Spatial Metabolomics by Mass Spectrometry Imaging using Desorption Electrospray Ionization (DESI)

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INTRODUCTION

- Spatial mapping of metabolites can increase our understanding of the biological functions of those molecules within the tissue
- Mass spectrometry imaging, such as Desorption Electrospray Ionization (DESI), can be used to map the distribution of molecules from any flat surfaces, including tissue sections without much sample preparation
- Mass spectrometry imaging using DESI have been developed to image metabolites directly off tissue sections, such as rodent brain
- Examples of metabolites detected included amino acids (e.g., taurine, glutamine, arachidonic acid) , neurotransmitters (e.g., GABA, serotonin) along with lipids (e.g., phosphatidylcholine, lysophosphatidylcholine)
- This preliminary work indicated the utility of DESI imaging for clearly distinguishing localized metabolites and lipids to provide insights for spatial metabolomics research.

METHODS

- **Tissue.** Rat brain was harvested and flash-frozen in liquid nitrogen before cryosectioning. Tissue sections were mounted on a glass microscope slides, vacuum dried, and analyzed without any other sample preparation.
- **DESI Mass Spectrometer.** DESI imaging platform was coupled with a quadrupole time-of-flight mass spectrometer (SYNAPT G2-XS or Xevo G2-XS) was used for the imaging data acquisition .
- **Data Processing Platform.** Molecular maps were processed by High Definition Imaging (HDI) 1.5 and overlaid with an optical image of the tissue to co-register the molecular distribution based on the anatomical features of the brain, such as the corpus callosum. Spatial correlation between detected metabolites and lipids were explored using analysis based on Pearson product-moment correlation coefficient in HDI software.
- **Molecular Annotation.** Molecular identification was aided using high mass accuracy database searches against curated databases, e.g., Human Metabolome (HMDB)

DESI MS IMAGING CONDITIONS

Mass Spectrometer: Xevo G2-XS Quadrupole Time of flight (Q-ToF)
Acquisition range: 50-1200 Daltons
Acquisition mode: MS in resolution mode
DESI solvent : 98% Methanol and 2% Water with 0.1 % formic acid

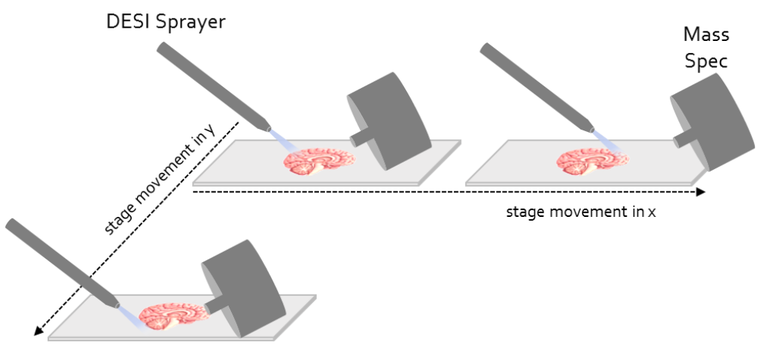

Figure 1. *During the DESI mass spectrometry imaging process, the molecules on the tissue sections are sampled when charged solvent droplets hit the tissue and lift them off inside a mass spectrometer (e.g., Q-Tof) for detection. By moving the sample stage in a prescribed manner, spatial information of molecules on each defined pixel can be obtained. The ion intensities of detected molecules are plotted in false-color heatmap as DESI-MS images.*

RESULTS & DISCUSSIONS

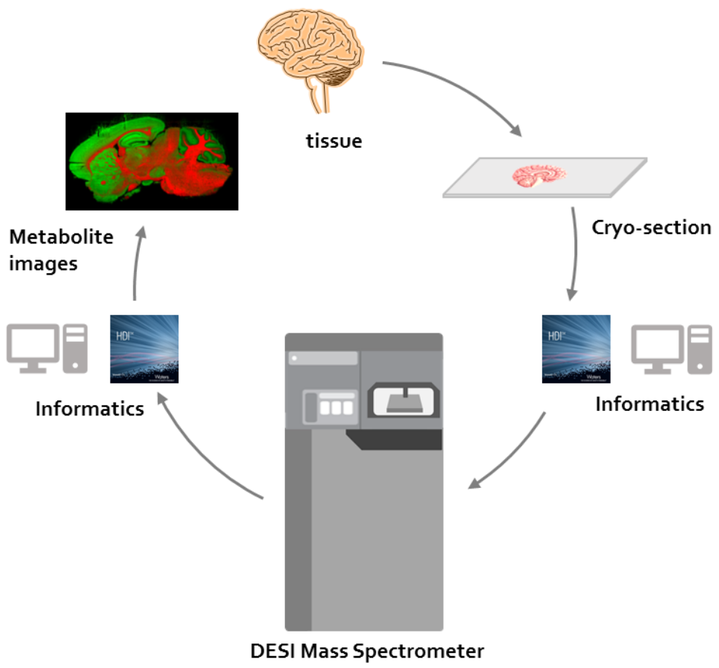

Figure 2. *Workflow for performing molecular imaging using a DESI mass spectrometer is shown. DESI does not require any sample preparations beside sectioning tissue. In the workflow, an MS imaging experiment is defined in software (e.g., HDI), MS data is acquired on a mass spectrometer, and finally images are processed using the same informatics platform.*

