Near-infrared rechargeable “optical battery” implant for irradiation-free photodynamic therapy

Lidan Hu, 1, Peiyuan Wang, 1, Mengyao Zhao, a, Lu Liu, a, Lei Zhou, a, Benhao Li, a, Fahad H. Albaqami, e, Ahmed Mohamed El-Toni, d, Xiaomin Li, a, **, Yang Xie, b, Xiaofei Sun, c, Fan Zhang, a, *  

a Department of Chemistry, Shanghai Key Laboratory of Molecular Catalysis and Innovative Materials, i-Chem, State Key Laboratory of Molecular Engineering of Polymers, Fudan University, Shanghai, 200433, PR China  
b Department of Orthopedics, Changhai Hospital, Second Military Medical University, Shanghai, 200433, PR China  
c Department of Spine Surgery, Changzheng Hospital, Second Military Medical University, Shanghai, 200003, PR China  
de King Abdullah Institute for Nanotechnology, King Saud University, Riyadh, 11451, Saudi Arabia  
ed Department of Physics and Astronomy, College of Science, King Saud University, Riyadh, 11451, Saudi Arabia  

A R T I C L E  I N F O  

Article history:  
Received 8 December 2017  
Received in revised form 10 February 2018  
Accepted 11 February 2018  
Available online 12 February 2018  

Keywords:  
Persistent luminescence  
Near-infrared  
Upconversion  
Rechargeable  
Photodynamic therapy  

A B S T R A C T  

As a minimal or noninvasive therapeutic method for tumors, photodynamic therapy (PDT) induced by the external laser irradiations has attracted great attentions. However, the UV–visible responsive property with low tissue penetration and photothermal effect from the prolonged irradiation impedes their further applications. Herein, a near-infrared (NIR) rechargeable “optical battery” for irradiation-free PDT is fabricated by embedding upconversion materials, persistent luminescence materials, photosensitizer into biocompatible polydimethylsiloxane. After 5 s quickly charged by 980-nm NIR laser, the PDT “optical battery” can generate green persistent luminescence and produce cytotoxic singlet oxygen for continuous irradiation-free PDT (~30 min) without external irradiation. Due to deep tissue penetration and discontinuous short exposure of NIR light charging source, the “optical battery” can still be charged to continuously generate singlet oxygen in deep tissue (~4 mm) with low photothermal effect. The PDT implant can be easily optimized in size and shape aiming at different nidus sites and achieved different functions by adding other functional components (e.g. CaO2 for oxygen envolving to overcome hypoxia tumor). The effective tumor proliferation inhibiting capability of this NIR rechargeable “optical battery” may give rise to next generation of intelligent stimuli-responsive nanomedicine and noninvasive photo bio-stimulation research for future clinical applications.

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1. Introduction  

Over the past decades, photodynamic therapy (PDT) with unique advantages and low systematic toxicity has been proposed as a relatively less invasive tool, widely applied in the anticancer therapy and nanomedicine fields [1–11]. A few photosensitizers (PSs), such as Porfimer sodium, have been approved by the United States Food and Drug Administration (FDA) to treat certain cancers [12–15]. However, most of the available PSs for PDT can only active under the UV–visible light (<700 nm) with low tissue penetration, beyond which the energy gets attenuated dramatically such that insufficient reactive oxygen species (ROS) is generated to produce an appropriate photodynamic effect [16–18]. Furthermore, the optimized PDT output is strongly dependent on the prolonged use of light, which inevitably causes severe damage to normal tissues because of the photothermal effect [19–22]. The last but not the least, the effectiveness of PDT is restricted by an inadequate oxygen supply in hypoxia tumors [23–27].  

Persistent luminescence, the so-called “optical battery”, is the afterglow emission of phosphors after excitation ceases, which allows complete separation of the excitation and emission processes [28–37]. Due to the ultra-long decay time of persistent luminescence after the excitation ceases, the multicolor (400–700 nm, matched well with the PSs for PDT) persistent luminescence...
materials with intriguing optical properties have been tried out in bioimaging and PDT to avoid the side effects induced by the prolonged light irradiation [38–41]. However, most of the reported recharging light sources for the “optical battery” are located in the UV–visible region, which is not suitable for the deep tissue biological applications.

