

Ambient MS Based Analytical Platform for Identification of Brain Tumor Tissues as a Method for Interoperation Monitoring

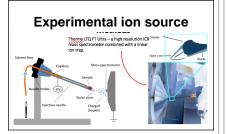
Igor A. Popov PhD; Vsevolod Shurkhay MD; Evgeny Zhvansky; Alexey S. Kononikhin; Anatoly Sorokin; Alexander Potapov;

Eugene Nikolaev

Moscow Institute of Physics and Technology

Introduction

Rapid and reliable tumor tissue identification during neurosurgical operation is a challenging problem despite the recent advances in intraoperative imaging and neuronavigation. Degree of resection still is the one of the most important prognostical factors for progression-free survival and overall survival in patients with intracranial low and high grade glial tumors. In most cases residual tumor cells or peritumoral border is the main source of tumor reccurence so determination of this border zone during surgery is extremely important. Ambient ionization mass spectrometry based on "in situ" molecular fingerprinting of tissue is an attractive and confident solution for real-time tracking of tumor cell concentration in a borderline zone.



Methods

All brain tumor tissue samples were collected during the surgery. A special spray-from-tissue ambient ion source was developed for tumor samples profiling. In this source liquid extraction is immediately followed by ionization. For classification of tumor samples by lipid profiles a database filled by the results of investigation from more than 100 tumor samples was created. Low and high resolution massspectrometry data was obtained using Thermo LTQ FT Ultra and ultrahigh resolution data was obtained using Bruker Apex Ultra FTICR instrument with a dynamically harmonized cell Pathological tissues were dissected during the neurosurgical procedure and divided into two parts: the first one was sent for routine examination by pathologists, and the second was frozen in normal saline and sent to the laboratory for mass-spectrometric analysis.

Defferent spectra obtained during the tissue profiling



Acknowledgment

This study was supported by grant # 16-15 -10431 "The development of methods and techniques for automated identification of brain tumor tissues as a key element of intelligent neurosurgical scalpel data processing system based upon database of multidimesional molecular profiles" from Russian Scientific Fund

Mass-spectra analysis

Results of the machine-learning based algorhytm analysis of different molecular spectra allows to differentiate between hystologically distinct parts of tumor.

Results

As a result of analysis of more than 200 MS profiles it could be suggested that MS profile analysis of brain tissue samples gives sufficient information for the tissue identification and the type of pathology. In this assay we demonstrated that in the border zone each tumor sample can be represented as a linear combination of profiles from mixture of different parts of tumor (necrosis and live tumor). In this situation validation of identification of compounds, forming each profile, is essential and could be performed by using ultra high resolution FTICR. High and ultrahigh resolution data (accurate mass and fine isotopic structure of mass spectra) could be used to identify lipids, metabolites and other compounds forming molecular profiles. Determination of the fine isotopic structure allows us to prove the identification results of compounds, which form the lipid profiles and are used for identification of tumor samples. Another important problem solved in our research was a consolidation of different types of data (imunohistochemistry, medical information and tumor molecular profiling). In order to build a procedure for validation and consolidation of such different types of data experiments on detailed investigation of pieces of tumor located very close to each other were performed. Finally, we demonstrated that the developed analytical platform allows us not only to classify brain tissue types, but also to determine the border between different types of tissues during the neurosurgical

Conclusions

In our work we demonstrate the possibility to use high and ultrahigh resolution data (accurate mass and fine isotopic structure of mass spectra) to identify lipids, metabolites and other compounds giving molecular signatures of the whole tissue.

Learning Objectives

Mass spectrometry profiling could become one of possible methods for development of technology for intra surgery control and characterization of dissected tissues and theirs rapid identification.

References

1. A novel direct spray-from-tissue ionization method for mass spectrometric analysis of human brain tumors. Kononikhin A et al., Anal Bioanal Chem. 2015 Oct;407(25):7797-805. doi: 10.1007/s00216-015-8947-0.

2. Navigation systems in neurosurgery Shurkhay VA, et al., Zh Vopr Neirokhir Im N N Burdenko. 2016;80(6):107-114. doi: 10.17116/neiro2016806107-114

3. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. Cancer Genome Atlas Research Network, Brat DJ et al., N Engl J Med. 2015 Jun 2 5 ; 3 7 2 (2 6) : 2 4 8 1 - 9 8 . do i : 1 0 . 1 0 5 6 / N E J M o a 1 4 0 2 1 2 1 .