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Porous Silicon as a Sensitizer for Biomedical Applications

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Abstract: Porous silicon (PSi) can activate (sensitize) biochemical reactions and physical processes of the energy dissipation under excitation (stimulus) by light illumination, ultrasound (US), and electromagnetic radiofrequency (RF) irradiation. Photosensitized biochemical effects of PSi layers and nanoparticles (NPs) were explored in numerous physical studies and biomedical experiments *in vitro*. The photothermal sensitizing with mesoporous PSi NPs was demonstrated to be efficient for the hyperthermia of cancer cells and tumors in small animal models. The sonosensitizing properties of bare PSi NPs and dextran-coated ones were revealed by both the physical studies and biomedical experiments, which indicated a good prospect for their applications in sonodynamic therapy of cancer. RF-induced hyperthermia sensitized by PSi NPs has been successfully used to destroy cancer cells and tumors *in vitro* and *in vivo*, respectively. Here, we review the results on the preparation, physical properties, and applications of PSi NPs as sensitizers for mild therapy of cancer.

Keywords: Porous silicon; nanoparticles; photoluminescence; sensitization; photosensitizer; sonosensitizer; sonodynamic therapy; radiofrequency; hyperthermia; theranostics

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1 Introduction

Nowadays, chemically pure silicon (Si), which is the basic element for semiconductor microelectronics and solar cell industry, demonstrates a great potential for different biomedical applications [1–6]. In particular, porous silicon (PSi) is nontoxic, biocompatible and biodegradable material for various applications in life sciences and food industry [2, 3]. PSi particles and nanoparticles (NPs) have been successfully examined as containers for brachytherapy of cancer [4] and drug delivery [5–11] as well as sensitizers for the photodynamic and photothermal therapy [12–19]. Moreover, PSi NPs with bright photoluminescence (PL) were used for bioimaging of cancer cells [11, 20]. The PL properties and photosensitizing ones can be used simultaneously to realize so-called *theranostics, i.e.* both therapy and diagnostics [20]. Beside of the photosensitizing properties of PSi NPs, their aqueous suspensions possess sensitization of the energy dissipation of ultrasound irradiation (USI) [21–26] and radiofrequency (RF) electromagnetic fields [27, 28].

In this mini-review, the preparation details and physical properties of PSi NPs, which are important for their sensitizing functionalities, as well the most interesting examples of *in vitro* and *in vivo* studies are analyzed. Along with the photosensitization, the attention is paid on the sensitization of USI (sonosensitizing) and RF-induced processes, which are interesting because of deeper penetration depths of the corresponding radiations and applications in medicine. It is taken into account that PSi NPs as sensitizers possess the following properties: (i) tailored porous morphology, (ii) biocompatibility and biodegradability, (iii) presence of small Si nanocrystals.

The possible sensitizing modalities with PSi NPs are schematically shown in Fig. 1. It is assumed that PSi NPs can be delivered to cancer cells and tumors, because of an effect of the passive accumulation (Enhanced Permeability and Retention – EPR effect [29]) or/and due to active targeting [30].

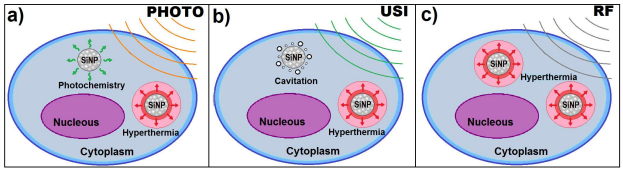

Figure 1: Schematic view of PSi NPs as sensitizers of photochemical reactions (green arrows), local hyperthermia (red arrows and circles), and cavitation (open circles) under (a) photoexcitation, (b) US irradiation (USI), and (c) RF- irradiation for cancer cell destruction.

2 Preparation of PSi particles

Many methods like ultrasonic fragmentation and mechanical milling of PSi films and silicon nanowires (SiNWs) are usually used to prepare suspensions of NPs. The mechanical milling can be done for dry powder of PSi flakes or SiNWs, i.e., *dry grinding*, and it also can be realized for those dispersed in water, i.e., *wet grinding* (see for example Refs. [20–24]).

PSi films are usually formed by using the standard method of electrochemical etching of crystalline silicon (c-Si) wafers in hydrofluoric acid solutions (see for example Refs. [25, 31]). Fig. 2(a) shows a typical cross-sectional SEM image of a PSi film, which consists of interconnected Si nanocrystals and pores. Inset in Fig. 2(a) shows a photographic image of the PSi film grown on a 4-inch c-Si substrate. Mesoporous (mPSi) and microporous (μPSi) silicon films are commonly formed from boron-doped c-Si substrates with specific resistivity of 1–50 mΩ·cm and 10-20 Ω·cm, respectively. Typical electrolyte composition and current density for etching are the following: HF(49%):C_2H_5OH=1:1 and 50–100 mA/cm^2, respectively. The prepared PSi films are lifted off by a short increase of the current up to 500–800 mA/cm^2. The dried free-standing films can be hand-milled in an agate mortar to get powders of micrometer-sized particles (see Fig. 2(b)). Then the powders are ground in ethanol or distilled water in an ultrasound bath (see for example Ref. [11]) or in a planetary-type mill (see for example Refs. [2, 25]).

