Application Note

LIPID SPECIES FROM BRAIN TISSUE SECTIONS

Using LESA^{PLUS} Liquid Extraction Surface Analysis^{PLUS} LC Separation

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INTRODUCTION

Spatial lipid composition, distribution and regulation are very important factors for mediating lipid functionality and, when disrupted, can cause pathophysiological processes leading to cancer, obesity, atherosclerosis, and neurodegeneration. The novel LESA^{PLUS} surface analysis approach combines the standard liquid extraction surface analysis with an additional step of a nano liquid chromatography separation (Figure 1). This combination is ideally suited to investigate small molecule drugs, metabolites or lipids from thin tissue sections and here, we will make a comparison between LESA^{PLUS} and LESA in the analysis of lipids from mouse brain (Figure 2).

THE LESA^{PLUS} ADVANTAGE:
In-line nanoLC column

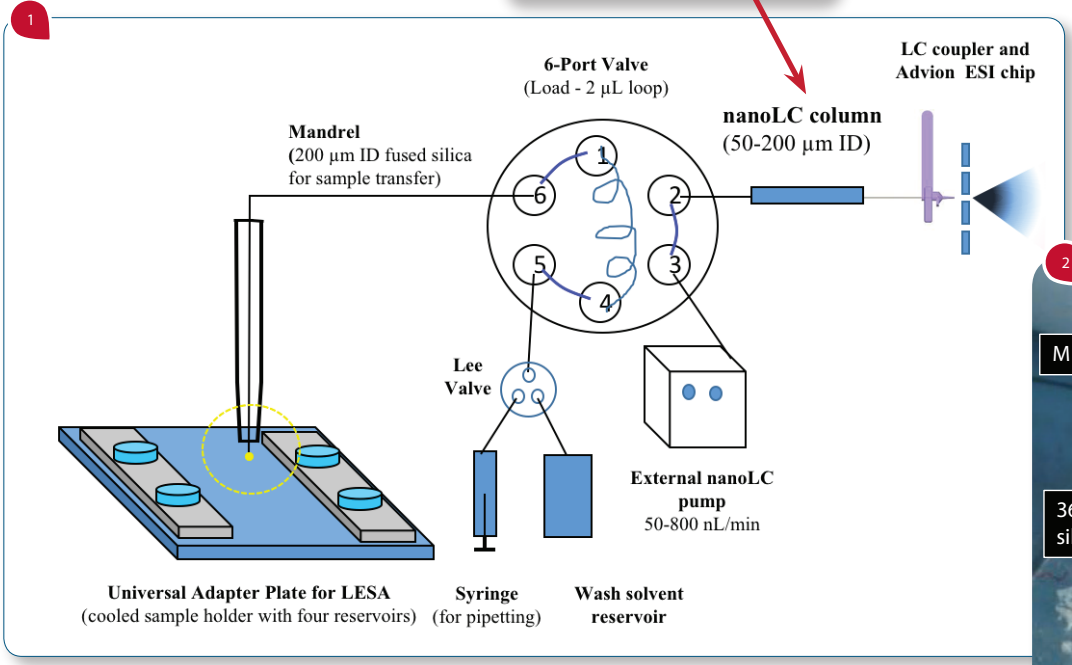

Figure 1: LESA^{PLUS} set-up schematic for automated surface analysis

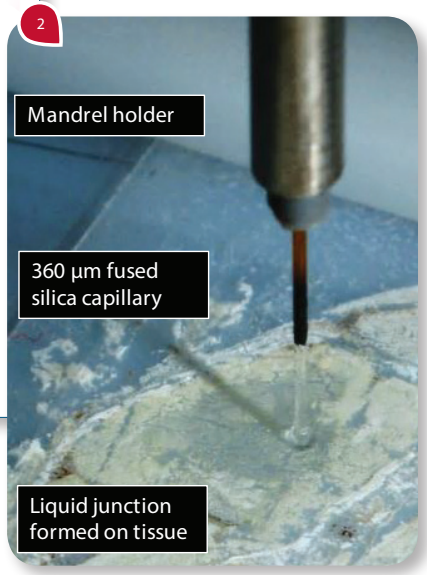

Figure 2: Figure 2: LESA^{PLUS} liquid junction formed between extraction capillary and brain tissue section, ca. 400 µm diameter. Extracted analytes are loaded into the loop of the injector and then directed onto the nanoLC column when the injector is switched to the inject position.

RESULTS

Standard liquid extraction surface analysis allows for a rapid sample analysis from a multitude of locations across tissue sections. For a shotgun lipidomics analysis approach, a 5 minutes infusion experiment provides sufficient time to investigate lipid composition in detail (Figure 3A); However, due to the sample complexity and matrix involved, some minor components may show a signal intensity insufficient for detailed MS analysis[1,2].

In those cases, LESA^{PLUS} adds an additional dimension of analyte separation and allows an improvement in both spatial resolution (Figure 2) as well as analyte sensitivity (Figure 3B). Furthermore, LESA^{PLUS} can separate isobaric lipid species (Figures 4A and 4B) and therefore, allows a more in-depth analysis of the lipidome.

The TriVersa NanoMate offers both modes of operation within the same automated nanoelectrospray source with minimal intervention between the two analyses and enables both rapid analyte screening for surface profiling as well as in- depth lipid analysis.

