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Ferromagnetic nanoparticles for tumor hyperthermia: in vivo study

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Local hyperthermia (tumor temperature increase up to 43-44^{0}C) is actively used in combined antitumor therapy resulting in significant enhancement of treatment efficacy. At the same time technical difficulties of microwave hyperthermia do not allow to obtain the optimal therapeutic effect. Ferromagnetic nanoparticles were proposed to enhance hyperthermia effect in tumor therapy. It was shown that tumor may be heated with magnetite nanoparticles under alternating magnetic field (AMF).

Different methods of synthesis were realized to obtain nanoparticles with requested characteristics: slightly agglomerated, small sized (5-30 nm), single-domained, easily excretable from the body, able to demonstrate high values of the SLP (specific loss power) and to exhibit superparamagnetic properties.

In our laboratory weakly-agglomerated nanocristalline ferromagnetic nanoparticles both with spinel structure, in particular AFe_2O_4 (A = Mn, Fe, Co, Ni, Zn) and perovskite, in particular $La_{1-x}Sr_xMnO_3$ were synthesized by precipitationfrom nonaqueous solution and sol-gel methods, respectively. Nanoparticles have size 3-5 nm (magnetite) and 14-48 nm (manganite). SLP of magnetite is 8-10 W/g and manganite – 2300-2350 W/g. Magnetic fluid (MF) was prepared using 0.025% aqueous agarose solution as organic matrix. MF is heated up to 56^{0}C (magnetite) and 72^{0}C (manganite) under AMF (300 kHz, 7.7 kA/m), respectively.

Administration of MF in the tumor followed by AMF resulted in the increase of tumor temperature up to 50^{0}C and inhibition of tumor growth. The distribution of MF magnetite was evaluated: intratumoral injection of MF at a dose of 200 mg/kg resulted in the accumulation of nanoparticles in tumor only, but at a dose of 400 mg/kg also in spleen; intravenous administration resulted in the accumulation of nanoparticles in spleen, lung and liver, but not in kidney; nanoparticles were not detected in mentioned organs after intraperitoneal administration at a doses of 400 or 800 mg/kg. Testing of MF in experiment with rodent transplanted tumor demonstrated significant antitumor effect in the regime of thermoablation. Obtained result allow to recommend MF manganite for the preclinical testing.