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Supporting Information

Radiopharmaceutical-Activated Silicon Naphthalocyanine Nanoparticles towards Tumor Photodynamic Therapy

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Experimental procedures

Synthesis of SiNc NPs

Silicon naphthalocyanine nanoparticles (SiNc NPs) were prepared *via* solvent evaporating method. Firstly, SiNc (0.6 mg) and methoxy poly(ethylene glycol)-b-poly(ε-caprolactone) (PEG−PCL, 20 mg) were dissolved in 2 mL of tetrahydrofuran (THF). The solution was transferred into 25 mL round-bottom flask, and 4 mL deionized water was added. THF was removed under vacuum using rotary evaporator. The three-stage evaporation cycle was operated as previous report. The final volume of obtained samples was adjusted to 1 mL with saline.

Characterization of SiNc NPs

The transmission electron microscopy images of SiNc NPs were acquired using JEOL JEM-F200. UV-ViS-NIR spectrum of SiNc NPs was recorded on the Cary 5000 Scan UV-Vis-NIR spectrophotometer.

The detention of $^1O_2$

Singlet oxygen sensor green (SOSG) probe was utilized for the detection of $^1O_2$ on multimode reader (SpectraMax i3x). Firstly, SOSG (100 μg) was dissolved in the methanol (330 μL) to form the mother solution (0.5 mM). Then, 30 μL mother solution of SOSG was added into the saline and saline + ^{18}F-FDG to acquire their fluorescence intensity (E_x = 504 nm, E_m = 525 nm) as F_0 and F values, respectively. Finally, 30 μL mother solution of SOSG was added into SiNc NPs and SiNc NPs + ^{18}F-FDG to obtain their fluorescence intensity (Ex = 504 nm, Em = 525 nm) as F_0 and F values, respectively. The ability of SiNc NPs for generating $^1O_2$ under the CR activation was identified by comparing the F/F_0 value in saline group and SiNc NPs group.

Cytotoxicity assay

The cytotoxicity assay of SiNc NPs was measured by cell counting kit-8 (CCK8) assay. Firstly, 4T1 cells were cultured at 37 °C in RPMI 1640 medium containing 10% fetal bovine serum (FBS), penicillin (100 U mL^{-1}) and streptomycin (100 μg mL^{-1}). After adding SiNc NPs solution with increasing concentrations and co-cultured for 24 h, 80 μL medium containing 4 μg CCK8 reagent was added to each well. Then, this cell-

culturing plate was incubated at 37 °C for 1 h and subsequently being slowly shaken for 15 min. Finally, the cytotoxicity of the SiNc NPs was detected by measuing the absorbance of each well at 450 nm on multimode reader.

Cell-level therapeutic effect of SiNc NPs-based CR-PDT was also evaluated by CCK8 assay as above, replacing the cell co-cultured samples with ^{18}F-FDG (200 μCi), SiNc NPs (100 ppm) or ^{18}F-FDG (100 μCi or 200 μCi) + SiNc NPs (100 ppm).

Construction of tumor models

All animal experiments complied with the relevant regulations of the Animal Care and Use Committee of the First Affiliated Hospital of Zhejiang University School of Medicine (No. 2023-986). The 4T1 subcutaneous tumor models were performed by subcutaneous injection of 60 μL cell culture medium without serum containing 1×10^6 4T1 cancer cells on the right rear legs of mice. After the inoculation for 6 days, the tumor with the size of around 60 mm^3 ~ 80 mm^3 could be used for the living fluorescence imaging and *in vivo* treatment.

Living fluorescence imaging

4T1 subcutaneous tumor-bearing mice (n = 3) were intravenously injected with SiNc NPs solution (100 μL, 0.5 mg mL^{-1}). At 2 h, 4 h, 8 h, 12 h and 24 h post-injection of SiNC, the mice were subjected to living fluorescence imaging using IVIS Lumina II imaging system (Caliper Life Science, USA). The acquired data were processed using the Living Image 4.5 Software.

PET imaging

4T1 subcutaneous tumor-bearing mice (n = 3) were intravenously injected with clinically used ^{18}F-FDG (50 μL, 100 μCi) which was provided by the first affiliated hospital of school of medicine of Zhejiang university. At 60 min post-injection, the mice were subjected to PET imaging (Inveon scanner (Siemens, USA)), the acquired data was edited using the built-in software of the instrument.

