Evaluation of an in-line low temperature plasma device for post-ionisation in atmospheric pressure MALDI imaging

Efstathios A. Elia[1], Marcel Niehaus[1], Jan-Christoph Wolf[2], Bin Yan[1], Kenneth N. Robinson[1], Rory T. Steven[1] and Josephine Bunch[1]

[1]National Centre of Excellence in Mass Spectrometry Imaging (NiCE-MSI), NPL, Teddington, [2]Plasmion GmbH, Augsburg, Germany

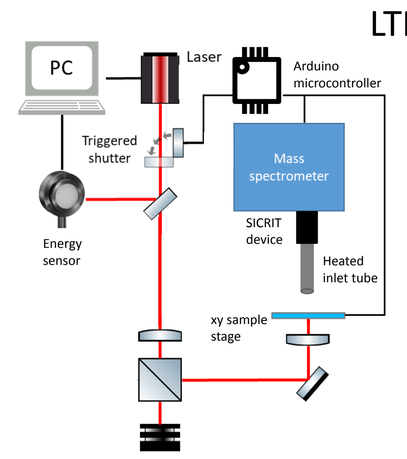
Introduction

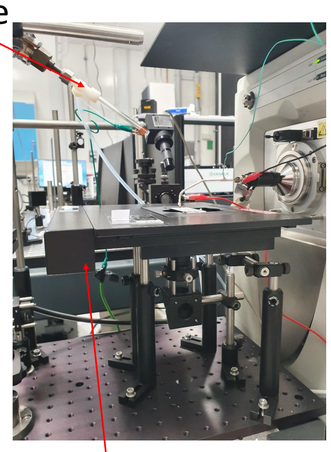
It is well known that ambient ionisation methods have a great advantage over more traditional vacuum based techniques. Their ease of hyphenation to mass spectrometers as well as their simplistic designs have made them attractive to many. For atmospheric pressure (AP-)MALDI, the major drawbacks however are low limits of detection, poor ion transmission and high variance in data. To try and reduce these effects, we have developed a second-generation transmission mode (TM) AP-MALDI imaging platform with in-line plasma post-ionisation using the commercially available SICRIT® device, replacing the previously used low-temperature plasma (LTP) probe from our developmental TM-AP-MALDI source[1].

Methods

A modified microscope stage (Märzhäuser Wetzlar, Germany) was coupled to an Orbitrap Elite (Thermo, Germany) mass spectrometer. The stage was controlled through the supplied software (Switchboard 1.76). An Nd:YLF laser (349nm, Spectra Physics, USA) was coupled to the ion source with standard opto-mechanics, triggering of MS acquisition was achieved using an Arduino microcontroller. The SICRIT® device (Plasmion, Germany) was mounted onto the ion block of the mass spectrometer, with a stainless-steel inlet tube extension fitted in front of it, heated to ≈ 550 °C with the use of a standard laboratory power supply. A LTP probe, as described previously[1,2], was also used to compare post-ionisation efficiency between the two plasma devices. Murine brain samples were sectioned at 10 µm thickness, thin films of standards were prepared using a TM Sprayer (HTX Technology). 2,5-dihydroxybenzoic acid and 2,6-dihydroxyactophenone (Sigma, UK) were used as matrix in 80% methanol and applied using a TM Sprayer or via a sublimation/recrystallization protocol. Data was converted to imzML by imzMLconverter and analysed in MatLab (2018a) via the SpectralAnalysis software package[3].

TM-AP-MALDI setup





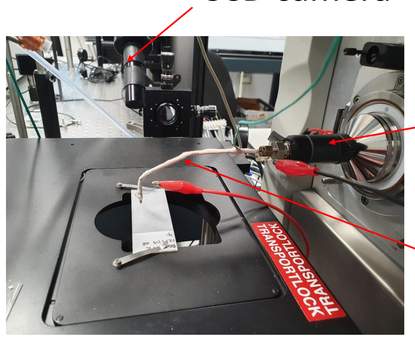


Figure 1. Schematic of updated TM-AP-MALDI source with both LTP probe and SICRIT® device attached. The extended inlet tube is bent in order for the orifice to be exactly above the point of ablation, at a distance of ≈ 3 mm from the sample's surface.

