Knowledge E
Engaging minds

Conference Paper

Spectral-optical Properties of Nutrient Coated Optical Fibers for Glioma Cells Growth Orientation

Sharova A. S.[1,2], Maklygina YU. S.[2], Volkov V.V.[2], Ryabova A.V.[2], and Loschenov V. B.[1,2]

[1]National Research Nuclear University MEPhI (Moscow Engineering Physics Institute), Kashirskoe shosse 31, Moscow, 115409, Russia
[2]Prokhorov General Physics Institute of Russian Academy of Sciences (GPI RAS), 38 Vavilov street, Moscow, Russia

Corresponding Author:
A. S. Sharova
alina.s.sharova@gmail.com

Received: 17 January 2018
Accepted: 25 March 2018
Published: 17 April 2018

Publishing services provided by Knowledge E

Selection and Peer-review under the responsibility of the PhysBioSymp17 Conference Committee.

Abstract

This study is based on the approach of guiding randomly proliferated deep lying brain tumor cells to the external surface where they could be registered and therapeutically affected. Optical fibers coated with nutrient medium (agar) act like neuro-scaffold for tumor cells growth orientation. Research of neuro-scaffold spectral-optical properties was carried out by photodiagnostics method using the model sample: the brain tissue phantom with aluminum phthalocyanine photosensitizer addition. Such neuro-scaffolds conduct and allow obtaining optical signal from the deep with high accuracy, comparable to direct measurement ”in contact” with the tissue, that will provide multiple phototheranostics and monitoring of processes occurring in the brain probed area.

Keywords: Optical fibers, neuro-scaffold, photodiagnostics (PD), agar ($C_{14}H_{24}O_9$), aluminum phthalocyanine (AlPc)

1. Introduction

Brain neoplasms considered to be the most dangerous and difficult to treat tumors due to their anatomical location. The new approach of such neoplasms type treatment is to control deep-lying brain tumor random proliferation by guiding tumor to the external surface where malignant cells could be registered and therapeutically affected without additional surgical intervention [1]. Neuro-scaffolds based on optical fibers structurally imitating white matter channels and blood vessels [2] seem to be promising for brain tumor cells growth orientation [3]. Moreover, one of the new methods aimed on deep-lying brain tumors therapy, is based on the concept, where ionizing radiation act as the key link in the antitumor effect implementation. Radiosensitizing agents could be used as the ionizing radiation sources for such an approach [4]. At the same time,

How to cite this article: Sharova A. S., Maklygina YU. S., Volkov V.V., Ryabova A.V., and Loschenov V. B., (2018), “Spectral-optical Properties of Nutrient Coated Optical Fibers for Glioma Cells Growth Orientation” in *The 2nd International Symposium on Physics, Engineering and Technologies for Biomedicine*, KnE Energy & Physics, pages 470–475. DOI 10.18502/ken.v3i2.1853

ionizing radiation, propagating in the depth of the tissue, acts as a source of Vavilov-Cherenkov radiation, whose energy can also transfer photosensitizer (PS) molecules from the ground state to the excited one, thereby exerting a photodynamic effect [5]. It is significant to mention, that optical-fibers neuro-scaffolds are suitable for carrying out subsequent photodiagnostics (PD), photodynamic therapy (PDT) and laser hyperthermia as they conduct optical signal [6]. Laser therapy and hyperthermia for glioblastoma multiforme are considered to be the part of a growing armamentarium for malignant glioma treatment [7-8]. The development of user-friendly fiber-optic toolkit, which allows obtaining spectral information during surgery and relapse observation, is very urgent [9]. To control tumor cells spreading and enhance the likelihood of their proliferation along the neuro-scaffold to the external surface, it is suggested to coat optical fibers with nutrient compound layer [10] (Figure 1). In this way, current paper introduces the results of spectral-optical properties research of nutrient agar coated optical fibers.