***In vivo* antitumor treatment**

4T1 subcutaneous tumor-bearing mice were divided into 4 groups (n = 5): Saline (control), ^{18}F-FDG, SiNc NPs and SiNc NPs + ^{18}F-FDG (CR-PDT). Taking CR-PDT group for example, firstly, SiNc NPs (200 μL, 0.5 mg/mL) was intravenously injected

into the mice. At 12 h post-injection of SiNc NPs, ^{18}F-FDG (100 μL, 800 μCi) was intravenously injected into the mice to activate tumor accumulated SiNc NPs (first-round treatment). At day 3, the administrations of SiNc NPs and ^{18}F-FDG were repeatedly operated as above for second-round treatment. The mice in ^{18}F-FDG group or SiNc NPs group were only intravenously injected with ^{18}F-FDG or SiNc NPs for two rounds. The volume of tumors and the weights of mice were measured per 2 days. The mouse model whose tumor exceeded 800 mm^3 would be recorded as death.

Statistical analysis

All the data were presented as the mean (±) standard deviation (SD). The statistical analyses were conducted and plotted using OriginPro 2023b software. Asterisks represented the significant differences (*$P < 0.05$, **$P < 0.01$ and ***$P < 0.001$).

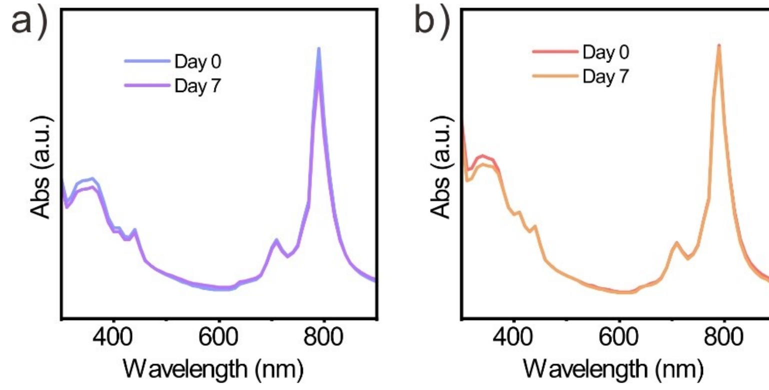

Figure S1: UV-Vis-NIR absorption spectrum of SiNc NPs dispersed in saline and in water containing 10% fetal bovine serum for 7 days.

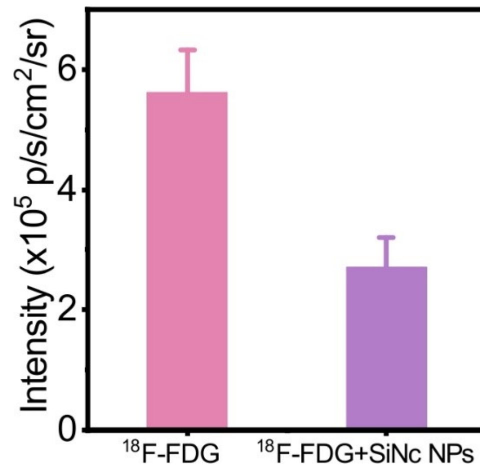

Figure S2: Quantitative analysis of luminescent intensity of ^{18}F-FDG and ^{18}F-FDG + SiNc NPs.

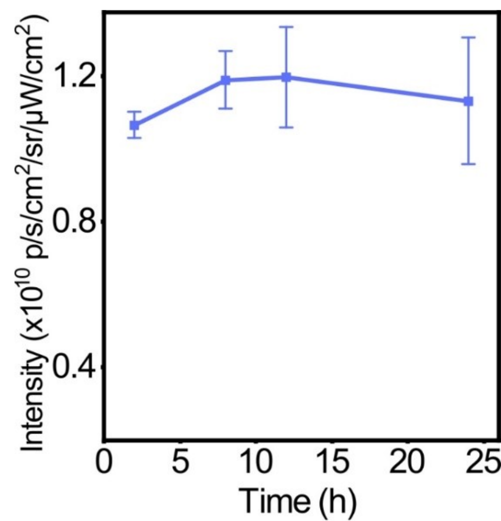

Figure S3: Fluorescence intensity in tumor sites at different time-point post-injection.

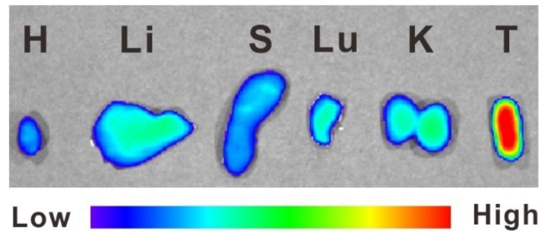

Figure S4: *Ex vivo* fluorescence imaging of major health organs and tumors at 24 h post-injection.

