Supporting Information

Photonic Cancer Nanomedicine using the Near Infrared-II Biowindow Enabled by Biocompatible Titanium Nitride Nanoplatforms

Chunmei Wang†[a], Chen Dai †[c], Zhongqian Hu*[b], Hongqiang Li [a], Luodan Yu [d], Han Lin [d], Jianwen Bai*[a] and Yu Chen*[d]

[a]Department of Emergency Medicine and Critical Care, Shanghai East Hospital, Tong Ji University, Shanghai 200120, People's Republic of China.

Email: baijianwen1019@163.com (J. Bai)

Department of Ultrasound, Zhongda Hospital, School of Medicine, Southeast University, Nanjing, Jiangsu, 210009, People's Republic of China.

Email: hzq920@126.com (Z. Hu)

[c]Department of Ultrasound, Shanghai East Hospital, Tong Ji University, Shanghai 200120, People's Republic of China.

[d]State Laboratory of High Performance Ceramic and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Shanghai, 200050, People's Republic of China.

Email: chenyu@mail.sic.ac.cn (Y. Chen)

Calculation of the Extinction Coefficient and Photothermal-Conversion Efficiency.

a. Calculation of the Extinction Coefficient

To access the NIR-II (1064 nm) absorption capability of TiN-PVP NPs, the extinction coefficient *ε(λ)* of the TiN-PVP NPs is measured according to the Lambert-Beer Law:

$$A(\lambda)=\varepsilon LC \tag{1}$$

where A represents the absorbance at a wavelength λ of 1064 nm, ε represents the extinction coefficient, L represents path-length (1 cm), and C is the molar concentration of the TiN-PVP NPs (in g L^{-1}). The extinction coefficient ε is determined by plotting the slope (in Lg^{-1} cm^{-1}) of each linear fit against wavelength. The 1064 nm laser extinction coefficient (ε) of TiN-PVP NPs can be measured to be 22.0 Lg^{-1} cm^{-1}. Similarly, the 1064 nm laser extinction coefficient (ε) of TiN NPs can be calculated to be 17.34 Lg^{-1} cm^{-1}.

b. **Calculation of the Photothermal Conversion Efficiency**

According to previous report[1], the total energy balance for this whole system is

$$\sum_i m_i C_{p,i}\frac{dT}{dt} = Q_{TiN-PVP} + Q_D - Q_S \tag{2}$$

where m and C_p are the mass and heat capacity of solvent (water) and T is the solution temperature, $Q_{TiN-PVP}$ refers to the photothermal energy input of TiN-PVP NPs. Q_D refers to the baseline energy input of the sample cell and Q_S is heat conduction away from the system surface by air.

$Q_{TiN-PVP}$, which refers to the 1064 nm laser induced source term, displays heat dissipated by electron-phonon relaxation of plasmons on the TiN-PVP NPs surface irradiated by 1064 nm laser.

$$Q_{TiN-PVP} = I\left(1 - 10^{-A_{1064}}\right) \tag{3}$$

where I is incident laser power (1.0 W cm^{-2}) , A_{1064} is the absorbance of the TiN-PVP NPs at wavelength of 1064 nm, and η represents the photothermal transduction efficiency of TiN-PVP NPs. Furthermore, Q_D expresses heat dissipated from light absorbed by the sample cell itself, and it was calculated independently to be $Q_D = (5.4 \times 10^{-4})I$ (in mW) by utilizing a sample cell containing pure aqueous solution without TiN-PVP NPs under 1064 nm laser irradiation. Q_S, in this system, is thermal energy lost to the ambient environment and is linear with the output of thermal energy

$$Q_S = hS(T - T_S) \tag{4}$$

where h represents the heat transfer coefficient, S refers to the surface area of the container, T represents the solution temperature, and T_S represents ambient surrounding temperature.

