Talanta 132 (2015) 579–582

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Short communication

Application of laser microdissection ICP–MS for high resolution elemental mapping in mouse brain tissue: A comparative study with laser ablation ICP–MS

Alessandra Sussulini *, J. Sabine Becker

Zentralinstitut für Engineering, Elektronik und Analytik, Analytik (ZEA-3), Forschungszentrum Jülich, D-52425 Jülich, Germany

ARTICLE INFO

Article history:
Received 19 August 2014
Received in revised form
29 September 2014
Accepted 1 October 2014
Available online 14 October 2014

Keywords:
Laser microdissection
Laser ablation
Inductively coupled plasma mass spectrometry
Mouse brain
Mass spectrometry imaging
Quantification

ABSTRACT

Mapping of elements in biological tissue by laser induced mass spectrometry is a fast growing analytical methodology in life sciences. This method provides a multitude of useful information of metal, nonmetal, metalloid and isotopic distribution at major, minor and trace concentration ranges, usually with a lateral resolution of 12–160 μm. Selected applications in medical research require an improved lateral resolution of laser induced mass spectrometric technique at the low micrometre scale and below. The present work demonstrates the applicability of a recently developed analytical methodology – laser microdissection associated to inductively coupled plasma mass spectrometry (LMD ICP–MS) – to obtain elemental images of different solid biological samples at high lateral resolution. LMD ICP–MS images of mouse brain tissue samples stained with uranium and native are shown, and a direct comparison of LMD and laser ablation (LA) ICP–MS imaging methodologies, in terms of elemental quantification, is performed.

1. Introduction

Laser microdissection (LMD) is a technology that isolates specific cell populations from heterogeneous tissue sections under direct microscopic visualization by means of a highly focused laser beam [1,2]. The development of laser-based tissue microdissection systems has provided the basis for the rapid acquisition of specific morphologically and/or phenotypically distinct types of cells for different types of molecular analysis. This has permitted the cell-type specific molecular analysis of solid tissues, especially biopsies (samples of tissue taken for determine the presence or extent of a disease), and has provided new insights into both physiological cell mechanisms and pathomechanisms [3]. For example, a specific part of the hippocampus of brain tissue, cornu ammonis (CA1) pyramidal neurone layer, could be isolated for targeted proteome analysis from a transgenic rat carrying a human amyloid precursor protein transgene using LMD [4].

Recently, Becker and coworkers [5–8] proposed the coupling of LMD to an inductively coupled plasma (ICP) mass spectrometer in order to obtain elemental images of thin biological tissues. In this methodology, LMD acts as an ablation system, where a glass chamber is placed over the sample and a flow of a carrier gas transports the ablated material, and the ICP mass spectrometer operates as the detector for metals, semimetals and non-metals that are present in the biological tissue sample [7].

In the pioneer LMD ICP–MS work [5], a lateral resolution of 3 μm was obtained for a brain tissue impregnated with a droplet of highly concentrated copper solution (1000 mg L^{-1}). It is expected that with the insertion of a more powerful laser in the LMD microscope and the coupling to a more sensitive mass spectrometer (sector field ICP–MS instead of the currently used quadrupole ICP–MS), a lateral resolution up to 300 nm range should be possible in future investigations, opening up the field of quantitative single cell analysis and imaging.

The improvement of LMD ICP–MS analytical features can make possible to acquire more precise and detailed information on elemental distribution in brain samples and other biological tissues at low-micrometre and nanometre scale, as a LMD microscope allows the observation and selection of specific structures and single cells, which can be ablated by the focused laser beam with a lateral

Table 1
LMD ICP–MS imaging applications described in the literature.

Detected analytes	Sample	Refs.
^{63}Cu, ^{65}Cu	Mouse brain (Cu-stained)	[5]
^{13}C, ^{23}Na, ^{24}Mg, ^{31}P, ^{39}K, ^{56}Fe, ^{63}Cu, ^{64}Zn	Mouse brain	[6]
^{13}C, ^{23}Na, ^{24}Mg, ^{31}P, ^{39}K, ^{56}Fe, ^{64}Zn	Rat brain	[7]

* Correspondence to: Department of Analytical Chemistry, Institute of Chemistry, Universidade Estadual de Campinas, PO Box 6154, 13083-970 Campinas, SP, Brazil. Tel.: +55 19 35213060.
E-mail address: sussulini@iqm.unicamp.br (A. Sussulini).

http://dx.doi.org/10.1016/j.talanta.2014.10.001
0039-9140/

resolution down to the low and sub-micrometre scale [5,9]. Table 1 illustrates the LMD ICP–MS imaging experiments described in the literature until the present moment.

In this work, the application of LMD ICP–MS to elemental imaging of native and metal-stained mouse brain tissues is shown. Uranium was chosen for tissue staining since it is important when