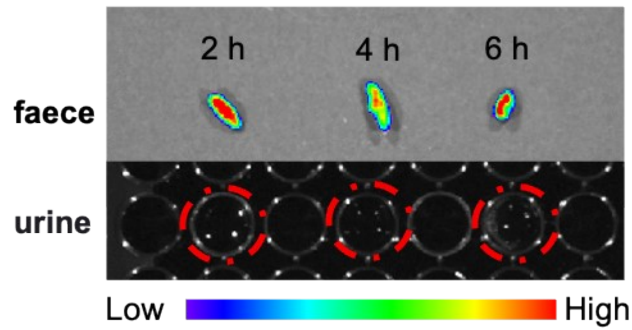

Figure S5: Fluorescence imaging of feces and urine which collected at 2 h, 4 h and 6 h post-injection of SiNc NPs.

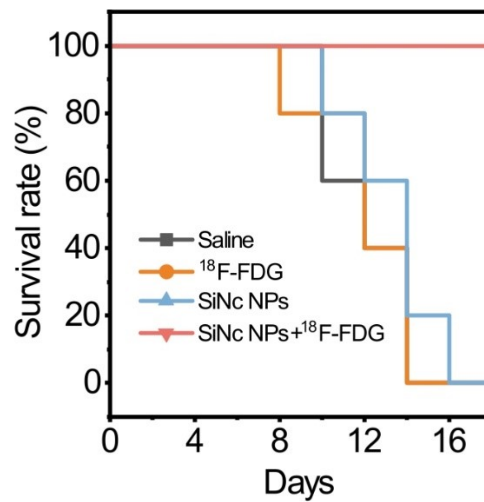

Figure S6: The survival rate curves of mice in various treatment group.

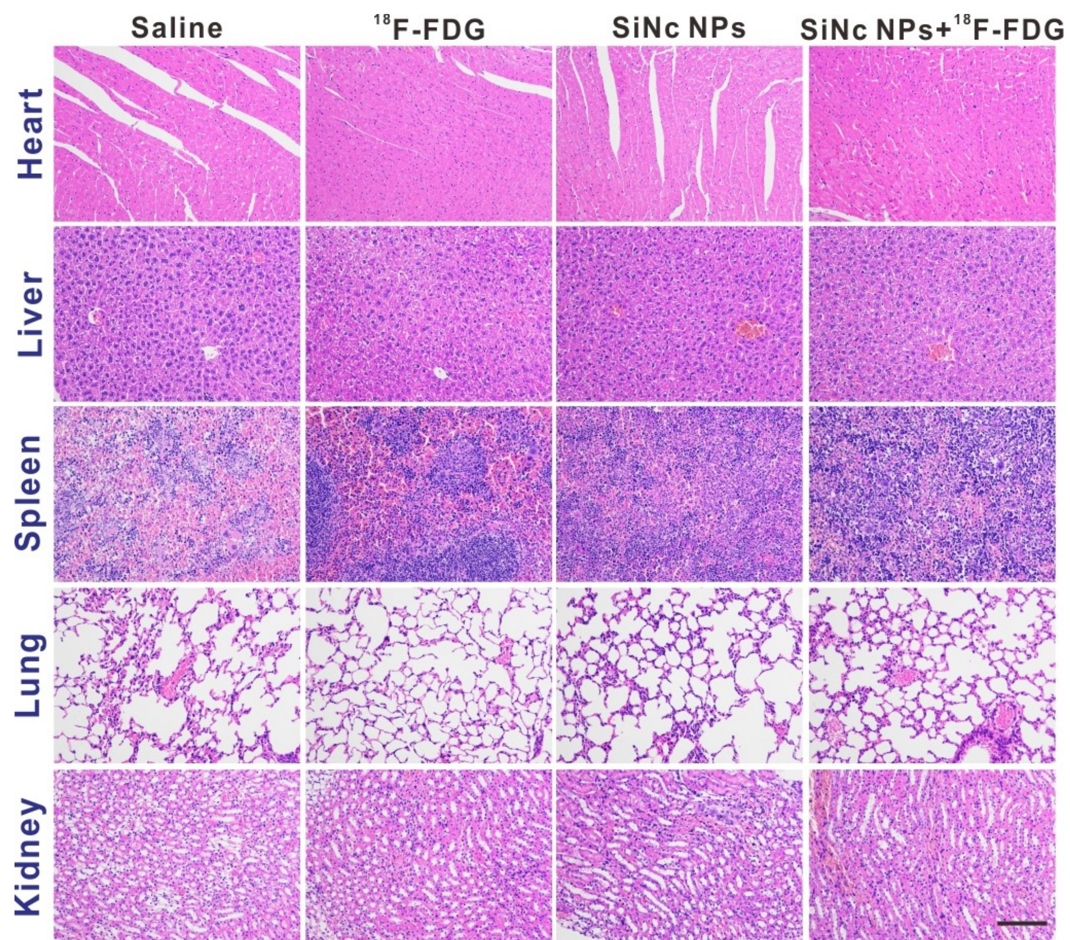

Figure S7: H&E staining images of major health tissues including heart, liver, spleen, lung and kidney of mice in each therapeutic group (Scale bar = 50 μm).