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In vitro feasibility study of the use of a magnetic electrospun chitosan nanofiber composite for hyperthermia treatment of tumor cells

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ABSTRACT

Hyperthermia has been reported to be an effective cancer treatment modality, as tumor cells are more temperature-sensitive than their normal counterparts. Since the ambient temperature can be increased by placing magnetic nanoparticles in an alternating magnetic field it has become of interest to incorporate these magnetic nanoparticles into biodegradable nanofibers for possible endoscopic hyperthermia treatment of malignant tumors. In this preliminary investigation we have explored various characteristics of biodegradable electrospun chitosan nanofibers containing magnetic nanoparticles prepared by different methods. These methods included: (1) E-CHS-Fe_3O_4, with electrospun chitosan nanofibers directly immersed in a magnetic nanoparticle solution; (2) E-CHS-Fe^{2+}, with the electrospun chitosan nanofibers initially immersed in Fe^{+2}/Fe^{+3} solution, followed by chemical co-precipitation of the magnetic nanoparticles. The morphology and crystalline phase of the magnetic electrospun nanofiber matrices were determined by scanning electron microscopy, transmission electron microscopy, selected area electron diffraction, and X-ray diffraction spectroscopy. The magnetic characteristics were measured using a superconducting quantum interference device. The heating properties of these magnetic electrospun nanofiber matrices in an alternating magnetic field were investigated at a frequency of 750 kHz and magnetic intensity of 6.4 kW. In vitro cell incubation experiments indicated that these magnetic electrospun nanofiber matrices are non-cytotoxic and can effectively reduce tumor cell proliferation upon application of a magnetic field.

1. Introduction

Cancer is a large, heterogeneous class of diseases in which groups of cells display uncontrolled growth, invasion that intrudes upon and destroys adjacent tissues, and often metastasis, wherein the tumor cells spread to other locations in the body via the lymphatic system or the bloodstream. Current therapies employed for the treatment of cancer include surgery, chemotherapy, radiation therapy, among others. While these methods have been accepted and practiced for decades, they have their drawbacks and side-effects [1].

The basis for hyperthermia as a treatment for cancer is that several types of cancer cells are more sensitive to temperatures in excess of 41 °C than their normal counterparts. At applied temperatures in the range 41–45 °C the damage to normal tissue is reversible, while tumor cells are irreversibly damaged. Hyperthermia has often been used in multimodality strategies as it can enhance the tumor killing effects of chemotherapy, radiotherapy, and immunotherapy [2–5]. The treatment works by rendering cells more sensitive to these therapies. In recent years various technologies, such as radio frequency irradiation, ultrasound, microwaves and inductive needles [6–9], have been developed to raise the temperature of target tissues. The technical challenge with hyperthermia is to locally heat the region of the tumor to the desired temperature without damaging the surrounding healthy tissues.

The possibility of treating cancer using artificially induced hyperthermia has led to the development of many different devices designed to heat malignant cells but not surrounding healthy tissue [10]. Magnetic fluid hyperthermia uses iron oxide nanoparticles, which are superparamagnetic, as a heating source due to their strong magnetism and low toxicity. These accumulate at the tumor site and are subsequently heated in an alternating magnetic field [11]. If iron oxide nanoparticles are exposed to an alternating magnetic field, the harmless magnetic particles become powerful heat sources, transforming the energy of the magnetic field into heat. Moreover, magnetic fields are not absorbed by living tissues and can be applied to deep regions in the living body [12].

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