Supporting Information

Facile preparation of hybrid core-shell nanorods for photothermal and radiation combined therapy
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Experimental section

Materials
All chemicals involved in this work were analytical grade and used without further purification. Oleylamine (99%), 1-octadecene (99%) and Fe(CO)₅ were purchased from Sigma-Aldrich. Pt(acac)₂ and 3,4-dihydroxyhydrocinnamic acid (DHCA) were purchased from Alfa Aesar Co. Sodium oleate was purchased from Shanghai Chemical Industrial Co. Tetrahydrofuran (THF) was purchased from Nanjing Chemical Reagent Co. Ltd. Dimethyl sulfoxide (DMSO) was purchased from Aladdin Industrial Co. High Q water was used throughout the research.

Methods

Synthesis of platinum nanorods
200 mg of Pt(acac)₂ and 150 mg of sodium oleate were added to 20 mL of oleylamine. The reaction mixture was degassed at 120 °C by bubbling nitrogen. The solution was kept at this temperature for 15 min until it turned brown yellow. A drop of Fe(CO)₅ (~5μL) was injected into the hot solution causing the solution to darken rapidly and then the temperature was raised to 220 °C for half an hour without stirring, resulting in nanorods formation. The solution was then cooled to room temperature, and the sample was centrifuged in excess ethanol. The supernatant was discarded, and the precipitates collected were reserved.

Synthesis of hybrid platinum@iron oxide nanorods
The above Pt nanorods were dispersed in 20 mL of 1-octadecene. The reaction mixture was degassed by bubbling nitrogen and heated to 180 °C, then 0.15 mL of Fe(CO)₅ was injected into the hot solution and the temperature was maintained for 30 min to form a Pt@Fe core-shell nanorods. Then the solution was cooled to 80 °C and bubbling air through the solution for another 30 min. The solution was then cooled to room temperature. The sample was centrifuged in excess ethanol and the precipitates collected were dispersed in tetrahydrofuran (THF) for further use.

Aqueous phase transfer of hydrophobic core-shell nanorods
50 mg of 3, 4-dihydroxyhydrocinnamic acid (DHCA) was dissolved in 6 mL of THF
in a three-neck flask (25 mL). The resulting solution was heated to 50 °C under nitrogen flow. Then, 20 mg of hydrophobic nanorods dispersed in 1 mL of THF were added dropwise. After 3 hours, the reaction was cooled to room temperature, and 600 μL NaOH (0.5 M) was introduced to the solution to precipitate the nanorods. The precipitates were collected by centrifugation and redispersed in 2 mL water for further use.

**Photothermal experiments of the hybrid core-shell nanorods in aqueous solutions**

To study the photothermal effect of the synthesized hybrid core-shell nanorods, 1 mL aqueous solutions containing different concentrations (0, 50, 100, 200 μgFe/mL) of core-shell nanorods were irradiated under 808 nm laser at a power density of 0.75W/cm² for 10 min. An IR thermal camera was used to record the temperature of the solution at each time point. To evaluate the photothermal stability of core-shell nanorods, 200 μgFe/mL of core-shell nanorods were irradiated for 10 min at a power density of 0.75 W/cm² and then turn off the laser. This procedure was repeated for 4 times to assess its photothermal stability.

**Cell cytotoxicity of the hybrid core-shell nanorods**

We tested cytotoxicity of the core-shell nanorods using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay with 4T1 murine breast cancer cells. Typically, 4T1 cells were incubated in the culture medium at 37 °C in an atmosphere of 5% CO₂ and 95% air for 24 h. Subsequently, the culture medium was removed. The cells were incubated in culture medium containing nanorods with different concentrations for another 24 h and washed with phosphate buffer saline (PBS) twice. 100 μL of the new culture medium containing MTT reagent (10%) was added to each well of the 96-well assay plate. After incubated for 4 h, the medium was removed. Then 100 μL of dimethyl sulfoxide (DMSO) was added to each well to dissolve the purple formazan product for 10 min. Finally, the optical absorption of formazan at the characteristic peak of 490 nm was measured by the microplate reader (Thermo SCIENTIFIC, MULTISCAN MNK3).

