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# (612g) Multi-Stage Delivery of Gold Nanoparticles for Detection of Early Stage Oral Cancer Using Optical Coherence Tomography


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Early detection is an inarguably indispensable requirement for achieving successful cancer therapy. Among many clinically available imaging modalities, Optical Coherence Tomography (OCT), a technology visualizing heterogeneous structures of a tissue by quantifying local mismatches in refractive indices, offers noninvasive and fast visualization of tumor tissues at micro-resolution with several millimeter depths. However, early stages of cancer do not induce remarkable changes of tissue structures, which necessitates use of contrast agents to detect premalignancy at a molecular level. Among a number of nanomaterials considered as OCT contrast agents, gold nanoparticles offer high optical scattering properties, clinically acceptable biocompatibility, and ease of bioconjugation with additional functional modalities. In this study, engineering questions of how to overcome highly limited penetration and distribution of gold nanoparticles in an early oral tumor, where efficient transport via vasculature is not available, were explored.

Tumors in hamster cheek pouch were induced by treatment with DMBA (9,10 dimethyl-1,2 benzanthracene) for 5 months. Spherical gold nanoparticles (70 nm in diameter) conjugated with anti-epidermal growth factor receptor (EGFR) monoclonal antibodies were administrated to the cheek pouch of an anesthetized hamster. Before topical administration of gold nanoparticles, microneedles (isosceles shape with 170 μm base and 300 μm height) were used to create passages for gold nanoparticles to penetrate through epithelial layers. To mildly disturb cellular junctions in order to enhance distribution of gold nanoparticles in the tissue, ultrasound waves with the clinically accepted frequency of 1MHz and the density of 0.3 W/cm2 were applied to the area where gold nanoparticles had been administered. Results obtained by 3D spectral domain OCT (SD-OCT) showed remarkably enhanced OCT images with clearly differentiated epithelial layers in the tissue. Histological analysis was also used to confirm and correlate distributions of gold nanoparticles in the tissue with the OCT images. Parameters involved in the penetration and distribution of gold nanoparticles using this multi-stage delivery approach will also be discussed with theoretical and experimental evidence.