Poster Note 43316

High Resolution Elemental Mapping of Biological Samples by High Sensitivity, Fast-Scanning LA-ICP-MS

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Overview

Purpose: To demonstrate the use of LA-ICP-MS for high spatial resolution metallomic imaging mass spectrometric analysis of biospecimens relevant to medical research on traumatic brain injury.

Methods: Samples were prepared and subsequently analyzed by LA-ICP-MS. Metallomic distribution images were constructed using in-house built MATLAB scripts.

Results: Elemental and isotopic images for a series of biological samples were produced and evaluated with results from optical imaging.

Introduction

We have developed a technique – metallomic imaging mass spectrometry (MIMS) tissue mapping – to localize and quantify neuroinflammation and disruption to the blood-brain barrier (BBB) following experimental traumatic brain injury (TBI). This novel method provides a wide detection range and permits single-run, multi-elemental and/or isotopic mapping in tissue specimens with variable elemental/isotopic concentration and composition .

Methods

Instrumentation

Mouse brain samples were sampled using a Teledyne CETAC LSX-213 G2+™ laser ablation system equipped with the HelEx II active 2 volume laser cell for optimum washout. Laser parameters:

- Spot size: 20 µm
- Shot frequency: 20 Hz
- 100% laser energy
- Single line scan
- Pause between lines: 30 s.

The ablated material was carried in a helium stream to either a quadrupole (Thermo Scientific™ iCAP™ Q) or high resolution (Thermo Scientific™ ELEMENT XR ™) ICP-MS for analysis.

FIGURE 1. Combined LSX-213 G2+ / iCAP Q LA-ICP-MS system

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Results

Mapping the metallome of the mouse hippocampus by MIMS (ELEMENT XR ICP-MS).

FIGURE 2. Mouse brain, Nissl stain. Red box, hippocampus and dentate gyrus, critical brain regions for memory formation. Allen Institute for Brain Science.

FIGURE 3. Mouse hippocampus and dentate gyrus showing areas of zinc enrichment by Timms stain. (Frederickson CJ, *et al.*, *J Nutr* 130:1471, 2000).

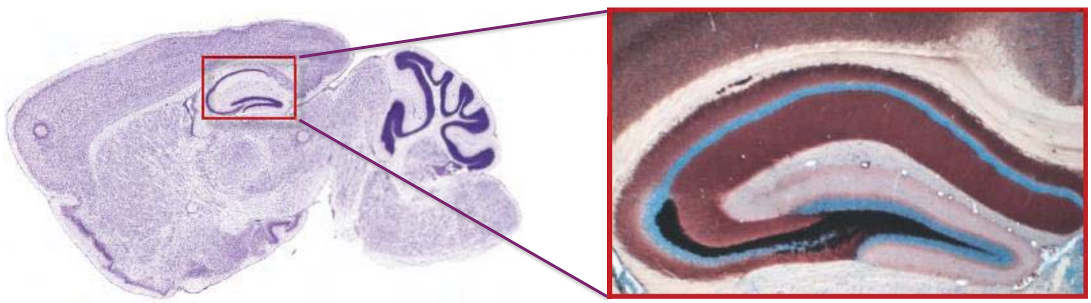


FIGURE 4. ^{56}Fe MIMS map (20 µm resolution)

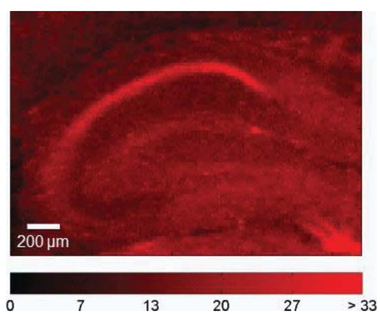


FIGURE 5. ^{65}Cu MIMS map (20 µm resolution)

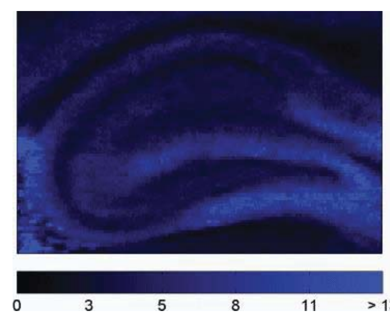


FIGURE 6. ^{70}Zn MIMS map (20 µm resolution)