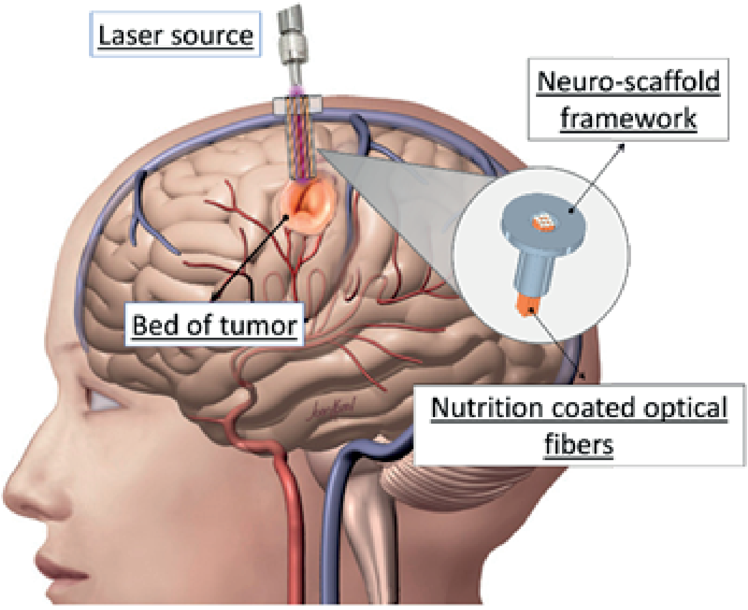

Figure 1: The model of nutrient coated fiber-optic neuro-scaffold implanted into the bed of tumor after resection. Such approach will provide setting the direction of malignant cells growth from the deep to the external surface and carrying out multiple phototheranostics of the probed area.

2. Materials and methods

A system of seven silica fibers with flat tips (20 mm length and 350 μm diameter each) lies at the basis of the developed neuro-scaffold construction of an enlarged scale [11-12]. The optical fibers were partially cleaned from the primary protective-strengthening cover to provide a steady radiation output from fibers around the neuro-scaffold perimeter. Then, the optical fibers were fastened by a polymer framework and fixed with a biocompatible adhesive solution. After that, the fibers tips were grinded followed by wiping of the peeled ends with a soft material to obtain a smooth, well-treated tip surface for qualitative radiation conduction.

As agar ($C_{14}H_{24}O_9$) is a nutritional medium favorable for cells seeding and growing in vitro, the oriented tumor cells proliferation improvement along the scaffolds can be achieved by coating neuro-scaffold' optical fibers with agar compound. Melting temperature of agar gel is 85-95° that is significant for solid coating of optical fibers in vivo conditions.

The study of the developed neuro-complex was carried out by PD method using the model sample: a brain tissue phantom with PS agent addition. The phantom of following composition: 1.1% intralipid in aqueous solution repeats optical and structural properties of the brain tissue with a high accuracy. Aluminum phthalocyanine (AlPc) molecular solution (c = 0.1 mkg/ml) was used as PS (synthesized by Organic Intermediates & Dyes Institute (NIOPIK), Russia).

The spectral- optical neuro-scaffold properties were investigated using LESA-01 "BIOSPEC" spectrometer (Russia). The fluorescence was excited by a laser source at a power density of $\sim$ 100 mW / cm^2 and λ = 632.8 nm wavelength, chosen in accordance with the AlPc absorption maximum. Experimental measurements were carried out for different conditions by fiber-optic diagnostic probe with receiving and emitting fibers (Figure 2).

3. Results

The spectral-optical properties of neuro-scaffold and adjuvant components were investigated during the study. It was found that silica fibers, agar and the brain tissue phantom do not show fluorescent properties on their own. During the fluorescent signal obtaining through fiber-optic neuro-scaffold (Figure 2b), the slight decrease of intensity (15%) was registered due to the optical losses at the junction of diagnostic probe and neuro-scaffold (Figure 3). After agar surface layer application on the optical fibers structure of neuro-scaffold the fluorescent signal intensity reduced insignificantly **(**Figure 2c, 3**).** Thus, the developed neuro-scaffold based on optical fibers coated with nutrient agar compound contributes obtaining a fluorescent signal

