SHIMADZU

Application News

MALDI-TOF Mass Spectrometry No.B10

On-Tissue Direct Analysis: MALDI Mass Spectrometric Imaging for Peptides/Protein

MALDI imaging refers to a technique in which mass spectrometric analysis is conducted directly on a biological tissue sample. The distribution of biomolecules (low-molecular weight metabolites, lipids, peptides and proteins, etc.) on the tissue are mapped as a two-dimensional image based on measurement site location information and mass spectral information. This makes it possible to visually grasp the localization of biomolecules of interest.
The application of the MALDI imaging technique has previously been reported for biomolecules in various tissues, and there are numerous recent manuscripts citing spatial distribution of disease-specific biomarker candidate compounds. Thus, the MALDI imaging is an effective technique for understanding the spatial distribution of molecules, and not only is there expectation for this technique with respect to the search for disease-specific biomarkers, but for its application in drug kinetics as well.

Here we present an example of MALDI imaging of peptides and proteins in which we used a cross-section of rat kidney tissue as the sample.
First, the matrix was coated on a frozen tissue section of rat kidney which was placed on an electrically conductive glass slide. Generally, when conducting MALDI imaging, the matrix must be coated uniformly on the tissue sample to ensure highly reproducible mass spectral data acquisition. One of these coating techniques uses a spotter instrument to deposit micro volumes of matrix solution.
Here we used a chemical inkjet printer (CHIP-1000), a micro volume dispensing instrument, to conduct repeat deposition of 300 pL of matrix solution (5 mg/mL sinapinic acid) at 200 μm intervals from spot center-to-center over the surface of the tissue section. Fig. 1 shows an image of the kidney tissue section and the other with the matrix deposited on the tissue.
Next, after drying the matrix-applied sample in a desiccator, the AXIMA Confidence was used to conduct linear-mode mass spectrometric analysis (positive mode) on all of the matrix spots. Fig. 2 shows the mass spectrum results obtained from the measurement.

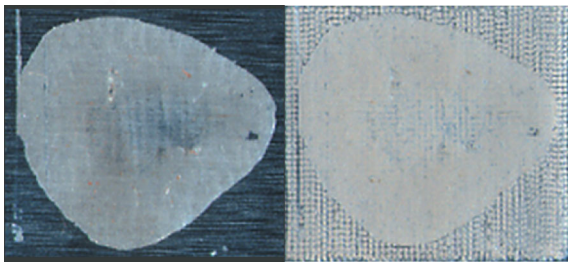


Fig. 1 Kidney Tissue Section without/with Matrix Deposition

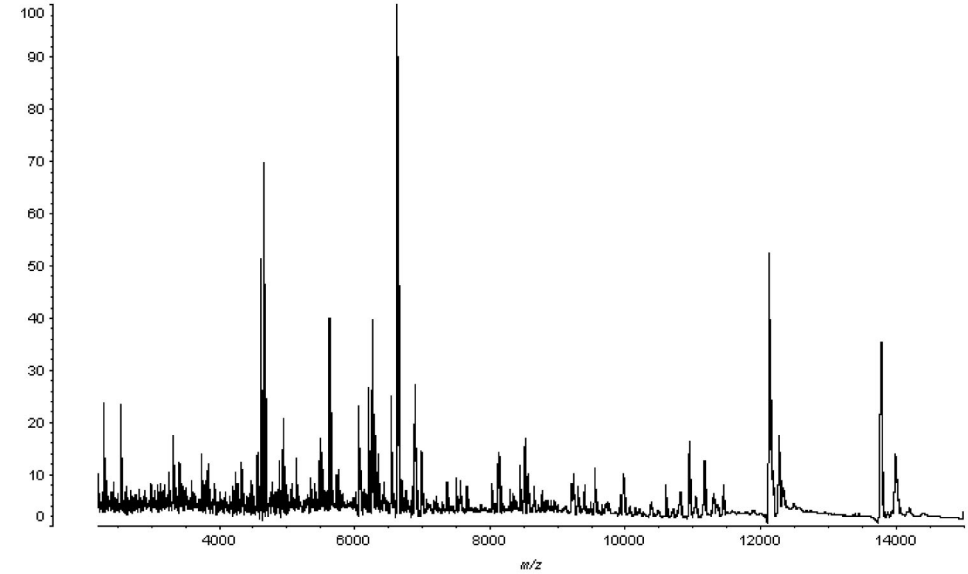


Fig. 2 Mass Spectrum of Rat Kidney Tissue Cross-Section

From the results of Fig. 2, several MS peaks presumed to be peptides and proteins were detected directly from the tissue. For some of the MS peaks, we created an MS image based on the peak intensity and matrix spot location coordinates using the BioMap software (http://www.maldi-msi.org/) (Fig. 3). The results indicated that the spatial distribution of compounds that corresponded to each of the mass values agreed with the characteristic structures of the kidney cortex and medulla, and localization of the various biomolecules was confirmed (spatial resolution 200 μm).

