MALDI orthogonal TOF imaging Mass Spectrometry with continuous laser raster sampling

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Abstract

Imaging mass spectrometry can be used to reveal the relative distribution of lipids, peptides and proteins present on or near the surface of materials with micro scale spatial resolution. MALDI imaging mass spectrometry is a recent development, but the field has grown dramatically in the last few years. Most of the research in MALDI imaging involves a time consuming sampling technique (*spot-to-spot laser raster sampling*) coupled with axial-injection TOF instruments. Recently, orthogonal-injection TOF mass spectrometry has been used with *continuous laser raster sampling* to speed up the MALDI imaging process with a higher spatial resolution and sensitivity. This thesis is based on improving the performance of MALDI imaging in orthogonal-injection TOF mass spectrometry with continuous laser raster sampling.

The research group at the TOF laboratory, University of Manitoba has developed a novel MALDI ion source for imaging, in which the MALDI target is oriented from the typical direction such that, the laser incident angle is perpendicular to the sample surface. This modification reduced the size of laser spot on the MALDI target and hence improved the spatial resolution of ion imaging. One of the objectives of this thesis is to study the optimum conditions of parameters (pressure and de-clustering voltages) of the novel ion source for protein imaging, minimizing cluster ions.

The quality of MALDI imaging highly depends on the matrix application protocol. The application of matrix prepared in liquid base disturbs the actual chemical distribution pattern on tissue samples and affects on spatial resolution of ion images. A spray of matrix droplets produced by an artistic air brush is one of the popular matrix application techniques used in MALDI imaging. To maintain a higher spatial resolution of MALDI ion images produced with continuous laser raster sampling, it is important to have a coating of tiny matrix droplets over the sample. To achieve this requirement, the sprayer parameters (spraying time / distance and pressure on the liquid) have been empirically selected in present matrix applications in imaging. Here a method is proposed to optimize the matrix sprayer parameters to obtain smaller size of droplets over the sample and applied in an orthogonal-injection TOF mass spectrometer coupled with continuous laser raster sampling.

Very recently, vacuumed sublimation technique which is traditionally used in chemistry was introduced for matrix applications in MALDI lipid imaging. Conventional glass ware system used in chemistry and high vacuumed evaporator used in electron microscopy for sublimation are generally used for the matrix sublimation in MALDI imaging. An attempt is made here to develop a dedicated vacuumed sublimation system for matrix deposition in MALDI lipid imaging.

In continuous laser raster sampling, the laser continuously moves over the sample surface while firing at a high repetition rate. The influence of sample stage velocity on ion intensity is studied for different laser spot sizes with a Nd-YAG laser at 500 Hz repetition rate. According to the results, the homogeneously prepared thin layer of Glyceryl trioleate (885.43 Da) samples and human brain tissue sections show an increment of lipid ion intensity with the sample stage velocity up to a certain value and then a decrement at a slower rate.

In orthogonal-injection TOF mass spectrometers, quadrupoles are used as ion transmission channel between the ion source and orthogonal injector. It is assumed that the spatial resolution of ion images produced by continuous laser raster sampling will be effected due to the mixing of ion packets while they are traveling through the quadrupoles. This ion packet mixing is investigated by studying their width at the ion detector for different laser firing frequencies and axial voltage gradients of the quadrupoles. It is found that the ion packets which are generated with consecutive laser shots are mixed together at the higher laser frequencies and lower axial voltage gradients.