Introduction:

Early detection of invasions and metastases by magnetic resonance imaging (MRI) is an important problem in the detection of malignant tumors. During imaging of early stage oncogenesis and metastases by BIOSPEC BC 70/30 (Bruker), we have found that we can separate signals from small sites of pathological cells generated by strong signals from normal tissues. To reveal the tumors by contrast-enhanced MRI, we have synthesized and tested Dextran-Fe (DF) as the first step of our research. DF is a new type of material that can be used for the following purposes: (1) it can be made of different substances currently used contrast agents. The second step was the treatment by combinations of several different drugs and procedures. For all of the drugs, we used Cy5-dextran (CP) and Melphenalin (MP), which are well-known chemotherapeutic drugs for treatment of the breast, lung, ovarian and others cancer. Besides, CP’s and MP’s activities can be increased by combining them with DFS [1,2]. The complex treatment method that combines the magnetically controlled antitumor drugs, namely, CP and MP containing DFS, targeting the tumor by a gradient of a permanent magnetic field (MF), heating tumor by AC MF with necrotic time drip aspiration, is a well-known treatment method named as magnetothermochemotherapy [1].

A more comprehensive combination of the treatment together with 3D MR-imaging as well as with quantification of magnetic agents we call as combined MRI-thermo-magneto-chemotherapy (Fig. 3). This paper is devoted to the description of results of the study on the in vivo assessment of the magnetic nanoparticles for the diagnosis and treatment of the melanoma Ca 75-5 adenocarcinoma (Tables 1-3). We studied the accumulation of nanomagnetic substances in the lungs, heart, and brain, and also determined the size of their aggregates for the estimation of the biocompatibility and ability to be used in clinical therapy. MRI-quantification of the magnetic nanoparticles as well as their accumulation was performed by bioluminescence monitoring associated with bioluminescent actinometry. MRI-quantification was performed by T1-weighted [500/15 [repetition time msec/echo time msec] and T1-weighted (1/000/80) spin-echo and T2-weighted gradient-echo (GRE) (500/15) sequences. This made it possible to diagnose the accumulation of the magnetic nanoparticles in the tumor tissues and was performed in (1-3) days after the treatment.

The initial development of tumor progression and bioluminescence monitoring was performed. The decrease of the signal intensity was recorded, and visual analysis was performed. We used T2- and T1-weighted images for the accumulation of the magnetic nanoparticles in tumor tissues was studied in (1-3) days after the treatment.

Results:

Conclusions:

Dextran-Fe synthesized from DF304 nanoparticles by covering their Dextran T70 was obtained from Sigma and the coated nanoparticles were separated magnetically. DF nanoparticles cores had diameters between 3 and 10 nm, with the hydrodynamic diameter of the coated nanoparticles being between 24 and 40 nm. Treating of the drugs in hypotensive conditions with tumor tissues was performed by using Ca575 nanobeads according to recommendations [8,9] or by superconducting magnet (up to 7 T). Results of magnetic imaging and time evolution of DF concentrations were monitoring by “BioMag” device [7]. We tested a 0.1% DFs in 7% of magnetic resonance imaging (MRI) for tumor tissue diagnosis. For this purpose, the doses at 0.01, 0.05, and 0.08 mmol Fe/kg were injected into mice with mammary Ca 75-5 adenocarcinoma. Lewis lungs carcinoma and B16 melanoma. To prepare tumor-bearing animals, the Ca 75-5 adenocarcinoma was implanted subcutaneously into the right axillary region in 150 female C57Bl/6j mice which were 6 - 10 weeks old by injection of 106 viable tumor cells in 0.2 ml of saline, pH 7.4. The B16 melanoma was implanted similarly in 60 female C57Bl/6j mice. The Lewis carcinoma was implanted intramuscular into the right femoral region in 60 female C57Bl/6j mice. The Cy5-dextran and Melphenalin containing 40% dextran-free sol were used as chemotherapeutic drugs having anti-cancer properties for CAT, MRI, and photodynamic therapy.

Within the groups, Ca 75-5 adenocarcinoma and B16 melanoma with the presence of the nanomagnetic substances were studied using BIOSPEC BC 70/30 USR (Bruker), supplied by Model 1025 Small Animal Monitoring and Gating system. MRI-quantification was performed with T1-weighted [500/15 [repetition time msec/echo time msec] and T2-weighted (1/000/80) spin-echo and T2-weighted gradient-echo (GRE) (500/15) sequences. Then 0.01 and 0.10 DF dose (up to 12 mg Fe/kg) were injected in mice caudal veins.

Table 1 shows the accumulation of the magnetic nanoparticles in the tumor tissues was studied in (1-3) days after the treatment. This study was essential for characterization of the formed magnetic nanoparticles for the estimation of the biocompatibility and ability to be used in clinical therapy.

Table 2 shows the accumulation of the magnetic nanoparticles in the tumor tissues was studied in (1-3) days after the treatment. This study was essential for characterization of the formed magnetic nanoparticles for the estimation of the biocompatibility and ability to be used in clinical therapy.

Table 3 shows the accumulation of the magnetic nanoparticles in the tumor tissues was studied in (1-3) days after the treatment. This study was essential for characterization of the formed magnetic nanoparticles for the estimation of the biocompatibility and ability to be used in clinical therapy.

References:


Fig. 1(a, b), MRI of tumor of Ca 75-5 after Dextran-Fe sol (DFS) intravenous injections (a) an injection of the tumor in normal muscles in group 2 mice: a place of injection of the tumor in a gauze (G) and the yield of the tumor (black arrow); a place of an insert, inducing the G and injection of the tumor (black arrow), and (b) in normal muscle tissues (short white arrows), - negative sites.

Fig. 2(a, b), MRI-monitoring of globular form Ca 75-5 (a) an injection of cells in lymphatic system and other normal tissue reference (b) negative tissues - as reverse opposite.

Table 1: MRI monitoring of microspheres of Ca 75-5 adenocarcinoma tumors in C57Bl/6j mice. 24 days after the start of the treatment.

Table 2: MRI-monitoring of microspheres of Ca 75-5 adenocarcinoma tumors in C57Bl/6j mice. 24 days after the start of the treatment.

Table 3: MRI-monitoring of microspheres of Ca 75-5 adenocarcinoma tumors in C57Bl/6j mice. 24 days after the start of the treatment.