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Multilayered, core/shell nanoprobes based on magnetic ferric oxide particles and quantum dots for multimodality imaging of breast cancer tumors

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ABSTRACT

Multilayered, core/shell nanoprobes (MQQ-probe) based on magnetic nanoparticles (MNPs) and quantum dots (QDs) have been successfully developed for multimodality tumor imaging. This MQQ-probe contains Fe_3O_4 MNPs, visible-fluorescent QDs (600 nm emission) and near infrared-fluorescent QDs (780 nm emission) in multiple silica layers. The fabrication of the MQQ-probe involves the synthesis of a primer Fe_3O_4 MNPs/SiO_2 core by a reverse microemulsion method. The MQQ-probe can be used both as a fluorescent probe and a contrast reagent of magnetic resonance imaging. For breast cancer tumor imaging, anti-HER2 (human epidermal growth factor receptor 2) antibody was conjugated to the surface of the MQQ-probe. The specific binding of the antibody conjugated MQQ-probe to the surface of human breast cancer cells (KPL-4) was confirmed by fluorescence microscopy and fluorescence-activated cell sorting analysis *in vitro*. Due to the high tissue permeability of near-infrared (NIR) light, NIR fluorescence imaging of the tumor mice (KPL-4 cells transplanted) was conducted by using the anti-HER2 antibody conjugated MQQ-probe. *In vivo* multimodality images of breast tumors were successfully taken by NIR fluorescence and T_2-weighted magnetic resonance. Antibody conjugated MQQ-probes have great potential to use for multimodality imaging of cancer tumors *in vitro* and *in vivo*.

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1. Introduction

The development of molecular imaging probes is crucial for imaging technologies such as magnetic resonance imaging (MRI), X-ray computed tomography (CT), positron emission tomography (PET), and fluorescence imaging [1]. A variety of imaging nanoprobes of those modalities have been developed for their biological and biomedical applications [2–8]. Among various modalities that can be used for *in vitro* and *in vivo* imaging research, fluorescence imaging is a most popular modality due to its high sensitivity with a high temporal resolution [9–11]. Although there are number of fluorescent probes based on organic dyes and fluorescent proteins, most of the fluorescent probes emit in the visible region (400–700 nm). Visible-emitting fluorescent probes have a disadvantage in the application to *in vivo* imaging. The light in the visible region is strongly absorbed by intrinsic chromophores such as hemoglobin, and scattered by tissues [12,13]. In addition, emission spectra of visible fluorescent probes overlap with the autofluorescence of the tissues [14,15]. This results in the difficulty of the resolution of probe fluorescence and tissue autofluorescence. In contrast, NIR light has a high permeability in living tissues. NIR spectral region (700–900 nm) is called as an “optical window” at a whole body level [14]. In this region, absorption and scattering of the NIR light by tissues are significantly decreased compared to the case of visible light. Thus the imaging modality using NIR light is suitable for *in vivo* imaging [14]. MRI is a popular modality for noninvasive *in vivo* imaging. The remarkable advantage of MRI is its ability to image in three dimension with a high spatial resolution [16,17]. MRI, however, has a low temporal resolution compared to the fluorescence imaging modality. Although CT and PET can be

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