In addition, using the BioMap software, we created overlay images of only those MS images that displayed characteristic distributions (Fig. 4). It is clear from the overlay image results that the distributions of these peptides and proteins correspond to characteristic structure of the kidney.

These results confirm the usefulness of the MALDI Imaging technique utilizing the chemical inkjet printer and the MALDI-MS (AXIMA Series) in investigating biomolecule distributions in biological tissue sections.

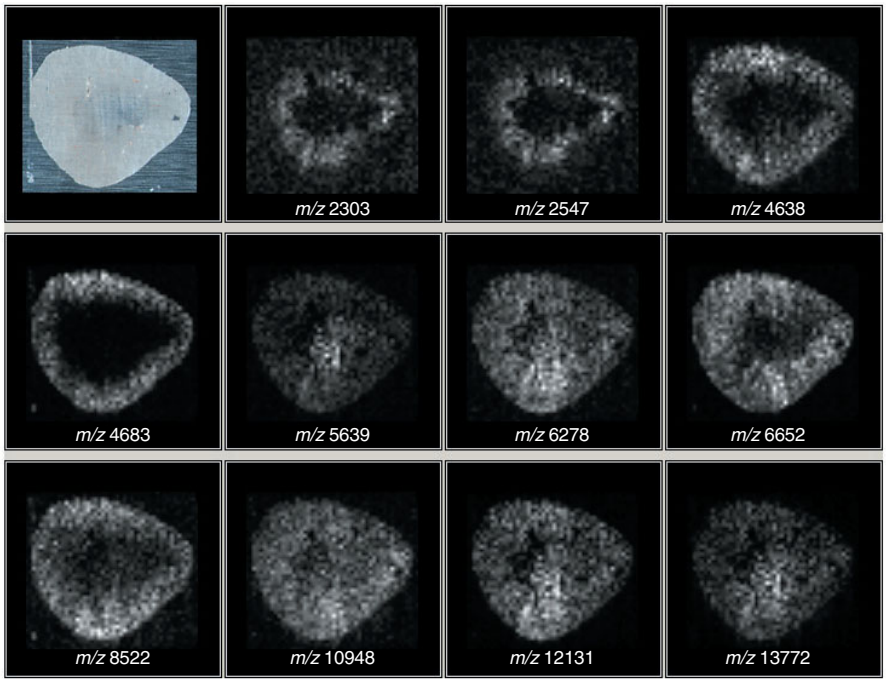
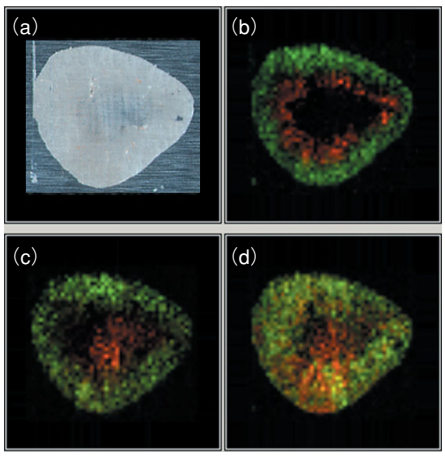


Fig. 3 MS Images of Rat Kidney Tissue Cross-Section



(a) Kidney tissue section
(b) Overlaid MS image (green: *m/z* 4683, red: *m/z* 2547)
(c) Overlaid MS image (green: *m/z* 4638, red: *m/z* 5639)
(d) Overlaid MS image (green: *m/z* 6652, red: *m/z* 6278)

Fig. 4 Overlaid MS Images

NOTES:
✻This Application News has been produced and edited using information that was available when the data was acquired for each article. This Application News is subject to revision without prior notice.

SHIMADZU

SHIMADZU CORPORATION. International Marketing Division

3. Kanda-Nishikicho 1-chome, Chiyoda-ku, Tokyo 101-8448, Japan Phone: 81(3)3219-5641 Fax. 81(3)3219-5710
Cable Add.:SHIMADZU TOKYO

Printed in Japan 3295-09905-10A-IK