Theranostic performance of photothermal bubbles from the phase transition of nanodroplets via concurrent laser and ultrasound irradiation

Dui Qin[1,2], Yi Feng[1], Hongrui Zhu[1], Daocheng Wu[1], Ayache Bouakaz[1,3], Mingxi Wan[1]
[1]School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, China, [2]School of Bioinformatics, Chongqing University of Posts and Telecommunications, Chongqing, China, [3]UMR Inserm U930, Université François-Rabelais de Tours, Tours, France.

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Background, Motivation and Objective

Near-infrared absorbing perfluorocarbon nanodroplets can vaporize to form photothermal bubbles for ultrasound (US) imaging-guided/monitored photothermal therapy (PTT). While concurrent laser and US were used, the phase-transition threshold can be reduced and the US-induced bubble cavitation effects may also improve the PTT efficacy. In our study, the synergistic photothermal/cavitation effects during concurrent laser and US irradiation were further investigated with the theranostic nanodroplets composed of a perfluoropentane core and an optically-absorbing polypyrrole shell (PFP@PPy ND) to achieve highly effective and safe tumor therapy.

Statement of Contribution/Methods

PFP@PPy ND was synthesized by *in-situ* oxidative polymerization on the surface of PFP nanodroplet, and its characterization was performed by transmission electron microscopy, dynamic light scattering, UV-vis spectrophotometer and photothermal effect evaluation. Then, enhanced US images of PFP@PPy NDs were acquired using a diagnostic US scanner with a 10 MHz linear probe, and their cavitation mapping was achieved by sonochemiluminescence (SCL). Finally, the treatment outcomes were evaluated with HeLa cells when exposed to either laser, US or their combination and further compared the results.

Results/Discussion

The PFP@PPy NDs with an average diameter of 245±13 nm (n = 3) were synthesized, and it showed a broadband absorption spectrum and an obvious photothermal effect (Fig. 1). Under concurrent laser and US irradiation, the phase transition of PFP@PPy NDs generated numerous photothermal bubbles compared to PFP NDs. These bubbles significantly increased the echo amplitudes in both B-mode and contrast-enhanced mode (Fig. 2a), indicating its great potential for US imaging. Moreover, the cavitation of photothermal bubbles occurred (Fig. 2c), which caused a significant increase ($p < 0.05$) in cell death (Fig. 3a) and an obvious cell detachment (Fig. 3b-II) compared to laser/US irradiation alone. The results demonstrate the synergistic photothermal effect and mechanical bioeffects of cavitation to improve therapeutic efficiency of PFP@PPy NDs. The simultaneous enhancement in US imaging and therapeutic efficiency offer opportunities for theranostic applications with PFP@PPy NDs.

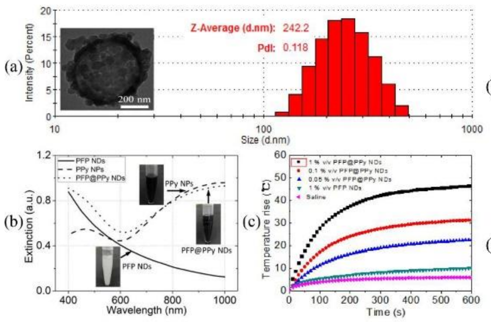

Fig. 1. Characterization of prepared PFP@PPy ND, including its (a) structure and size distribution, (b) UV-vis spectra and (c) photothermal effect evaluation. (Laser: 980nm, 1W/cm^2)

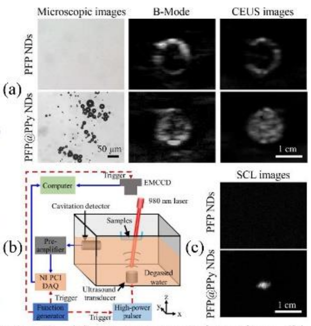

Fig. 2. (a) *In vitro* US imaging, (b) experimental system and (c) SCL images. (Laser: 1W/cm^2; US: 1MHz, 2.2MPa, 50μs, 10Hz; Time: 1min)

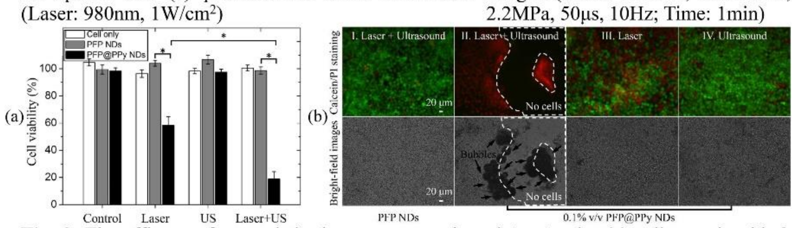

Fig. 3. The efficacy of synergistic therapy was evaluated *in vitro* by (a) cell-counting kit-8 (CCK-8) assay and (b) calcein-AM/propidium iodide staining. (Laser: 1W/cm^2; US: 2.2MPa, 50μs, 10Hz; Time: 1min)