By means of UV–visible emissions of upconversion materials under the excitation of NIR light (980 nm), herein, we report a NIR rechargeable “optical battery” implant for irradiation-free PDT by embedding upconversion materials, persistent luminescence materials, PDT photosensitizer in biocompatible polydimethylsiloxane (PDMS) (Fig. 1). Because of the protection of PDMS, the obtained implant exhibit enhanced afterglow green emission after a quick charging of 5 s by 980-nm NIR light (the effective PDT time is ~30 min for one cycle after 5 s NIR recharging). This continuous PDT under a short discontinued external charging irradiation can not only effectively generate ROS with high therapeutic efficacy, but also minimize the photothermal effect of the external irradiation. Furthermore, the PDT “optical battery” implant can still be charged to continuously generate singlet oxygen even in deep tissue as high as 4 mm because of the deep tissue penetration of the NIR charging source. Due to the facile preparation, flexible and bio-stability of PDMS, the irradiation-free PDT implant can be easily optimized in size and shape aiming at different nidus sites and achieved different functions by adding other functional components (e.g. CaO2 for oxygen envolving to overcome hypoxia tumor). Both in vitro and in vivo results demonstrated that this NIR rechargeable irradiation-free PDT implant could efficiently inhibit the proliferation of tumor, even for the hypoxia tumor.

2. Experimental section

2.1. Fabrication of PDT optical battery

Green persistent luminescence materials (GPM) were added to Rose Bengal (RB) hexanoic acid ester ethanol solution (1 mg/mL) and stirred in the dark for 24 h. Then, excess RB was removed by centrifugation and washing with deionized water for several times and the GPM-RB phosphors were dried at 50 °C in the dark overnight. The obtained GPM-RB phosphors were mixed with upconversion phosphors and CaO2 with a mass ratio of 10: 1: 5 by using a ball mill for 30 min. The mixture was added into PDMS (with a curing agent in a 10:1 ratio) with a mass ratio of 2: 5. After thoroughly mixed, the composites were placed to special moulds and degassed under vacuum for 30 min. The PDT optical battery can be obtained after solidify at 60 °C for 1 h.

2.2. Preparation of buffers in different pH

\[ pH = 1.0 \] buffer: 1.0 g NaCl was dissolved to 500 mL deionized water, then the pH was adjusted to 1.0 using 1 M HCl.

\[ pH = 5.0 \] buffer: 1.36 g KH2PO4 and 0.304 g NaOH were dissolved to 200 mL deionized water, then the pH was adjusted to 5.0.

\[ pH = 8.0 \] buffer: This buffer was obtained by adjusting the pH of the \[ pH = 5.0 \] buffer to 8.0 using 1 M NaOH.

2.3. Persistent luminescence induced toxicity to HT29 cells

CCK-8 assay was used to evaluate the in vitro therapeutic efficacy of PDT optical battery: HT29 cells were seeded onto 96-well plates with a cell intensity of \( 1 \times 10^4 \) cells per well and incubated for 12 h to allow the attachment of cells. After cultivation for 12 h, different membranes with or without charging were added, respectively, and incubated with cells for 4 h. Cells without treatment were set as controls. After treatments, the solution of CCK-8 assay was added into each well. After 4 h incubation, the plate was read by a spectrometer at 490 nm. The cell viability was calculated as:

\[
\text{cell viability} = \frac{\text{Mean absorbance of test wells} - \text{Mean absorbance of medium control wells}}{\text{Mean absorbance of control wells} - \text{Mean absorbance of medium control well}} \times 100%.
\]

2.4. Antitumor efficacy of the PDT optical battery

Subcutaneous tumors were induced to the right arm of 5 weeks old female nude mice by injection of \( 5 \times 10^6 \) HT29 cells under irradiation-free PDT implant. Both in vitro and in vivo results demonstrated that this NIR rechargeable irradiation-free PDT implant could efficiently inhibit the proliferation of tumor, even for the hypoxia tumor.

Fig. 1. Schematic illustration of the NIR light rechargeable persistent luminescence activated PDT “optical battery” implant for tumor inhibition (GPM: green persistent luminescence materials; PSs: photosensitizers; UC: upconversion materials; TB: trapping band; VB: valence band). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
aesthetic conditions. All experimental protocols were in agreement with the guidelines of the Institutional Animal Care and Use Committee of Fudan University and performed in accordance with institutional guidelines on animal handling. For determination of tumor growth, individual tumors were measured by a caliper and the tumor volume was calculated as: tumor volume \((\text{mm}^3) = \text{length} \times \text{width} \times \text{height}/2\).

