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Imaging Mass Spectrometry Using Ultra-high Mass Resolution Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometer, SpiralTOF

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Imaging mass spectrometry (IMS) has been used for biological applications, to assess the distribution of proteins, peptides, lipids, drugs, and their metabolites in a tissue specimen. IMS has expanded during the last decade using matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) mass spectrometer, which adopted a linear and a reflectron ion optical systems. A reflectron MALDI-TOF mass spectrometer, using a delayed extraction technique, has higher mass resolution than linear MALDI-TOF mass spectrometer. However, its high mass resolution is available only within limited mass range, which isn't sufficient for analysis in low-molecular compounds such as lipids, drugs and drug metabolites. It is necessary to extend flight path length to improve mass resolution and mass accuracy in wide mass range. However, the flight path length of a reflectron TOF mass spectrometer is limited by its instrument size, and is difficult to be extended beyond certain length restricted by the instrument dimension. We developed a MALDI-TOF mass spectrometer with a spiral ion trajectory, SpiralTOF[1], to solve the issue. It has 17 m flight path length within a cubic vacuum housing of approximately 0.6m x 0.6m x 0.7m.

The schematic of SpiralTOF, which consists of four toroidal electrostatic sectors, is shown in Figure 1. Each has eight stories made by nine Matsuda plates piled up inside a cylindrical electrostatic sector. The ions pass the four toroidal electrostatic sectors sequentially and revolve along a figure-eight-shaped orbit on a certain projection plane. During multiple revolutions, the ion trajectory shifts perpendicular to the projection plane every revolution cycle, thus generating a spiral trajectory. The flight path length of one revolution is 2.1 m. The total flight path of SpiralTOF was 17 m, which is 5-10 times longer than a reflectron TOF mass spectrometer.

SpiralTOF achieved ultra-high mass resolution that could separate isobaric compounds, which differed only 0.1 u each other. The advantage of isobaric separation in IMS will be shown to take the IMS for lipids distribution on mouse brain tissue section as an example. The isobaric mass separation at m/z 820–825 is shown in Figure 2. Three types of lipid peaks were well separated in mass spectrum and could show the different localization respectively. The high selectivity for drawing mass image is important for understanding clear localization of compounds, especially in low mass region. Further IMS measurements for drugs distribution on mouse brain tissue section will be reported in the presentation.

References:

[1] T. Satoh, T Sato, A. Kubo, J. Tamura, J. Am. Soc. Mass Spectrom. **22** (2011), p. 797.

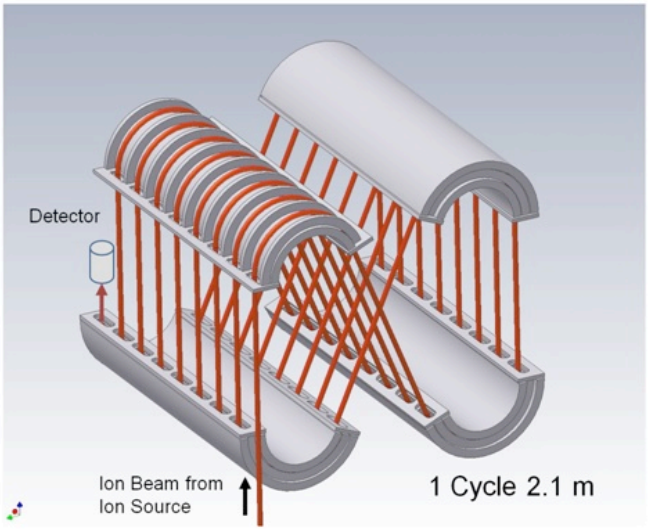

Figure 1. Schematic of time-of-flight mass spectrometer with spiral ion trajectory (SpiralTOF). The outer electrode of the left-top electrode is not included to show the ion trajectory (red line).

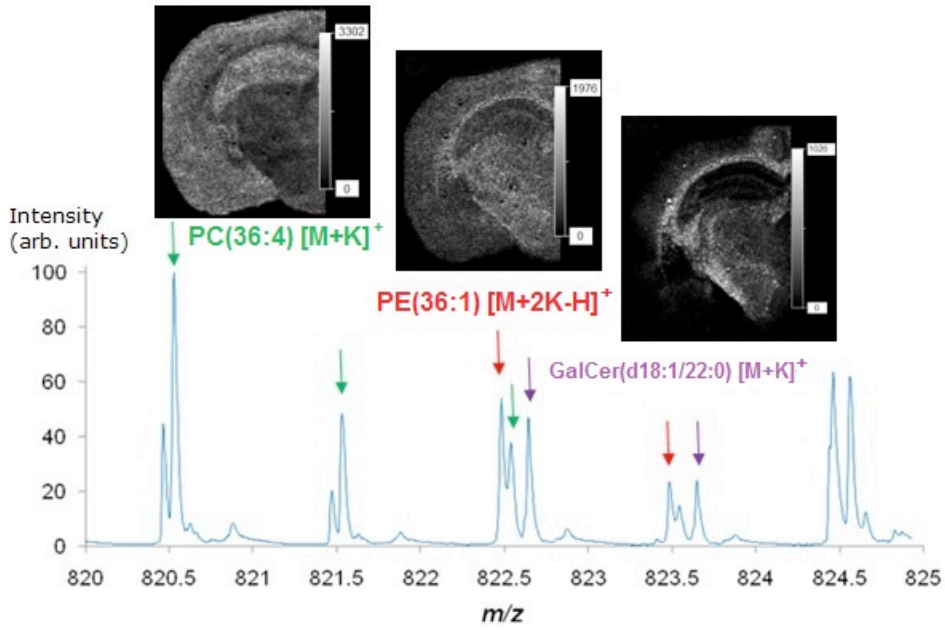

Figure 2. Ultra-high resolution mass spectrum at *m/z* 820–825 in imaging mass spectrometry for lipids in a mouse brain tissue section. Three types of lipids were well separated in mass spectrum and could draw different mass images from them.