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Advances in MALDI Imaging Mass Spectrometry - Adding a New Dimension of Separation for Direct Tissue Analysis

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Abstract

A major limitation of MALDI MS imaging using conventional MALDI Tof and Tof-Tof analysers is the absence of any additional dimension of separation. Owing to the complexity of the samples under investigation this poses a major risk of isobaric ions distorting the ion distribution and thus invalidating results. With the introduction of the Waters MALDI SYNAPT HDMS System, it is possible to separate ions using ion mobility separation (IMS) prior to mass analysis.

Introduction

A major limitation of MALDI MS imaging using conventional MALDI Tof and Tof-Tof analysers, which separate by *m/z*, is the absence of any additional dimension of separation. Owing to the complexity of the samples under investigation, this poses a major risk of isobaric ions distorting the ion distribution and thus invalidating results.

With the introduction of the Waters MALDI SYNAPT HDMS System, it is possible to separate ions using ion mobility separation (IMS) prior to mass analysis. IMS allows for the separation of ions according to their size, shape, and charge state. Using this technique it is possible to separate different compound classes, giving additional confidence that the true distribution of an ion of interest is observed. On the MALDI SYNAPT HDMS System, Waters' unique high efficiency IMS system has been combined with a state-of-theart imaging solution. Figure 1 shows two ways in which a MALDI HDMS imaging dataset can be mined, firstly imaging data analysis using BioMap and secondly HDMS data analysis of the same data using DriftScope.

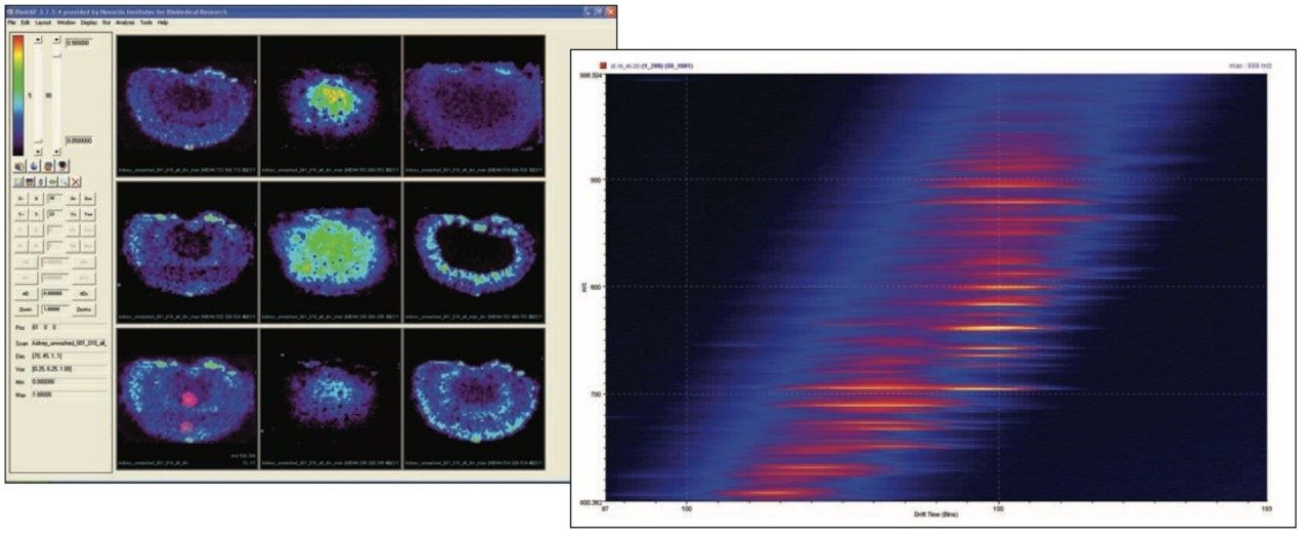

Figure 1. Illustration of image analysis of the kidney section using BioMap and visualization of ion mobility data from the same sample combined across the tissue section using DriftScope.

