MALDI Imaging with a Time-of-Flight Mass Spectrometer with a Spiral Geometry and Silver Nanoparticles

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Matrix-Assisted Laser Desorption/Ionization (MALDI) imaging provides information about the spatial distribution of chemical compounds. Although MALDI imaging has relatively poor spatial resolution in comparison with electron microscopy, MALDI has the advantage that it can detect, identify, and image intact molecules, including biomolecules. High mass-resolving power is required to achieve accurate imaging of specific compounds in a complex biological sample such as a mouse brain section, where compounds of interest and interferences may have exact masses that differ by only a fraction of a mass unit.

Time-of-flight mass spectrometers are well suited for MALDI imaging because they can combine high mass-resolving power with rapid data acquisition. However, small differences in the sample topography can introduce differences in flight time, leading to a loss in mass-resolving power for samples that are not perfectly flat (e.g. tissue slices). One way to overcome this limitation is to use a time-of-flight mass spectrometer with a long flight path. We have developed an ultrahigh-resolution time-of-flight mass spectrometer with a unique “Spiral” geometry that compresses a 17-meter flight path into approximately a 1-meter distance, while still maintaining “perfect focusing” ion optics[1, 2]. The advantage of this design for imaging lipids in mouse-brain sections was demonstrated by obtaining separate images for two phospholipids with exact masses that differ by only 0.09u [3].

Sample preparation for MALDI imaging is critical and requires that the sample be uniformly coated with a light-absorbing matrix compound. Organic compounds that are commonly used as MALDI matrices can be lost through vacuum sublimation over the long data acquisition times needed to obtain an image of a biological specimen. Furthermore, uniform deposition of an organic matrix by spraying or sublimation requires skill and patience. An alternative approach has been devised using a silver nanoparticle matrix and a particle implanter that provides a means to control the uniformity, depth, and particle size[4-6]. This provides a uniform matrix deposition and eliminates the problem of matrix sublimation. Because silver has two major isotopes with nearly equal abundance, the need for high mass-resolving power is reinforced.

Here we report the use of silver nanoparticle implantation for MALDI imaging with a time-of-flight mass spectrometer to image lipids in mouse brain tissue. A new feature added to the imaging software provides continuous drift correction to ensure constant mass accuracy over a long data acquisition period [7].
References:


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Figure 1. Silver-nanoparticle MALDI-SpiralTOF images of two lipids in a mouse brain section.