# Peculiarities of biomedical applications of silicon nanoparticles (Review)

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**Abstract.** The review highlights today directions in biomedical applications of silicon nanoparticles for the tasks of early diagnostics and minimum invasive treatment of cancer. It reveals the important issues related to their biocompatibility, toxicity, biodegradation, functionalization and targeting of drugs carried by porous silicon nanocontainers, making stress on theranostic applications of this novel material.

## 1. Introduction

The national projects launched in Russia more than 10 years ago aim at global reconstruction of primary and specialized medical aid including the high-tech medicine [1]. Significant efforts are focused in the oncology domain as the cancer morbidity is claimed to be one of the leading causes of death in the population. More than 600,000 cases of the primary cancer have been detected in the Russian Federation in 2018 which is 1,2% more compared to the level of the previous year. More than 20% of these cases were found in the neglected state and revealed presence of distant metastases. By the end of 2018, the number of oncology patients amounted to 3.76 million i.e. 2.6% of the country's population.

The methods of cancer treatment used broadly nowadays are: surgical, medicinal, chemo- and radiotherapy and combinations of those. Detection of the illness at the very early stage and personalized approaches are the clues to the effective and minimum invasive treatment. This calls for drastic enhancement of the existing methods of diagnostics and therapy of cancer. Novel medical technologies which are now widely under discussion are based on using the structures with their dimensions belonging to the range of few dozen nanometers which is comparable to the size of a large protein molecule [2]. As a result, a direction exploring behavior of nanoparticles in organisms and their prospective applications to diagnostics and therapy, called “cancer nanotechnology”, appeared at the boundary between several sciences: physics, chemistry, biology, medicine, material science and the technologies of nanofabrication [3]. Modern techniques of the cancer detection based on X-ray computed tomography and magnetic resonance imaging, are capable of revealing the tumor when it is grown large enough to contain more than 10 billion cells [4]. That is why the research aiming at increase of sensitivity and resolution of the diagnostic methods is of vital importance. It is assumed that nanoparticles will be of help to solve this problem.

## 2. Biomedical applications of silicon nanoparticles

Cancer therapy using nanoparticles is being developed both ways: in terms of the traditional and the novel approaches [2]. Applying the nanoparticles as photosensitizers in photodynamic therapy (PDT) can already be considered as the conventional one. While, using of biodegradable nontoxic nanomaterials for diagnostic and therapeutic modalities gives an example of a modern research direction in biomedicine. Silicon nanoparticles (SiNP) attract attention of researches due to inexpensive and well controlled technology of their synthesis and variety of possible morphologies and structures depending of the particular procedure of fabrication. Their specific features like luminescent response, biodegradation in organisms, non-toxicity, an extensive surface area, in the case of the porous silicon nanomaterial, and capability to further functionalization make them suitable for the use as biocompatible pharmaceutical additives for the advanced nano-biomedical technology applications. As a result, silicon-based nanomaterials may play an important role in in vivo theranostic applications for cancer diagnostics and treatment [5-13].

Biocompatibility is mandatory for nanoparticles used for drug delivery [5]. This property of the nanoforms of silicon, in addition to biodegradation, make it very promising not only for biological and medical applications but also for the broad use in the beauty product and food industries. It was demonstrated in in vivo experiment that oxidized films of porous silicon are biocompatible with eye tissues and allow using for medical treatment of the retina and cornea disorder [6-8]. It is of crucial importance for the therapy and diagnostic applications that medications based on nanomaterials could be excreted from the organism without harm and within a short period of time after their mission in the body is complete [5]. Looking for nanomaterials with the highest level of biological compatibility, the researchers found that porous silicon nanoparticles used as nanocontainers for the drug delivery come completely apart after the time period of few days turning into variety of silicon acids which are known to be vitally important for the functioning of the connective tissues. Fluorescence and Raman spectroscopy tools were applied to examine uptake and biodegradation of SiNP monitoring the size and chemical composition of the material [9]. The result of monitoring of SiNP in cellular organelles revealed their complete biodegradation to happen within 13 days of incubation [10].

In [11], aiming at theranostic applications and target delivery of nanopharmaceuticals, a comparative analysis of the functionalized silicon nanoparticles was performed. Compared were the multifunctional porous silicon nanoparticles and nonfunctionalized particles. Diagnostic modality was realized using X-ray or fluorescence response of the material. Using the isotope of 111In and single photon emission computed tomography tools (SPECT) allowed to display distribution of nanoparticles in vivo. Fluorescens marking by Alexa Fluor 488 was successfully applied to map the long living distribution of the nanocarrier. Due to fundamental characteristic of the porous surface oxidized SiNP, this material can also play role of the contrast agent in magnetic resonance imaging (MRI) [12].

Targeting features of the particles based on porous silicon were provided by their modification using the peptide iRGD which is a 9-amino acid cyclical variation of the RGD peptide (Arg-Gly-Asp). It is identified as the guiding peptide aiming at tumor and penetrating through biological tissues, which is commonly used in cancer therapy as guiding agent [11]. Enhanced accumulation of SiNP in tumor was demonstrated at intravenous injection which resulted in an effective suppression of the tumor growth. Non-targeted nanocarriers can nevertheless be delivered into tumor due to the effect of enhanced permeability and retaining (EPR) through the defects of the blood vessel system supplying the tumor.

Both non-targeted and targeted SiNP were rapidly recognized and removed from the bloodstream by reticuloendothelial cells. Their cytotoxicity in vitro was measured after 24 hours incubation with the cells PC3-MM2 which are the highly metastatic variant of the cell line of prostate cancer PC-3. No toxicity was observed in both groups of nanomaterials.

## 3. Conclusions

It is shown that SiNP featured by diagnostic and therapy modalities penetrate fast into the tumor and interstitial cells and can be used as the carrier of the antitumor drugs. In the case of transporting radionuclides, that results in higher radioactivity in the domain of tumor compared to molecular radiopharmaceutical. It was also shown that nonguided SiNP and those targeted by iRGD were quickly recognized and removed from the bloodstream by reticuloendothelial system cells which calls for further research. The multifunctional SiNP used in these experiments were successively demonstrated to be a prototype of the prospective materials for theranostic medical nanosystems allowing simultaneously to display their behavior in vivo and to deliver effectively drugs through their porosity.

**Acknowledgements**
The study was carried out with a grant from the Russian Science Foundation (Project No. 19-14-00171) "Non-toxic and biodegradable silicon-based nanoparticles for development of minimum invasive methods of cancer treatment".

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