Experimental

The sample under investigation was a thin section of rat kidney. A 12 µm section was produced using a cryostome and deposited on thick aluminum foil. a-cyano-4-hydroxycinnamic acid matrix was applied evenly to the sample in several coats using an airbrush. The sample was mounted on a target plate.

The area to be imaged was selected using MALDI Imaging Pattern Creator (Waters Corporation, Manchester,

UK) (see Figure 2). Data were acquired on a MALDI SYNAPT HDMS System operated in HDMS mode over the *m/z* range of 10 to 1000. Spatial resolution of 250 µm was selected and 600 laser shots were acquired per pixel at a laser repetition rate of 200 Hz. After acquisition, HDMS data evaluation was performed using Driftscope (Waters Corporation, Manchester, UK). Data were converted into Analyze file format using MALDI Imaging Converter (Waters Corporation, Manchester, UK) for image analysis using BioMap (Novartis, Basel, CH).

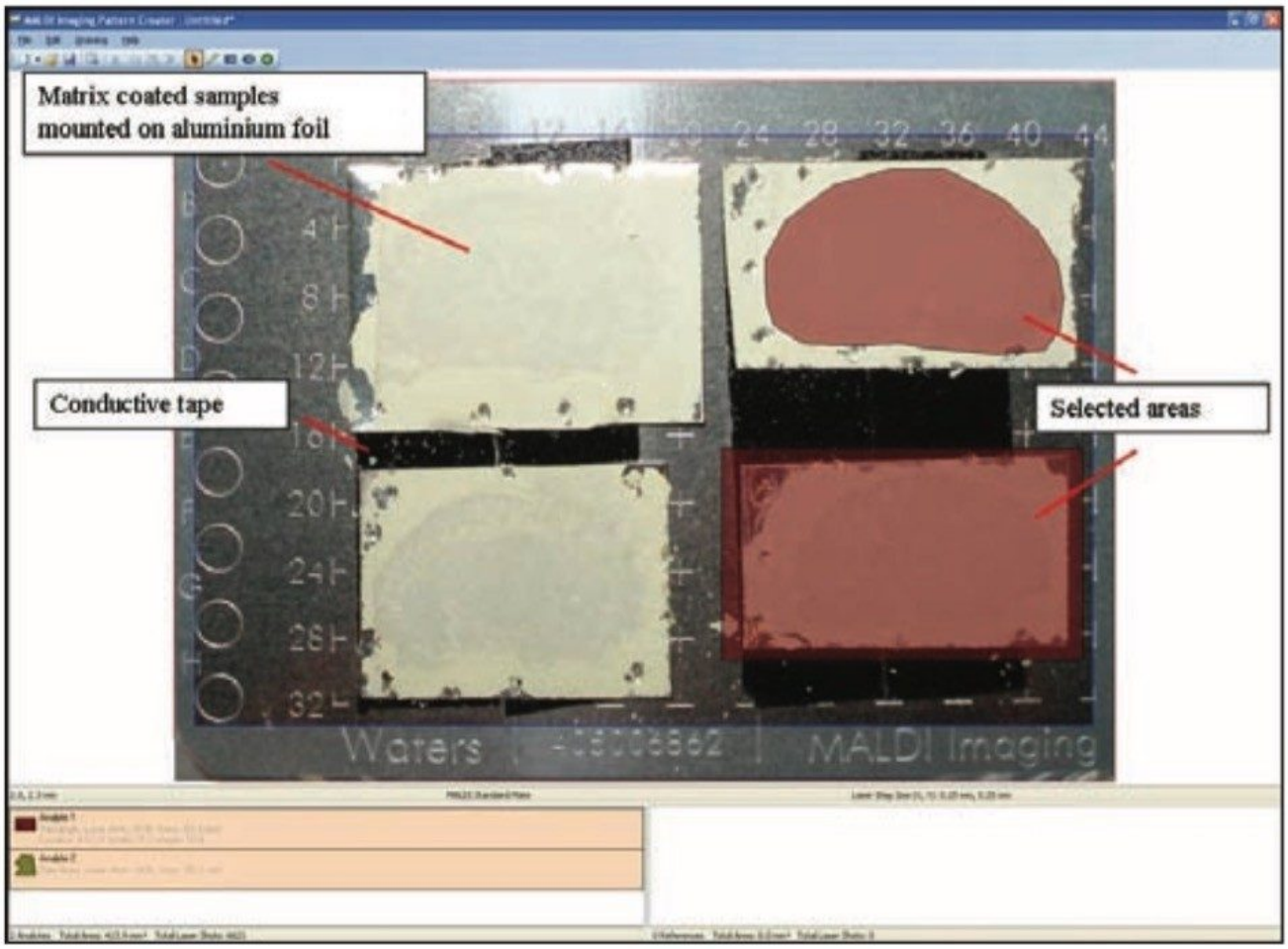

Figure 2. MALDI Imaging Pattern Creator is used to select area(s) to be automatically imaged using MALDI SYNAPT HDMS.

Results and Discussion

The combined Driftscope mobility plot showing drift time (x-axis) versus *m/z* (y-axis) obtained from the kidney sample is shown in Figure 3. It can clearly be seen that ions of similar *m/z* (on the same horizontal line in the plot) are separated in the ion mobility dimension. A full 3D data set is acquired at every spatial position consisting of *m/z*, IMS, and intensity, ensuring maximum flexibility for mining the data. It is also possible to perform a targeted experiment where only a small mobility and/or *m/z* range is acquired (not shown here).