Mouse brain sections

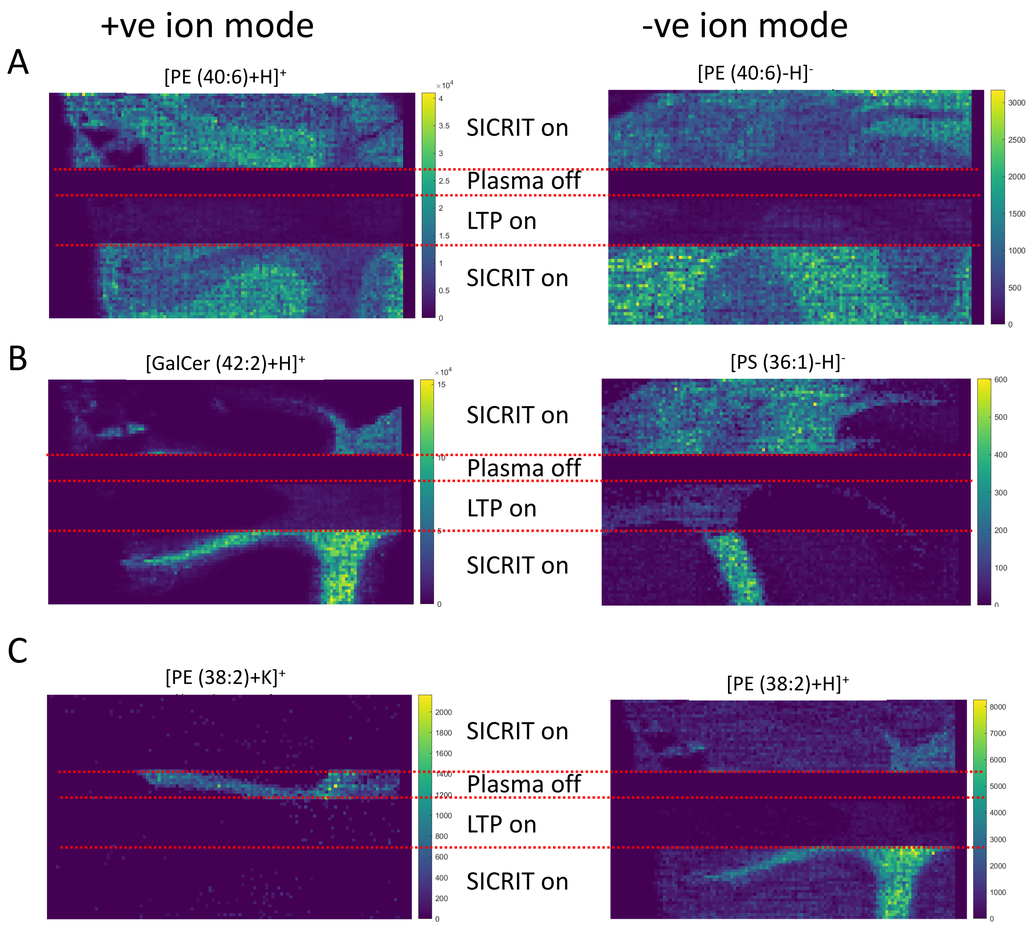


Figure 2. Selected single ion images of mouse brain sections acquired at 20 µm pixel size in both +ve and –ve ion mode. (A) A typically observed PE lipid (PE (40:6)) mainly localised in the white matter. (B) Evidence of plasma induced post-ionisation events; detection of GalCer (42:2) and PS(36:1) only when either plasma devices are on. (C) Plasma enhancement of protonation event over salt adduct formation.

Thin film analysis

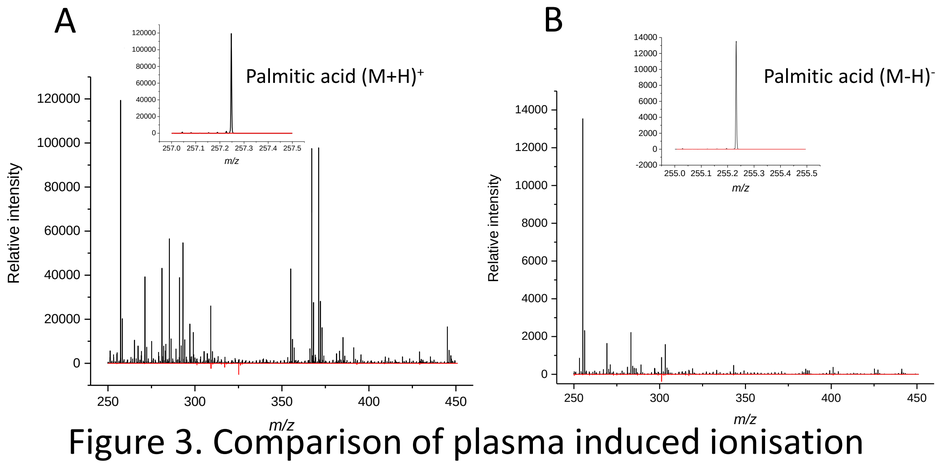


Figure 3. Comparison of plasma induced ionisation enhancement between the LTP probe (red trace) and the SICRIT device (black trace) in (A) +ve ion and (B) –ve ion mode.

Compound	Monoisotopic mass	SICRIT plasma enhancement	
		+ve ion mode	-ve ion mode
Glutamine	146.0691	20x	-
Lysine	146.1055	20x	-
Arginine	174.11167	-	-
Choline	104.10699	**No change**	-
Palmitic acid	256.2402	10000x	1000x
PC(36:1)	787.6091	100x	-
Raffinose	504.16904	-	-
Glutathione	307.0838	-	-
Arachidonic acid	304.2402	10000x	100x
Glutamate	147.0532	-	10x

Discussion

- We have successfully showcased the integration of the SICRIT® plasma device with an TM-AP-MALDI imaging setup. Ease of setup of SICRIT® device, as well as minimal user input makes this an ideal method for post-ionisation in MALDI-MSI
- An ionisation enhancement by at least an order of magnitude was observed for several small molecules from a thin films. Interestingly molecules that are already charged, such as choline, did not appear to be influenced by the plasma. These results confirm our previous observations using an LTP probe[1]
- Evidence of plasma post-ionisation observed when imaging biological tissue sections, evident by the detection of the post-ionised GalCers
- Higher ion intensities obtained by plasma post-ionisation now allow for AP-MALDI MSI at greater spatial resolution e.g. < 5 µm

References

[1] Steven et al., 2019, Analytica Chimica Acta
[2] Salter et al., 2013, Anal. Chem.
[3] Race et al., 2016, Anal. Chem.

Acknowledgements

- This work was supported by NPL Strategic Capability Program 'AIMS Higher'
- We greatly acknowledge Sue Kennerly for kindly providing the SICRIT device

Department for Business, Energy & Industrial Strategy
FUNDED BY BEIS