**Photothermal experiments of the hybrid core-shell nanorods**

To quantitatively evaluate the photothermal effect to cells of the hybrid core-shell nanorods, 4T1 murine breast cancer cells maintained in culture medium were cultured in 96-well plates at 37 °C in a humidified atmosphere containing 5% CO₂ for 24 h. Then the culture medium was removed. 100 μL of new culture medium with different concentrations of core-shell nanorods were added into the cells and further incubated
for 6 h. Afterwards, the cells were exposed to an NIR laser (808 nm, 0.75W/cm²) for 10 min, then incubated for another 8 h. The viability of 4T1 cells were evaluated by the MTT assay.

To further assess the photothermal effect of the nanorods, 4T1 cells were incubated in 6-well plates at a density of 1\times 10^5 per well and in the culture medium at 37 °C in an atmosphere of 5% CO₂ and 95% air for 24 h. Then the cells were set four groups. The first group had no dispose. The second group was irradiated by 808 nm laser at the power density of 0.75 W/cm² for 10 min. The third group was cultured with the Pt@Fe₂O₃ nanorods at the concentration of 50 µgFe/mL for 6 h. The fourth group was treated with Pt@Fe₂O₃ nanorods (50 µgFe/mL) for 6 h and then irradiated by 808 nm laser (0.75 W/cm²) for 10 min. After treatment, the cells were cultured for another 12 h. Then the culture medium was removed. The cells were washed with PBS and stained with both calcein AM and PI (propidium iodide) for 15 min. After staining, the fluorescence microscope was applied to take the images.

**Radiotherapy experiments of the hybrid core-shell nanorods**

4T1 cells were seeded into 96-well plates and then incubated for 24 h at 37 °C under 5% CO₂ and 95% air. Culture medium with different concentrations of core-shell nanorods (0, 3.75, 7.5 and 15 µgFe/mL) were added to the wells and incubated for another 6 h. Then the 4T1 cells were irradiated by X-ray at a dose of 4 Gy and incubated for 20 h again. Cell viability was evaluated by the MTT assay.

**Combined photothermal and radiotherapy experiments of the hybrid core-shell nanorods**

4T1 cells were seeded into 96-well plates and incubated for 24 h. Then 100 µL of culture medium with different concentrations of core-shell nanorods (0, 7.5 and 15 µgFe/mL) were coincubated with 4T1 cells for 6 h. Firstly, 4T1 cells were exposed to 808 nm laser (0.75W/cm²) for 10 min and incubated for 30 min (PTT treatment), followed by 4 Gy of X-ray radiations (RT treatment) and incubation again for 20 h. Cell viability was measured by MTT assay.
Results

Figure S1. HRTEM images of (A) Pt nanorods and (B) hydrophilic Pt@Fe$_2$O$_3$ nanorods.

Figure S2. UV-Vis-NIR absorption spectra of Pt@Fe$_2$O$_3$ nanorods and Pt nanorods at the same concentration.
Figure S3. The optical images of Pt@Fe$_2$O$_3$ nanorods (A) before ligand exchange (left) and after ligand exchange (right), (B) attracted by a magnet.

Figure S4. Synergistic therapeutic of 4T1 cells that have taken up Pt@Fe$_2$O$_3$ nanorods (7.5 $\mu$gFe/mL) subjected to NIR, RT and the combined NIR/RT treatments.
Figure S5. (A) The photo and (B) TEM image of hybrid nanorods dispersed in PBS buffer.

Table S1. The composition of hybrid Pt@Fe$_2$O$_3$ nanorods determined by ICP.

<table>
<thead>
<tr>
<th>Pt (µg/mL)</th>
<th>Fe (µg/mL)</th>
<th>Fe$_2$O$_3$ (µg/mL)</th>
<th>Pt% (mass)</th>
<th>Fe% (mass)</th>
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<td>0.84</td>
<td>0.58</td>
<td>0.82</td>
<td>50.6</td>
<td>35.0</td>
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</tbody>
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Figure S6. Cell viability of 4T1 cells treated with different concentrations of platinum@iron oxide nanorods with or without X-ray irradiation.

When the concentration of the nanorods increased, the cell viability of 4T1 cells decreased gradually under X-ray irradiation.
Figure S7. The cell viability of 4T1 cells with NIR laser, X-ray irradiation and both NIR laser and X-ray irradiation without platinum@iron oxide core-shell nanorods.