Discrimination of Human Astrocytoma Subtypes by Lipid Analysis Using Desorption Electrospray Ionization Imaging Mass Spectrometry


Department of Chemistry and Center for Analytical Instrumentation and Development, Purdue University, West Lafayette, USA
Department of Neurosurgery, Department of Radiology and Department of Medical Oncology, Brigham and Women’s Hospital and Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA
Prosolia, Inc., Indianapolis, USA


Amitava Srimany
6-11-10
INTRODUCTION

- Imaging technique is very important for accurate characterization of tissue to optimize resection specially for brain tumors

- Microscopy, fluoroscopy, magnetic resonance imaging and computed tomography are the common used tools

- Limited chemical information, low sensitivity and systematic administration of contrast agents are not possible

- DESI-MS imaging: No sample preparation, very little time, high quality analytical data and chemical information

- Work has been done on lipid distributions in mouse brain, images of antifungals in algae, distinction of cancerous and non-cancerous canine bladder tissue samples using multiple marker lipids

- Little work with human tissue: Observation of distinctive lipid markers associated with tumor and non-tumor regions in human liver adenocarcinoma tissue sections
World Health Organization (WHO) recognizes over 125 types of brain tumors according to histopathological evaluation

- Classified them according to cellular characteristics
- Grades malignancy according to proliferation, cellular and nuclear morphology, vascularization, and a few biomarkers

Gliomas are the most common human primary brain tumors with astrocytomas comprising the most common subtype ranging in grade from WHO grade II to WHO grade IV

Current diagnosis is based on neuropathological examination of a biopsy sample and characteristic cytogenetic aberrations which needs an expert neuropathologist and longer time

MS imaging rapidly provides extensive chemical information from biopsy samples, which could differentiate brain tumors from healthy and functional brain
IN THIS PAPER

- 7 glioma specimens from seven human subjects were examined using DESI-MS. Those 7 were categorised by an expert neuropathologist as:
  1. Diffuse astrocytoma (WHO grade II) :1
  2. Anaplastic astrocytoma (WHO grade III) :2
  3. Glioblastoma (GBM) (WHO grade IV) :4

- Tissue specimens were analyzed for obtaining lipid profile using DESI-MS in both positive and negative ion mode and confirmed by tandem MS

  Positive mode: Glycerophosphocholines (PC), Sphingomyelins (SM) and Galactoceramides (GalCer)
  Negative mode: Glycerophosphoinositol (PI), Glycerophosphoserines (PS), Plasmenyl glycerophosphoethanolamines (plasmenyl-PE) and Sulfatides (ST)

LIPID: The major component of brain tissue and alteration of composition associated with several diseases
NEGATIVE ION MODE DESI SPECTRA

Major lipids
ST, PS, PI

ST decreases

PS increases

PI increases

Major lipids
PS, PI, plasmankyl-PE
Most abundant peaks are from the lipids PS(40:6), PI(38:4), and PS(36:1)
DESI-MS IMAGES FOR THE MAIN IONS IN THE NEGATIVE ION MODE

a) PS (36:1)  
   m/z 788.8  
Sample G2  
Astrocytoma  
WHO grade II

b) PS (40:6)  
   m/z 834.2  
Sample G4  
Astrocytoma  
WHO grade III

c) PI (38:4)  
   m/z 885.4  
Sample G5  
Astrocytoma  
WHO grade IV

d) ST (24:1)  
   m/z 888.4  

f) Optical Image  
H&E stained

e) ST (26:1)  
   m/z 916.5  

Scale: 3 mm  
Resolution: 200.3 μm
POSITIVE ION MODE DESI SPECTRA

Major peaks
- PC(34:1)+Na⁺
- PC(34:1)+K⁺
- PC(32:0)+Na⁺

PC(34:1)+K⁺ increases
PC(32:0)+Na⁺ increases
GalCer decreases
Most abundant peaks are from the lipids PC
REPRODUCIBILITY OF DATA

Negative ion mode DESI-MS in different labs
POSITIVE ION MODE DESI SPECTRA IN DIFFERENT TIME

a) 1-12-09
   10 AM

b) 1-12-09
   5 PM

c) 3-12-09
   5 PM

d) 8-12-09
   9 AM
SUMMARY

- DESI imaging of lipid profile is an important tool to differentiate various degrees of malignancy in astrocytic tumors in both positive and negative ion mode.

- With increased malignancy of astrocytomas, abundance of STs decreases in negative ion mode and GalCers also decreases in positive ion mode.

- These reports also corroborate previous reports based on classical lipid extraction methodologies.

- Sample size has to be increased to establish this as a proper diagnostic tool for various astrocytomas.

- Same m/z lipids have to be differentiated by using high resolution MS.
CONCLUSIONS

- DESI-MS can be used to diagnosis of various diseases
- If we can find bio-markers for different diseases then we can easily monitor it accurately in very short time and without any expert histopathologist
- The fast analysis can help in taking decision during critical surgeries
THANK YOU