

APPLICATION OF FERRIMAGNETIC NANO-PARTICLES IN CHEMOTHERAPY, HYPERTHERMIA AND MRI CONTRASTING

*Brusentsov N.A.¹, Pirogov Yu.A.², Polyanski V.A.³, Golubeva I.S.¹, Anisimov N.V.², Gulyaev M.V.²,
Nikitin M.P.⁴, Yuriev M.V.⁴, Brusentsova T.N.⁴, Nikitin P.I.⁴*

¹ N.N. Blokhin Russian Cancer Research Center, RAMS, Moscow, 115478, Russia

² Research Center for Magnetic Tomography and Spectroscopy,

M.V. Lomonosov Moscow State University, Moscow, 119991, Russia

³ Institute of Mechanics, Moscow State University, Moscow, 117192, Russia

⁴ A.M. Prokhorov General Physics Institute, RAS, Moscow, 119991, Russia

Last time, developments of chemotherapy drugs on the base of ferrimagnetic substances became high interest subject in medicine and medical physics. Tissues absorbing the preparation change sharply magnetic characteristics - magnetic susceptibility and times of spin relaxation. Therefore selective accumulation of drug just in a lesion zone creates good conditions for monitoring and forcing of treatment process for account of magnetic hyperthermia application with following extraction of breakup substances. For visualization of lesion, it is suitable to use magnetic resonance imaging (MRI) method. In the case, ferrimagnetic preparation may be considered as a contrast agent which stimulates strong lowering of MRI-signal in the drug accumulation zone.

We synthesized citrate-ferrite (CF) particles containing Fe_3O_4 with size 25-50 nm, applied them for early diagnostics of tumor in metastasis stage and tested the preparation in experiments on the female mice C57Bl/6j with inoculated adenocarcinoma of mammary gland in nodule form (the size about 10 mm). Besides electric sensor control with application of BioMag equipment [1], it was used 7 Tesla MRI scanner BioSpec 70/30 (Bruker Co.) to inspect the process. The mice were anesthetized by intra-abdominal injection of Zoletil 100 preparation. Hyperthermia (heating up to +46 °C during 30 min) fulfilled with help of NdFeB bandage creating alternate (0.88 MHz) magnetic field 0.2 Tesla from 150 W power current source [2,3].

Citrate-ferrite accumulation in tumor affected hypodermic region was revealed on MRI images in some (2-24) hours as MRI signal lowering. It was particularly visible on T2* images resulted by gradient echo method that is equivalent to negative contrast agent influence [3]. Additional tool promoting to higher CF concentration in tumor tissue appeared using of the foregoing alternate magnetic field. Variable gradient magnetic fields of MRI scanner also promoted to the same process.

CF preparation was injected to 8 mice in 1.0 ml quantity. Combination of chemotherapy and magnetic hyperthermia for Ca755 tumors with dimensions about 10 mm diameter supplies 60% lowering of metastasis volume and raises survival rate of female mice up to 300%. In the case of 15-mm tumors, application of the procedure described above with systematic repetition of the therapy after relapse enlarges survival potential up to 220%.

Citrate-ferrite nano-particle drugs for chemotherapy in combination with magnetic hyperthermia are the good tool of tumor treatment. Simultaneously, these particles act as powerful contrast agent during MRI observation of the process because they are accumulated inside tumor and give strong magnetic resonance signal from paramagnetic Fe_3O_4 clusters.

[1] M. Nikitin, P. Vetoshko, N. Brusentsov, P. Nikitin, *J. Magn. Magn. Mat.*, **321** (2009) 1658.

[2] U. Hafeli, K. Gilmor, A. Zhou, S. Lee, M. Hayden, *J. Magn. Magn. Mat.*, **311** (2007) 323.

[3] N. Brusentsov, Yu. Pirogov, N. Anisimov, et al., *Am. Inst. Phys.*, **1311** (2010) 447-451.