Application of infrared spectroscopy to the study of biopsies of patients with glial brain tumors

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Abstract. The treatment of each pathology directly depends on the effectiveness of diagnostics. Brain tumors (BT) are often detected only at late stages, since most existing instrumental diagnostic methods are mainly used after the manifestation of signs of the disease, when the tumors reach clinically significant sizes. Despite significant advances in neurosurgery and oncology, glial brain tumors continue to be an acute problem in modern healthcare. The relevance of developing new diagnostic methods is due to the prevalence and social significance of glial tumors, the great need to develop minimally invasive methods of early diagnosis to improve the overall duration and quality of life of such patients, as well as express diagnostic methods to reduce the time of diagnosis using traditional methods. **Purpose of the study.** The work assessed the possibility of using infrared spectroscopy of attenuated total internal reflection (FTIR ATR) as a method for early diagnosis of glial tumors on biopsies of patients (blood serum) in comparison with control samples; as well as an express method of classification within a given type of tumor (brain tissue).

Research materials. The work was carried out jointly at the Russian Research Neurosurgical Institute named after prof. A. L. Polenov - a branch of the Federal State Budgetary Institution "Northwestern Federal Medical Research Center named after V. A. Almazov" and the Federal State Autonomous Institution of Higher Education ITMO Research University.

An IR spectroscopy study of various types of glial tumors was conducted in 19 patients undergoing treatment at the A.L. Polenov Russian Scientific Research Institute. Primary medical records from the Polenov Russian Scientific Research Institute, including histopathological examination results (Table 1), served as the source of information.

Tumor type	Classification	Number of patients	
		Abs.	%
Astrocytoma	II	3	15,78
Astrocytoma	III	2	10,53
Oligodendroglioma	III	6	31,58
Glioblastoma	IV	6	31,58
Epileptic leukoencephalopathy	-	2	10,53
Total		19	100

**The study was conducted in accordance with the Declaration of Helsinki (June 1964, Helsinki, Finland) and approved by the Ethics Committee of the LEC 12-20 on December 21, 2020. Informed consent was obtained from each patient.*

Chemometric analysis of IR spectroscopic data from brain tissue

First, PCA analysis was performed to examine overall differences between the control group and individual brain tumor groups. Then, PLS and LDA were used to classify the spectra into different classes. Multivariate classification allows for the identification of diagnostic spectral patterns that remain valid for all spectra within a class, even though there may be significant interclass variability between spectra.

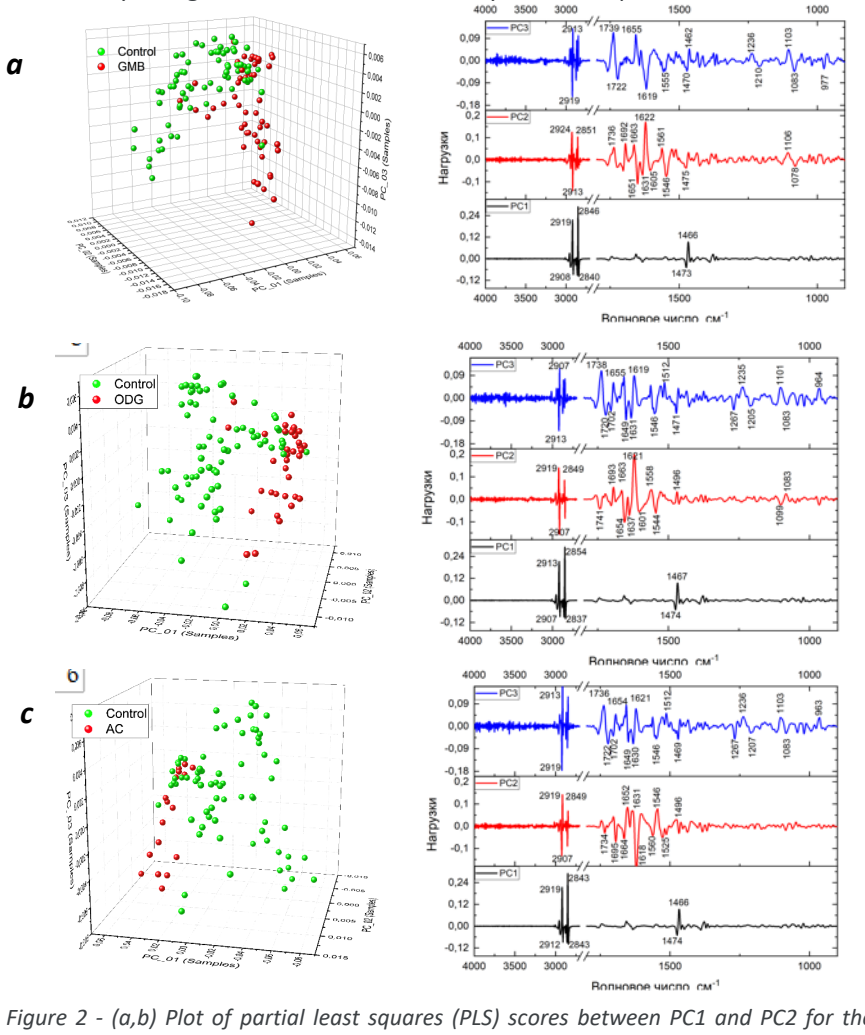
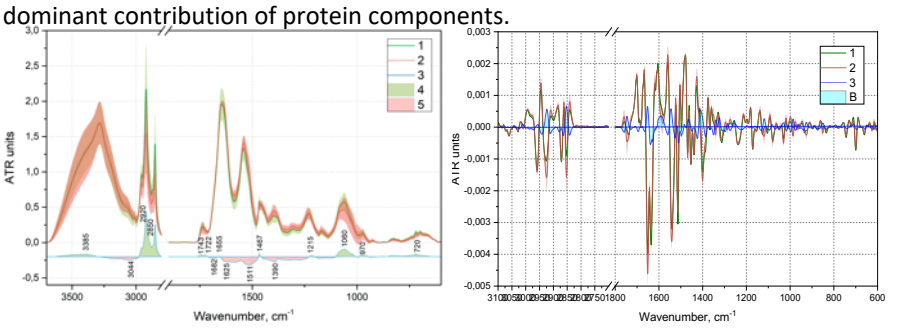


