

Magneto-hydrodynamic thermochemotherapy and MRI of malignant tumorigenesis

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Abstract Citric-ferrite sol (CFS) has been synthesized and successfully tested as MRI negative contrast preparation for revealing primary tumors, and also invasions and metastases at the tumor relapses. Magneto-hydrodynamic thermochemotherapy (MTC) by Cysplatin (CP), Mitoxantron (MX), Melphalan (MP) combined with CFS, which were carefully monitoring in vivo and quantified by an electronic detector, improved results of cancer treatment. At various stages of oncogenesis, MTC with CFS at a dose of 62 mg Fe/kg combined with chemotherapeutic drugs was performed at +48° C for 30 min. While such MTC, treatment of ~30 mm³ B 16 melanoma tumor by AC magnetic field led to tumor regression in female mice up to 40 %, and an increase of life span up to 300 % was achieved.

1. Introduction

In this work, we continue investigation of magneto-hydrodynamic thermochemotherapy (MTC) [1-3] performed with a scanning electronic detector (ED) [4-6] of magnetic nanoparticles as well as MRI of malignant tumors oncogenesis by BIOSPEC BC 70/30 (Bruker). To reveal the tumors by contrast-enhanced MRI, we have tested Citric-ferrite sol [7]. Then the tumors were treated by combination of several procedures and drugs. We used Cysplatin (CP), Mitoxantron (MX) and Melphalan (MP), Dacarbazine (DC), Docetaxel (DT), which are well-known chemotherapeutic drugs for treatment of breast, lung, ovarian and other cancer types. The effect of CP's, MX's and MP's can be increased by combining them with CFS [3,6]. A complex treatment, which combined magnetically controlled anticancer drugs such as CP and MP containing CFS, targeting them to the tumor tissue by a constant magnetic field, heating the tumor by AC magnetic field with necrotic slime aspiration, and with intraperitoneal (IP) and intracavitary (IC) introduction of Cyclophosphan, was performed [8]. This paper is devoted to development of MTCs for murine B 16 melanoma, mammary Ca 755 adenocarcinoma and Lewis lungs carcinoma (LLC) based on novel methods for quantification of magnetic agents [4,5] and optimization of the treatment of oncogenesis by 3D near-real-time MRI.

2. Materials and methods

To obtain Fe₃O₄ nanoparticles, 5 g of FeCl₂ 4H₂O and 10 g FeCl₃ 6H₂O were dissolved in 200 ml water, solution was heated at 70 to 80 °C. 25 ml 25% NH₄OH was added with vigorous stirring. After 40 min concentrated sol has separated in NdFeB 5x5 cm magnet, has washed out and was diluted by water to 200 ml. Then 10 g of citric acid (Sigma) in 30 ml H₂O was added. The mixture was actively and continuously stirred for another 120 min at 70-80° C. CFS was magnetically separated. The cores of CF nanoparticles had diameters between 3 and 10 nm, the hydrodynamic diameters of the coated with citric-ions nanoparticles ranged between 6 and 30 nm, pH 7.4; ζ +8 mV; Ms 8.2 kA/m; SAR 330 W/g Fe) [7,8]. Targeting of the drug sol in hypodermic and skin tumor