Ultrasonic fragmentation of porous SiNWs formed by metal-assisted chemical etching (MACE) of c-Si wafer with specific resistivity of 1-5 mΩ·cm is also used for preparation of aqueous suspensions of PSi NPs with mean sizes ~200 nm [24]. The oxide coating of SiNWs grown by MACE facilitated stability of the prepared suspensions.

After the wet grinding, NP suspensions are usually centrifuged to remove larger aggregates and to prepare supernatants for further studies. For as-prepared suspensions the concentration of NPs is about 5-10 g/L and the suspensions are diluted to obtain the PSi concentration below 1–2 g/L for biomedical experiments. Fig. 2(c, left) shows a digital image of standard optical cells filled by aqueous suspensions of PSi NPs with concentration of 1 mg/mL.

Transmission electron microscopy (TEM) studies reveal that PSi NPs obtained by the wet grinding appear as clusters of size 10–300 nm with a maximum of the distribution function at 30-100 nm (see Fig. 2(d)) [23–25]. The dry-ground NPs are characterized by larger dispersion of sizes in the range from 50 nm to 600 nm with a maximum at about 150–250 nm [23]. Scanning electron microscopy (SEM) analyses confirmed the larger sizes of dry-ground NPs in comparison with the wet-ground ones [23]. The smaller sizes of the latter are probably related to lower efficiency of NP agglomeration because of their wetting and partial dissolution in water during the mechanical milling [22, 23]. The electron diffraction patterns of PSi NPs show periodically arranged reflexes, which are more pronounced for dry-ground NPs, indicating their crystalline structure. Partial disordering of the crystalline lattice in wet-ground NP appears as diffusive rings in the electron diffraction pattern [23]. It is worth mentioning that the wet grinding influences partially the porosity and specific surface area of NPs and the latter can be changed up to 2 times for μPSi (lowering) and mPSi (increasing) samples, respectively [32].

Medical applications of PSi NPs with their intravenous administration are possible when special surface coating is used to ensure stability and to prevent fast dissolution of NPs [11]. It can be done by using coating with biodegradable polymers as dextran and PEG [11, 25]. Dextran coated NPs are mainly accumulated in cancer tumor, while an increase of the silicon concentration in different organs of mice is also observed for weeks after the injection [11]. During the coating process, dextran is adsorbed on the surface of PSi NPs that leads to an increase of the size of dextran-coated ones, i.e. DPSi NPs (see Fig. 2(e)). Fig. 2(c, right-hand) shows a typical view of suspension of DPSi NPs. Fig. 2(f) and (g) shows the corresponding electron diffraction pattern obtained in the "transmission" geometry for PSi NPs and DPSi NPs, respectively. The diffraction pattern indicates that Si atoms in the prepared NPs arrange mainly as the crystalline structure of c-Si. While the diffraction pattern of PSi NPs contains both the diffraction rings and bright spots, DPSi NPs are characterized by the diffraction rings only. This fact indicates larger degree of misorientation of nc-Si in DPSi NPs in comparison with PSi ones. Indeed 2-10 nm-sized silicon nanocrystals within individual DPSi NPs are assembled in a porous sponge-like structure (see Fig. 2(h)).

