Medical & healthcare, Bio-imaging, Material analysis

Research on mass spectrometry imaging technique using picoliter liquid and its application to human disease tissues

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Abstract

Mass spectrometry imaging, which extracts and ionizes various components in a sample and performs mass spectrometry, can visualize the distribution of multiple chemical components in a sample in a single measurement. We have been developing a unique extraction and ionization method called "tapping-mode scanning probe electrospray ionization (t-SPESI)" using a vibrating capillary probe and picoliter liquid. In order to stabilize the measurement of real samples with non-flat surfaces, we developed the measurement technique of probe vibration amplitude and the amplitude feedback control. This enabled simultaneous acquisition of high-spatial-resolution mass spectrometry imaging and surface topography imaging. We have also succeeded in visualizing the various distributions of lipid components in human heart disease tissues through collaborative research with the graduate school of medicine and engineering, Osaka University.

Background & Results

In the cells that constitute our bodies, it is known that the chemical reactions necessary for life activities proceed through the interaction of various molecules with different molecular weights and chemical properties, such as lipids, metabolites, and proteins. Imaging technology to investigate the distribution of complex chemical species in biological tissues is important for detailed understanding and diagnosis of disease states in biological tissues, where various cells form a network.

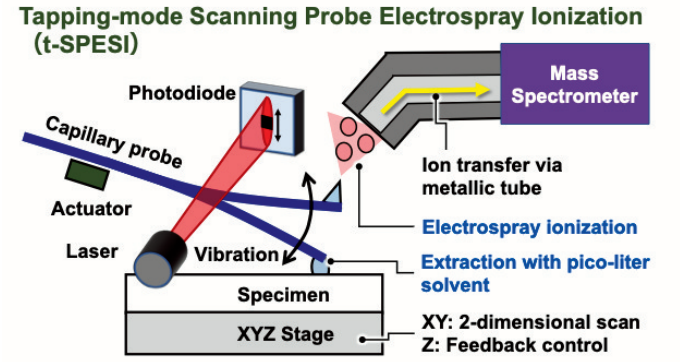
t-SPESI can rapidly extract and ionize chemical components contained in a localized region of a sample by intermittently supplying a picoliter of solvent with high voltage applied to the sample through a fast vibrating capillary probe ("probe"). Electrospray ionization is used for ionization, and biomolecules are changed into gas-phase ions without breaking their structures. By scanning the probe in a two-dimensional direction with respect to the sample surface, we can obtain mass spectra associated with the coordinate information of a sample and visualize the distribution of specific chemical components in a sample.

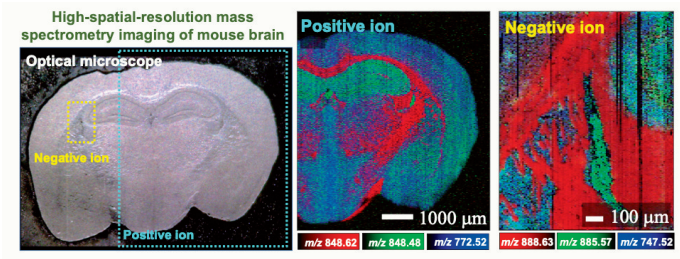
We integrated the elemental technology of atomic force microscopy, which can measure the unevenness of a sample at the nanoscale, with t-SPESI. Using this technique, we were able to image multiple lipids in a mouse brain tissue section with a spatial resolution of 6.5 micrometers, and showed that it is possible to classify brain structures based on differences in the mass spectral patterns of multiple lipids.

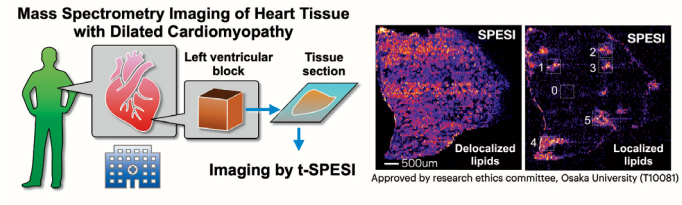
As a medical application of t-SPESI, we are also conducting collaborative research on human disease tissues. As a result of measurement of cardiac tissue donated by a patient with dilated cardiomyopathy, we found that multiple lipids were localized in the tissue, indicating that the type and distribution of lipids can be precisely measured.

Significance of the research and Future perspective

This technique, which enables high-spatial-resolution imaging of biological tissue sections without pretreatment, is effective for visualizing a variety of chemical information in diseased tissues. In the future, we will continue our research on multi-dimensional chemical distribution information measurement and feature extraction methods for human disease tissues. We expect that this technology will contribute to the elucidation of pathological conditions and be applied to diagnostic techniques.







Patent

Treatise
Otsuka, Yoichi; Kamihoriuchi, Bui; Takeuchi, Aya et al. High spatial resolution multimodal imaging by tapping-mode scanning probe electrospray ionization with feedback control, Anal. Chem. 2021; 93: 2263–2272. doi: 10.1021/acs.analchem.0c04144
Otsuka, Yoichi; Satoh, Shuya; Naito, Junpei et al. Visualization of cancer-related chemical components in mouse pancreas tissue by tapping-mode scanning probe electrospray ionization mass spectrometry, J. Mass Spectrom. 2015; 50; 1157-1162. doi: 10.1002/jms.3634

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Keyword mass spectrometry, bioinformatics, imaging, extraction ionization, multidimensional information