Magnetic nanoparticles as new labels for biosensing directly in living organisms

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Abstract – Various magnetic nanoparticles (MP) have been investigated as the nanomarkers for *in vivo* biosensing directly in the living organisms. A novel method of non-invasive real time detection of MP has been proposed and realized. The method allows measuring MP content in blood and tissues as well as selecting the promising MP for biomedical applications. MP detection method is based on the non-linear MP magnetization and its sensitivity is on the level of the radioactive technique. An external induction probe allows monitoring of MP content in tissues of small experimental animals. The method can be extended for immunoassay in patient's body.

Magnetic particles (MP) have become very popular in scientific research as labels. They are stable unlike fluorescent labels and safe as compared to radioactive agents. MP can also be used in magnetic drug delivery as driving agents and as heating agents in hyperthermia. Quantitative detection of magnetic nanoparticles (MP) *in vivo* is very important for many biomedical applications, especially because MP are already approved for injections in humans. Possibility of magnetic immunoassay (MIA) realization directly inside a human body (Fig. 1,A) is of our special scientific interest. It looks promising for diagnostics of cancer, atherosclerosis or other diseases by detecting with a remote induction probe of localization of MP, targeted with antibodies (AT) against antigens specific for the disease. In the present work, a novel highly sensitive room-temperature method of MP detection *in vivo* has been realized and tested. The method provides real-time quantitative measurements of MP concentration in blood or tissues of a living organism [1,2]. This method is based on non-linear MP magnetization [3,4]. The sensitivity of the method of few ng of MP in 0.1-0.5 ml volume is on the level of radioactive technique for MP with ^{59}Fe isotope [1]. The developed new class of instruments has a remote probe with a special coil system that allows external MP excitation at several frequencies and measuring the response at combinatorial frequencies [3]. The output signal linearly depends on MP quantity in wide dynamic range of up to five orders of magnitude. The influence of parameters of the coil and electronic systems on spatial resolution and the depth where MP could be detected have been established. The developed instruments were tested to study magnetic drug delivery (Fig. 1B), for feasibility check of magnetic immunoassay carried out in a live body, which was previously tested *in vitro* [3,4].

Non-invasive monitoring of MP content in tissues up to 2 cm in depth has been performed with an external induction probe. In our experiments, MP dynamics has been recorded in tissues and in tumor of a mouse, which was placed on the top of the probe or near it as shown in Fig.2. The sensing depth can be significantly increased. It has also been shown that anesthesia of mice can alter MP dynamics in blood. That emphasizes advantages of research methods that do not require anesthesia.

The developed method of MP detection and related devices are highly sensitive and robust, they are not sensitive to linear dia- or paramagnetics that always surround MP in quantities nine-ten orders of magnitude higher than that of tested MP.

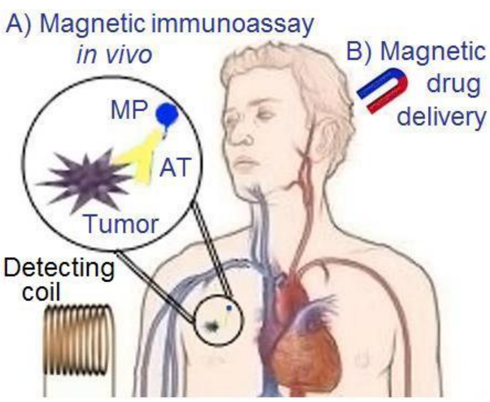

Fig. 1. MIA *in vivo* and drug delivery

Fig.2. Detection of MP in mouse by remote probe

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