In order to obtain hS, a dimensionless θ is introduced,

$$\theta = \frac{T - T_S}{T_{max} - T_S} \tag{5}$$

where T_{max} is the maximum system temperature. A sample system time constant τ_s is also needed to be introduced,

$$\tau_s = \frac{\sum_i m_i C_{p,i}}{hS} \tag{6}$$

which needs to be substituted into eq 2 and rearranged to become

$$\frac{d\theta}{dt} = \frac{1}{\tau_s}\left[\frac{Q_{TiN-PVP} + Q_D}{hS(T_{Max} - T_S)} - \theta\right] \tag{7}$$

After the 1064 nm laser pump is turned off, the heat input become zero, $Q_{TiN-PVP} + Q_D = 0$, reducing eq 7 to give the expression,

$$t = -\tau_s \ln \theta \tag{8}$$

Thus, τ_s was measured to be 190.59 from the data in **Figure 3I**. Furthermore, m is 0.1 g and C is 4.2 J g^{-1}. According to eq 6, the hS was determined to be 2.2 mW °C^{-1}.

When the temperature of system reaches an equilibrium, the heat output is equal to the heat input:

$$Q_{TiN-PVP} + Q_D = Q_S = hS(T_{Max} - T_{Surr}) \tag{9}$$

where T_{Max} represents the equilibrium temperature. The 1064 nm laser photothermal conversion efficiency (η) can be calculated by substituting eq 3 for $Q_{TiN-PVP}$ into eq 9 and rearranging to yield

$$\eta = \frac{hS(T_{Max} - T_S) - Q_D}{I\left(1 - 10^{-A_{1064}}\right)} \tag{10}$$

where the $(T_{Max} - T_S)$ was determined to be 29.0 °C according to **Figure 3k**. Substituting these values into equation (10), the 1064 nm laser photothermal conversion efficiency (η) of TiN-PVP NPs can be calculated to be 22.8%. Similarly, the 1064 nm laser photothermal conversion efficiency (η) of TiN NPs can be calculated to be 22.7%.

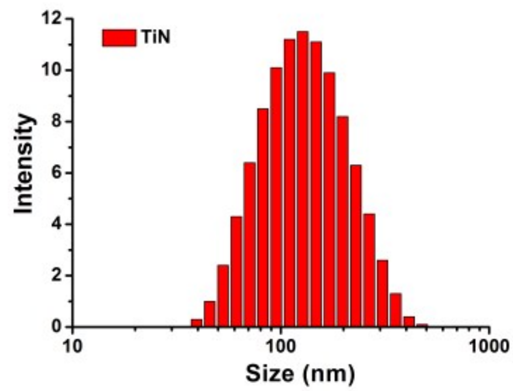

Figure S1. Dynamic light scattering (DLS) of TiN NPs in aqueous solution.

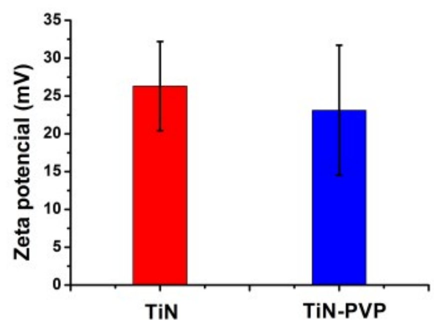

Figure S2. Zeta potential of TiN and TiN-PVP NPs dispersed in deionized water. n = 3, mean ± s.d.

