Combined MRI-adaptive Magneto-thermo-polychemotherapy for Improved Cancer Treatment

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The early detection of invasions and metastases by MRI-monitoring (MRM) is an important problem in the detection of malignant tumors. We synthesized and tested dextran-ferrite (DF) for the early detection of invasions and metastases at combined MRI-adaptive magneto-thermo-polychemotherapy (CAT) with slime aspiration to improve cancer treatment. During investigation of invasions by BIOSPEC USR 70/30 (Bruker), we have found that weak signals of protons from small sites of pathogenic cells are neutralized by intensive signals from normal tissues. To solve the problem ferrite nanoparticles can be used as MR-negative contrast agents [1]. Contrast enhanced MR-images of invasions are represented in Fig. In our experiments hypodermic and skin tumors were treated with magnetically controllable drugs. Increase of drug concentration in tumor tissues due to the magnetic field was achieved by use of $SmCo_5$ or NdFeB bandages (0.2-0.3 T induction) according to recommendations [2] and by superconducting electromagnet (7T). Quantification of magnetic nanocarriers of such antitumor drugs *in vitro* and *in vivo* in mice bodies were carried out by "BioMag" device based on non-linear magnetization of nanoparticles [3]. Initially 60 female mice C57Bl/6j with mammary adenocarcinoma Ca 755, 60 female mice with Lewis lungs carcinoma and 60 male mice with melanoma B16 underwent native MR-imaging with T_1-weighted (TR/TE=500/15ms) and T_2-weighted (TR/TE=1900/80ms) spin-echo and T_2-weighted gradient-echo (GRE) (TR/TE=500/15) sequences. Then 1.0 ml DF sol (particles diameter 24–40 nm, dose 10.0 mg Fe/kg) were injected in mice caudal vein and after 2-24 hours second MRM and DF-enhanced T_2-weighted GRE sequences were performed. Signal intensity decrease was recoded and visual analysis was performed. At early stages of oncogenesis thermochemotherapy at +46 ºC for 30 min using DF with the dose 60 mg Fe/kg containing of Cysplatin (CP) or Melphalan (MP) were performed. The DF (Fe_3O_4 weight -83 mg; CP - 20 μg; MP -2 μg; pH 7.4) was injected into multiple tumor sites and was concentrated in the tumor tissue with magnetic bandages. Mammary adenocarcinoma Ca 755 tumor ~45 mm^3 treatment by AC magnetic field (0.88 MHz, 7.3 kA/m, 0.15 kW) led to regression in female mice before metastases up to 40 % and increased up to 280 % life span was achieved, tumor ~300 mm^3 CAT with slime aspiration and the invasions and metastases (Fig.) systemic treatment by Cyclophosphamide led to 200 % increased life span.

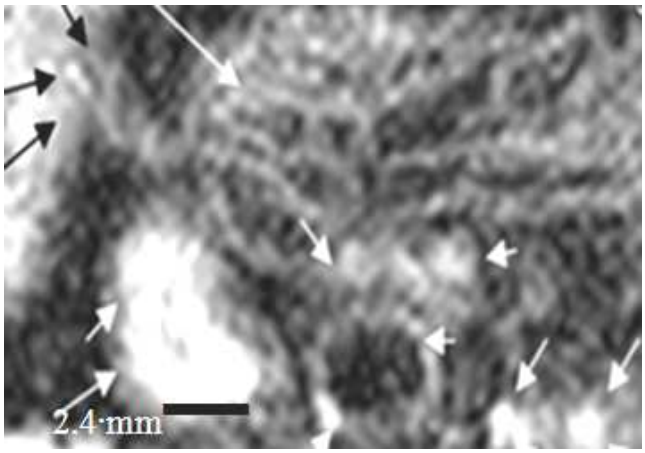

Fig. MRI of invasion and metastases of Ca 755 tubs in normal tissues, which was implanted subcutaneously in the female mice C57Bl/6j with subsequent DF intravenous injections: a place of intertwisting of the tubs in a tumor in a garrot (G) and yield of G from a tumor (black arrows); a place of an inlet, untwisting of G and invasion of the tubs in normal tissues (major white arrow); metastases (short white arrows).

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