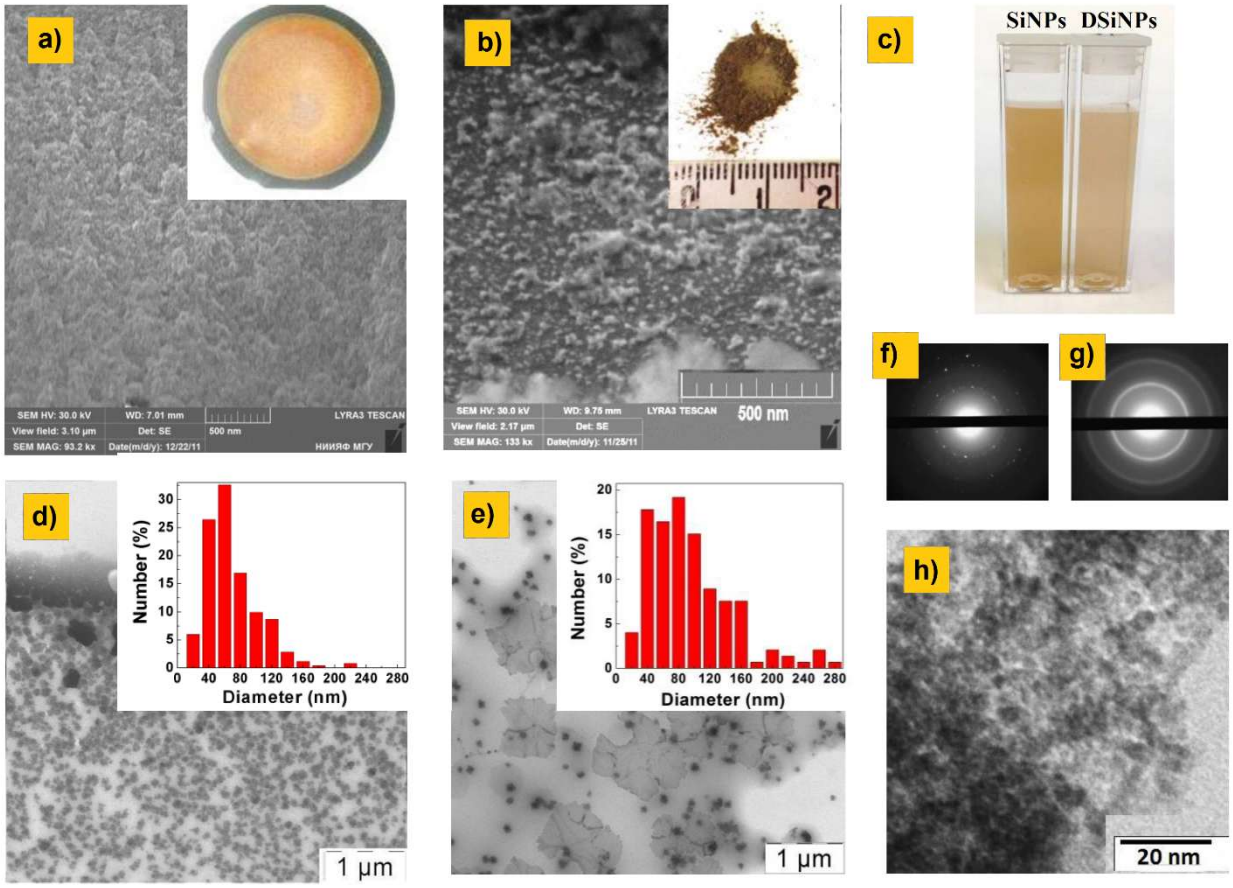

Figure 2: (a) Cross-sectional SEM image of a PSi film; inset shows a photographic image of the PSi film grown on a 4-inch c-Si substrate. (b) SEM image of a powder of PSi NPs obtained by the hand milling of PSi films; inset shows a photographic image of the powder. (c) Photographic images of PSi NPs (left) and DPSi NPs (right) aqueous suspensions with the concentration of 1 mg/mL. (d) TEM image of PSi NPs; inset shows the size distribution of PSi NPs obtained from the TEM data. (e) TEM image of DPSi NPs; inset shows the size distribution of DPSi NPs obtained from the corresponding TEM image. (f) Electron diffraction pattern for PSi NPs. (g) Electron diffraction pattern for DPSi NPs. (h) TEM image of the porous morphology of DPSi NPs. (Ref. [25])

The electron and optical properties of NPs prepared by the above-described methods inherit those inherent for the corresponding PSi films and SiNWs. For example, NPs prepared by the wet grinding of μPSi and SiNWs possess the visible PL similar to that for the corresponding initial films (see Fig. 3) [20, 24, 25]. A small high-energy shift of the PL band for NPs can be attributed to partial oxidation of small Si nanocrystals inside the NPs [20]. The PL emission of SiNWs and corresponding suspensions of NPs can be easily seen with a naked eye (insets in Fig. 3).

It was found that the coating of PSi NPs by biopolymers as PVA/PLGA [33] and dextran could significantly improve both the PL efficiency and stability [25]. These results look very promising for the bioimaging with PSi NPs and they can be combined with the photosensitizing and photothermal properties in order to realize the optical theranostic modalities [12–21].

3 Photosensitization

PSi as a photosensitiser is aimed to be applied in photodynamic therapy (PDT), which is a kind of phototherapy of malignant tumors and other tissue pathology. Usually PDT combines three steps, i.e. (i) injection of a drug (photosensitizer), (ii) the drug accumulation, (iii) the drug activation by illumination (photoexcitation). The photosensitization results in formation of singlet oxygen (SO) and/or other reactive oxygen species (ROS) as superoxide and peroxide, which interact (oxidize) cancer cells and malignant tumors [12]. The photochemical effect of PSi NPs in a cancer cell is schematically shown in Fig. 1a.

