Supporting Information

Bismuth Sulfide Nanorods as a Precision Nanomedicine for *in Vivo* Multimodal Imaging-Guided Photothermal Therapy of Tumor

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1. Supporting Discussion

Measurement of Photothermal Performance.

To examine photothermal properties of Tween 20 modified Bi₂S₃ NRs, the temperature trends of the aqueous dispersion of Bi₂S₃ NRs with different concentrations (0.05, 0.1, 0.25, 0.5, 0.8, and 1 mg mL⁻¹) was measured under the irradiation of 808 nm CW laser (Connet Fiber Optics Co., Ltd.) with a power density of 1 W cm⁻², and pure water was used as control. The power of 808 nm CW laser was calibrated by a PM310D-S310C power meter bundles (Thorlabs, Inc). Real-time thermal imaging of samples was recorded using a FLIR thermal camera (FLIR ThermoCAM E40) and quantified by FLIR Examiner software.

The photothermal conversion efficiency of Tween-Bi₂S₃ NRs was determined according to the reported method.^{1,2} To measure the photothermal conversion efficiency (η), the Bi₂S₃ NRs aqueous dispersion samples were exposed to 808 nm

CW laser (1 W cm^{-2}) for 10 min, and then the laser was shut off. The heating and cooling temperature trends of samples were recorded by FLIR thermal camera. The photothermal conversion efficiency was calculated according to the eq 1:

$$\eta = \frac{hS(T_{\max} - T_{\text{surr}}) - Q_0}{I(1 - 10^{-A_{808}})}$$

(1)

Where h is the heat transfer coefficient, S is the sample container surface area, $T_{\max}$ is the steady state maximum temperature, T_{surr} is the ambient room temperature, Q_0 is the baseline energy input by the solvent and the sample container without NRs, I is the laser power, and A_{808} is the absorbance of NRs at 808 nm. The value of hS is calculated by eq 2:

$$\tau_s = \frac{m_d C_d}{hS}$$

(2)

Where τ_s is the characteristic thermal time constant, The mass of the nanoparticle solution (m_d) was g, and its heat capacity (C_d) was approximated to be $4.2 \text{ J g}^{-1} \text{ K}^{-1}$ (the heat capacity of water). The heat energy (Q_0) of the sample container and solvent without nanoparticles was measured independently, using the following eq 3:

$$Q_0 = hS(T_{\max} - T_{\text{surr}})$$

(3)

References

1. Tian, Q.; Hu, J.; Zhu, Y.; Zou, R.; Chen, Z.; Yang, S.; Li, R.; Su, Q.; Han, Y.; Liu, X. Sub-10 nm $\text{Fe}_3\text{O}_4@\text{Cu}_{2-x}\text{S}$ Core-Shell Nanoparticles for Dual-Modal Imaging and Photothermal Therapy. *J. Am. Chem. Soc.* **2013**, *135*, 8571-8577.

2. Ayala-Orozco, C.; Urban, C.; Knight, M. W.; Urban, A. S.; Neumann, O.; Bishnoi, S. W.; Mukherjee, S.; Goodman, A. M.; Charron, H.; Mitchell, T.; *et al.* Au Nanomatryoshkas as Efficient Near-Infrared Photothermal Transducers for Cancer Treatment: Benchmarking against Nanoshells. *ACS Nano* **2014**, 8, 6372-6381.

2. Supporting Figures

Figure S1. SEM image of Bi₂S₃ NRs prepared by solvothermal method.

Figure S2. Photos of larger-scale prepared OA-Bi₂S₃ NRs dispersed in cyclohexane and Tween-Bi₂S₃ solutions in saline, PBS, and DMEM, respectively.

Figure S3. (a) XRD, (b) EDS spectrum, (c) XPS spectra of Bi_2S_3 NRs. (d) FT-IR spectra of Bi_2S_3 NRs before and after modification with Tween20.

Figure S4. (a) Photothermal effect of the irradiation of the aqueous dispersion of Bi_2S_3 NRs (1 mg mL^{-1}) with the 808 nm NIR laser (1 W cm^{-2}). The irradiation lasted for 10 min, and then the laser was turned off. (b) Plot of cooling time versus negative natural logarithm of the temperature driving force which is obtained from the cooling stage. Time constant for heat transfer from the system is determined to be $\tau_s = 278.72$

s.

Figure S5. UV-vis absorption spectra of Bi_2S_3 NRs dispersion in water before and after laser irradiation for 1 h (808 nm , 1 W cm^{-2}).

Figure S6. The measured CT values of Bi_2S_3 NRs and the clinical CT agent Ultravist[®] 300. Inset: the color-mapped phantom CT images.

Figure S7. *In vivo* X-ray CT imaging with different position in 4T1 tumor bearing mice. (a) CT images of mice before injection. (b) CT images of mice 5 min post i.v. injection with Bi_2S_3 NRs. (c) CT images of mice 3 h post i.v. injection with Bi_2S_3 NRs: liver (L), spleen (S), and tumor (T).

Figure S8. The weight of 4T1 tumor-bearing mice and their major organ.

Figure S9. The biodistribution of Bi₂S₃ NRs in BALB/c mice (data expressed as percentage of the injected dose per gram of tissue (% ID/g)).

Table S1. Blood biochemistry analysis of the mice treated with Bi₂S₃ NRs. The results show mean and standard deviation of total bilirubin (TBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (CREA), uric acid (UA), blood urea nitrogen (BUN), creatine kinase (CK).

group	TBIL ($\mu\text{mol/L}$)	ALT (U/L)	AST (U/L)	AST/ALT	CREA ($\mu\text{mol/L}$)	UA ($\mu\text{mol/L}$)	BUN (mmol/L)	CK (U/L)
PBS	0.63 $\pm$ 0.10	36.5 $\pm$ 12.3	128 $\pm$ 23.4	3.99 $\pm$ 2.05	3.75 $\pm$ 0.96	114 $\pm$ 21.6	10.8 $\pm$ 2.02	1112 $\pm$ 46.1
Laser only	0.70 $\pm$ 0.36	37.8 $\pm$ 16.3	214 $\pm$ 56.7	6.18 $\pm$ 2.30	3.00 $\pm$ 1.41	125 $\pm$ 14.7	13.6 $\pm$ 1.42	1287 $\pm$ 265
Bi ₂ S ₃	0.98 $\pm$ 0.41	31.3 $\pm$ 4.60	148 $\pm$ 42.7	4.95 $\pm$ 2.04	2.00 $\pm$ 2.31	136 $\pm$ 30.0	11.4 $\pm$ 1.78	1404 $\pm$ 250
Bi ₂ S ₃ + laser	0.63 $\pm$ 0.42	42.0 $\pm$ 20.8	154 $\pm$ 53.2	4.15 $\pm$ 1.90	0.25 $\pm$ 0.50	157 $\pm$ 15.2	8.96 $\pm$ 0.70	1094 $\pm$ 359
Normal mice	1.03 $\pm$ 0.21	49.3 $\pm$ 4.64	127 $\pm$ 33.2	2.55 $\pm$ 0.52	6.00 $\pm$ 2.94	140 $\pm$ 24.6	9.40 $\pm$ 0.45	1132 $\pm$ 455