A Method for Introduction of Magnetic Nanoparticles into Tissues by Means of Magnetic Field Gradient: An Experimental Study

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Targeted effects of magnetic nanoparticles were studied. Solution with iron-containing nanosubstance was applied to resected nasal bone and cartilage tissues. Magnetic field was generated by a Polus-101 device for low-frequency magnetotherapy, which provided permanent work of one inductor (10.14±19.56 mT). The results indicate that magnetic nanoparticles placed into magnetic field gradient penetrate into the thickness of the cartilage and bone tissues.

Key Words: *nanoparticles; magnetic field*

Controlled delivery of drugs on nanocarriers attracts special attention of scientists [4,3,10,11]. However, there is no universal viewpoint on the methods of nanosubstances administration. The intravenous route is used most often [1,2,12]. Nanoparticles are also administered endotracheally, intramuscularly, subcutaneously, and orally [8,3,10]. There is virtually no data on local application of nanoparticles and no information about local administration of magnetic nanoparticles. The advantages of local administration of nanoparticles are lower concentration of the substance, targeted effect, and absence of negative systemic effects.

We evaluated experimentally the possibility of local application of magnetic nanoparticles to tissues by means of the magnetic field gradient.

MATERIALS AND METHODS

Magnetic nanoparticles were obtained by culturing of *Klebsiella oxytoca* bacteria isolated from the Borovoe Lake sapropel (Krasnoyarsk Territory). Previous studies have shown that the bacteria synthesized ferrihydrite ($5Fe_2O_3 \times 9H_2O$) nanoparticles in the course of their vital activity [6,7]. Ferrihydrite is an antiferromagnetic. Due to small size of the particles (2-7 nm), the magnetic moments of Fe^{3+} ions on the surface of the particle are uncompensated and form a "parasitic" integral magnetic moment of a separate particle. The precipitate annealed at 550°C was used in the study (Fig. 1).

The absorption spectrum indicates that iron-containing nanoparticles are superantiferromagnetic. The results of absorption spectrum processing are presented in Table 1.

The parameters of superfine structure of the detected Fe^{3+} states are presented in the nanoparticles (Table 1). Positions Fe1, Fe2, Fe3, Fe4 correspond to Fe^{3+} ion states in the ferrihydrite nanoparticles. The sextet which appeared after thermal processing is explained by small amount of the resultant αFe_2O_3.

The magnetic field was generated by Polus-101 device, providing continuous work of one inductor (10.14±19.56 mT) [5].

The study was carried out on cartilage and bone tissue of the nasal septum resected in 10 patients. The operation was carried out for nasal respiration dys-

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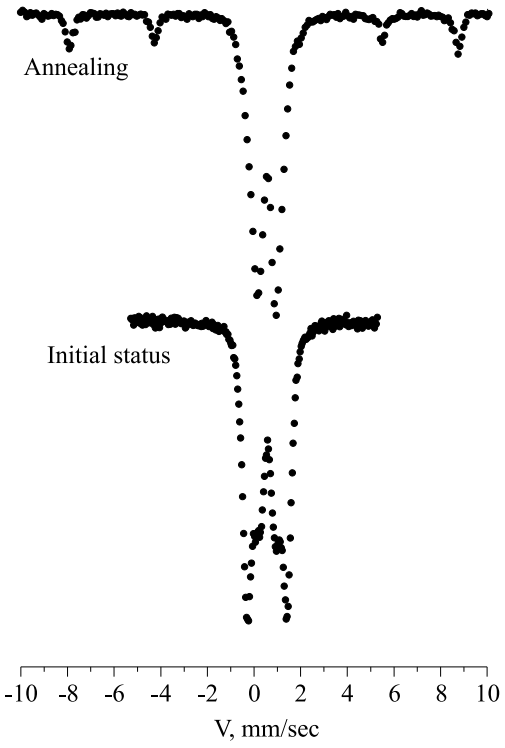

Fig. 1. Mossbauer spectra of nanoparticles initially and after thermal processing.

function without signs of inflammation or other abnormalities of cartilage and bone tissues.

The weight of the studied magnetic nanoparticles was 0.125 g. Magnetic powder was added to 1 ml 0.9% NaCl solution. The entire material was divided into equal portions and studied in 3 experimental series. In series I, fragments of the cartilage and bone tissue were plunged in a flask with nanoparticles suspended in saline for 20 min, after which they were washed and their histology was studied. In series II and III, fragments of the bone and cartilage tissues were plunged in the flask with nanoparticles and exposed in a magnetic field generated by Polus-101 device for 20 (series II) and 40 (series III) min, after which they were washed and their histology was studied. For histological study, the nanoparticles were detected in tissues by Perls' reaction.

