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ORIGINAL RESEARCH

Chemical nature and structure of organic coating of quantum dots is crucial for their application in imaging diagnostics

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Background: One of the most attractive properties of quantum dots is their potential to extend the opportunities for fluorescent and multimodal imaging in vivo. The aim of the present study was to clarify whether the composition and structure of organic coating of nanoparticles are crucial for their application in vivo.

Methods: We compared quantum dots coated with non-crosslinked amino-functionalized polyamidoamine (PAMAM) dendrimers, quantum dots encapsulated in crosslinked carboxyl-functionalized PAMAM dendrimers, and silica-shelled amino-functionalized quantum dots. A multimodal fluorescent and paramagnetic quantum dot probe was also developed and analyzed. The probes were applied intravenously in anesthetized animals for visualization of brain vasculature using two-photon excited fluorescent microscopy and visualization of tumors using fluorescent IVIS® imaging (Caliper Life Sciences, Hopkinton, MA) and magnetic resonance imaging.

Results: Quantum dots coated with non-crosslinked dendrimers were cytotoxic. They induced side effects in vivo, including vasodilatation with a decrease in mean arterial blood pressure and heart rate. The quantum dots penetrated the vessels, which caused the quality of fluorescent imaging to deteriorate. Quantum dots encapsulated in crosslinked dendrimers had low cytotoxicity and were biocompatible. In concentrations <0.3 nmol quantum dots/kg bodyweight, these nanoparticles did not affect blood pressure and heart rate, and did not induce vasodilatation or vasoconstriction. PEGylation (PEG [polyethylene glycol]) was an indispensable step in development of a quantum dot probe for in vivo imaging, based on silica-shelled quantum dots. The non-PEGylated silica-shelled quantum dots possessed low colloidal stability in high-salt physiological fluids, accompanied by rapid aggregation in vivo. The conjugation of silica-shelled quantum dots with PEG1100 increased their stability and half-life in the circulation without significant enhancement of their size. In concentrations <2.5 nmol/kg bodyweight, these quantum dots did not affect the main physiological variables. It was possible to visualize capillaries, which makes this quantum dot probe appropriate for investigation of mediators of vasoconstriction, vasodilatation, and brain circulation in intact animals in vivo. The multimodal silica-shelled quantum dots allowed visualization of tumor tissue in an early stage of its development, using magnetic resonance imaging.

Conclusion: The present study shows that the type and structure of organic/bioorganic shells of quantum dots determine their biocompatibility and are crucial for their application in imaging in vivo, due to the effects of the shell on the following properties: colloidal stability, solubility in physiological fluids, influence of the basic physiological parameters, and cytotoxicity.

Keywords: quantum dot, organic shell, biocompatibility, in vivo imaging, two-photon excited fluorescent microscopy, magnetic resonance imaging

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Introduction

One of the most attractive properties of quantum dots is their potential to extend the opportunities for fluorescent and multimodal imaging in vivo. The high quantum yield

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