For the first time the photosensitizid SO generation by PSi was observed as the spectrally-selective quenching of the PL intensity of μPSi layers in molecular oxygen ambient followed by an appearance of the SO luminescence line

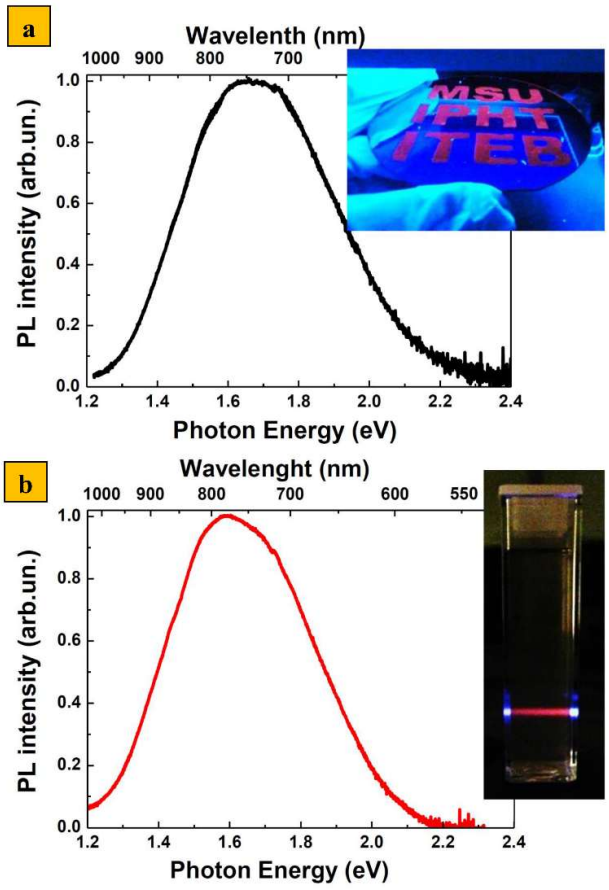

Figure 3: (a) PL spectrum of SiNW layer (inset shows a digital photo of the silicon wafer with SiNWs under UV excitation). (b) PL spectrum of aqueous suspension of Si NPs prepared from SiNWs (inset shows a digital photo of the suspension under irradiation with UV beam of an Ar+ laser). (Ref. [24])

at 0.98 eV [34, 35]. The first observation of the photosensitization with PSi *in vitro* was reported in Ref. [36] (see Table 1). Fig. 4(a) shows dependence of the cell viability in the presence of PSi NPs, relative to the control, on incubation time [20]. Part of the cells with PSi NPs was in the darkness (black curve) and the other part of cells was irradiated by visible light of a Hg-lamp with intensity about 1 mW/cm^2 near the sample (red curve). The illumination for 20–150 min led to a continuous decrease of the cell viability to 80–30%. At the same time, the number of cells incubated with PSi NPs in darkness was nearly equal to the number in the control group. Note that in both cases (see Fig. 4(b) and 4(c)) the cells with the amount of DNA less than in the diploid chromosome set (sub G1) were detected. However, the peak of sub G1 phase (see Fig. 4(b)) was close to the uniform distribution on the number of DNA that is typical for cellular debris. In the case of the cells with photoexcited PSi NP shown in Fig. 4c, the distribution of cells in the sub G1 is typical for ones in the process of programmed cell death, i.e. apoptosis. This fact can be attributed to the cytotoxic effect of SO photosensitized by PSi NPs [20].

The generation of reactive oxygen species (ROS) by PSi microparticles in solution was also detected by means of the fluorescent probe *in vitro* [37]. Photoluminescent NPs from both μPSi [20] and mPSi [38] were found to penetrate into cancer cells. The results on the phototoxic effect of PSi NPs are summarized in Table 1.

4 Photothermal sensitization

Photothermal therapy (PTT) is another kind of the phototherapy, which is based on light-induced overheating (hyperthermia) of cells and tumors above 40–41°C. Phototreatment up to the tissue temperature above 46°C is usually termed as thermoablation [12].

PSi NPs were used as PTT sensitizers upon exposure to NIR light with wavelength of 0.78–1.4 μm [39]. *In vitro* studies showed a strong destruction of cancer cells after interaction with PSi particles excited by NIR light [40]. It was found that the PTT induced cell death was mostly due to necrosis rather than apoptosis [41]. Malignant tumors were found to be completely resorbed after the PTT sensitized by mPSi NPs *in vivo* [42]. Besides of the bare PSi NPs it was reported that DMSO-modified ones could be successfully used for nearly complete destruction of cancer cells *in vitro* [43].

The main advantage of PSi as a PTT agent consists of a broad spectral region of the light absorption in PSi that is much more attractive in comparison with gold, silver and other plasmonic NPs, which are usually discussed for PTT applications. The biodegradability of PSi NPs and possibility to use them as nanocontainers for drug delivery are also extremely important for biomedical applications.

