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Lipidomic analysis in the diagnosis of brain tumors

Fast and accurate diagnosis of brain tumors can be one of the key steps in patient therapy. However, due to the hard-to-reach location of the lesion in the brain, as well as the late manifestation of disease symptoms, diagnosis is often difficult. Therefore, interdisciplinary research on the borderline of analytical chemistry, medical diagnostics and chemical engineering is necessary to develop new diagnostic approaches that would facilitate the analysis of neoplastic changes in the brain. In recent years, various types of tools have been developed to enable the differentiation of neoplastic and healthy tissue as well as the metabolomic profile of the examined tissues. One such technology is solid-phase microextraction (SPME), also known as chemical biopsy. Although, the choice of the right tool is not a sufficient to solve entire problem. It is also important to select compounds that could indicate and differentiate pathophysiological changes in the examined tissue and enable the selection of appropriate therapy. Lipids are the compounds which are recently more often being reported as important in cancer processes.

The aim of this doctoral dissertation was to test the applicability of SPME probes in the analysis of brain tumors. In addition, the lipid profile of gliomas was assessed depending on the degree of malignancy and the presence of genetic changes: mutations in the IDH gene and 1p/19q codeletion. Another goal of this doctoral dissertation was to assess the possibility of using SPME in *in vivo* brain studies in humans.

The use of chemical biopsy in the analysis of brain tumors showed that the lipidomic profiles of benign meningiomas differed from those obtained from malignant lesions such as gliomas. It was also possible to classify samples taken from the same lesion on the basis of the extracted set of lipids, which indicates the reliability of the obtained results. Studies of gliomas showed that the lipidome of brain tumors varied depending on the grade of malignancy and IDH mutation status.

Due to the significant role of acylcarnitines in the fatty acid metabolism, their profile in gliomas was analyzed. It has been observed that the content of carnitine esters in neoplastic tissue increases in tumors with a worse clinical prognosis, that is in lesions with a higher degree of malignancy, and in samples without mutations in the IDH gene.

Detection of compounds with diagnostic potential *ex vivo* is not sufficient to develop a clinically useful method of brain sample collection. The desired one should also enable rapid analysis during surgical procedures. Therefore, to the best of our knowledge, this is the first time when SPME probe was optimized and tested under surgical conditions in the study of the human brain. Although, due to the various localizations and heterogeneity of brain tumors, the pilot proof-of-concept studies were focused on profiling of brain structures rather than differentiating healthy and neoplastic tissue. This study was designed to characterize the white and gray matter of brain using the SPME probe, which allowed simultaneous sampling of both structures. As a result, it was possible to extract a set of metabolites with a wide range of physicochemical properties. Still, the obtained metabolomic and lipidomic results did not show differentiation between gray and white matter, which was probably due to too small study group and too high inter-individual variability.

To sum up, the research conducted within this doctoral dissertation indicates the usefulness of microextraction probes in the study of brain tumors as well as in lipidomic profiling of meningiomas and gliomas, taking into account the degree of malignancy and genotype. It has also been observed that chemical biopsy may be useful tool in *in vivo* brain research, what provides a future direction for studies of brain tumors during neurosurgical procedures.

Key words: solid-phase microextraction, brain tumor, diagnostics, lipidomics