In vivo PDT experiments were performed when the tumors reached 100 mm\(^2\) in average diameter (14 days after implant). The tumors embedded mice were divided into seven groups (include four mice in each group): 1. Control (without treatment); 2. NIR charging; 3. PDMS; 4. \(\text{O}_2\)-generating PDT optical battery; 5. GPM + RB + PDMS & NIR charging; 6. & NIR charging; 7. Normal PDT optical battery & NIR charging; 8. \(\text{O}_2\)-generating PDT optical battery & NIR charging. NIR charging was conducted each day by 980-nm laser \((2 \text{ W/cm}^2\) 980 nm) for 5 s, and the volume of tumors was measured every other day. To further confirm the treatment efficiency of PDT optical battery for tumor therapy, all the tumors tissues were sectioned into slices and H&E, TUNEL stained for histological analysis. The organs of heart, liver, spleen, kidney, and lung were dissected for H&E staining and examined under a microscope.

For ex vivo bio-compatibility analysis, mice were sacrificed after PDT therapy, and tissue of implant site were collected, measured and weighed for ICP-MS.

3. Results and discussion

3.1. Fabrication of NIR light rechargeable PDT “optical battery” implant

By combining the NaYF\(_4\):25\%Yb,0.5\%Tm upconversion materials with typical UV/blue upconversion emission \((350/475 \text{ nm})\) and UV rechargeable SrAl\(_2\)O\(_4\):2\%Eu\(^{2+},4\%\text{Dy}^{3+}\) persistent phosphors (mass ratio, 1: 10), the green persistent luminescence at ~520 nm can be activated by 980-nm NIR excitation due to the spectra overlapping between the upconversion emissions and absorption of persistent phosphors (Fig. 2A). In the optical charging step (Fig. 1), photons of UV/blue emission from upconversion materials are absorbed by the persistent phosphors, populating the excitation state levels and leading to the energy storage in electron traps. After ceasing the 980-nm excitation, the energy trapped in the persistent phosphors can be released and transferred to the activator to realize the long-lasting luminescence (Fig. 1). Then the persistent luminescence can be used for the irradiation-free PDT (Fig. 1). As a proof of concept, we choose the RB as the photosensitizer because it’s strong absorbance on the green light to generate the singlet oxygen (Fig. 2A). The RB can be loaded on the surface of persistent phosphors \((1.565 \text{ mg/g})\) according to the electrostatic interaction (Fig. S2, S3). In order to suppress the quenching effects of the persistent luminescence in physiological environment for long term lasting PDT (discussed in following), the upconversion and persistent luminescence materials \((\text{bulk materials with broad size distribution of 1–10} \text{ \mu m, Fig. S1})\), photosensitizer are embedded in biocompatible PDMS to form a PDT “optical battery” implant.

After being charged by 980-nm laser, the PDT “optical battery” implant can generate strong naked-eye certifiable green persistent luminescence (Fig. 2B, inset). According to the intensity and decay kinetics of the persistent luminescence, there is not apparent difference when the charging time prolonged from 5 to 30 s at 2 W/cm\(^2\), which means that a very short NIR exposure time of 5 s is enough to full charge the persistent materials (Fig. 2B). So, the overheating and cell damages induced by the long-lasting irradiation can be effectively suppressed (discussed in following). The persistent luminescence of the PDT “optical battery” implant is allowed to experience multiple cycles of recharging without noticeable intensity weakening (Fig. 2C), which is much useful for the lasting irradiation-free therapy. The luminescence of “optical battery” can persist more than 2 h (Fig. 2D). Moreover, it is found that the intensity of persistent luminescence is greatly enhanced under protection of PDMS, which is about 2 times stronger than that of the directly environment exposed composites without protection of PDMS (Fig. 2D). We consider that this diversity is mainly result from the non-radiative quenching by the moist environment. To verify this assumption, the long-term stability of the persistent materials was further investigated under different physiological buffers. The results show that the persistent luminescence intensity of PDMS encapsulated persistent materials is very stable in PBS (Fig. 2E, Fig. S4), serum medium (Fig. S16) and buffers of different pH value (Fig. 2F) in 15 days. In contrast, the persistent luminescent property of the bare persistent materials without the protection of PDMS is almost wiped out after only 5 days in PBS solution (Fig. 2E, Fig. S4).

