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Superparamagnetic PLGA-iron oxide microcapsules for dual-modality US/MR imaging and high intensity focused US breast cancer ablation

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ABSTRACT

Organic/inorganic, hybrid, multifunctional, material-based platforms combine the merits of diverse functionalities of inorganic nanoparticles and the excellent biocompatibility of organic systems. In this work, superparamagnetic poly(lactic-co-glycolic acid) (PLGA) microcapsules (Fe_3O_4/PLGA) have been developed, as a proof-of-concept, for the application in ultrasound/magnetic resonance dual-modality biological imaging and enhancing the therapeutic efficiency of high intensity focused ultrasound (HIFU) breast cancer surgery *in vitro* and *in vivo*. Hydrophobic Fe_3O_4 nanoparticles were successfully integrated into PLGA microcapsules by a typical double emulsion evaporation process. In this process, highly dispersed superparamagnetic Fe_3O_4/PLGA composite microcapsules with well-defined spherical morphology were obtained with an average diameter of 885.6 nm. The potential of these microcapsules as dual contrast agents for ultrasonography and magnetic resonance imaging were demonstrated *in vitro* and, also, preliminarily *in vivo*. Meanwhile, the prepared superparamagnetic composite microcapsules were administrated into rabbits bearing breast cancer model for the evaluation of the *in vivo* HIFU synergistic ablation efficiency caused by the introduction of such microcapsules. Our results showed that the employment of the composite microcapsules could efficiently enhance ultrasound imaging of cancer, and greatly enhance the HIFU ablation of breast cancer in rabbits. In addition, pathological examination was systematically performed to detect the structural changes of the target tissue caused by HIFU ablation. This finding demonstrated that successful introduction of these superparamagnetic microcapsules into HIFU cancer surgery provided an alternative strategy for the highly efficient imaging-guided non-invasive HIFU synergistic therapy of cancer.

1. Introduction

Organic poly(lactic-co-glycolic acid) (PLGA) nano-/micro-particles have been extensively employed in the applications of drug delivery, tissue engineering and molecular imaging [1–3]. Comparatively, the inorganic superparamagnetic Fe_3O_4 nanoparticles have found their application in either T_1- or T_2-weighted magnetic resonance imaging (MRI), magnetically targeted drug delivery and hyperthermia [4–9]. By combining the advantages of PLGA microcapsules and magnetic Fe_3O_4 nanoparticles, organic/inorganic hybrid composite biomaterials with broader and more feasible applications could be produced compared to standalone applications of either PLGA or magnetic Fe_3O_4 nanoparticles.

High intensity focused ultrasound (HIFU) ablation has been shown as a successful non-invasive, complication-free treatment, and is also known as focused ultrasound ablation, or focused ultrasound surgery (FUS) [10]. HIFU was introduced by Lynn for the first time in the 1940s in the performance of neurologic surgery [11]. Over the past few decades, HIFU as a promising non-invasive modality in the treatment of solid tumors has been developed rapidly [12–15]. Abundant scientific investigations have concluded that HIFU ablation was safe, effective and feasible and could be used for clinical destruction of tumor tissues [16–18].

Among all cancers, breast cancer is one of the most common type of cancer and the second leading cause of cancer-related death among women [19]. Surgery has been the standard of

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