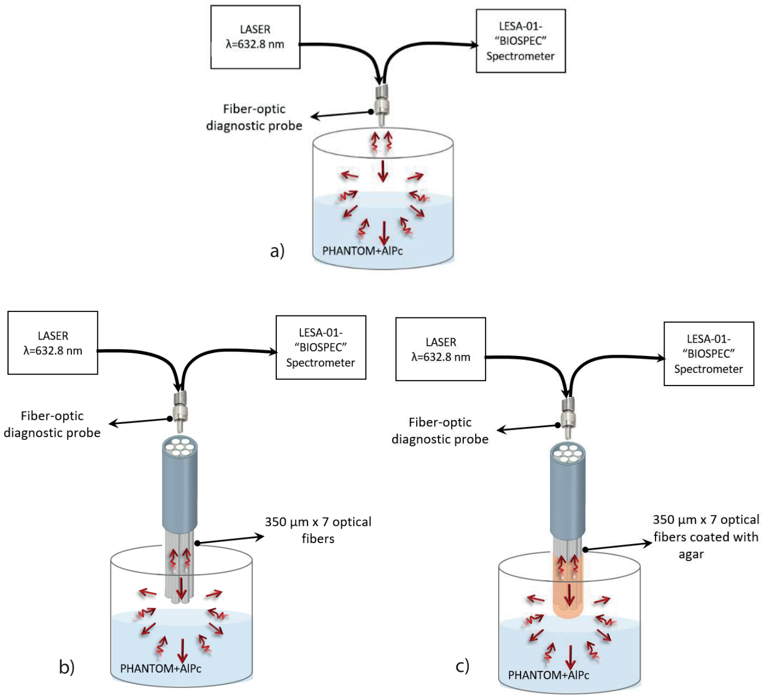

Figure 2: Scheme of the experiment in a PD mode. Direct fluorescence measurements "in contact" with the modal sample (brain tissue phantom with AlPc addition) (a), fluorescence measurements of the modal sample through neuro-scaffold (b), fluorescence measurements of the modal sample through neuro-scaffold coated with agar (c).

with high accuracy, comparable to direct measurement "in contact" with the tissue (Figure 2a, 3).

4. Conclusion

The spectral-optical properties of the developed neuro-scaffold based on optical fibers with nutrient agar coating were investigated in the framework of this study. The neuro-scaffold structure allows obtaining a fluorescent signal from the deep with high accuracy, comparable to direct measurement "in contact" with the tissue. It was also found that agar optical fibers coating does not interfere with photodiagnostics. Moreover, it is significant to note that neuro-scaffold construction and nutrient coating are still develop and can be varied until optimal configuration achievement. Overall, to carry out deep-lying tumor phototheranostics by guiding tumor cells to the external surface, and monitor processes occurring in the brain probed area, further studies of the developed nutrient coated neuro-scaffolds in vivo seem to be perspective. This system will also find application for various photosensitizers research, including organic dyes,

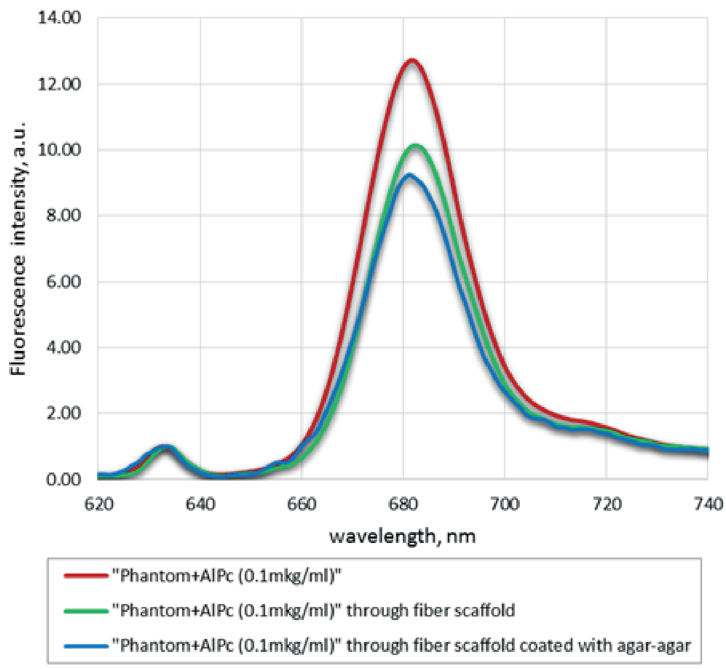

Figure 3: The fluorescence spectra of modal sample (brain tissue phantom with AlPc addition) obtained during: • direct diagnostic probe measurement; • through fiber-optic neuro-scaffold; • through fiber-optic neuro-scaffold coated with agar.

rare-earth nanoparticles, not only for PD and PDT, but also for deep layers temperature evaluation during laser hyperthermia (for instance, with rare-earth nanocrystals containing neodymium or dysprosium ions).