3.2. ROS generation of “optical battery” implant under NIR irradiation

The in vitro biosafety of PDT “optical battery” implant was assessed by cck-8 kit assay. It can be seen that the viability of the HT29 cells is maintained at more than 95% even when the weight percentage of inorganic species in implant increased as high as 50%, indicating the high biocompatibility of the implantable device (Fig. S5). Due to the hydrophobicity of PDMS (Fig. S19), the liquid water is difficult diffused into the PDMS, but the gas molecule, including gaseous water molecule, can easily permeate into the framework of PDMS, thus an atmosphere environment would be formed in PDMS. For the lifetime of \(\text{O}_2\), it has been demonstrated that the lifetime of \(\text{O}_2\) in atmosphere (~1 h) is much longer than that in the liquid environment \([42,43]\), which is long enough for diffusion out from the PDMS to destroy the membranes of the appressed cells by introducing a variety of reversible and irreversible oxidative modifications on proteins, lipids \([44–47]\). The generated \(\text{O}_2\) from RB under persistent luminescence from the PDT “optical battery” implant was examined by the single oxygen indicator 9,10-anthracenediylbis (methylene) dimalonlic acid (ABDA). The typical absorbance of ABDA at 342, 359, 378 and 400 nm decreased with an increase in the concentration of \(\text{O}_2\) in solution after being charged with 980-nm NIR laser \((2 \text{ W/cm}^2)\) (Fig. 3A, B, Fig. S6). The absorbance intensity of ABDA gradually decreased in the following 30 min after ceasing of NIR light, indicating continuous generation of \(\text{O}_2\) under the excitation of the persistent luminescence (Fig. 3A, B, Fig. S6). This result was further confirmed by detecting the emission of \(\text{O}_2\) at 1270 nm (Fig. S20). With multiple circulating of the recharging process, the cumulative producing of singlet oxygen can be further increased (Fig. 3A and B).

The statistic results of the absorbance intensity decreasing of ABDA gradually decreased after each charging also proved the charging stability of this PDT device. To investigate the PDT effect of the “optical battery” implant in deep tissue, we further compared the \(\text{O}_2\) generation capability of the PDT device recharged by UV (365 nm) and NIR (980 nm) light crossing different thickness of pork tissue (Fig. S7). Due to the poor tissue penetration of UV light, the PDT implant can be recharged to generate \(\text{O}_2\) by 365-nm light only when the thickness of tissue within 1 mm. In contrast, when using the 980-nm NIR light as the charging source, the PDT implant can generate \(\text{O}_2\) in deep tissue as high as ~4 mm (Fig. 3C). All these results demonstrated that \(\text{O}_2\) could be persistently produced from the PDT implant after short-time charging, which further confirms the feasibility of NIR rechargeable “optical battery” for irradiation-free PDT implants.

On the other hand, the photothermal effect from 980-nm
charging source can be greatly suppressed because of the discontinuous short exposure of the laser. As shown in Fig. 3D, the multiple short time irradiation manner (5 s * 12 times) possess negligible photo-toxicity with a high cell viability of 99.1%. However, after a continue exposure of equal time (1 min * 1 time), the cell viability decreased to 93.4%. The photo-toxicity becomes worse (the cell viability decreased to 87.7%) when the irradiation time further increased to 5 min. The in-vivo temperature monitoring of the irradiation points (Fig. 3E and F) showed that the temperatures of the exposure point could be well controlled below 48 °C by using the intermittent irradiation manner (55 s interval after each 5 s of irradiation) in our rechargeable irradiation-free PDT, and the temperature was much lower than that of the constant light irradiation (>60 °C) in traditional PDT. It can be seen that the skin of the nude mice was obviously burned after only 1 min prolonged 980-nm irradiation (2 W/cm²).

