The possibilities of optical methods in the early diagnosis of gliomas

O. Cherkasova^{1,2}, A. Mankova³, M. Konnikova², P. Solyankin², D. Vrazhnov^{4,5}, Yu. Kistenev^{4,6}, A. Sinko², Y.Peng⁷, E. L. Zavjalov⁸

¹Institute of Laser Physics, Siberian Branch of the RAS, Novosibirsk, Russia

²Institute on Laser and Information Technologies - Branch of the Federal Scientific Research Centre "Crystallography and Photonics" of RAS, Shatura, Moscow Region, Russia

³Faculty of Physics and International Laser Center, Lomonosov Moscow State University, Moscow, Russia

⁴Tomsk State University, Tomsk, Russia

⁵Institute of Strength Physics and Materials Science of Siberian Branch of the RAS, Tomsk Russia

⁶Siberian State Medical University, Tomsk, Russia

⁷University of Shanghai for Science and Technology, China

⁸Federal Research Center "Institute of Cytology and Genetics of the Siberian Branch of the RAS", Novosibirsk, Russia

Abstract—A novel approach based on the Raman and absorption spectroscopy for detection of gliomas molecular markers in brain tissue and blood will be discussed. Using the mice model of the U87 human glioblastoma, we have shown the possibility of glioma development control by a combination of Raman, infrared (IR), and Terahertz (THz) pulsed spectroscopy.

Keywords— terahertz spectroscopy, Raman spectroscopy, infrared spectroscopy, glioma, human glioblastoma model

I. INTRODUCTION

The glioma is occurred in about 80% of primary malignant brain tumors. It causes substantial social and economical loss connected with the damage of the employable part of the population. Glioblastoma (GBM) is the most common and devastating primary malignant brain tumor in adults. Even in case of applying an aggressive therapy of the brain glioma, such as surgical resection, radiotherapy and chemotherapy, many types of gliomas have the pessimistic prognosis for survival of a patient [1]. Thereby, early diagnosis and assessment of lesion stage of brain by glioma are important problems. It is the reason for the importance of development the non-invasive and low-invasive methods of early detection of gliomas and control of treatment.

One of the main directions of diagnostics and treatment of malignant tumors is investigation of the reasons of formation and the routes of the generation of molecular markers of carcinogenesis for the elaboration of new methods of early diagnostics and therapy [2]. Traditional methods of methabolomics cannot render operatively fully reliable information due to complicated sample preparation, long testing time, and the impossibility of timely intra-operation analysis [3].

Recently, enantiomers of 2-hydroxyglutarate (L-2HG and D-2HG) in tissues and blood were shown to be highly specific markers for the differential diagnostics of gliomas [4]. It was demonstrated the use of THz Time-domain Spectroscopy (THz-TDS) for the measurement and identification of 2-HG

isomers [5]. The goal of work is early diagnosis of brain gliomas with a complex of methods including THz-TDS, IR absorption and Raman spectroscopy, machine learning.

II. RESULTS

A novel approach based on the Raman and absorption spectroscopy for detection of enantiomers of 2hydroxyglutarate (L-2HG and D-2HG) in tissues and blood are discussed. We are focusing on gliomas molecular markers detection in brain tissue and the blood. Using the mice model of U87 human GBM [6], we have shown the possibility of glioma development control by a combination of THz-TDS, Raman, and IR spectroscopy. 1H-Magnetic resonance spectroscopy is used as reference method for detection of glioma molecular markers at different stage of the tumor growth.

References

- [1] G. M. Yusubalieva, V. P. Baklaushev, O. I. Gurina et al, "Treatment of Poorly Differentiated Glioma Using a Combination of Monoclonal Antibodies to Extracellular Connexin-43 Fragment, Temozolomide, and Radiotherapy," Bulletin of Experimental Biology and Medicine, vol. 157, pp. 510–515, 2014.
- [2] M.Touat, A. Duran-Peña, A.Alentorn et al, "Emerging circulating biomarkers in glioblastoma: promises and challenges", Expert Review of Molecular Diagnostics, vol. 15 (10), pp.1311-1323, 2015.
- [3] E.Miyauchi, T.Furuta, S.Ohtsuki et al, "Identification of blood biomarkers in glioblastoma by SWATH mass spectrometry and quantitative targeted absolute proteomics", PLoS ONE, vol. 13 (3), pp. e0193799, 2018.
- [4] M. S. Waitkus, B. H. Diplas, H.Yan, "Isocitrate dehydrogenase mutations in gliomas", Neuro-Oncology, vol. 18(1), pp. 16–26, 2016.
- [5] W.Chen, Y.Peng, X.Jiang, J.Zhao, H.Zhao, Y.Zhu, "Isomers Identi cation of 2-hydroxyglutarate acid disodium salt (2HG) by Terahertz Time-domain Spectroscopy", Sci.rep., vol.7, p. 12166, 2017.
- [6] E. L. Zavjalov, I. A. Razumov, L. A. Gerlinskaya, A. V. Romashchenko, "In vivo MRI Visualization of U87 Glioblastoma Development Dynamics in the Model of Orthotopic Xenotransplantation to the SCID Mouse", Russian Journal of Genetics: Applied Research, vol. 6, (4), pp. 448–453, 2016.

The work was supported by the RFBR and National Natural Science Foundation of China, research project № 19-52-55004.