Nanoparticle Mapping in Tissues by LA-ICP-MS

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Laser Ablation ICP-MS

In Laser Ablation ICP-MS, a high powered pulsed laser is directed onto a solid surface whereby surface materials are ejected into a helium stream, which rapidly carries the particles to the ICP-MS for detection.

This allows the full detection power of the ICP-MS to be applied directly to solid samples without the need for digestion, as well as retaining spatial information. Figure 1 displays a laser ablation ICP-MS schematic.

The ability to spatially resolve elements of interest allows for LA-ICP-MS to function as an elemental microscope that can complement other imaging techniques to give more complete information about a sample.

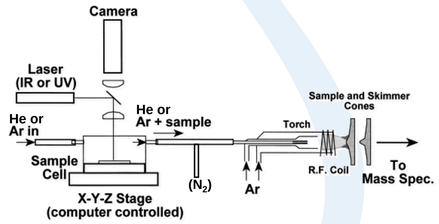


Figure 1: LA-ICP-MS schematic

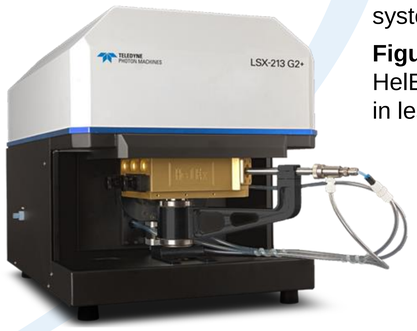
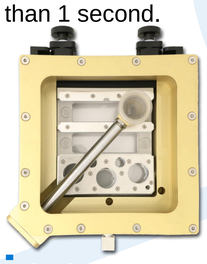


Figure 2a (left): Teledyne CETAC LSX-213 G2+ laser ablation system used in this study.

Figure 2b (below): Two volume HelEx Cell allows for 99% washout in less than 1 second.



Introduction

Silver nanoparticles are increasingly used in medical and daily life products owing to a greater likelihood of exposure and uptake.
In this study the gastrointestinal tract of a rat given a daily oral dosage of nanopartlces is investigated. The gastrointestinal tract consists of stomach, small intestine (divided into duodenum, jejunum, and ileum) and the large intestine. The objective of this method development was to answer:

How are nanoparticles distributed in the gastrointestinal tract after oral uptake?

Nanoparticle Mapping

Treatment of the rat: Oral application of 1000 mg/kg bodyweight per day of AgNP ranging in size from 30 – 90 nm. Treatment over a time period of 4 weeks. Rats were sacrificed and the small intestine divided into duodenum, jejunum, and ileum embedded in paraffin and cut into thin sections (7 micron).

Quantification strategy: Size dependent external calibration using chicken liver. AgNP were spiked and homogenized with chicken liver then frozen. The frozen homogenized livers were cut into thin sections of 7 micron thickness and then ablated with the ICP-MS collecting in single particle mode. The quantification strategy resulted in a sized dependent calibration curve.

Elemental Mapping: Single line scans using the Teledyne CETAC LSX-213 G2+ laser were made across each sample with the ICP-MS collecting data in single particle mode. Data was collected for ^{107}Ag and then mapped using the size specific calibration. Figure 2 displays an example line scan from the Ileum.

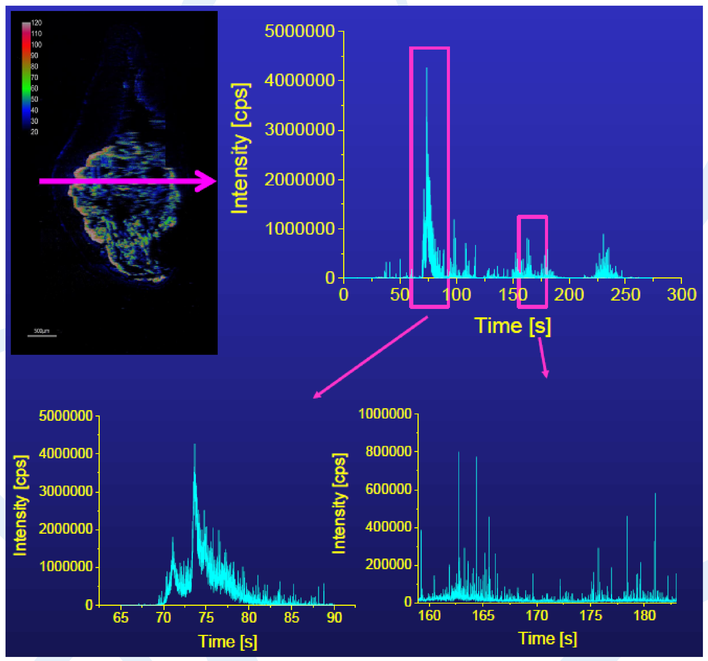
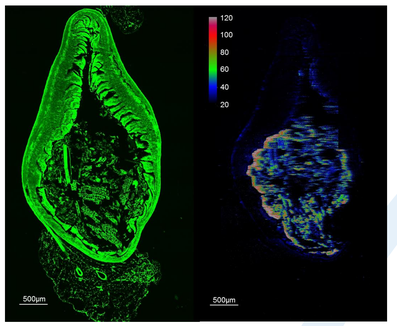


Figure 3a (top) Single line scan of the duodenum (bottom)
Figure 3b (bottom) Further investigation of the high intensity indicates intensity due to detection of multiple particles

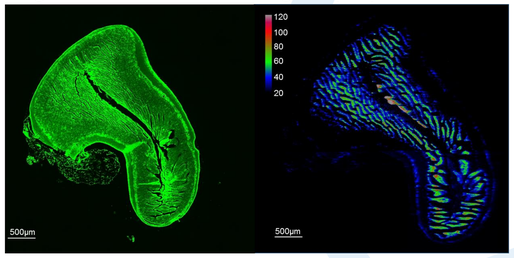
Results

The results below show two images for each of the three portions of the small intestine that were evaluated. The images on the left show an autofluorescence microscope image of the sample and the image on the right show the response for ^{107}Ag. Detected nanoparticles give transient signals. Size dependent calibration curve allows to calculate the diameter of a nanoparticle according to the intensity of the ICP-MS signal. In the plots below the color scale shows particle diameter (nm).



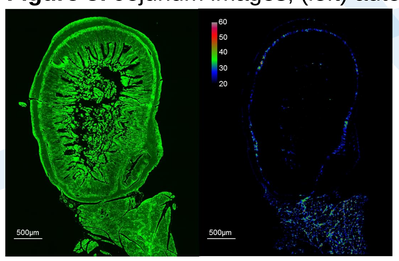
- Silver distribution shows good correlation to the structure of the organ
- AgNP are mainly in the intestinal villi of the deodenum and jejunum
- Little silver found in the outer connective tissue

Figure 4: Duodenum images, (left) autofluorescence, (right) ^{107}Ag



- Silver is not found in the muscle layer of any of the intestinal sections

Figure 5: Jejunum images, (left) autofluorescence, (right) ^{107}Ag



- In the Ileum, silver is only found in the outer connective tissue
- No evidence for nanoparticles in the spectrum of the ileum (figure 6) and no uptake into intestinal villi

Figure 6: Ileum images , (left) autofluorescence, (right) ^{107}Ag

Conclusions

Resolution of single particles in most parts of the organs was accomplished. Signals from single nanoparticles and other silver can be distinguished. LA-ICP-MS is a useful tool for elemental bioimaging.