

Application Magnetite of Nanoparticles (ICNB Preparation) as Magnetically-Resonant Contrasting Means During Visualization of Tumours

Andrey Belousov

Laboratory of Applied Nanotechnology
Kharkov Medical Academy of Postgraduate Education
pr. Lenina, 31-v, fl. 32 Kharkov, 61072 Ukraine
Mob.tel.:+38050-915-18-89 E-mail: an.belousov2012@yandex.ua
Web site: www.nanolab.com.ua

ABSTRACT

In investigation on animals (Vistar rats) was proof that magnetite of nanoparticles (ICNB) are contrast means for malignant tumour visualization. Was been shown that magnetite of nanoparticles have contrast effect when performing magnetic resonance imaging (MRI). Was established, that after intravenous inject preparation of nanotechnology (ICNB) the magnetite of nanoparticles have selective accumulate in tumour and alter brightness of picture in 24-hours. On 4-th day investigation was established significant decries of dynamic brightness of the picture of tumour and muscles. This fact is connected with elimination the ICNB out of rat's organism.

Keywords: nanoparticles, magnetite, MRI, tumour, contrast, selectively.

INTRODUCTION

The first medical preparations of nanotechnology were synthesis in Ukraine in 1998. One of them is intracorporal nanobiocorrector (ICNB) [1]. ICNB is authorial development intravenous form of nanosorbent. A basis of ICNB is colloid magnetite particles (Fe_3O_4) size from 6 till 12 nm.

Presently magnetic materials have lager interest for modern medicine and pharmacology at development methods of treatment and diagnostic different diseases, including oncologic [2-4].

The commensurability size of nanoparticles and magnetic domen of magnetite results in appearance of the phenomenon of superparamagnetism. Magnetite of nanoparticles has a substantial change of magnetic properties with reduction of size of particles. Water solutions of magnetite with the middle size of 6-12 nm correspond to with the size of domen and possess superparamagnetic properties.

Such magnetite of nanoparticles can become the optimal magnetically-resonant substance of contrasting mean which allow to look after the seats of diseases on two relaxation parameters, in contrast to preparations which content gadolinium [5,6].

Foregoing was founding in the choice of theme of the real investigation. The problem was set in an experiment on animals to check possibility of the use of biocompatible magnetite of nanoparticles (ICNB preparation) as contrasting means during visualization of tumours, ability to change relaxations of T1 and T2, i.e. to render a contrasting effect during realization magnetic resonance imaging (MRI).

Primary purpose of investigation - selective accumulate magnetite of nanoparticles (ICNB preparation) in a tumour.

MATERIALS AND METHODS

Investigations were performed on the males of rats of Vistar line, by age 26-27 months. Rats lived in individual cages with standard ration of vivarium with free access to water and food.

One rat was relatively health. Other – with the present fibroadenoma of mammary gland. Wait of rates was identical. During investigations with animals we observed the principles of humanity, which expounded in declaration of Helsinki.

For 5 minutes prior to research intramuscular the rats get sedation. In subsequent was carrying out control of MRI.

After the performed control of MRI, singly in a tail vein of the rat, from a calculation 0.6-0.8 ml/100 mg, 0.0225% was inserted colloid solution magnetite of nanoparticles (ICNB preparation). The repeated was performed of MRI studies. Conditionally all MRI studies were divided into 4 stages:

Stage I is control (before intravenous insert of nanoparticles);

Stage II - in 5 minutes after insert magnetite of nanoparticles;

Stage III - in 24 hours after insert magnetite of nanoparticles;

Stage IV - in 96 hour after insert magnetite of nanoparticles.

Physical and chemical properties of ICNB:

- Osmolality theoretical of colloid solution is 500 mosm/l

- Size of magnetite of nanoparticles is 6-12 nm;

- Total area of surface magnetite of nanoparticles $S_s = 800\text{-}1200 \text{ m}^2/\text{g}$;
- Magnetized of saturation $I_s = 2.15 \text{ kA/m}$;
- ζ - potential = $- 19 \text{ mV}$.

The investigations were performed on the MR-tomograph Magnetom Concerto of Siemens firm with power magnetic-field 0.2 T .

Got axial tomograms:

1. T1 - the self-weighted sequences of Echo Spin of TR 50 ms, TE 17 ms the field of review a 250 mm, the thickness of cut 2 mm.
2. T2 - the self-weighted sequences Echo Gradient of TR 500 ms, TE 17 ms the field of review a 180 mm, the thickness of cut 4 mm.

Concentration of accumulation magnetite of nanoparticles was estimated by measuring of brightness of image in a tumour and tissue of muscular of rats.

RESULTS AND DISCUSSION

As a result of research of the use magnetite of nanoparticles (ICNB preparation) it is set as contrasting means was establishment that magnetite of nanoparticles were able to change relaxation of T1 and T2, i.e. to render a contrasting effect during realization MRI. This fact is demonstrated by MRI study (fig.1, 2).

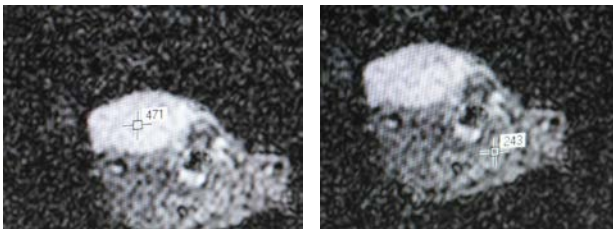


Fig. 1. Initial MRI study the brightness of image the rat's fibroadenoma of mammary gland and tissue of muscular (471 conventional sign – tumour; 243 conventional sign – tissue of muscular).