Acknowledgments

This work is supported by Ministry of Education and Science of the Russian Federation RFMEFI61615X0064.

References

[1] A. Jain, M. Betancur, G. D. Patel, C. M. Valmikinathan, V.J. Mukhatyar, A. Vakharia, S. B. Pai, B. Brahma, T. J. MacDonald, and R. V. Bellamkonda, “Guiding intracortical brain tumour cells to an extracortical cytotoxic hydrogel using aligned polymeric nanofibers,” Nature materials, vol.13, pp. 308-316, 2014.

[2] A. Claes, A. J. Idema, and P. Wesseling, “Diffuse glioma growth: a guerilla war,” Acta Neuropathol, vol. 114, pp. 443-458, 2007

[3] Yu. S. Maklygina, A. V. Ryabova, V. B. Loschenov, E. N. Sokolov, D. I. Nevzorov, E.Yu. Grigoreva, M. B. Dolgushin, and B. I. Dolgushin, “Depth independent

Cherenkov radiation-mediated therapy with 5-ALA photosensitizer," *Abstracts of the International Conference on Lasers, Applications and Technologies (LAT2016)*, Photon Lasers Med., vol.5, no.4, pp. 309-310, 2016.

[4] D.A. Tzerkovsky, "Photosensitizers as radiosensitizing agents in experimental and clinical neurooncology," Biomedical Photonics, vol.6, no.2, pp.27-33, 2017

[5] Yu.S. Makligina, A.V. Ryabova, V.B. Loschenov, E.N. Sokolov, D.I. Nevzorov, E. Yu. Grigorieva, M.B. Dolgushin, and B.I. Dolgushin, "The use of the Cherenkov radiation for C6 rat glioma cells destruction with the combined effect of FDH and 5-ALA induced protoporphyrin IX, Pilot experimental research," Vestnik RONTS, vol.27, no.4, pp.133-139, 2016

[6] V.B. Loschenov, V.I. Konov, A.M. Prokhorov, "Photodynamic Therapy and Fluorescence Diagnostics," Laser Physics, vol. 10, no. 6, pp.1188–1207, 2000.

[7] M. Jaber, J. Wölfer, C. Ewelt, M. Holling, M. Hasselblatt, T. Niederstadt, T. Zoubi, M. Weckesser, and W. Stummer, "The Value of 5-Aminolevulinic Acid in Low-grade Gliomas and High-grade Gliomas Lacking Glioblastoma Imaging Features: An Analysis Based on Fluorescence, Magnetic Resonance Imaging, 18F-Fluoroethyl Tyrosine Positron Emission Tomography, and Tumor Molecular Factors," Neurosurgery, vol.78, no.3, pp. 401-11, discussion 411, 2016.

[8] T. W. Lee, G. J. Murad, B. L. Hoh, M. Rahman, "Fighting fire with fire: the revival of thermotherapy for gliomas," Anticancer Res., vol.34, no.2, pp.565-74, 2014.

[9] L. Liu, F. Ni, J. Zhang, C. Wang, X. Lu, Z. Guo, S. Yao, Y. Shu, and R. Xu, "Thermal analysis in the rat glioma model during directly multipoint injection hyperthermia incorporating magnetic nanoparticles," J. Nanosci. Nanotechnol., vol.11,no.12,pp.10333-8, 2011.

[10] Z. MA, W. He, T. Yong, and S. Ramakrishna, "Grafting of Gelatin on Electrospun Poly(caprolactone) Nanofibers to Improve Endothelial Cell Spreading and Proliferation and to Control Cell Orientation," Tissue Eng., vol. 11, pp. 1149-58, 2005.

[11] V.V. Volkov, V.B. Loshchenov, V.I. Konov, V.V. Kononenko, "Fibreoptic diffuse-light irradiators of biological tissues," Quantum Electronics, vol.40, no. 8, pp. 746-750, 2010.

[12] LTD Biospec, "Medical systems for photodynamic therapy, fluorescent diagnostics and optical biopsy," *online resource,* [http://www.biospec.ru/index_e.html]