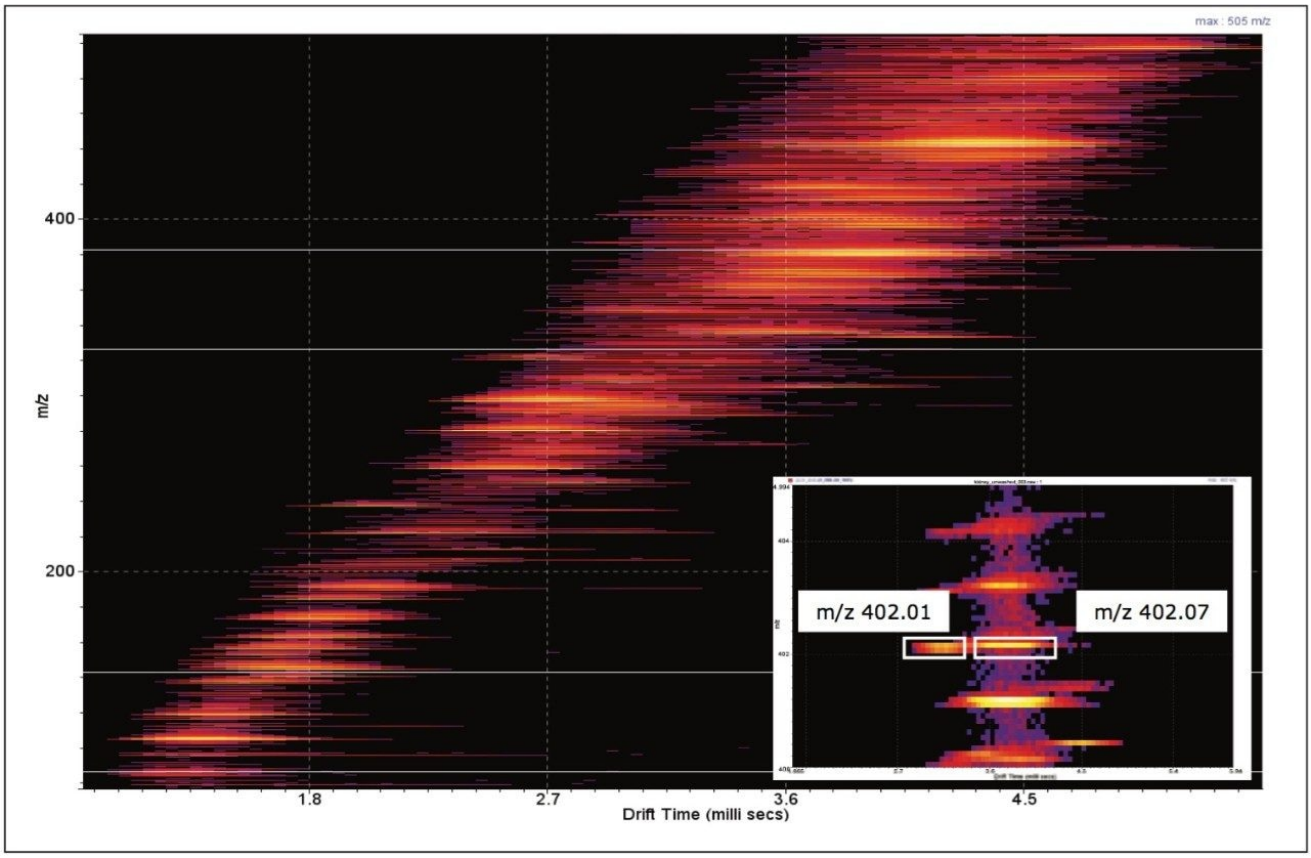

Figure 3. DriftScope data plot combined across the entire tissue section. Inset shows region (m/z 400.5 - 405, IMS 2.3 - 5.0 ms).

Figure 4 shows an ion image for the ion of *m/z* 402.01 without ion mobility separation. When the ion mobility range from 2.7 ms–3.3 ms is combined, the ion image for *m/z* 402.01 has a significantly lower background noise

level, as illustrated in Figure 5. Finally, Figure 6 shows the ion image of the interfering background ion with *m/z* 402.07 after it has been selected using ion mobility (drift time 3.4–4.1 ms).

The use of HDMS clearly helps to provide the true spatial tissue distribution of the endogenous metabolite of mass 402.01 Da by removing any contribution of the interfering matrix ion of *m/z* 402.07 Da.

