Influence of Nanoparticles on the Nervous Tissue Properties

I.Reshetov[*], V.Chissov[*], S.Sukharev[*], V.Timoshenko[**], V.Sidletsky[*] and P.Forsh[**]

[*]P.A.Hertzen Moscow Research Oncological Institute, 2-nd Botkinsky proezd 3, Moscow 125248, Russian Federation, hertz@portal.ru
[**]Physics Department, Moscow State M.V.Lomonosov University, 119999 Moscow, Russia, timoshen@phys.msu.ru

ABSTRACT

Interaction between nanoparticles and nervous tissue in the process of the damage healing is the object of study in the present work. The Nervus ishiadicus of rat was intersected and anastomosis performed. The electrical resistance of the nerve was measured above and below the anastomosis after place of anastamosis being underwent the action of AC field or heat. The electrical resistance of the nerve was measured above and below the anastomosis. Nanoparticles are biocompatible with respect to the nervous tissue. They decrease the pathological pulsation from the area of damage and the spread of changes in the macroscopic electrical parameters of the nervous tissue, including changes, caused by damage.

Keywords: nanoparticles, biodistribution, nervous tissue

1 AIMS AND INNOVATION

The surgical treatment of malignant tumors requires quite often the removal of nervous structures. This unavoidably leads to the patient invalidization, and also compromises the function of organs and muscles.

The development of nanotechnologies applications to the treatment of nervous system (both central and peripheral) defeats significantly lags behind the development of applications in other areas of medicine (orthopedics, DNA- sensors, drug delivery). Among the reasons for this delay it is possible to name the following circumstances:

- the difficulty of access to the divisions of central and peripheral nervous system;
- extremely diverse cellular and molecular environment, in which inanosobjects should act;
- the complexity of anatomical and functional connections and information streams in the nervous system.

Special features of nanoparticle's distribution and interaction with mammalian tissue were investigated earlier for muscle and epithelium tissues, tumor including. Interactions of living cells with porous silicon in-vitro were studied earlier [1,2]. Interaction between silicon nanoparticles and nervous tissue in the process of the damage healing is the object of study in the present work.

2 MATERIALS AND MODEL

2.1 Biological Model

In this study we used the rat femur model. For the purpose of this investigation 40 rats (250–300 g) were used.

Three groups of rats each comprises 10 – 15 animals were formed.

The first group (control) – no nanoparticles used.

The second one was subjected to action of AC field (Figure 1) after nanoparticles injection into anastomosis area.

Figure 1: Stimulation of anastomosis area by AC field.

The animals of third group underwent the action of heat after anastomosis performance.

An anesthetic solution containing phentanili and droperidoli was injected intraperitoneally. Surgery was performed on the front of the lower limb, unilaterally under sterile conditions.

The Nervus ishiadicus of rat was intersected and anastomosis performed. Rats were sacrificed at 1 – 49 days after operation.

Surgical procedures were conducted in compliance with ethical principles for animal research, as approved by

MROI and European (European Convention for the protection of vertebrate animals used for experimental and other scientific purposes) guidelines.

2.2 Preparation of Nanoparticles

Formation of stable silicon nanocrystals suspensions in biological liquids consists of the three stages.

1) Obtaining of porous silicon (PS) layers by electrochemical etching of monocrystal silicon wafers. The PS films were formed from (100)-oriented p^+-Si:B wafers (ρ=10÷20 $\Omega\cdot$cm) by electrochemical anodization in a 1:1 solution of HF acid and ethanol at a current density of 60 mA/cm^2 for an hour. Free-standing 70-μm-thick PS films were obtained by lifting during a short electropolishing step at a current density of 500 mA/cm^2.

2) Mechanical crushing of received PS films in a powder.

3) Dispersion in water and in biological liquids of the obtained powder. According to high-resolved electron microscopy the maximum size of silicon nanocrystals in suspension didn't exceed 50 nm.

