

Low-Level Laser Treatment Induces the Blood-Brain Barrier Opening and the Brain Drainage System Activation: Delivery of Liposomes into Mouse Glioblastoma

Arina Evsukova¹, Andrey Terskov¹, Ivan Fedosov¹, Egor Ilyukov¹, Inna Blokhina, Alexander Shirokov^{1,2}, Nikita Navolokin^{1,3}, Oxana Semyachkina-Glushkovskaya¹

¹Saratov State University, Scientific Medical Center, laboratory “Smart Sleep” (Saratov, Russia)

²Saratov Scientific Centre of the Russian Academy of Sciences (IBPPM RAS), Institute of Biochemistry and Physiology of Plants and Microorganisms, (Saratov, Russia)

³Department of Pathological Anatomy, Saratov Medical State University, (Saratov, Russia)

✉ arina-evsyukova@mail.ru

Glioblastoma (GBM) is the most common central nervous system (CNS) tumour, which can occur at any age. Small patients with GBM have a comparably dismal clinical outcome to older patients with morphologically similar lesions. Only a few children with GBM achieving long-term survival despite a variety of therapies applied.

The blood-brain barrier (BBB) limits the delivery of vast majority of cancer therapeutics that creates challenge of pharmacological therapy of GBM, especially treatment of satellite tumor areas that grow along healthy cerebral vessels with an intact. Therefore, the effective therapy of recurrent GBM depends on the development strategies of bypassing an intact BBB at the GBM border to prevent tumor migration and progression.

Low-level laser treatment is considered as a promising least-toxic method tool in treating both pediatric and adult GBM.

In this study, we discovered that transcranial laser stimulation 1268 induces temporary BBBO in the mice brain which is accompanied by activation of the brain drainage system contributing to the effective delivery of liposomes to GBM. The BBBO-mediated increase in the interstitial fluid movement leads to a stronger accumulation of liposomes in the GBM tissues that we observe in mice treated with the 1268 nm laser compared with intact animals. Thus, during the increase in BBB permeability, the movement of brain fluids increases, which contributes to the transport of liposomes to GBM and their effective accumulation in tumor tissues. Based on the results, it was concluded that a noninvasive increase in BBB permeability using transcranial laser stimulation the 1268 nm-BBBO can be a new strategy for brain drug delivery in surrounding GBM places for the effective GBM therapy.

Key words: neurotechnology, medicine, photodynamic therapy, glioblastoma, blood-brain barrier

Acknowledgments: The research was supported by the Russian Science Foundation (project No. 23-25-00296).