SPATIAL MAPPING OF LIPIDS AND NEUROTRANSMITTER IN RAT BRAIN SECTIONS USING DESI ION MOBILITY MASS SPECTROMETRY

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ABSTRACT

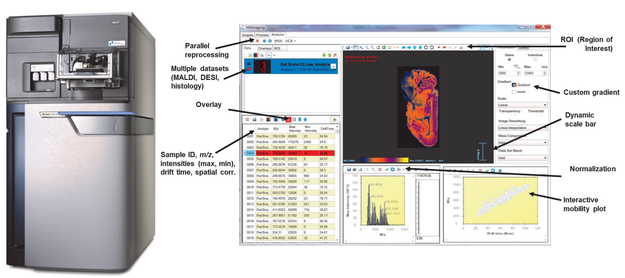
Desorption Electrospray Ionization (DESI) mass spectrometry imaging (MSI) is utilized to map distribution of lipids alongside with metabolites, such as neurotransmitters, from brain tissue sections. Small molecules such as amino acids (e.g., taurine, glutamine) and neurotransmitters (e.g., GABA, serotonin) were simultaneously detected along with lipids (e.g., arachidonic acid, phosphatidylcholine, lysophosphatidylcholine). DESI-MSI data were collected and processed on a high definition mass spectrometer with ion mobility separation (SYNAPT HDMS G2-Si, QToF) using High Definition Imaging (HDI) 1.4 software. Mass accuracy of DESI-MSI analysis was improved by the elimination of systematic mass drift, using either in-line lock mass or other endogenous ions off tissue. This preliminary work indicated the utility of DESI imaging for clearly distinguishing localized metabolites and lipids to provide insights for neuro-molecular research.

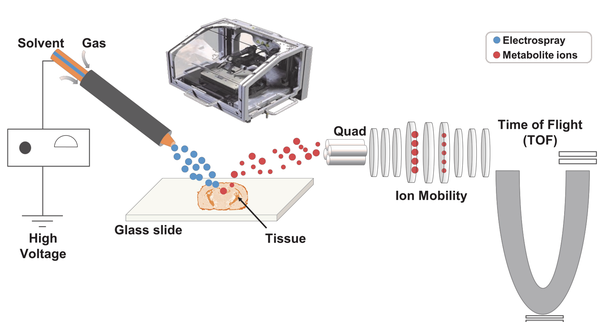
INTRODUCTION

- Spatial distribution of small molecules, such as neurotransmitters, alongside lipids, in brain improve our understanding of their biological functions
- Mass spectrometry imaging (MSI), such as Desorption Electrospray Ionization (DESI), can be used to map distribution of lipids and metabolites on tissue sections
- DESI is an ambient ionization technique that does not require any sample preparation steps, such as matrix deposition
- DESI often provides complementary information to matrix-assisted laser desorption ionization (MALDI), such as distribution of small metabolite and drug molecules that are amenable to electrospray ionization
- Here we show the utility of DESI imaging to detect neurotransmitters, such as serotonin, adenosine, and glutamine and several different lipids directly in brain tissue samples
- Ion mobility separation enhanced the detection of lipids and metabolite signal by discriminating from electrospray background species produced during the DESI analysis
- Ion mobility allowed for calculation of collisional cross sections (CCS) values for lipids and metabolites with aided in their confident identification

METHODS

- Coronal tissue sections of rat brain were mounted on microscope slides and imaged without any further sample preparation
- DESI imaging platform was coupled with a high definition mass spectrometer (HDMS) with ion mobility separation (SYNAPT G2-S*i*)
- DESI-MSI data were processed using High Definition Imaging (HDI) 1.4 software with MassLynx 4.1 data acquisition control
- Molecular identification was done using high mass accuracy (low PPM) database searches against curated databases, such as METLIN; ID confidence was increased by high-fidelity isotopic distribution, and collisional cross sections (CCS) measurement obtained from ion mobility experiments





