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"Smart" nanoscalpel for microsurgery of glial tumors of the human brain

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Abstract. We studied the effectiveness of magnetomechanical therapy in the treatment of brain glial tumors using magnetic nanodiscs functionalized with DNA aptamers to human brain tumor glial cells. • Materials and methods. The formation of a model of human glioblastoma was carried out by intracranial injection of tumor cells of glioblastoma obtained from a patient with glioblastoma. Antitumor therapy was carried out using nanodiscs modified with the Gli233 aptamer. The growth of the glial tumor was monitored using NMR tomography. • Results and discussion. Therapy of a glial tumor during 4 sessions of magnetomechanical therapy using a "smart" nanoscalpel in MF (10Hz, 100Oe) led to a significant reduction in its size, while glial tumors in mice that were treated with nanodiscs modified with nonspecific aptamers continued to increase in size. • Conclusion. Microsurgery using three-layer magnetic nanodisks with a quasi-dipole structure (Au/Ni/Au) modified with the specific for glial cells Gli233 aptamer ("smart" nanoscalpel) is effective for the treatment of human glial tumors in the brain.

Key words: aptamers, glial tumor, NMR tomography, «smart» nanoscalpel, nanodiscs, magnetomechanical therapy.

Conflict of interest. The authors declare the absence of obvious and potential conflicts of interest associated with the publication of this article.

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Introduction

Glial tumors are primary human brain tumors with a high mortality rate due to their malignancy [1]. The high invasion of tumor cells into the surrounding tissues makes it impossible to completely resect the tumor, and conventional therapies are ineffective for its treatment. Currently, one of the promising methods for therapy is the cell surgery, where a "smart" nanoscalpel acts as a surgical instrument. A nanoscalpel is a remotely controlled magnetic nanodisc targeted at a tumor with DNA aptamers specific to human brain glial tumors, capable of transforming a magnetic moment into a mechanical one in an alternating magnetic field [2]. Here we evaluated the effectiveness of a "smart" nanoscalpel (unique three-layer magnetic nanodisks with a quasi-dipole structure (Au/Ni/Au) modified with the Gli233 aptamer) under the influence of an alternating magnetic field to destroy a glial brain tumor *in vivo*.

Material and methods

The objects of the study were laboratory male ICR mice with immunosuppression, weighing 20-25g. The formation of a model of human glioblastoma was carried out by intracranial injection of tumor cells of glioblastoma obtained from a patient with glioblastoma. The growth of the glial tumor was monitored using NMR tomography. Antitumor therapy was carried out using nanodiscs modified with the Gli233 aptamer. The selection of optimal magnetic field parameters for microsurgery with magnetic nanodisks was carried out on ascitic cells of Ehrlich carcinoma.

Results and discussion

The effectiveness of magnetomechanical therapy was evaluated on cell cultures of Ehrlich's ascitic carcinoma *in vitro* at the following frequencies of an alternating magnetic field (MF): 1, 5, 10, 20, and 50 Hz (MF intensity was 100 Oe). Ascitic cells were destroyed using magnetic nanodiscs modified with a AS42 aptamer, which was specific to ascitic cells. Studies have shown that MF with a frequency of 10 Hz led to the maximum death of ascitic cells. MF with a frequency of 10 Hz was used for microsurgery of a glial brain tumor *in vivo*.

The development and treatment of glial tumors in mice was monitored using NMR imaging. Studies have shown that within 14 days the tumor has increased to a large size (Fig. 1, a, d). Therapy of a glial tumor during 4 sessions of magnetomechanical therapy using a "smart" nanoscalpel in MF (10Hz, 100Oe) led to a significant reduction in its size (Fig. 1, b-c), while glial tumors in mice that were treated with nanodiscs modified with nonspecific aptamers continued to increase in size (Fig. d-f).

Conclusion

Microsurgery using three-layer magnetic nanodisks with a quasi-dipole structure (Au/Ni/Au) modified with the specific for glial cells Gli233 aptamer ("smart" nanoscalpel) is effective for the treatment of human glial tumors in the brain.

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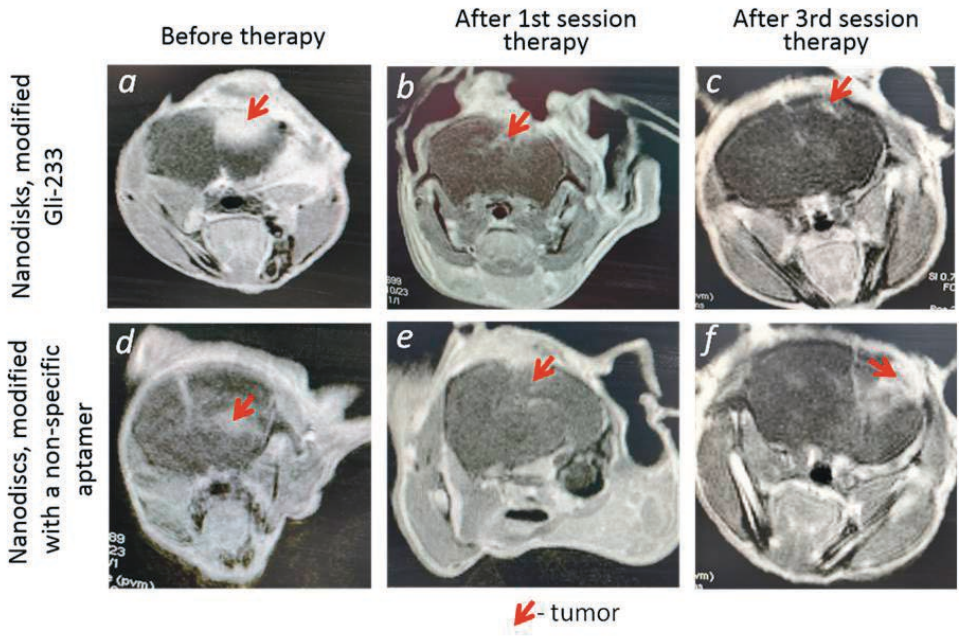

Figure. Efficiency of "smart" nanoscalpel in microsurgery of glial tumors: a) and d) the tumors before treatment; b) and c) treatment with nanodisks modified with Gli233 aptamer; e) and f) treatment with nanodisks modified with nonspecific aptamer.

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References

1. WirschingH-G, Galanis E, Weller M. Glioblastoma. *Handbook of Clinical Neurology*. 2016;(134):381-97. DOI: 10.1016/B978-0-12-802997-8.00023-2

2. Zamay TN, Prokopenko VS, Zamay SS, Lukyanenko KA, Kolovskaya OS, Orlov VA, Zamay GS, Galeev RG, Narodov AA, Kichkailo AS. Magnetic nanodiscs - a new promising tool for microsurgery of malignant neoplasms. *Nanomaterials*. 2021;11(6):1459-147.

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