RESULTS

In series I, the nanoparticles did not penetrate into the cartilage tissue, but were located at the cartilage edge (Fig. 2). Despite loose structure of the cartilage tissue, the nanoparticles did not penetrate into the depth.

A similar picture was observed for bone tissue. Stained nanosubstance was located mainly in the lumen and around the bone channels. Iron-containing substance did not penetrate into the thickness of the bone tissue.

Exposure of tissues in the magnetic field for 20 min (series II) resulted in a significant increase of activity of iron-containing nanoparticles (Fig. 3). Nanosubstances penetrated into the thickness of the cartilage and bone under the effect of magnetic field gradient and diffused in tissues. This can be due to the structure of extracellular substance of the cartilaginous tissue consisting of the main amorphous substance and collagen fibers. The same was observed in the bone tissue. Nanoparticles penetrated into bone plates virtually through the entire bulk of the bone fragments.

Hence, penetration of iron-containing nanosubstance into the thickness of tissues confirms its supermagnetic quality and suggests that it can be regulated by magnetic field exposure.

Despite 2-fold lengthening of the magnetic exposure in experimental series III, the content of iron-containing substances in tissues virtually did not increase. This indicates that 20-min exposure of nanoparticles in a magnetic field is sufficient for their penetration into tissues.

TABLE 1. Mossbauer Parameters of the Studied Nanoparticles

Appurtenance	IS	H	QS	W	S	Belonging
Initial nanoparticles	0.419	0	0.56	0.39	0.26	Fe1
	0.397	0	1.04	0.41	0.21	Fe2
	0.405	0	1.60	0.34	0.30	Fe3
	0.404	0	1.90	0.33	0.23	Fe4
Annealed nanoparticles	0.373	517	-0.42	0.20	0.15	αFe_2O_3
	0.406	0	0.54	0.40	0.28	Fe1
	0.383	0	0.92	0.43	0.45	Fe2
	0.362	0	1.40	0.25	0.07	Fe3
	0.364	0	1.79	0.30	0.06	Fe4

Note. IS: isomeric chemical shift *vs*. αFe, ±0.01 mm/sec; QS: quadrupole splitting, ±0.02 mm/sec; W: width of absorption line at the half-peak, ±0.02 mm/sec; S: part of the position population, ±0.03.

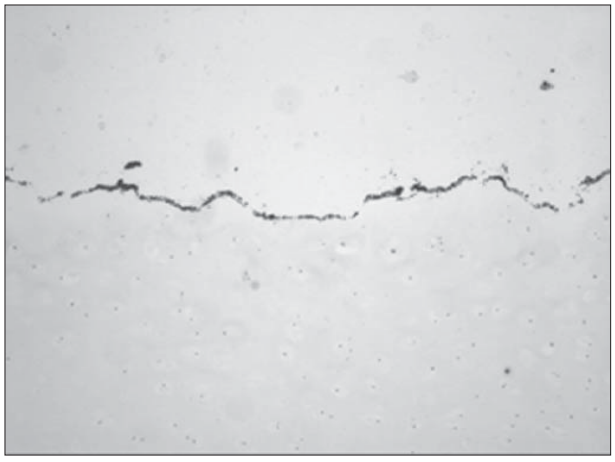

Fig. 2. Histology of the cartilage tissue (series I). Iron-containing nanoparticles on cartilage surface. Perls' reaction, ×100.

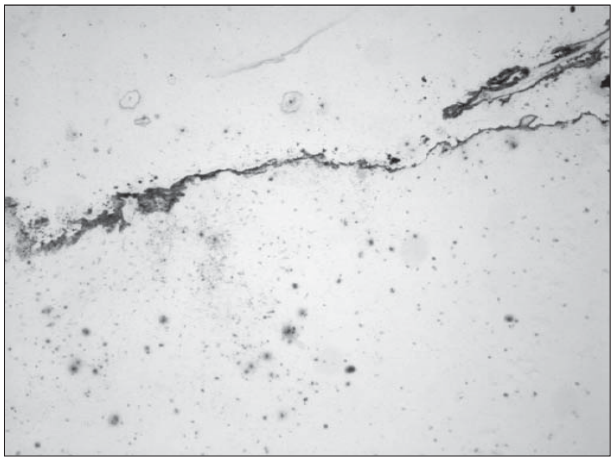

Fig. 3. Histology of the cartilage tissue after magnetic exposure (series II). Iron-containing particles in the cartilage thickness. Perls' reaction, ×100.

Hence, our findings indicate that magnetic exposure of iron-containing nanosubstances for 20 min leads to penetration of nanoparticles into the thickness of the cartilage and bone tissues. Prolongation of magnetic exposure of the nanoparticles virtually did not increase the amount of nanosubstances diffusing in tissues.

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