5 Sonosensitization

Sonodynamic therapy (SDT) of malignant tumors is a method of mild cancer therapy, which can be realized with USI sources similar to the diagnostic ones. SDT typically requires more simple and cheap set-up in comparison with other methods based on high-intensity focused ultrasound [44, 45].

The essence of SDT is an enhancement (sonosensitization) of the physical processes induced by as called therapeutic USI with MHz frequency and relatively low intensity

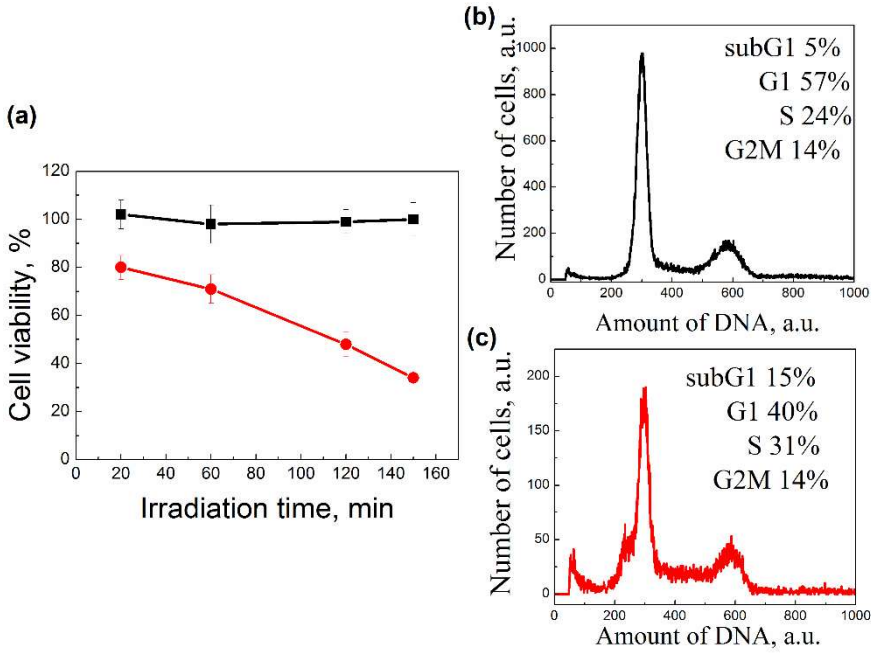

Figure 4: (a) Dependence of the viability of 3T3NIH cells with PSi NPs, relative to the control, on exposure time. Black curve corresponds to the cells with PSi NPs in darkness, while red curve plots the cell viability for PSi NPs irradiated by a Hg-lamp with intensity 1 mW/cm^2. (b) The phase distribution of 3T3NIH cells with PSi NPs incubated in darkness for 150 min. (c) The phase distribution for 3T3NIH cells with PSi NPs irradiated for 150 min by a Hg-lamp with intensity near the sample ~1 mW/cm^2. (Ref. [20])

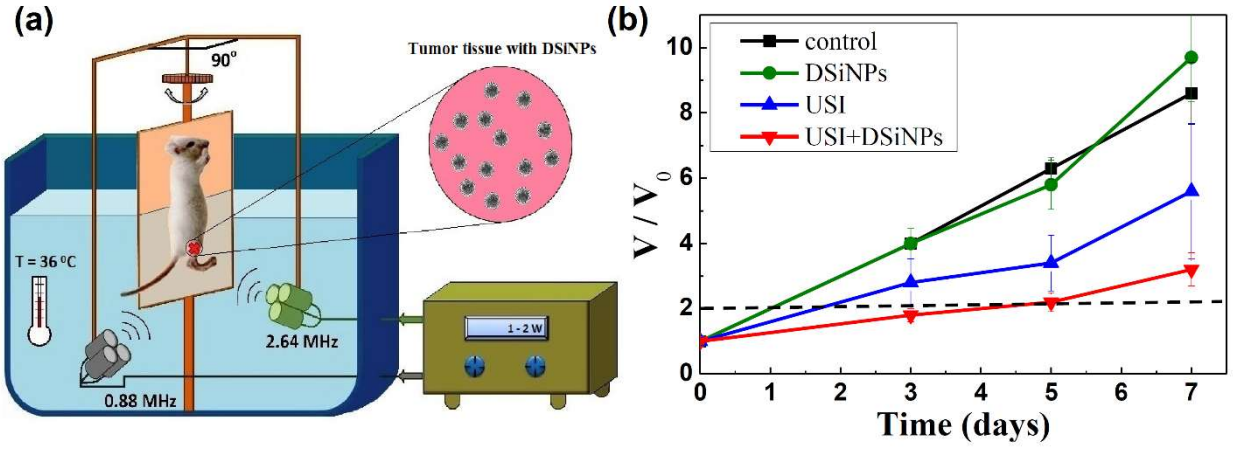

Figure 5: (a) Schematic image of the experimental setup for USI experiments *in vivo*. (b) Dynamics of the melanoma B16 growth for mice with intravenously injected DPSi NPs followed by the USI treatment (red down triangles), for mice with intravenously injected DPSi NPs only (green circles), for mice with the USI treatment only (blue up triangles), and for the control group of mice (black squares). The horizontal dashed line indicates the doubled tumor volume. (Ref. [25])