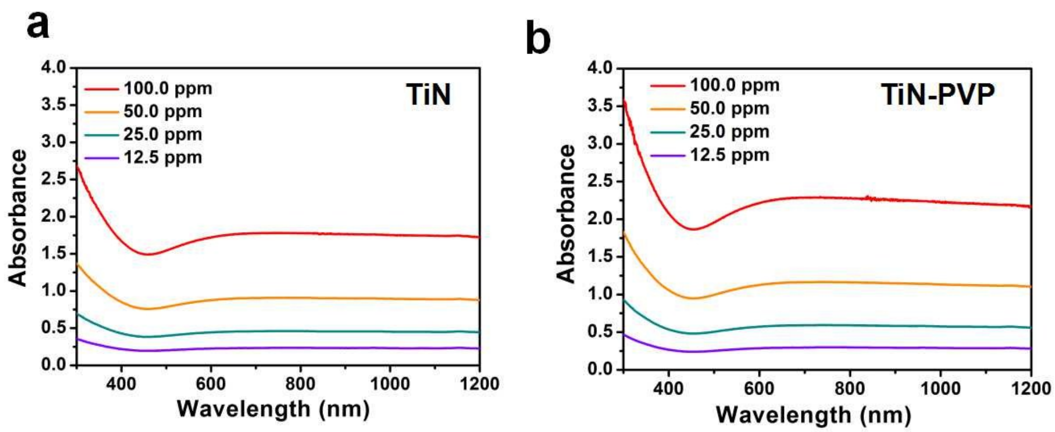

Figure S3. UV-vis spectra of (a) TiN NPs and (b) TiN-PVP NPs dispersed in aqueous solution at elevated concentrations (12.5, 25, 50 and 100 ppm).

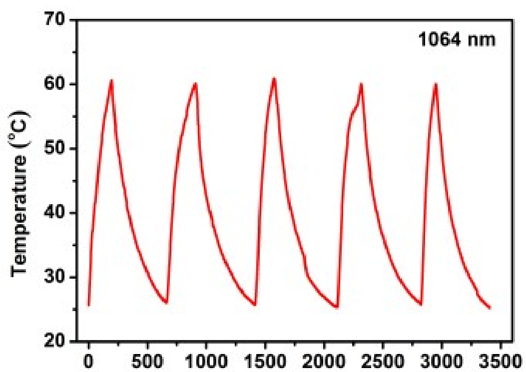

Figure S4. Recycling-heating profiles of TiN-PVP NPs (200 ppm) aqueous solution after 1064 nm laser irradiation at 1.0 W cm^{-2} for five laser on/off cycles.

Figure S5. Equipment for assessing tissue-penetration performance of NIR laser at 808 nm, 980 nm and 1064 nm employing different thicknesses (0, 2.5 mm and 5.0 mm) of chicken breast tissues.

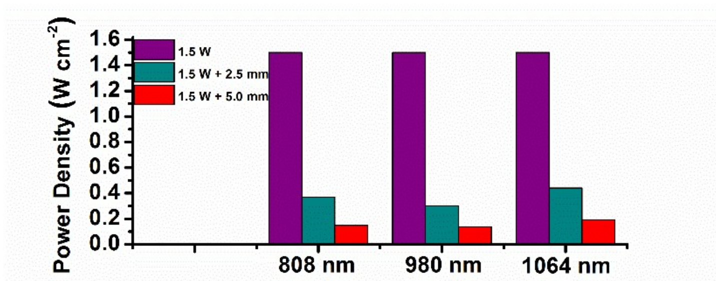

Figure S6. Residual power density after penetrating through the chicken breast tissues of varied thickness of 0, 2.5 mm and 5.0 mm under 808 nm, 980 nm, and 1064 nm laser irradiation at the power density of 1.5 W cm^{-2}.

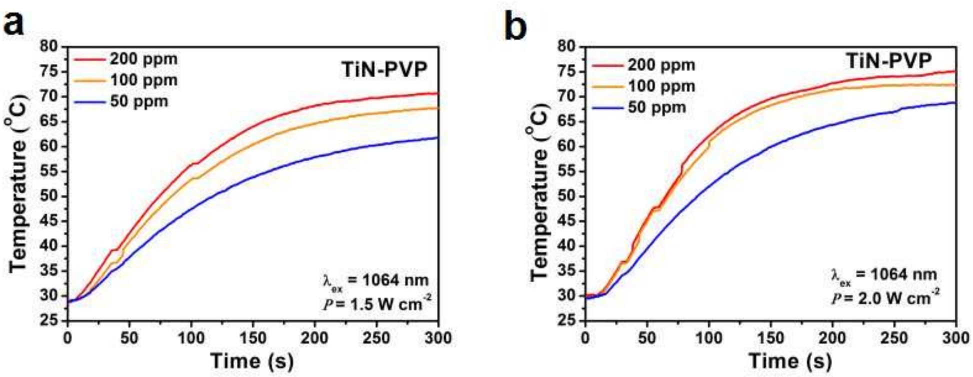

Figure S7. The photothermal-heating curves of TiN-PVP at elevated concentrations (50, 100 and 200 ppm) under 1064 nm laser irradiation at the power densities of (a) 1.5 W cm^{-2} and (b) 2.0 W cm^{-2}.

