A NOVEL PROTOTYPE MALDI SOURCE ON A OA-TOF MASS SPECTROMETER COMBINED WITH ION MOBILITY SEPARATION

Sahidole Sangar1; Mark Towers2; Paul Murray3; Nicole Lawes1; Shaia Jarvis4; Richard M. Caprioli1
1. Waters Corporation, Beverly, MA, USA; 2. Waters Corporation, Wilmslow, UK; 3. Vanderbilt Mass Spectrometry Research Center and Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, TN, USA; 4. Surgery and Cancer, Imperial College London, London, UK

INTRODUCTION

Mass spectrometry imaging (MSI) is a rapidly growing technology and has become the preferred technique for a range of research areas. Some areas of particular interest are those of clinical research and omics in particular. In both cases high throughput and spatial resolution along with reliability and ease of use are essential success within these fields. Currently within these areas, MSI is being driven primarily by matrix-assisted laser desorption/ionization (MALDI) as a key technology. Here we present a prototype MALDI source mounted on a SYNAPT G2-S/HDMS. The source has been designed specifically for high throughput, high spatial resolution MSI experiments. It incorporates a number of key features tailored to aid and circumvent some of the common MSI related issues such as source contamination and maintenance.

METHODS

Investigations have been performed at the University of Würzburg and the Department of Biochemistry at Vanderbilt University. The SYNAPT G2-S/HDMS was purchased from Waters. All MALDI-TOF-MS and MS/MS analysis was performed using the MassLynx 4.1 software (Waters, Wilmslow, UK) and some custom executables. Software suite (WREnS) (Waters, Wilmslow, UK) and some custom executables. Due to the orthogonal nature of the source the ability to perform MS/MS analysis was not affected. Further information with regard to source contamination and maintenance.

RESULTS / DISCUSSION

Prototype source description

The prototype MALDI source was mounted on the front of a SYNAPT G2-S/HDMS (Figure 1). The conventional source was removed with no modifications to the front of the instrument using the existing fixings of the conventional source. Figure 2 shows a CAD drawing of the current iteration of the prototype source with the door in the open position and the novel hexapole partially removed.

Figure 3 shows the hexapole in the loaded position. The hexapole has been designed so that it can be easily removed for cleaning and maintenance. The removal of the hexapole can be performed via a tool-free mechanism (spring loaded catch).

Figure 4 shows the hexapole housing with the removed hexapole. The hexapole is guided into the assembly by a set of rails giving two key advantages. 1. Easy removal and inserting of the hexapole with exact alignment each time. 2. Prevention of accidental interaction with the mirrors of the hexapole and the camera guide to the hexapole. This means that the mirror for the laser can be placed within the hexapole housing close to the hexapole itself allowing for a more perpendicular angle of incidence for the laser (22°). A photograph of the hexapole can be seen in figure 4.

The hexapole has been designed so that the whole assembly can be easily removed in maintenance/water for cleaning by soaking. All electrical contacts are made via contact pin so no further disassembly is required. As the entire source opens, the hexapole can be easily inspected prior to each sample loading and the front surface can be wiped if necessary.

The ability to load samples without using a load tool is achieved thanks to a specially designed isolation valve which can be seen in figure 5. The hemispherical shape of the valve combined with the tapped set of the hexapole allows the valve to be swung into position whilst minimizing the distance between the exit of the hexapole and entrance to the step wave ion guide of the mass spectrometer. The isolation valve enables basic maintenance and cleaning of the source with the user to break vacuum on the main system, helping to increase instrument uptime.

The prototype MALDI source allows for high pixel rate imaging utilizing the existing fixing of the conventional source and is designed to be more robust and easier to clean. The source can be lowered or raised using the gas spring giving the option for cleaning and maintenance. The removal of the hexapole can be performed via a tool-free mechanism (spring loaded catch).

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The unique hexapole design and isolation valve enables fast cleaning of the source ion optics (3 min) without the need to break vacuum improving reliability and robustness.

CONCLUSION

Figure 8 shows images acquired at 240µm using the traditional static method. The laser was expanded to match the pixel size maximizing signal intensity and signal to noise. Representative spectra can be seen in figure 9. The source is fitted with an Nd:YAG frequency tripled solid state laser. The focusing lens is on a translation stage allowing it to be refocused depending on the image resolution needed. In order to maximize signal to noise response the laser can be focused in a range of 50µm down to 15µm where MALDI MSI images can be acquired with good signal to noise at a pixel size of 10µm with over sampling. Figures 6 and 7 show examples of images acquired at 10µm acquired using a continuous master acquisition controlled using the custom script in WRESS.

Figure 6: Hexapole images acquired in bulk positive and negative ionization mode. The laser beam was expanded to match the pixel size maximizing signal intensity and signal to noise. Representative spectra can be seen in figure 9. The source is fitted with an Nd:YAG frequency tripled solid state laser. The focusing lens is on a translation stage allowing it to be refocused depending on the image resolution needed. In order to maximize signal to noise response the laser can be focused in a range of 50µm down to 15µm where MALDI MSI images can be acquired with good signal to noise at a pixel size of 10µm with over sampling. Figures 6 and 7 show examples of images acquired at 10µm acquired using a continuous master acquisition controlled using the custom script in WRESS.

Figure 7: Hexapole images acquired in bulk positive and negative ionization mode. The laser beam was expanded to match the pixel size maximizing signal intensity and signal to noise. Representative spectra can be seen in figure 9. The source is fitted with an Nd:YAG frequency tripled solid state laser. The focusing lens is on a translation stage allowing it to be refocused depending on the image resolution needed. In order to maximize signal to noise response the laser can be focused in a range of 50µm down to 15µm where MALDI MSI images can be acquired with good signal to noise at a pixel size of 10µm with over sampling. Figures 6 and 7 show examples of images acquired at 10µm acquired using a continuous master acquisition controlled using the custom script in WRESS.

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