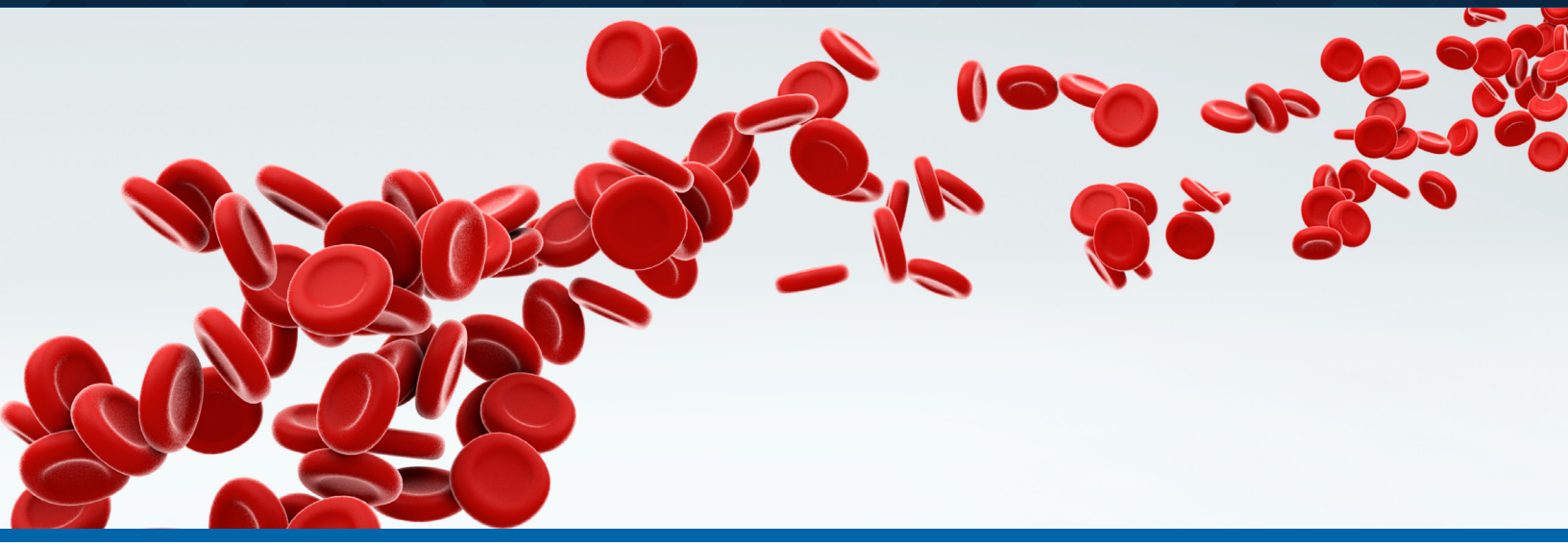
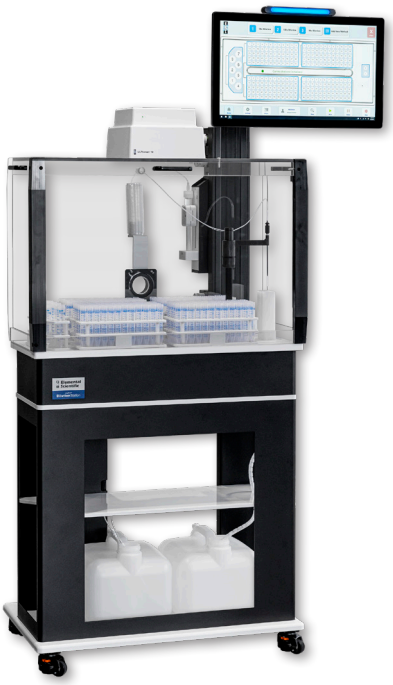
Elemental Scientific