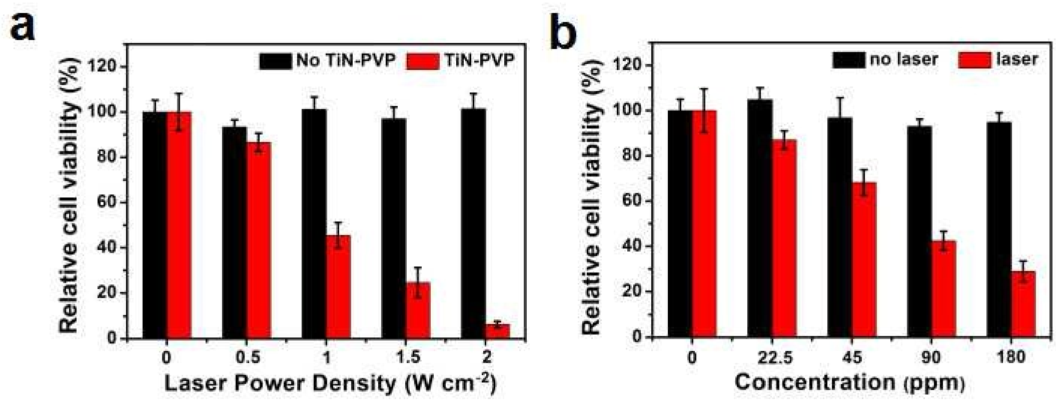

Figure S8. (a) Relative viabilities of 4T1 cells after incubation with TiN-PVP NPs (200 ppm) followed by the exposure to 1064 nm laser irradiation at different laser power densities (0, 0.5, 1, 1.5 and 2.0 W cm^{-2}). (b) Relative viabilities of 4T1 cells after incubation with TiN-PVP NPs at various concentrations (22.5, 45, 90 and 180 ppm) followed by laser irradiation at the power density of 1.0 W cm^{-2}.

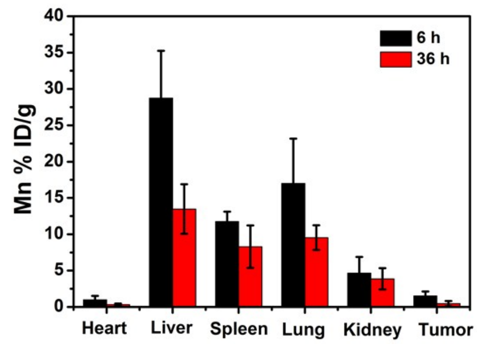

Figure S9. Biodistribution of Ti (% ID of Ti per gram of tissues) in main tissues and tumor after intravenous administration of TiN−PVP NPs dispersed in PBS for 6 h and 36 h (n = 3).

Figure S10. Digital photos of 4T1 tumor-bearing mice from each group including control group, TiN-PVP group, NIR-I laser group, NIR-II laser group, TiN-PVP + NIR-I laser group, and TiN-PVP + NIR-II laser group.

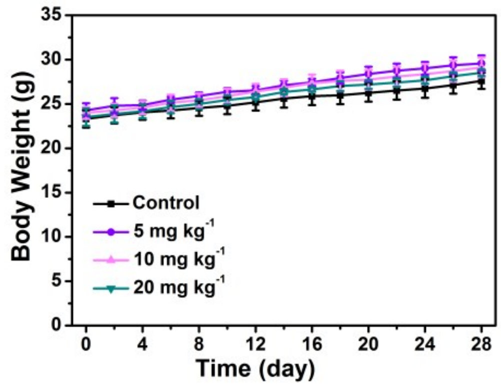

Figure S11. Time-dependent body-weight curves of Kunming mice during one-month feeding period.

References

[1] D. K. Roper, W. Ahn, M. Hoepfner, *J. Phys. Chem. C.*, 2007, **111**, 3636.