World Academy of Science, Engineering and Technology
International Journal of Materials and Metallurgical Engineering
Vol:9, No:04, 2015

Magnetic Single-Walled Carbon Nanotubes (SWCNTs) as Novel Theranostic Nanocarriers: Enhanced Targeting and Noninvasive MRI Tracking

Authors : Achraf Al Faraj, Asma Sultana Shaik, Baraa Al Sayed

Abstract : Specific and effective targeting of drug delivery systems (DDS) to cancerous sites remains a major challenge for a better diagnostic and therapy. Recently, SWCNTs with their unique physicochemical properties and the ability to cross the cell membrane show promising in the biomedical field. The purpose of this study was first to develop a biocompatible iron oxide tagged SWCNTs as diagnostic nanoprobes to allow their noninvasive detection using MRI and their preferential targeting in a breast cancer murine model by placing an optimized flexible magnet over the tumor site. Magnetic targeting was associated to specific antibody-conjugated SWCNTs active targeting. The therapeutic efficacy of doxorubicin-conjugated SWCNTs was assessed, and the superiority of diffusion-weighted (DW-) MRI as sensitive imaging biomarker was investigated. Short Polyvinylpyrrolidone (PVP) stabilized water soluble SWCNTs were first developed, tagged with iron oxide nanoparticles and conjugated with Endoglin/CD105 monoclonal antibodies. They were then conjugated with doxorubicin drugs. SWCNTs conjugates were extensively characterized using TEM, UV-Vis spectrophotometer, dynamic light scattering (DLS) zeta potential analysis and electron spin resonance (ESR) spectroscopy. Their MR relaxivities (i.e. r1 and r2*) were measured at 4.7T and their iron content and metal impurities quantified using ICP-MS. SWCNTs biocompatibility and drug efficacy were then evaluated both in vitro and in vivo using a set of immunological assays. Luciferase enhanced bioluminescence 4T1 mouse mammary tumor cells (4T1-Luc2) were injected into the right inguinal mammary fat pad of Balb/c mice. Tumor bearing mice received either free doxorubicin (DOX) drug or SWCNTs with or without either DOX or iron oxide nanoparticles. A multi-pole 10x10mm high-energy flexible magnet was maintained over the tumor site during 2 hours post-injections and their properties and polarity were optimized to allow enhanced magnetic targeting of SWCNTs toward the primary tumor site. Tumor volume was quantified during the follow-up investigation study using a fast spin echo MRI sequence. In order to detect the homing of SWCNTs to the main tumor site, susceptibility-weighted multi-gradient echo (MGE) sequence was used to generate T2* maps. Apparent diffusion coefficient (ADC) measurements were also performed as a sensitive imaging biomarker providing early and better assessment of disease treatment. At several times post-SWCNT injection, histological analysis were performed on tumor extracts and iron-loaded SWCNT were quantified using ICP-MS in tumor sites, liver, spleen, kidneys, and lung. The optimized multi-poles magnet revealed an enhanced targeting of magnetic SWCNTs to the primary tumor site, which was found to be much higher than the active targeting achieved using antibody-conjugated SWCNTs. Iron-loading allowed their sensitive noninvasive tracking after intravenous administration using MRI. The active targeting of doxorubicin through magnetic antibody-conjugated SWCNTs nanoprobes was found to considerably decrease the primary tumor site and may have inhibited the development of metastasis in the tumor-bearing mice lung. ADC measurements in DW-MRI were found to significantly increase in a time-dependent manner after the injection of DOX-conjugated SWCNTs complexes.

Keywords : single-walled carbon nanotubes, nanomedicine, magnetic resonance imaging, cancer diagnosis and therapy
Conference Title : ICNN 2015 : International Conference on Nanoscience and Nanotechnology
Conference Location : Paris, France
Conference Dates : April 27-28, 2015