. Histological analysis of FUS damaged cancer tissue

Figure S5. (A) H&E staining of pathological sections of burned area of focused ultrasound where is pointed by white arrow. (B) Pathological slides of damaged blood vessels in cancer tissue which is
caused by ultrasound mediats BBRNPs cavitation (black arrow). Left column shows objective images with 20 times magnification, while right column shows 40 times magnification images.

**Part 6. HeLa xenograft mice photographs**

![HeLa xenograft mouse photographs](image)

**Figure S6.** HeLa xenograft mouse photoes taken before and after treatement of drug intraperitoneal injection.