After diffusion out from the PDT optical battery, 1O2 can destroy the membranes of the appressed cells by introducing a variety of reversible and irreversible oxidative modifications on proteins, lipids, etc.[44–47]. In the in vitro PDT efficiencies were further evaluated by detecting the ROS generation in HT29 cells under different treatments. 2, 7-Dichlorofluorescin diacetate (DCFH-DA) was used as a fluorescence probe for detecting intracellular ROS that was produced by PDT damaged cells. As shown in Fig. 4A, after incubated with pre-charged PDT “optical battery” implant, the strong green fluorescence from the ROS probe can be observed clearly, indicating the presence of ROS in the cell. Due to the continuously decreasing of the persistent luminescence, the intensity of fluorescence from ROS probe gradually decreased with prolonging of time. The green fluorescence from ROS probe can also be detected at 30 min after charging (Fig. 4A, Fig. S8), which indicating the effective cell damage time of this PDT device is 30 min. In contrast, there is not ROS generation in HT29 cells in the other groups (PDT implant without charging, GPM & PDMS with 980 charging, UC & RB & PDMS with 980 charging) (Fig. S9), indicating no PDT effect was produce to the treated cells by these groups. Compared with PDT implant without charging group, GPM & RB & PDMS and UC & RB & PDMS with 980 charging groups, the NIR charged PDT “optical battery” implant group showed an obvious cell toxicity for the tumor cell (~25% of the cells were killed) (Fig. 4B). To investigate the persistent luminescence dependent toxicity to HT29 cells, the effective PDT can last ~30 min (Fig. 4C). The cell toxicity decreased as the prolonging of the persistent luminescence because of the decreasing of the intensity of persistent luminescence (Fig. 4C), which is consistent with the results of the intracellular ROS determination (Fig. 4A). Moreover, the therapeutic efficiency of PDT implant can be further increased with the multiple charging process (Fig. 4B).

3.3. O2-generating PDT “optical battery” implant for tumor proliferation inhibiting

Another important character of the developed PDT implant is that the species embedded in it can be handily changed as the requirements of clinic features. In most PDT process, 1O2 is formed by the electronically excited PSs react with surrounding O2. However, the hypoxic is a common phenomenon in many tumors. So, to increase the PDT efficiency in the hypoxic tumor, we can further encapsulate CaO2 adjuvant in the NIR rechargeable “optical

![Graph and Diagrams]

Fig. 2. A) Excitation spectrum (Ex) of SrAl2O4:Eu³⁺,Dy³⁺ green persistent materials (GPM), emission spectra (Em) of the NaYF4:Yb, Tm upconversion materials (UC) and GPM, and absorbance spectra (Ab) of Rose Bengal (RB). B) Persistent luminescence decay curve of the “optical battery” implant monitored at 520 nm after charging with 980-nm NIR laser for 5, 15, 30 and 60 s, respectively. Insets: Photographs of “optical battery” implants and persistent luminescence image of the implants after charged with 980-nm NIR laser. C) The multiple repeating charging of “optical battery” implant with 980-nm NIR laser for 5 s. All the decay curves were recorded 10 s after the cease of excitation. D) Persistent luminescence decay curve of GPM at 520 nm with and without of the protection of PDMS after charging with 980-nm NIR laser for 5 s. E) Persistent luminescence intensities of GPM after incubated in PBS for different lengths of time with and without of the protection of PDMS. F) Persistent luminescence intensities of “optical battery” implant after incubated in buffer of different pH value for different days. The power density of the 980-nm NIR laser is 2 W/cm². (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
battery" implant to realize the O₂ self-supporting irradiation-free PDT via the reaction shown in the following equation.

$$2\text{CaO}_2 + 4\text{H}_2\text{O} \rightarrow 2\text{Ca(OH)}_2 + 2\text{H}_2\text{O}_2 \rightarrow 2\text{Ca(OH)}_2 + 2\text{H}_2\text{O} + \text{O}_2$$

The O₂ generating property of this PDT implant is investigated in PBS. The dissolved O₂ were daily measured by dissolved oxygen apparatus. Fig. 4D shows the average oxygen concentration in stimulated hypoxia fluid when co-incubated with the O₂-generating or normal PDT "optical battery" implant. The results show that the dissolved O₂ in the CaO₂-free PDT membranes group remained at a very low dissolved O₂ of 1.68 mg/L. In comparison, the dissolved O₂ can increase to as high as 6.05 mg/L and maintain above 3.50 mg/L for 15 days in oxygen-generating PDT implant group, suggesting the CaO₂ adjuvant in the implant can persistently generate oxygen in a hypoxic environment. Furthermore, the O₂ generated from the implant in the hypoxia cytoplasm was also noninvasively monitored using oxygen sensors of tris(4,7-diphenyl-1,10-phenanthroline) ruthenium (II) dichloride (its fluorescence can be quenched by O₂). As shown in Fig. S10, strong red fluorescence can be observed in the cytoplasm because of the hypoxia condition of cell. However, the red fluorescence is totally quenched by the O₂ when the hypoxia cells were co-incubated with O₂ self-supporting PDT implant.