Figure 2 - (a,b) Plot of partial least squares (PLS) scores between PC1 and PC2 for the glioblastoma (GB) (a), oligodendroglioma (ODG) (b), actrocytoma (AC) (c) and control (green, Control) dataset, and (c) loadings for the 1st PCA component, PC2, and PC3.

FTIR spectra and average second derivatives of brain tissue spectra

Fig. 1 a, b show the mid-IR spectra and mid-IR derivatives of normal perifrontal cortex tissue and brain tumor tissue. Overall, the IR spectra of brain tumors appear to overlap with those of normal brain in the region of biochemical component fingerprints (1800 cm^{-1} to 900 cm^{-1}), making it difficult to discern any subtle but significant differences. These similarities are explained by the dominant contribution of protein components.



F1 - Average IR spectra of blood sera from healthy donors (1) and patients with brain tumors (2); Average second derivatives of IR spectra of blood sera from healthy donors (1), patients with brain tumors (2) and the result of subtracting the second derivatives (3)

However, upon closer inspection, noticeable differences are tentatively detected in the region from 1050 to 1000 cm^{-1} (carbohydrates and collagen), from 1300 cm^{-1} to 1150 cm^{-1} (amide III and ν_{as} PO2-) and from 1760 cm^{-1} to 1700 cm^{-1} (lipids, DNA/RNA and amide I) in the IR spectra and from 950 cm^{-1} to 850 cm^{-1} (protein, tyrosine and collagen), from 1265 cm^{-1} to 1240 cm^{-1} (amide III) and 1600 cm^{-1} to 1530 cm^{-1} (amino acids and DNA/RNA.

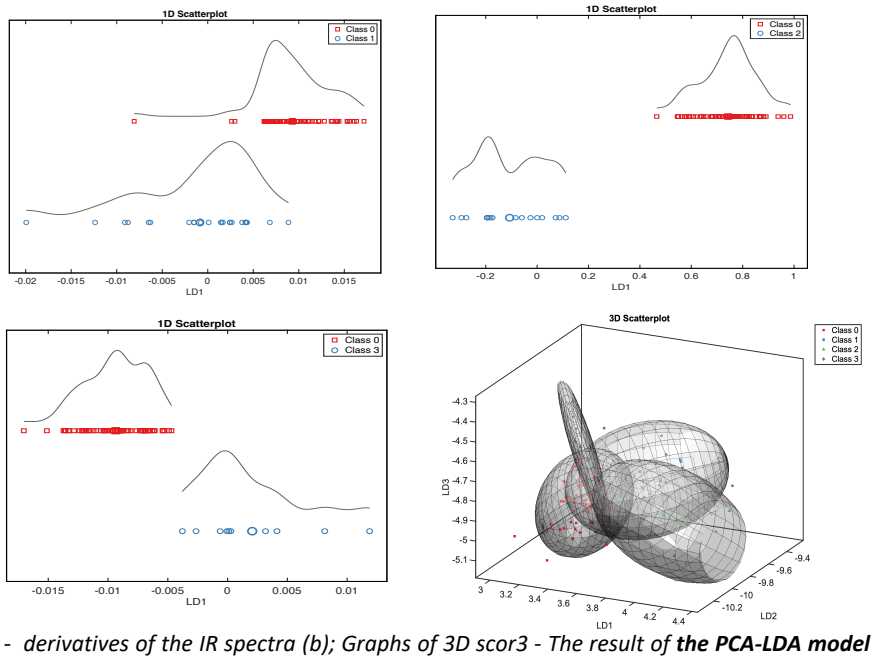


*Figure 3 - derivatives of the IR spectra (b); Graphs of 3D scor3 - The result of **the PCA-LDA model** between groups, constructed from the second es obtained after LDA of the second derivatives of the IR spectra, control tissue samples (Class0), tissues with glioblastoma (GBM) (Class1), tissues with oligodendroglioma (Class2) and astrocytoma (AC) (Class3).*

Similar chemometric analysis was performed on serum samples and cerebrospinal fluid samples for these patients.

Sensitivity and specificity of the analysis of the second derivative of the IR spectra of blood sera of healthy donors and patients with breast cancer in the range of 1306-1250 cm^{-1}

	Brain tissue		Blood serum		Cerebrospinal fluid	
	I	II	I	II	I	II
Accuracy (%)	84	80	92	89	95	78
Sensitivity (%)	93	92	91	83	96	85
Specificity (%)	96	92	80	86	92	83
Number of samples	115	115	130	130	32	32