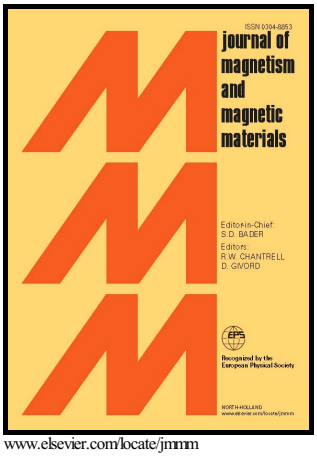

The magnetic introduction of magnetite nanoparticles into live cells for radiosensibility enhancement

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PII: S0304-8853(16)32964-X
DOI: http://dx.doi.org/10.1016/j.jmmm.2016.11.025
Reference: MAGMA62099

To appear in: *Journal of Magnetism and Magnetic Materials*

Received date: 26 June 2016
Revised date: 3 November 2016
Accepted date: 5 November 2016

Cite this article as: Anton Y. Yurenya, Mikhail A. Polikarpov, Aynur A. Chukalova, Elizaveta Y. Moskaleva, Alexander N. Taldenkov and Vladislav Y. Panchenko, The magnetic introduction of magnetite nanoparticles into live cell for radiosensibility enhancement, *Journal of Magnetism and Magnetic Materials* http://dx.doi.org/10.1016/j.jmmm.2016.11.025

The magnetic introduction of magnetite nanoparticles into live cells for radiosensibility enhancement.

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Abstract

Earlier we proposed a new radiotherapy enhancement method that entails the administration of ^{57}Fe iron-oxide nanoparticles into the cells [5]. Within this work we were prompt to investigate the capability of iron oxide nanoparticles with monolayer coating to penetrate into live cells. Magnetite particle samples were synthesized and stabilized with HCl or citric acid. The cells were incubated in the presence of nanoparticles for 1 hour, washed and dried. To distinguish inside-cell particles from outside ones a set of experiments with low temperature incubation was carried out. Several cell samples were prepared in the presence of an external magnetic field in order to study the possibility of the nanoparticle uptake enhancement. To evaluate the amount of particles in each cell sample we used a SQUID-magnetometer. The nanoparticle suspension with HCl stabilization turned to be inadequate for intracellular introduction. Approximately $2 \cdot 10^5$ particles with citric acid covering conjugated with each cell after incubation at normal conditions. An application of an external magnetic field increased this amount up to 10^7 particles/cell. Most probably much of these particles penetrated into cells.

Keywords
magnetite nanoparticles; radiotherapy enhancement; magnetofection; nanoparticle uptake; endocytosis

1. Introduction

The applications of iron oxide nanoparticles have been expanding to biological fields such as MRI contrast enhancement, drug delivery and hyperthermia [1]. Magnetite nanoparticles are relatively non-toxic, biocompatible [2,3] and exhibit magnetic properties. Moreover, the magnetic nanoparticles either solely or in combination with a drug are internalized into cells via endocytosis [4].

Earlier we proposed a new radiotherapy enhancement method that entails the administration of magnetic nanoparticles into the cells with its further irradiation [5]. The amplification of cell radiosensibility is based on the Mills' idea [6]. He suggested that the energy of an external monochromic 14.4 keV gamma-ray beam can be converted into secondary radiation in form of low-energy electrons by its scattering on ^{57}Fe-isotope agents embedded into the cells. It is thought that low-energy electrons exhibit very high biological efficiency (in comparison with gamma radiation) [7]. According to the calculations [6], this approach could reduce the magnitude of the standard dose of a radiotherapy treatment on several orders. Our method implies the use of isotopically-enriched iron oxide nanoparticles as ^{57}Fe carriers and its introduction into the malignant cells. However this method imposes some constraints on the particle coating. The fact is that electrons with energy less than 10 keV possess a very low free path length [8]. For this reason during irradiation of particles with massive polymer coating much of the secondary radiation energy can dissipate in it. In this paper the magnetite nanoparticles with two different types of stabilization were studied.

We used a magnetometer based technique for nanoparticle detection in the cell culture [9]. It was found that the presence of the magnetic nanoparticles in the cell culture after its incubation in nutrient solution with ferrofluid can be detected using a SQUID-magnetometer. We used this technique to estimate the capability of our nanoparticles to reach inside the cells. In order to study