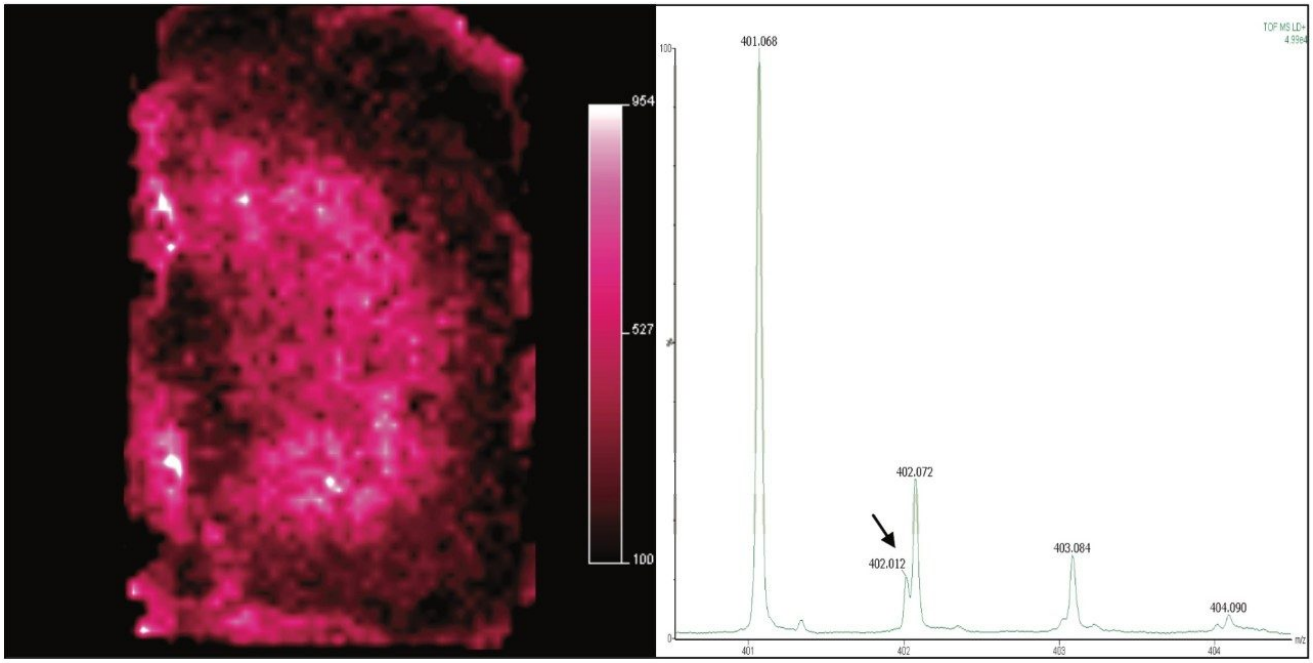

Figure 4. Ion image of m/z 402.01, without ion mobility separation.

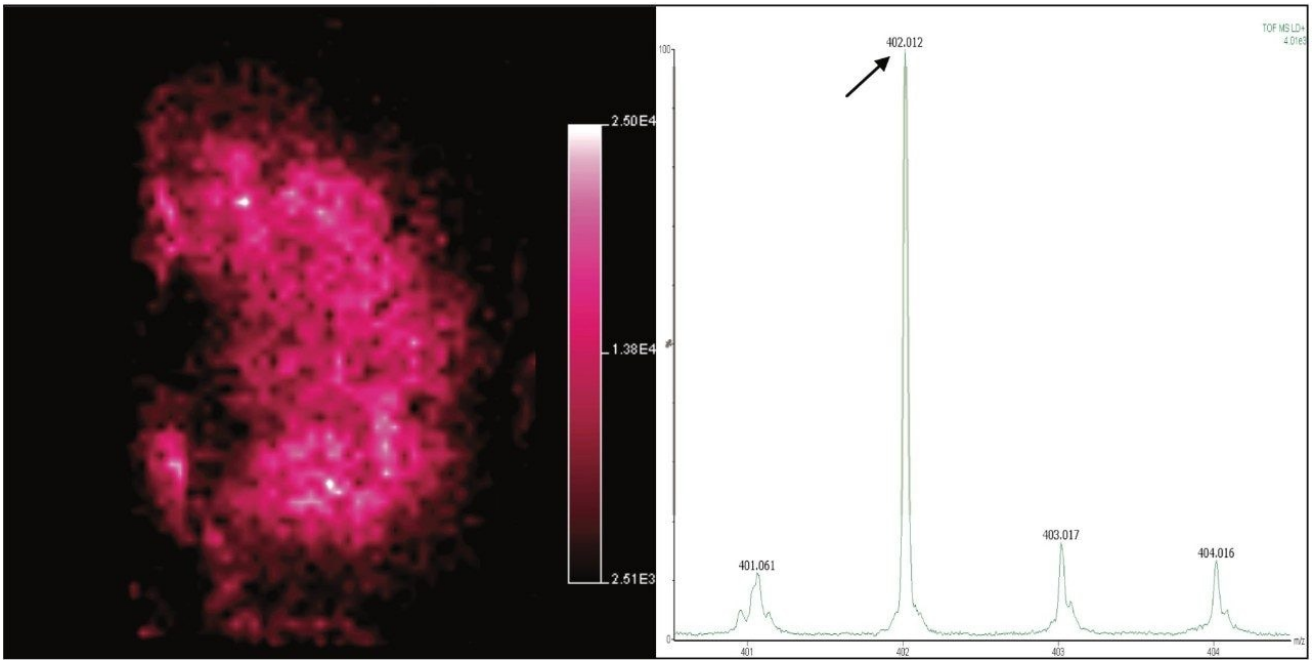

Figure 5. Ion image of m/z 402.01 (ion of interest), with ion mobility separation, selected ion mobility range 2.7 - 3.3 ms.