Figure 1 shows typical photoluminescence spectra of silicon nanocrystals dispersed in biological liquid. As follows from Figure 1 the received suspensions of silicon nanocrystals were characterized by intensive photoluminescence in visible and near IR range. After 120 minutes photoluminescence intensity and spectral shape of the silicon nanocrystals suspension didn't undergo significant changes. These experimental data as well as the visual control of samples condition testify the stability of the silicon nanocrystals suspension. The analysis of photoluminescence spectra and kinetics has shown that optical influence doesn't result in essential change of a surface covering and structural properties silicon nanocrystals in biological liquids.

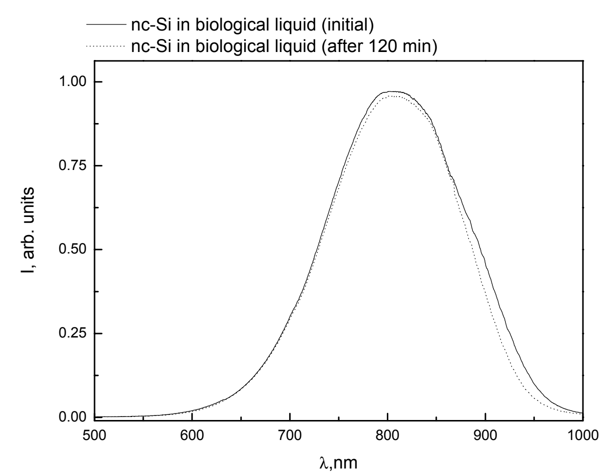

Figure 1: Photoluminescence spectra of silicon nanoparticles in biological liquids.

On the basis of the obtained data it is possible to conclude that silicon nanocrystal suspensions in biological liquids are stable during as a minimum of 2 hours, and retain in the mentioned time interval the initial structural and electronic properties.

Investigations of electrical characteristics were carried out on a sciatic nerve of a rat's hip. Measurements were carried out both on alternating and constant signals. The amplitude of a signal changed from tens millivolt up to several volt. To determine the resistance along a nerve tissue one of measuring electrodes was displaced lengthways of the nerve.

3 RESULTS

3.1 Clinical Observations

No disturbances of the behavioral features of animals was noted. Physiological functions and behavior conformed to severity and terms of surgical intervention.

The electrical resistance of the nerve was measured above and below the anastomosis after place of anastamosis being underwent the action of AC field or heat.

The portion of animals with the restored function of nerve at 49 days after operation comprised:

- control group (without nanoparticles application) – 70%;
- group, which received the powder of nanoparticles – 0%;
- group, which received the suspension of nanoparticles and than subjected tto action by heat – 60%;
- group, which received the suspension of nanoparticles and than subjected to action by AC field – 60%.

Most of animals in the control group, for which the restoration of innervation did not occur, formed the stump of the damaged extremity convenient in functional sense. None of animals of experimental groups did form stump.

3.2 Electrical Parameters

In Figure 2 the received dependences of nervous tissue resistance from distance between electrodes are given. These dependences were measured under the displacement of one of electrodes along a nerve and under constant voltage 1.7 V. Similar dependences were received on a variable signal. In Figure 2 typical dependence of investigated nervous tissue resistance is given without anastomosis and nanocrystals. Displacement of an electrode occurred in distant direction. Value of resistance is given in arbitrary units. Resistance of maximum distance L between contacts is accepted for resistance unit. One can see that resistance falls with distance decrease according to the Ohm law.

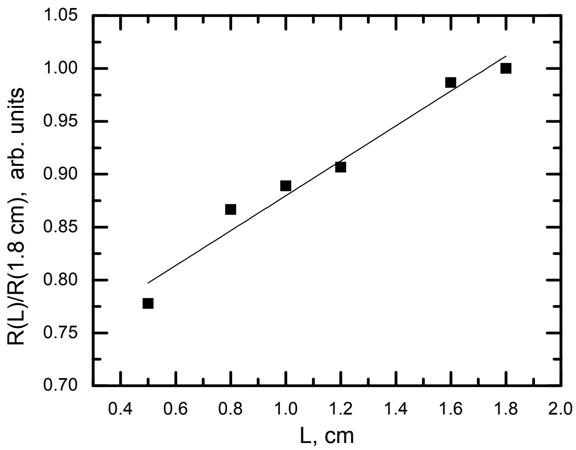

Figure 2: Dependences of nervous tissue resistance on distance between electrodes (without anastomosis and nanoparticles).