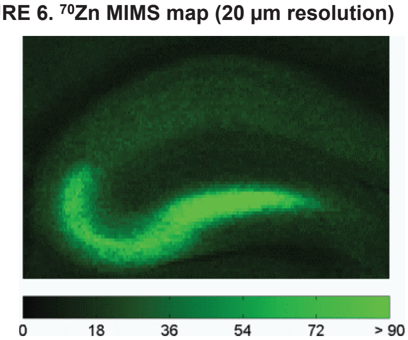


FIGURE 7. Composite ^{56}Fe, ^{63}Cu, ^{70}Zn MIMS map with elemental concentrations at a selected point (CA1 subfield), boxed region (dentate gyrus), and segmentation area (CA3 subfield).

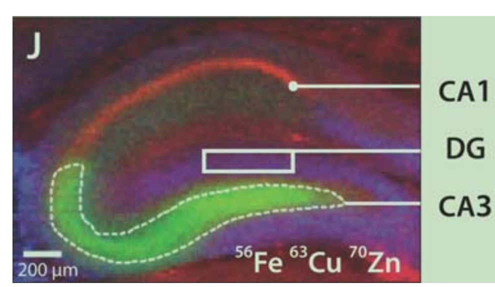
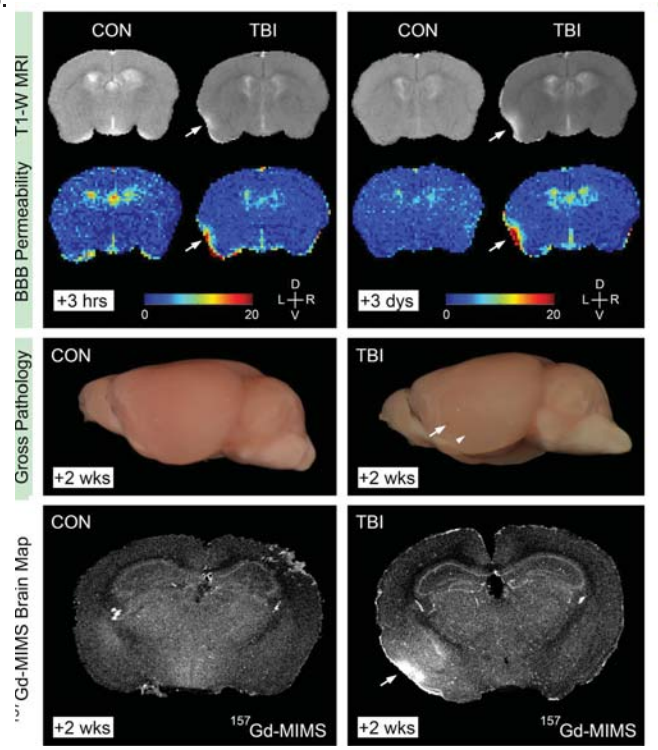


FIGURE 8. ^{157}Gd-MIMS (iCAP Q ICP-MS) mapping of the mouse brain after experimental traumatic brain injury (TBI).



Note the correspondence between the MRI-detectable enhancement in the left perirhinal cortex (arrows, top two rows) and Gd accumulation in the ^{157}Gd-MIMS map (arrow, bottom row). The ^{157}Gd-MIMS map provides direct quantitative evidence of anatomically localized BBB disruption following impact TBI. The closed-head concussive impact injury induced only minor contusion (third row). These MIMS results provide clinical insights into the pathophysiological mechanisms of concussion and acute neurotrauma (taken from Tagge et al., in preparation).

Conclusion

- MIMS analysis enables high-throughput, high spatial resolution, multi-elemental analysis of biological samples with definitive elemental/isotopic identification.
- Metallomic distribution provides clinical insights in the blood brain barrier dysfunction and neuroinflammation that are not provided by traditional techniques.

Acknowledgement

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