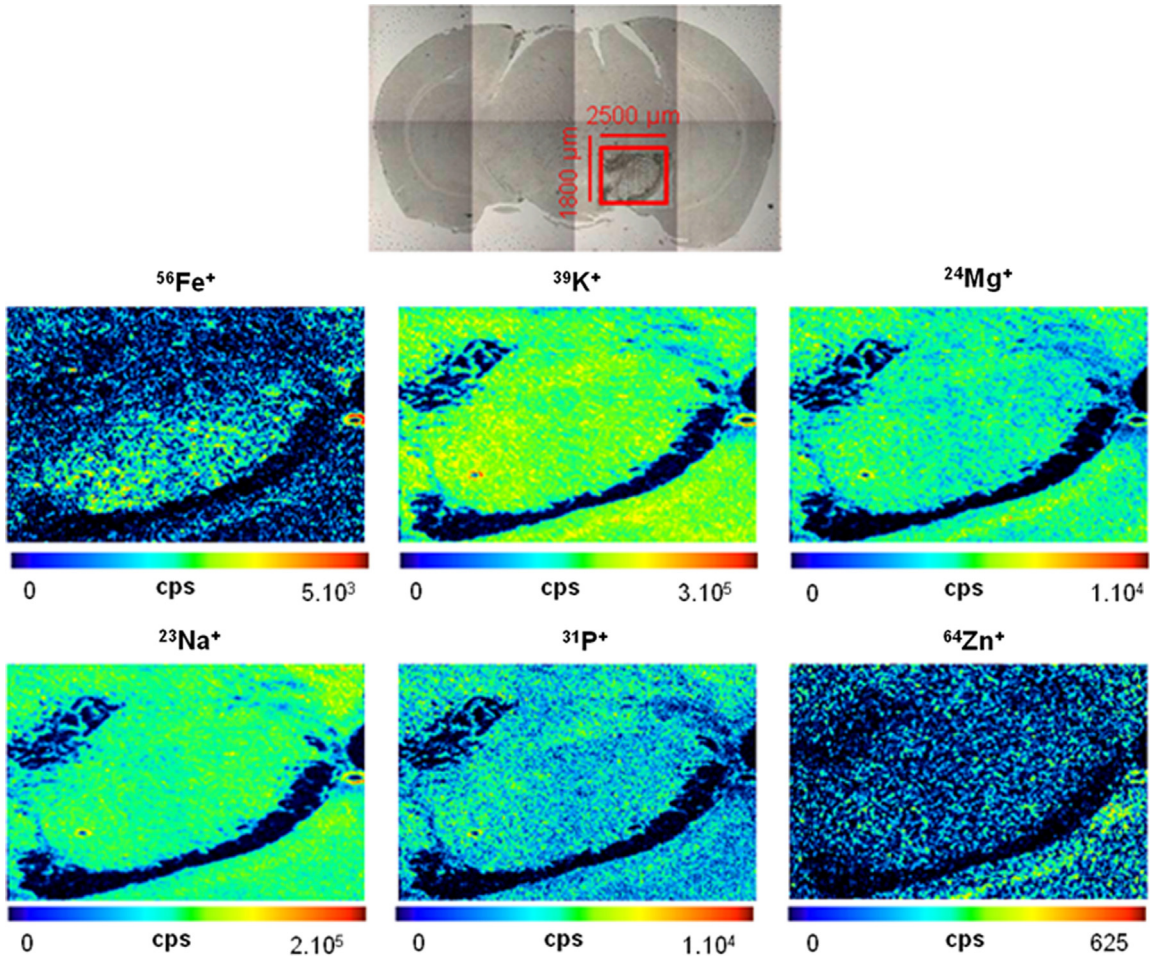

Fig. 1. LMD ICP–MS qualitative images with lateral resolution of 6 µm for a native mouse brain tissue (substantia nigra region).

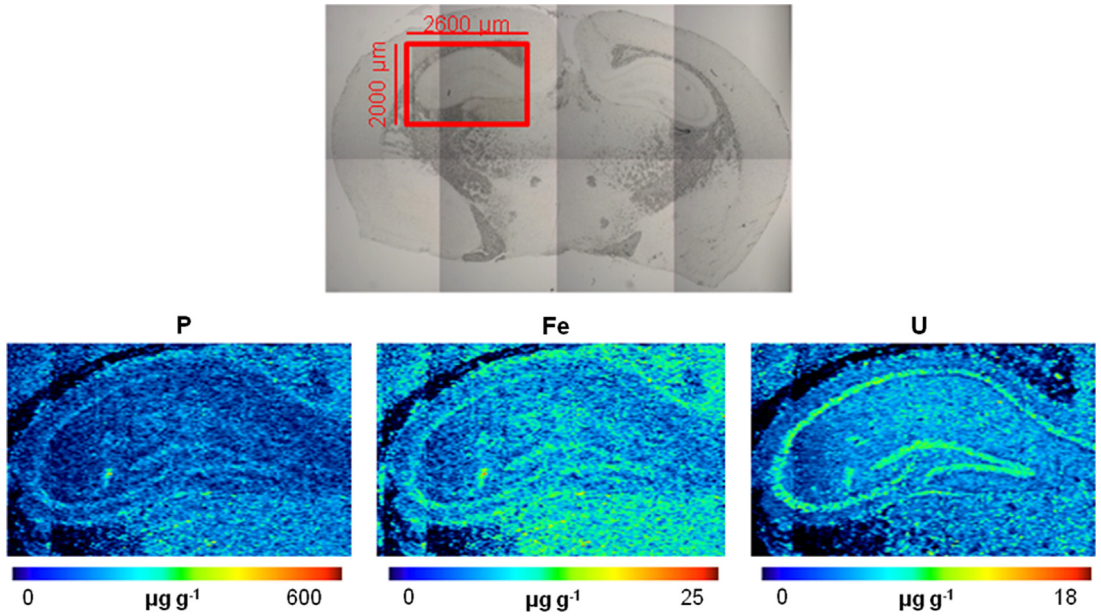

Fig. 2. LMD ICP–MS quantitative images with lateral resolution of 4 µm for a mouse brain tissue (left hippocampus region) stained with ^{238}U solution at 100 µg L^{-1}.