in the range of 1–10 W/cm^2. Various types of solid and soft NPs are considered as sonosensitizers [46]. The therapeutic effect is achieved because of (i) USI-induced destabilization of cellular structures, (ii) local hyperthermia, and (iii) cavitation process, which results in mechanical disruption of the cells and tumor [46]. The selectivity of SDT is determined by both a selective accumulation of sonosensitizer in tumor and a predominant effect of USI on the tumor in comparison with healthy tissue [25]. However, desired accumulation of the commonly used sonesensitizers in tumor is still complicated due to the residual toxicity problem [47]. In this regard, biocompatible and biodegradable PSi NPs [1–3] are promising sonosensetizers for SDT. PSi NPs incorporated in a cancer cell can be easily activated by therapeutic USI in order to sensitize the above discussed processes of the cell death (see Fig. 1b).

Table 1: Summary of the biomedical studies of sensitizers based on PSi.

Sensitization	Particles	Stimulus	*In vitro / in vivo*	Refs.
Photodynamic (photochemical)	Particles of μPSi, 0.5-2.5 g/L	Illumination with 360-600 nm, 1 mW/cm^2 for 1 h	*In vitro:* up to 80 % suppression of NIH-3 T3 cell proliferation	[36] [21]
	BioSilicon^{TM} microparticles and membranes	Native illumination, 24 h	*In vitro:* visible PDT effect for Human lens epithelial cells	[37]
	NPs of mPSi, 0.1 g/L	White (infrared filtered) light, 100 mW/cm^2 for 10 min	*In vitro:* 45 % death of HeLa and NIH-3 T3 cells	[38]
	NPs of μPSi, 0.05 g/L	Illumination with 360-600 nm, 1 mW/cm^2 for 0.5-2.5 h	*In vitro:* up to 70 % death of NIH-3 T3 cells	[20]
Photothermal (hyperthermia)	NPs of μPSi filtered with 200 nm membrane	NIR illumination with 0.3 W/cm^2 for 20 min	*In vitro:* 2.6 % viability of Breast cancer cells	[40]
	NPs of mPSi/ EtOH-PEG, ~140 nm, 0.7 g/L	Illumination with 808 nm, 1.5 W/cm^2, 4 times for 2 min	*In vitro:* 6.7 % CT-26 cell viability; *In vivo:* complete resorbtion of Murine colon tumor	[42]
	NPs of mPSi/ DMSO, ~67 nm	Illumination with 808 nm, 1.25 W/cm^2 for 20 min	*In vitro:* 5.7 % viability of Pancreatic cancer BXPC-3 cells	[43]
Sonodynamic (hyperthermia and cavitation)	NPs of mPSi with sizes 50-150 nm	US irradiation at 37 kHz with 0.2-2 W/cm^2 for 30 min	*In vitro:* destruction and complete suppression of the HEP2 cell proliferation	[21] [22]
	NPs ~135 nm from SiNWs	US irradiation at 0.88 MHz with 1 W/cm^2 for 10 min	*In vitro*: 50% suppression of the HEP2 cell proliferation	[24]
	NPs ~100 nm from μPSi/ Dextran, 0.1 mg/mL, 10 mg/kg of mouse weight	US irradiation at 0.88 and 2.64 MHz with 1-2 W/cm^2 for 5-20 min	*In vitro:* complete suppression of the HEP2 cell proliferation; *In vivo:* 60% suppression of the growth of melanoma B16 tumor	[25]
Radiofrequency hyperthermia	NPs of 50-200 nm from mPSi, 0.5 mL injection with1 mg/mL	RF 27 MHz, 5 W/cm^2, for 2 min	*In vivo:* 35% suppression of the lung carcinoma (3LL) tumor growth	[27]

NPs of mPSi were successfully used as sonosensitizers under USI at 37 kHz for the destruction of cancer cells *in vitro* [21, 22] (see for details Table 1). It was found that the NPs activated by USI with relatively low intensity about 0.2 W/cm^2 did not destroy directly the cells, while the cell death occurred for 1-2 days due to the apoptosis [22]. In order to explain the observed effect, the possible mechanisms of the cell death were proposed: (1) local heating (hyperthermia); (2) "nano-scalpel" effect of NPs, which destroy mechanically the cancer cells; (3) sensitization of cavitation, which results in the shock wave generation and additional dissipation of the ultrasound energy [21]. It is worth noting that the USI with frequency in the kHz range is usually accompanied by strong cavitation and the third mechanism should be dominant. However, the therapeutic USI is commonly operated at the MHz frequency and all the mechanisms can be important for the sonosensitizing properties of PSi NPs.

