**Biodegradable Silicon Nanoparticles for Multimodal Bioimaging**

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**Abstract:** Rationally designed biomaterials that provide high bioimaging signal intensity, high biosafety, precise targeting, and delivery of a variety of payloads are key toward effective treatment of diseases like cancer. This research investigates porous silicon nanoparticles (pSiNPs) based theranostics agent for multimodal imaging (photoacoustic imaging (PAI) and 2-photon fluorescence imaging (2PFI)), and load and delivery therapeutic payloads specifically to the diseased tissue. The advantages of pSiNPs over other nanomaterials include strong PAI and 2PFI signal enhancement, ablility to target the diseased tissue, and are safely cleared from the body as orthosilicic acid. We systematically evaluated photo-stability of the nanoparticles, degradation of the nanoparticles, their in-vitro and in-vivo contrast enhancement, and their targeting capabilities. The size of the pSiNPs was noted to be approximately 60 nm from the electron microscopy images and the dynamic light scattering. The pSiNPs displayed an approximately 7.5-folds in-vitro PA imaging (imaged using Vevo LAZR) signal enhancement compared to an FDA approved dye (Indocyanine Green, at comparable concentration). Similar PAI signal enhancement was achieved upon local injection of pSiNPs in mouse cadavers – encouraging us to study their targeting ability. The in-vitro cell targeting showed enhanced uptake of functionalized pSiNPs in the cells generating a 2-folds PAI enhancement compared to non-targeted pSiNPs. For 2PFI under in-vitro conditions, the pSiNPs were visible even at 0.5mW laser power, while the detector was saturated at 5mW of laser power. The 2PF imaging capabilities of pSiNPs were tested ex-vivo by injected 120 µm deep into microtome sectioned human skin. The pSiNPs were clearly visible at the side of injection in human skin when imaged under 2 photon excitation.