Then, the O₂ self-supporting NIR rechargeable irradiation-free PDT "optical battery" is implanted subcutaneously onto the surface of HT29 tumor (Fig. 5A). Photoacoustic (PA) imaging was used to evaluate the vascular saturated O₂ (sO₂) within HT29 solid tumors by measuring oxygenated hemoglobin. Compared with the CaO₂-free normal PDT "optical battery" group, both oxygenated hemoglobin and total hemoglobin in the tumor are significantly increase in the O₂ self-supporting PDT "optical battery" group, which further resulted in the enhancement of total sO₂ of tumors from 5.7% to 34.6% (Fig. 4E and F). Owing to the high efficient irradiation-free continuous PDT and oxygen-generating properties of the implantable O₂-generating PDT device, the tumor volume of the mice greatly decreased after the multiple circulation of NIR irradiation in 15 days (2 times each day) (Fig. 5B, C, Fig. S11, S12). The tumor cells and blood vessels appressed on the PDT optical battery are destroyed firstly, then deep into the tumor with...
gradually destruction of the outer most tumor cells and blood vessels. Moreover, oxidized phospholipids (cell membranes) can be recognized as damage-associated molecular patterns by numerous pattern recognition receptors on immune cells, thus initiating inflammatory and immunogenic responses [48,49], which would be a potential strategy for effective cancer immunotherapy.

No significant body weight variation (Fig. 5D) was observed. The H&E staining of the major organs (Fig. S13) on day 15 after treatments did not show any obvious tissue damage or any other side effect to the organs. After the whole treatment, PDT device can be removed from the implant position (Fig. S14). The elemental analysis of the tissue around the implant position show that there is

Fig. 4. A) Confocal laser scanning microscope images of \( ^1 \)O\(_2 \) generation in HT29 cells after co-incubated with PDT “optical battery” implant at different time after recharged with 980 nm NIR laser for 5 s (Scale bar, 100 \( \mu \)m). B). Viability of HT29 cells treated with various conditions. “+” 980” means recharged with 980 nm NIR laser for 5 s. C). Cell viability of HT29 cells after co-incubated with PDT implants at different time after charged with 980 nm NIR laser for 5 s. D) In vitro evaluation of \( O_2 \) generation from \( O_2 \)-generating PDT “optical battery” implant or normal PDT “optical battery” implant in stimulated hypoxia condition. E, F) 2D photoacoustic images of oxygenated hemoglobin within HT29 solid tumors after being implanted with \( O_2 \) self-supporting PDT “optical battery” implant (F) or normal PDT “optical battery” implant (E) (Scale bar, 1 mm). Cell viability was measured using the CCK-8 assay, \( N=4 \); Data are means ± S. D; the power density of 980-nm NIR laser is 2 W/cm\(^2\); OB: “Optical Battery”.

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not excessive allochthonous inorganic species leak from the implant (Sr is the intrinsic trace element in the organism) (Fig. S15). The last but not the least, with the development of microfabrication technology, such as 3D printing, the NIR rechargeable irradiation-free PDT implants can be easily fabricated into any size and shapes (Fig. 5E) to meet the requirements of special nidus sites. For example, the implantable canular device for the disease of digestive, intestinal tract without of the influence on the normal feeding and excretion. Furthermore, the NIR rechargeable self-sustained “optical battery” may provide a new platform for not only the implantable PDT device, but also the noninvasive photo-genetics and persistent photo bio-stimulation research.

4. Conclusion

In conclusion, we prepared a novel NIR rechargeable “optical battery” implant for irradiation-free continuous PDT. After short (5 s) charging process by 980-nm NIR laser, the “optical battery” implant can generate green persistent luminescence and further induce the production of cytotoxic singlet oxygen for the continuous irradiation-free PDT (~30 min) without external irradiation. The PDT “optical battery” implant can still be charged to continuously generate singlet oxygen even in deep tissue as high as 4 mm. The efficient tumor proliferation inhibit capability of this implantable irradiation-free continuous PDT device was evidently confirmed by in vitro and in vivo results. This continuous PDT under the short multiple discontinued external NIR charging can not only effectively generate reactive oxygen species with high therapeutic efficacy, but also minimize the photothermal effect of the external irradiation. Due to the facile preparation, flexible and bio-stability of PDMS, the PDT implant can be easily optimized in size and shape aiming at the different nidus sites and achieved different functions by adding other adjuvant (for example, CaO2 for hypoxia tumor therapy). We considered that this intelligent NIR rechargeable irradiation free “optical battery” implant with brilliant customizability will provide a new way to not only photo responsive biomedicine, but also the noninvasive photo bio-stimulation research.
Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.biomaterials.2018.02.029.

References