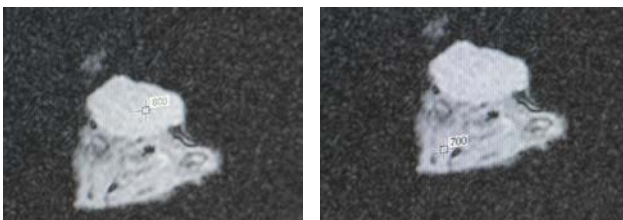


Fig. 2. MRI study the brightness of image the rat's fibroadenoma of mammary gland and tissue of muscular on the first minutes after intravenous insert magnetite of nanoparticles (800 conventional sign - tumour; 700 conventional sign - tissue of muscular).

In subsequent was revealed that in Stage III of research (in 24 hours after intravenous insert of ICNB) the nanoparticles in mainly accumulated in a tumour, than tissue of muscular. The index of growth of brightness of image of tumour (836 conventional sign) testified to it. In

too times the brightness tissue of muscular evidently went down and present 595 conventional sign (fig.3).

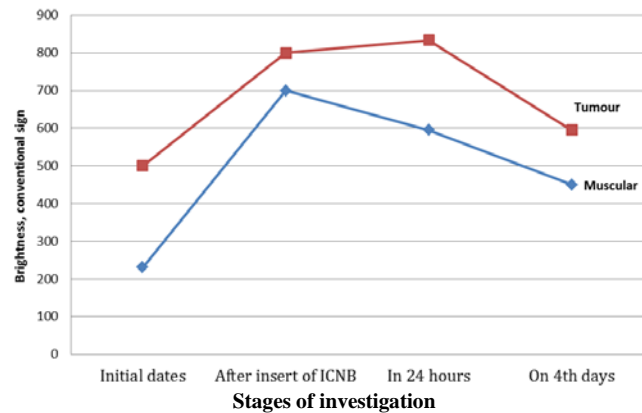


Fig. 3. Dynamic of change magnetite of nanoparticles concentration in rat's tumour and muscular after intravenous insert ICNB preparation on various stages for MRI studies.

Reduction of dynamics brightness of tumour was present only on Stage IV of research (4th days) and cause by the elimination of ICNB preparation from the organism of rat.

Dynamics of change brightness of image after intravenous insert ICNB preparation in tissue of muscular healthy rat and the rat with a tumour were presented on the fig. 4.

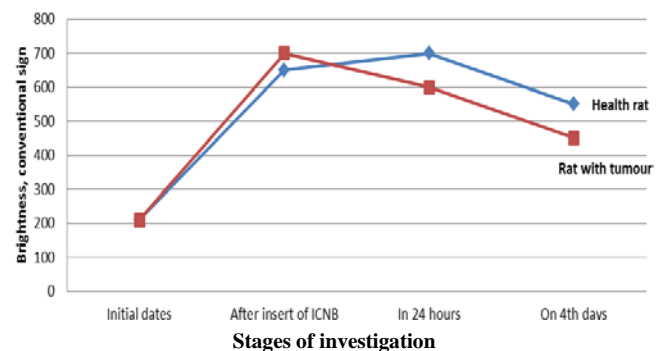


Fig. 4. Dynamic of change brightness of image rats muscles in both groups on various stages for MRI studies after intravenous insert ICNB preparation

The fig. 3,4 is demonstrated that on Stage III study (in 24 hours after insert magnetite of nanoparticles) was revealed decrease brightness of image tissue of muscular (595 conventional sign) in rat with tumour.

Opposite for a healthy rat on Stage III of research was revealed increase brightness of image tissue of muscular (700 conventional sign).

Taking into account a well-known fact, that the surface tumour of cells, by comparison to ordinary, has a higher negative charge and that the clutch of intercellular in tissue of tumour is weak, the mechanism of selective accumulation magnetite of nanoparticles between the tumours of cells is obvious.

CONCLUSION

1. In an experiment on animals possibility of the application of biocompatible magnetite of nanoparticles (ICNB preparation) is well-proven as contrasting means during visualization of tumours. Ability magnetite of nanoparticles to render contrasting effect during realization MRI is shown.

2. Was establishment that in 24 hours after intravenous insert of ICNB preparation the magnetite of nanoparticles has selective accumulation in a tumour, change the brightness of image here.

3. On 4th days of research was revealed expressed dynamics reduction the brightness of image tumour of muscular. This fact connect with process eliminate of ICNB preparation from rat's organism.

REFERENCES

1. www.nanolab.com.ua
2. Suzuki M., Honda H., Kobayashi T. et al. Development of a targetdirected magnetic resonance-contrast agent using monoclonal antibody-conjugated magnetic particles // *Brain Tumour Pathology*. 1996. V. 13. P. 127—132.
3. Pankhurst Q.A., Connolly J., Jones S.K., Dobson J. Applications of magnetic nanoparticles in biomedicine // *J. Phys. D. Appl. Phys.* 2003. V. 36. P. 167—181.
4. Salata O.V. Applications of nanoparticles in biology and medicine [Resources of electronic]. Access: <http://www.jnanobiotechnology.com/content/2/1/3>
5. Bonnemain B. Superparamagnetic agents in magnetic resonance imaging: physiochemical characteristics and clinical applications-a review // *J. Drug Target*. 1998. V. 6. P. 167—174.
6. Weissleder R., Bogdanov A., Neuwelt E.A. et al. Long circulating iron oxides for MR imaging // *Adv. Drug. Delivery Rev.* 1995. V. 16. P. 321—334.