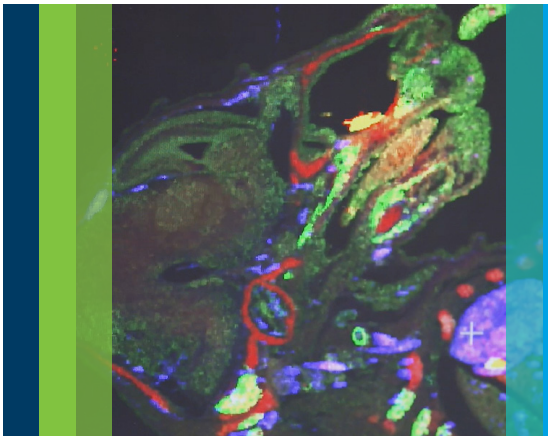


Agilent Case Study: Ghent University

Mapping Elements In Biological Tissue Using Laser Ablation ICP-MS

Measuring signals lasting only half a millisecond to map the quantitative distribution of elements across the surface of a tissue sample.

Agilent spoke to Dr. Thibaut Van Acker, a postdoctoral researcher in the Atomic and Mass Spectrometry (A&MS) research group at Ghent University in Belgium.

Q. Please describe your research project

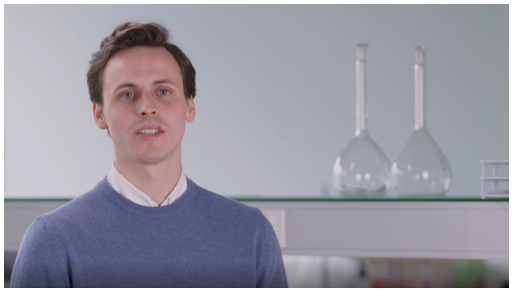
My research at A&MS is focused on developing new analytical methods for laser ablation ICP-MS, to reveal the quantitative distribution of elements in biological tissue. We collaborate with many internal groups here at Ghent University, but also with external partners.

Q. Can you describe the measurement process you are using?

Our research partners deliver biological tissue samples to us, usually as thin sections on a standard glass microscope slide. We load the slides into the sample holder, which is then placed inside the laser ablation chamber. The ablation chamber is supplied with a flow of helium, which generates a slight overpressure in the chamber. The helium acts as the carrier gas to transport the ablated material to the ICP-MS for analysis.

We focus the laser beam on the surface of the biological tissue and fire laser pulses to ablate material from the sample. By moving the sample holder using x/y stepper motors, we can control the point on the sample that we ablate, and we scan across the tissue line-by-line to build up a 2-dimensional map of the elemental content.

The material that is ablated from the sample is in the form of vapor and small particles, and this is carried from the ablation site via transport tubing into the ICP-MS. The sample material is vaporized, atomized and then ionized within the ICP-MS plasma. The mass spectrometer separates the ions as a function of their mass-to-charge ratio, so we can measure the ions and calculate the elemental content of each ablated spot on the sample.



"The information that can be gained from the biological tissue is just way more comprehensive than before."

Dr. Thibaut Van Acker
Postdoctoral researcher
Ghent University

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Q. What features of the ICP-MS are important for your measurements?

Due to recent hardware developments we've done, we've been able to achieve peak profiles for laser ablation ICP-MS that are approaching the profiles that are typically encountered in single-particle ICP-MS. These peak profiles typically last for only half a millisecond. To measure the elemental signals in the short-lived peaks, we really need to use short dwell times and a fast detector. And when you use very short dwell times, you also need a very high sensitivity—or rather, very high signal-to-noise ratio—to be able to detect elements at lower concentrations. The Agilent 8900 provides this capability. The instrument can detect the fast transient peaks we are generating with our laser ablation unit equipped with a fast ablation cell. The Agilent instrument delivers excellent sensitivity and spatial resolution across the tissue sample.

Q. What new measurement capabilities have you been able to achieve?

By using some hardware developments to minimize the dispersion of the plume of material created by each laser ablation shot, we can use much higher laser pulse repetition, with rates of up to 1 kiloHertz—1 thousand shots per second. We were also able to boost our signal-to-noise ratio and achieve much higher sensitivity. These improvements allow us to use smaller laser spot sizes, which improves spatial resolution. We can now generate elemental maps much faster and with better image resolution while still measuring elements at the concentrations of interest to our research partners.

Q. What are these measurements being used to study?

These measurements can be used to study the migration of pharmaceuticals into different tissue types. For example, we have been working with a pharmaceutical company to develop analytical methodology to reveal the quantitative distribution of platinum-based chemotherapeutic compounds in kidney tissue. Our measurements show the distribution of the drug compound at high spatial resolution. This allows us to identify the regions of the kidney tissue where the highest levels were detected, with the highest being in the renal cortex. We could also show damage to kidney cells when working at ultra-high spatial resolution, mapping the distribution of platinum at 1 micrometer spatial resolution.

Q. What other types of analysis are you planning?

One of the hot topics for ICP-MS is single-cell ICP-MS, which involves introducing a suspension of cells into the ICP. Laser ablation can also be used to analyze single cells if they are plated on a microscope slide or a glass cover slip. The laser can be focussed on each cell, ablating them one by one.

This technique is slower than measuring the cells in suspension, but we don't have to worry about the background signal or elemental contamination that the suspension solution can introduce. Laser analysis also avoids the possibility of cell lysis during the nebulization process.

Q. Where do you see the LA-ICP-MS technique being used in the future?

Ten years ago, laser ablation ICP-MS imaging was relatively slow and the resolution quite low. Pixel generation happened at only 1 or 2 hertz. We can now do 1,000 pixels per second. So that's multiple orders of magnitude faster. This means that imaging applications that were previously not possible are now possible. We can generate elemental maps at much higher spatial resolution. The information that can be gained from the biological tissue is just way more comprehensive than before.

We have established more and more collaborations, based on what our techniques can deliver in terms of the contribution to medicine and biomedical research. When people know what we can do, sometimes multiple collaborations pop up. There are many options which they take advantage of with our technique to increase the information they get from their samples.

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RA44789.6271412037

Published in the USA, February 15, 2023
5994-5235EN

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