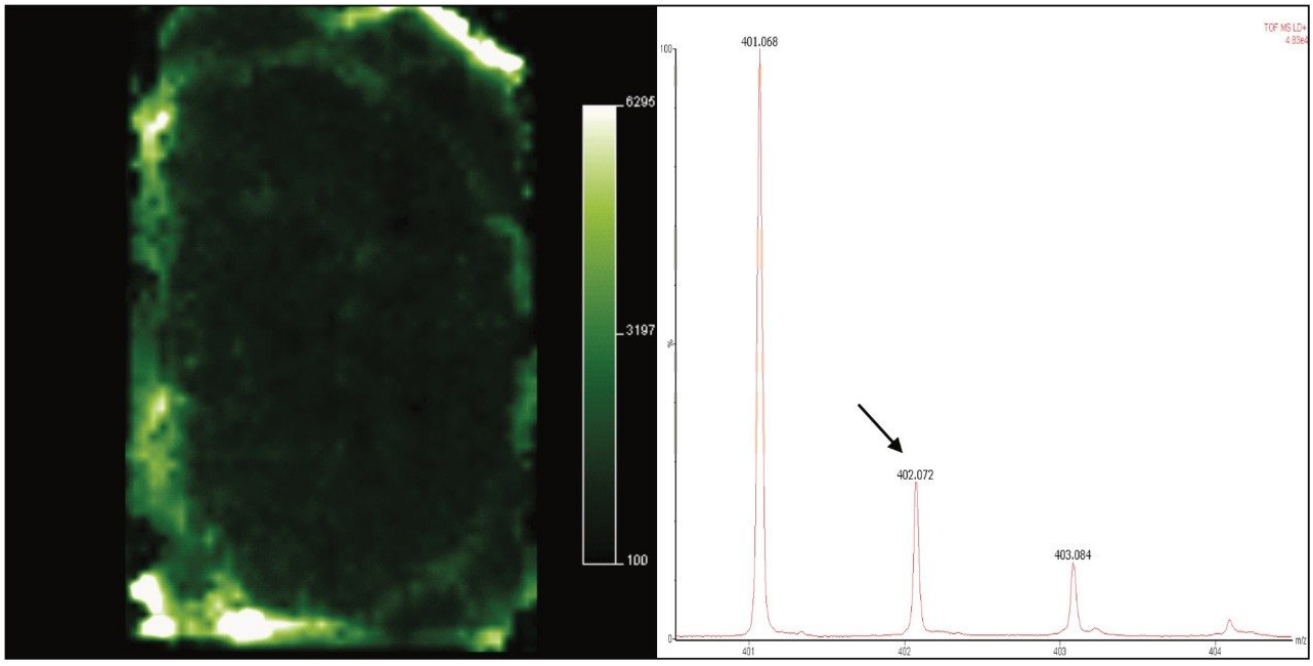

Figure 6. Ion image of m/z 402.07 (interfering background ion), with ion mobility separation, selected ion mobility range 3.4 - 4.1 ms.

Conclusion

- The combination of high efficiency ion mobility separation with MALDI provides a unique separation dimension to further enhance mass spectrometric imaging
- Through the use of ion mobility separation, isobaric species desorbed from tissue can be separated
- IMS can be used to produce images without interference from background ions of similar mass. This can remove ambiguity from imaging experiments and lead to more precise localisation of the compound of interest, such as drugs and metabolites
- HDMS has the potential to reduce the complexity and improve confidence in imaging experiments
- MALDI imaging offers a complementary approach to established imaging techniques, such as whole body autoradiography. It has the advantage that no labelling of the compounds of interest is required and that

multiple compounds can be monitored simultaneously, e.g. drugs and metabolites. As a result the experiments are rapid and the technique is relatively inexpensive

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720002443, December 2007