Numerical simulations and physical experiments showed that PSi NPs with sizes above 100 nm can efficiently sensitize the hyperthermia under therapeutic USI with frequencies of 1–2.5 MHz and intensities of 1–20 W/cm^2 [23]. It was noted that the dry-ground PSi NPs exhibited 2 times larger heating than the wet-ground ones and the effect was explained by the large sizes of the former, as well as by hydrophobic properties of their surfaces and, as a consequence, greater viscous friction [23].

The therapeutic USI essentially did not affect the cell viability, while the combined action of USI and NPs prepared from SiNWs led to 50% drop in the number of living cells as compared to the control [24]. The effect of USI and NPs on the cell viability was explained by the local hyperthermia induced nearby NPs. Also, the possibility of appearance of cavitation nearby NPs under ultrasound irradiation was not excluded. The role of cavitation was intentionally investigated in Ref. [26] where mPSi NPs with sizes about 100 nm were used to sensitize USI at 0.88 MHz with intensity 1 W/cm^2 at the constant temperature control. It was found that porous morphology of NPs promoted the nucleation of cavitation bubbles [26].

The sonosensitization under therapeutic USI was demonstrated both *in vitro* [24, 25] and *in vivo* [25] (see Table 1). Luminescent DPSi NPs with mean size about 100 nm were found to be efficient sensitizers for SDT [25]. In fact, the NPs with concentration up to 0.1 mg/mL were efficiently up-taken by cancer cells without any undesired cytotoxic effect *in vitro*. Furthermore the DPSi NP suspensions with doses up to 30 mg/kg could be easily intravenously injected *in vivo*. It was found that the combined impact of DPSi NPs and USI at frequencies of 1-3 MHz and intensity of 1-2 W/cm^2 resulted in a strong suppression of the cancer tumor growth (see Fig. 5) [25].

6 RF-induced hyperthermia

PSi NPs were found to act as efficient sensitizers of RF-induced hyperthermia [27, 28]. Due to a large penetration depth of the RF radiation the effect seems to be very promising to treat malignant tumors and even individual cells in metastases. The principle of RF-induced hyperthermia sensitized by PSi NPs is shown schematically in Fig. 1c.

The physical experiments showed that heating of aqueous suspensions of PSi NPs by tens of Celsius degrees could be achieved under RF irradiation at 27 MHz with relatively low intensity (1-5 W/cm^2). The heating effect was demonstrated for PSi NPs prepared by mechanical grinding of mPSi layers as well as for non-porous Si NPs synthesized by laser ablation of c-Si in water. The observed RF heating effect can be explained by considering the polarization of Si NPs and electrolyte in the electrical field of RF radiation and the corresponding release of the Joule heat. The polarization of electrolyte ensure relatively high ionic conductivity due to the electric current outside NP, I_{out} (see Fig. 6). The higher heating rate for laser-ablated NPs is related to their smaller sizes. The size-dependent specific heating rate per a mass unit of NPs can be estimated by the following expression:

$$S \sim E^2/D^2, \tag{1}$$

where E is the amplitude of the RF electrical field and D is the size of NP [27]. It was theoretically shown that the RF heating by the electrical current inside small NP, I_{in}, is weaker in comparison with I_{out} because of the significantly larger volume for the heat generation by the latter [28].

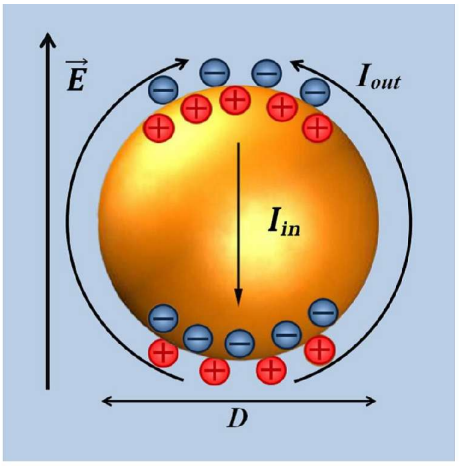

Figure 6: A schematic image of the RF-radiation induced electrical currents inside and outside a NP (Ref. [27]).