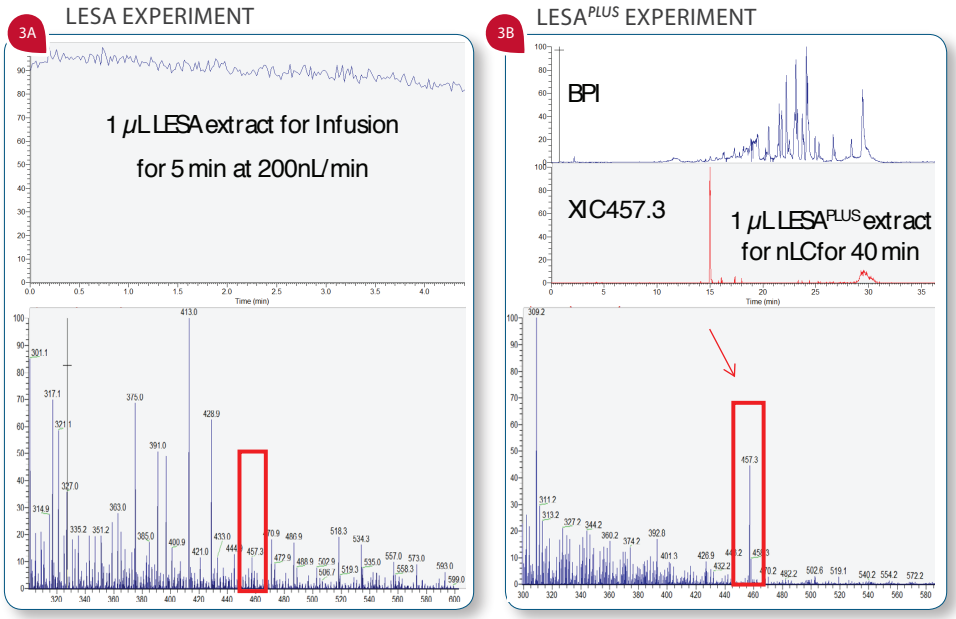

Figure 3: Comparison between a standard LESA experiment and a LESA^{PLUS} experiment from mouse brain tissue section (Figure 2). A: shows a multitude of *m/z* signals representing different lipid species with *m/z* 457.3 being a minor component. B: shows the LESA^{PLUS} experiment and the XIC of the same *m/z* signal at 457.3, now separated from matrix components and other lipid species resulting in higher overall detection sensitivity[1,2].

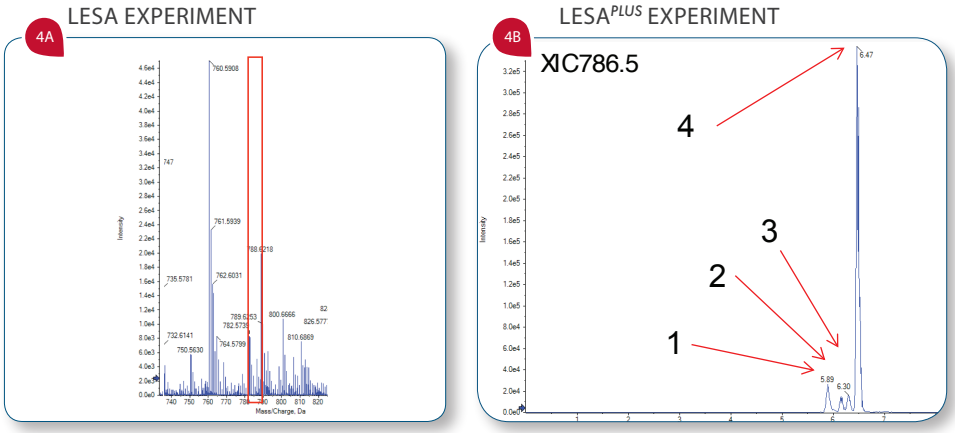

Figure 4: Top trace showing the standard LESA experiment from mouse brain section. *m/z* 786.5 is a minor component of the tissue in that location. Bottom trace showing the comparable LESA^{PLUS} experiment with XIC of *m/z* 786.5. LESA^{PLUS} is able to separate multiple isobaric lipid species with a major component eluting at 6.47 minutes and three minor components eluting earlier[1].

SUMMARY

Advantages of LESA^{PLUS} compared to standard LESA for lipid analysis from tissue sections are:

- Higher sensitivity due to separation of analytes from matrix components
- In-depth analysis of more lipid species
- Smaller extraction spots (400 µm) and better spatial resolution

LITERATURE

(1) Almeida R. Liquid extraction surface analysis (LESA) combined with nanoelectrospray MS for direct sampling of planar tissues. 1st AB SCIEX European Conference on MS/MS 2011, Noordwijkerhout, The Netherlands.

(2) Henion J, Eikel D, Linehan SL, Heller D, Murphy K, Rudewicz PJ and Prosser SJ. Liquid Extraction Surface Analysis Mass Spectrometry (LESA MS)-Drug Distribution and Metabolism of Diclofenac in the Mouse. 59th ASMS Conference on Mass Spectrometry and Allied Topics 2011 in Denver, CO, USA