RESULTS

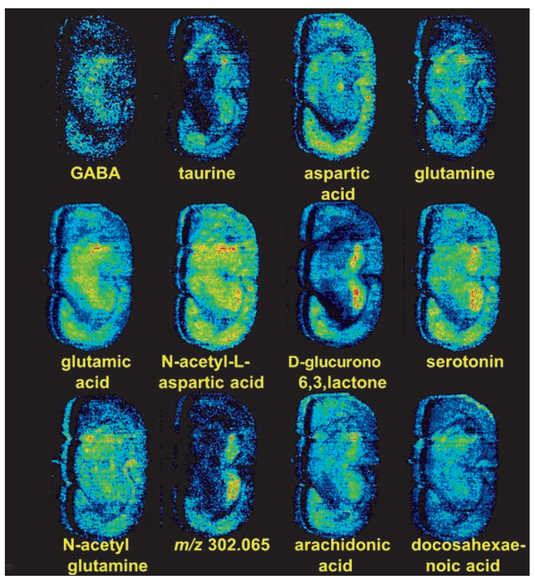
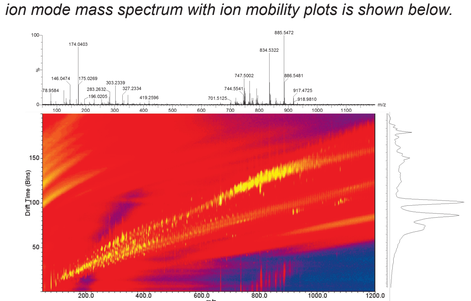


Figure 1. DESI MS images of metabolites such as amino acids (e.g., taurine, glutamine) and neurotransmitters (e.g., GABA, serotonin). The small molecules were simultaneously detected along with lipids (e.g., arachidonic acid, phosphatidylcholine, lysophosphatidylcholine). Negative ion mode mass spectrum with ion mobility plots is shown below.



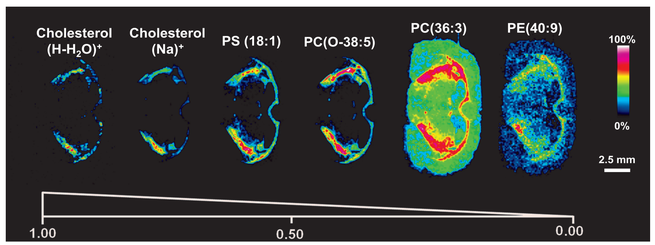


Figure 2. Spatial correlation between detected molecules were explored using spatial correlation analysis based on Pearson product-moment correlation coefficient. In shown example, spatial correlation of water-loss cholesterol ions is strongest with another cholesterol ions (sodiated) and weakest with PE.

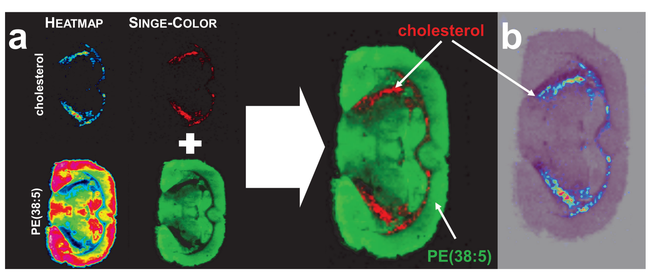


Figure 3. (a) Overlay of single-color channel distribution of discretely distributed small molecules such as cholesterol with abundant molecule shows contextual distribution of that molecule, and (b) such overlay on reference microscopy image also shows anatomical distribution of such molecule

CONCLUSION

- Simultaneous MS based spatial imaging of lipids and metabolites directly from tissue sections with no sample preparation by DESI-MSI
- Molecular identification was aided by improved mass accuracy by the elimination of systematic mass drift, using either in-line external lock mass, other endogenous ions treated as an internal lock mass
- Ion mobility separation prior to the MS was leveraged to increase coverage of the molecular species from tissue, as well as improving identification of molecules
- Ion mobility derived collisional cross sections (CCS) provided further confidence to lipid and metabolite identification

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