High Spatial Resolution Molecular Tissue Imaging by Desorption Electrospray Ionization (DESI) using Novel Sprayer Assembly

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INTRODUCTION

- Desorption electrospray ionization (DESI) mass spectrometry (MS)[1] is an ambient ionization source with a wide array of applications from high-throughput screening to molecular imaging
- DESI imaging is performed by obtaining a pixel-by-pixel mass spectrum of a sample by impinging the focused electrospray droplets on a confined area or pixel. Thus, the spatial resolution or pixel size of DESI imaging is primarily defined by the area of the electrospray impact on the surface.
- Here, we show DESI imaging MS the novel sprayer with electro-flow focusing technique that combined electrospray and flow focusing, was capable of high-resolution DESI imaging of metabolites in tissue sections

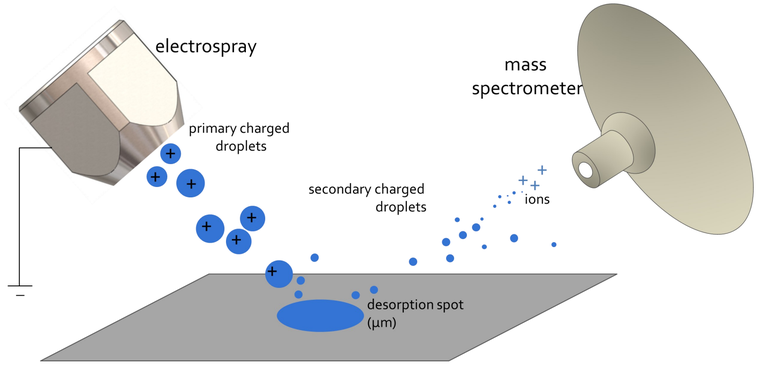

Figure 1. *DESI MS is performed by extracting and ionizing, in-concert, from a sample surface. Briefly, primary droplets produced by the sprayer forms a thin film of solvent at the surface extracting analyte molecules off tissue, the subsequent primary droplets colliding with the film generate secondary droplets that are ejected, desorbed, ionized, and analyzed by mass spectrometer.*

METHODS

- **DESI Sprayer.** Sprayer[2] from Waters Ikey technology was incorporated to improve DESI sprayer design
- **DESI MS Imaging.** DESI was coupled with a quadrupole time-of-flight mass spectrometer (SYNAPT G2-XS), samples were analyzed with 98% methanol and 2% Water with 0.1 % formic acid solvent; rat brain and chicken liver tissue sections were thaw mounted on a glass slides, vacuum dried, and analyzed without any other sample preparation
- **Data Processing .** Processed by High Definition Imaging (HDI) 1.5. Images are not interpolated.
- **Spatial Measurement.** The dimension of electrospray beam width was measured using laser illumination and performance was evaluated by imaging precision laser etched patterns of rhodamine dye

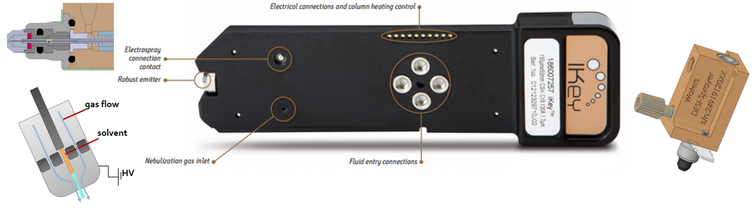

Figure 2. *The electrospray design within ionKey high-pressure microfluidic device was incorporated to improve DESI sprayer. Briefly, stainless steel emitter recessed behind critical orifice, nebulization gas sheathes primary solvent to create liquid jet. Schematic representation of prototype sprayer is shown on the right.*

RESULTS & DISCUSSIONS

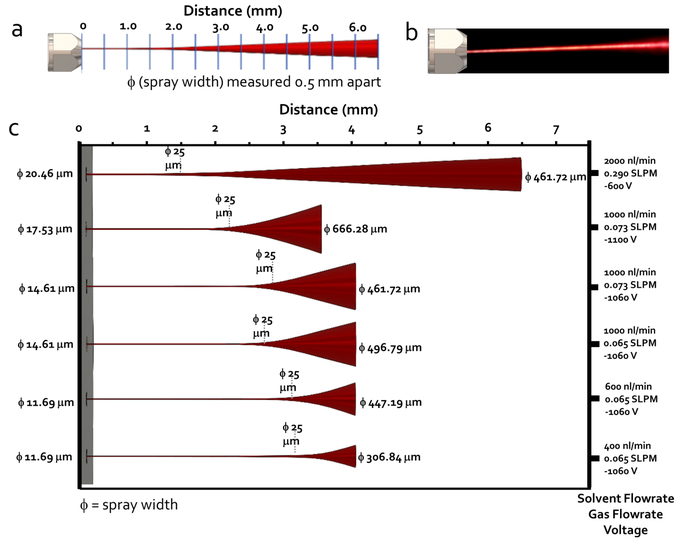

Figure 3. *(a) electrospray width dimension was measured every 0.5 mm from 0.0 to 6.5 mm using laser illumination; (b) example of shadowgraphy laser illumination images of electrospray beam used for measurement; (c) the width of spray dimension (denoted by symbol Φ) at various distance along the spray axis. E.g., left-most Φ value is spray width exiting the sprayer, and right-most Φ spray width at the indicated distance from the sprayer, distance where spray width reaches 25µm is also indicated. Critical parameters of solvent flow, nebulization gas flow, and voltage are listed on the right.*