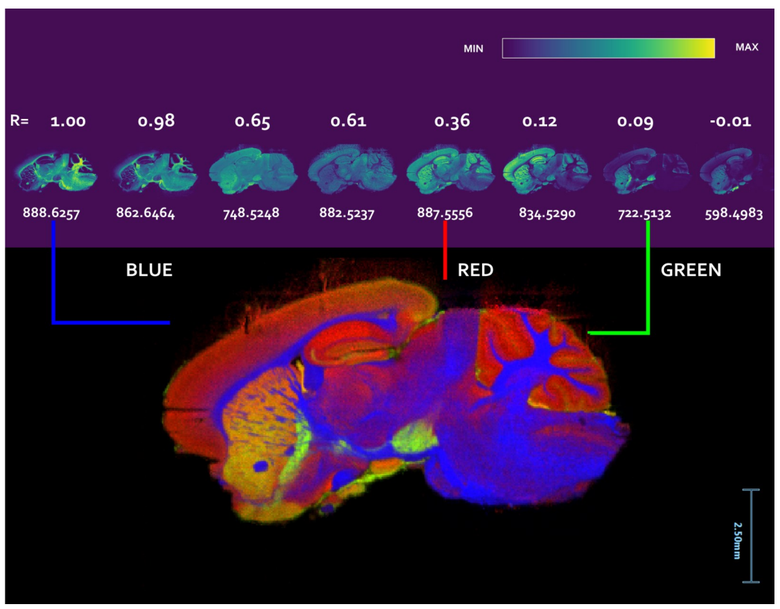

Figure 4. *Spatial correlation of one molecule against all the other molecules can be calculated to determine the spatial similarities between the selected molecules (m/z 888.6257) and other detected molecules. R of is the Pearson correlation coefficient. The higher positive R value represents strong spatial correlation, and negative value represent a negative correlation. The value of 1 is equivalent to 100% correlation, which is assigned to the selected molecule.*

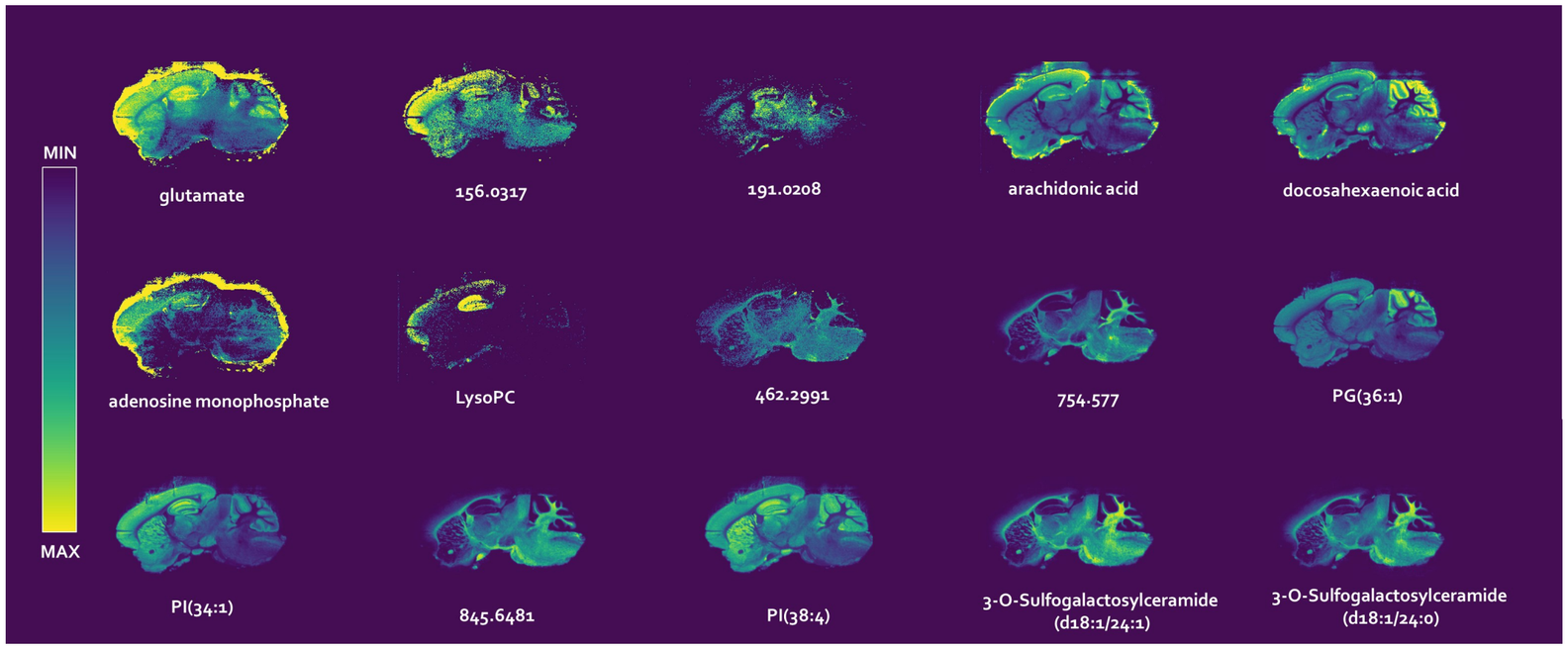

Figure 3 . *Examples of metabolite and lipid ion images collected in a quadrupole time of flight mass spectrometer using DESI are shown here. DESI images were acquired in the negative ion mode at a pixel size of 40 microns. Molecules were tentatively identified based on a low PPM mass accuracy match against a list of commonly known metabolites and lipids.*

CONCLUSION

- DESI mass spectrometer imaging excels at detecting and mapping several molecules simultaneously and directly from tissues such as rodent brain
- DESI is capable of producing molecular images with a high spatial resolution at a few hundreds microns pixel size, here DESI images were acquired with 40 µm pixel sizes
- Several metabolites such as taurine, glutamine, arachidonic acid, GABA, serotonin, phosphatidylcholine lipids, lysophosphatidylcholine lipids can be visualized with high specificity and sensitivity

REFERENCES

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