In-vitro and *in-vivo* tests evidence relative safety of PSi NPs and their efficient dissolution in physiological solutions, suggesting potential clearance of nanoparticles from a living organism without any side effects [28]. *In-vivo* experiments (see Fig. 7a) showed that PSi NPs under activation with RF radiation resulted in 35% suppression of the tumor growth [27, 28] (see Table 1). The inhibition of tumor growth can be calculated using the following expression:

$$\text{Inhibition} \sim \left(1 - \frac{V}{V_0}\right) \times 100\% \tag{2}$$

where, V and V_0 are the averaged tumor volumes for the experimental and reference groups of mice, respectively [27]. The positive value of inhibition indicates the inhibition of tumor growth, while the negative one signifies that the average volume for the exposed group of mice is larger than that for the reference group. As shown in Fig. 7(d), PSi NPs themselves can slightly inhibit the tumor growth. This effect was explained by the toxic effect of free radicals (dangling bonds) from the surface of Si NPs during the dissolution process. Similar slight inhibition of the tumor growth took place under the action of RF radiation

alone (Fig. 7(d)). However, the combined action of PSi NPs and RF excitation could drastically amplify the effect leading to a much stronger inhibition of the tumor growth.

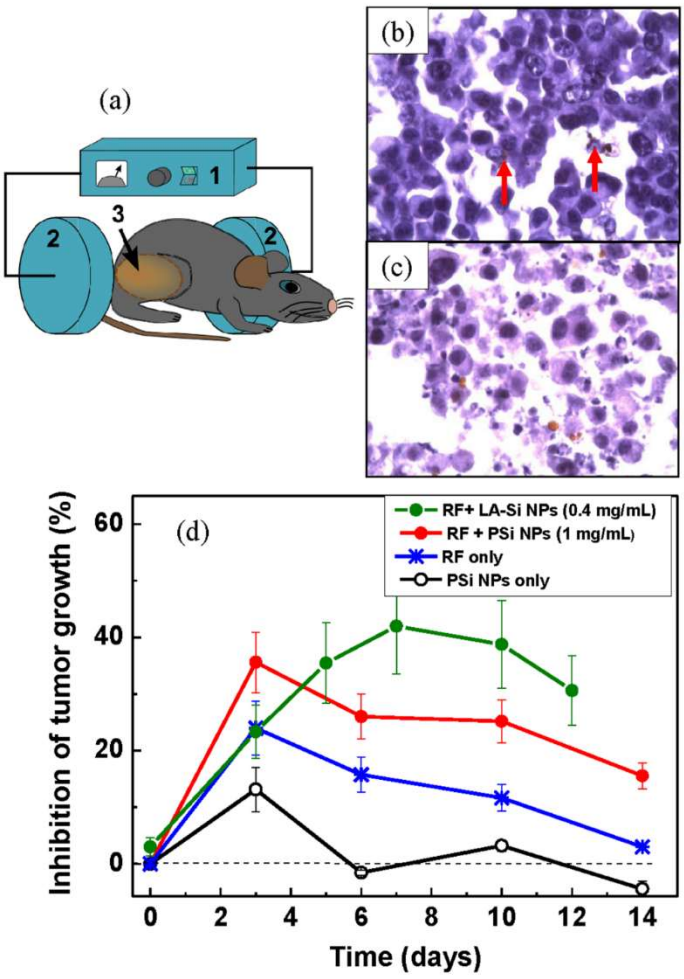

Figure 7: *In vivo* assessment of the efficiency of RF radiation-based hyperthermia using Si-based nanosensitizers. (a) Schematics of the RF radiation-based therapy setup where (1) is a RF radiation source, (2) are the RF electrodes, (3) is a mouse having a tumor area. (b) and (c) Histology images of a tumor area 1 h and 3 days after the PSi NP injection and RF-based treatment, respectively. Cancer cells are visible as dark blue spots and agglomerations of PSi NPs in the cells are indicated by red arrows. (d) Inhibition of the tumor growth after the following treatments: injection of PSi NPs suspension without RF irradiation (black curve); RF irradiation 2 min without PSi NPs (blue curve); injection of PSi NPs followed by 2 min RF irradiation (red curve); injection of a suspension of laser-ablated (LA-Si) NPs followed by 2 min RF irradiation (green curve). (Ref. [27])

7 Conclusions

Based on the data presented, it is argued that PSi micro- and nanoparticles are promising sensitizers of the cancer therapy based on the photo-, sono- and radiofrequency irradiations. Photoexcited PSi NPs were explored as sensitizers for PDT *in vitro*, while the toxicity of the NPs in darkness was negligible. Both the *in vitro* tests and *in vivo* experiments have revealed that the PTT effect sensitized by PSi NPs was rather strong to selectively destroy cancer cells without damaging the surrounding healthy cells. The investigation of physical processes and biomedical experiment *in vitro* and *in vivo* show good prospects of biocompatible and biodegradable PSi NPs for the application in sonodynamic therapy of cancer. The RF hyperthermia sensitized by PSi NPs promise a breakthrough in the development of mild methods of cancer therapy. Moreover, the sensitizing properties of PSi NPs can be combined with PSi-based cancer diagnostics, e.g. by means of the optical bioimaging, that opens new possibilities for applications of such biocompatible and biodegradable nanoparticles in theranostics of cancer.

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