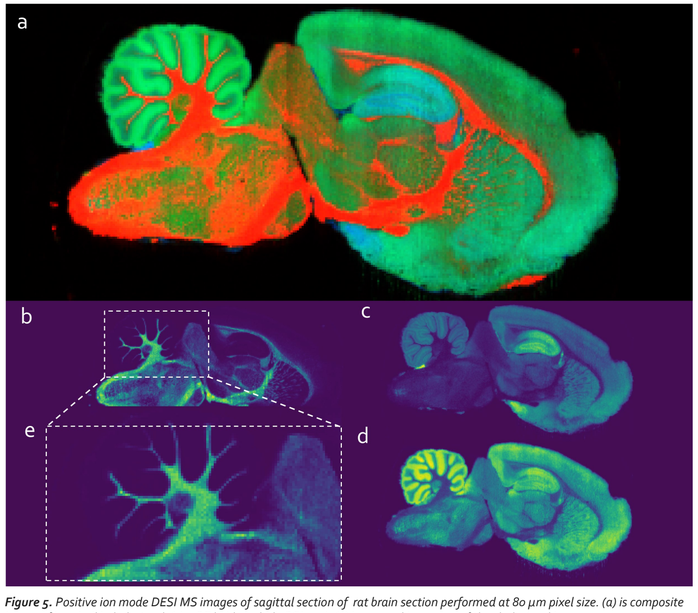

Figure 5. *Positive ion mode DESI MS images of sagittal section of rat brain section performed at 80 µm pixel size. (a) is composite image of ions in (b) cholesterol, (c) a PE lipid, and (d) PC(34:1); (e) is zoomed in version of the cholesterol ion.*

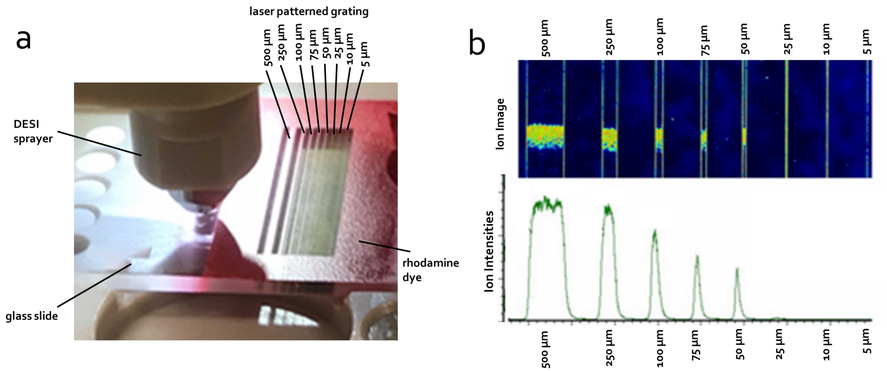

Figure 4. *(a) Precision laser etching was used to create pattern with defined spacing, from 5 µm to 500 µm over rhodamine dye coating; (b) images at the defined grating is shown on top, the image at 10 µm and 5 µm are may be below of limit of detection, the ion intensities for each spaces grating is shown below.*

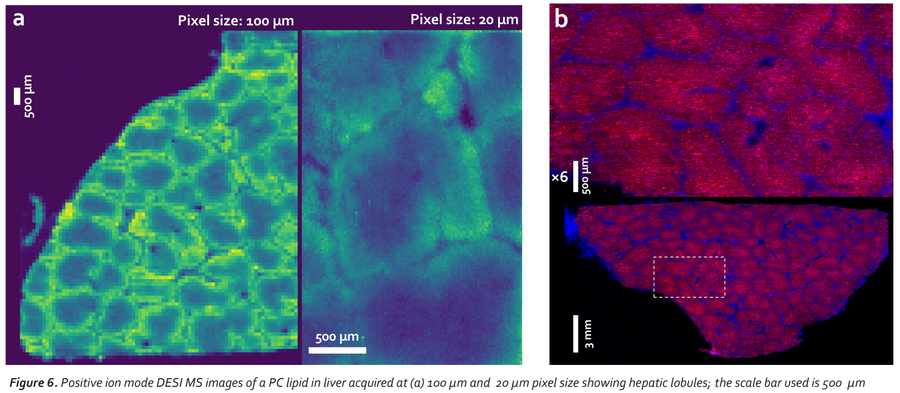

Figure 6. *Positive ion mode DESI MS images of a PC lipid in liver acquired at (a) 100 µm and 20 µm pixel size showing hepatic lobules; the scale bar used is 500 µm for both image , (b) a composite negative ion mode image of m/z 195.05 (blue) and 293.21 (red) ions imaged at 25 µm pixel size.*

CONCLUSIONS

- Study of sprayer beam width showed tunable dimension from 12 µm to 650 µm depending on distance from the emitter, sprayer voltage, flowrates used.
- The spatial resolution and signal sensitivity of DESI MS imaging was improved by incorporation of new designs in the sprayer assembly as shown.

REFERENCES

[1] Takáts, Zoltán, et al. "Mass spectrometry sampling under ambient conditions with desorption electrospray ionization." *Science* 306.5695 (2004): 471-473.

[2] Patent; Housing for converting an electrospray to an ion stream EP0622830B1 Michael J. Tomany, Waters Investments Limited Priority 1992-04-10 • Filed 1993-04-29 • Granted 2001-08-08 • Published 2001-08-08

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