In a case of anastomosis the dependence of resistance on distance between electrodes is shown in Figure 3. It is seen, that resistance decrease with decrease of L is weakened and in anastomosis area the plateau is observed. It is possible to conclude, that the anastomosis zone has different (smaller) resistance than nervous tissue one. This fact leads to smaller voltage decrease along nervous tissue.

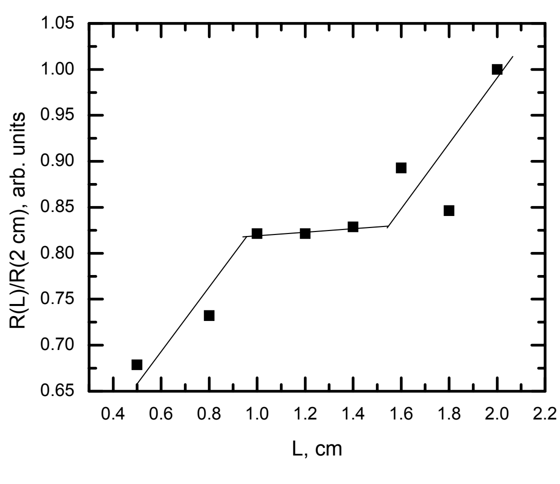

Figure 3: Dependence of resistance on distance between electrodes in a case of anastomosis.

On Figure 4 dependences of resistance on length of a site of a nervous tissue are given in case of anastomosis presence and introductions of nanocrystals suspension. For comparison on figure 4 the dependence of resistance on distance between electrodes for a nervous tissue without anastomosis and nanocrystals presence is shown. Introduction of nanoparticles compensates the changes caused by anastomosis and make plateau on the diagram smaller. In Figure 4 one can see that the change of resistance with distance in case of absence of anastomosis and silicon nanoparticles differs from resistance of a healthy nervous tissue. It can testify the insufficient contribution of silicon nanocrystals in process of nervous tissue restoration.

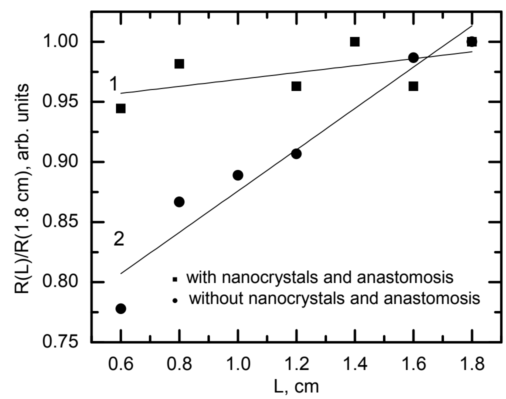

Figure 4: Dependences of resistance on distance with (1) and without nanocrystals (2) when the anastomosis is absent.

4 CONCLUSIONS

1.Nanoparticles are biocompatible with respect to the nervous tissue – when in suspension they do not worsen the results of the nerve damages treatment.

2. Nanoparticles decrease the pathological impulsation from the area of damage.

3. Nanoparticles decrease the spread of changes in the macroscopic electrical parameters of nervous tissue, including changes, which are caused by damage.

These observations are a basis for the therapeutic applications of silicon nanoparticles in treatments of the damaged nerves.

5 ACKNOWLEDGEMENTS

The work was supported by grants of the Ministry of Education and Science of the Russian Federation.

REFERENCES

[1] S. Ben-Tabou de-Leon, R. Oren, M. E. Spira, N. Korbakov, S. Yitzchaik, A.Sa'ar. "Porous Silicon substrates for neurons culturing and bio-photonic sensing", Physica Status Solidi (a) **202**, No.8, pp.1456-1461 (2005).

[2] F. Johansson, M. Kanje, C. Eriksson, L. Wallman. "Guidance of neurons on porous patterned silicicon", Physica Status Solidi (c) **202**, No.9, pp.3258-3262 (2005).