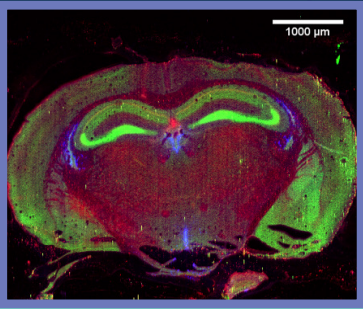


Clinical Product Portfolio

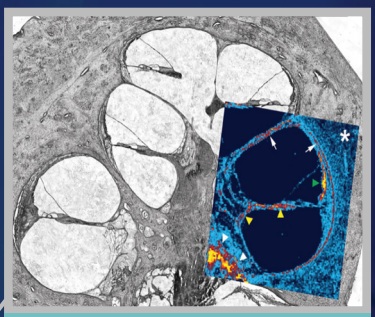
Liquid and Solid Sample Introduction Systems for ICP and ICPMS



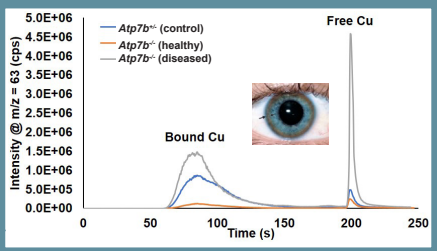
Elemental Scientific



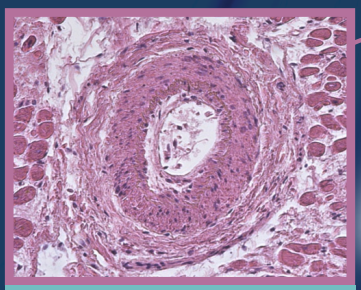
Age related changes in the brain



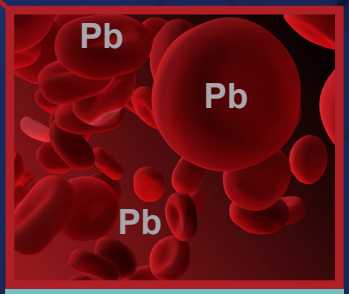
Cisplatin distribution in the ear



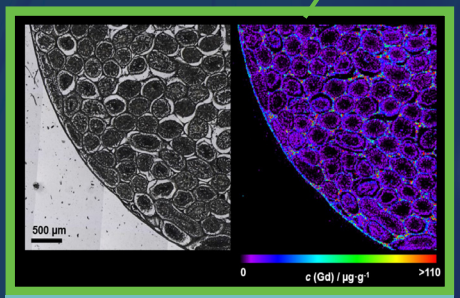
Free Cu determination in patients with Wilson disease



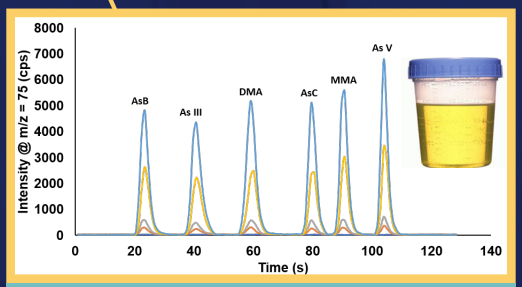
Microscope image of heart tissue



Detection of Pb levels in blood



Gd distribution in testicles after administration of MRI contrast agents



Toxicology - Arsenic exposure

Introduction

Three main areas of research – experimental, clinical, and epidemiological – cover a broad spectrum of application areas and disciplines that are critical for better understanding human longevity and survival. For the most part, the analytical instrumentation needed to support these areas of research is either molecular/organic or elemental/inorganic in nature. Historically, most research has focused on molecular applications, but a great deal of critical information can be obtained from inorganic analysis. The relatively new field of Metallomics, the study of how metals and metalloids interact within biological systems, originated as an effort to bring together research areas including various fields of chemistry – analytical, bioinorganic, medicinal, environmental, and biophysical – and cell, plant, and chemical biology. This multidisciplinary approach has provided key insights into the role of inorganic metals in biology in recent years.

Some of the areas of research in the field of Metallomics:

- Metalloproteins
- Metal regulation, protein receptors
- Metals in cells
- Metal chelation in the liver
- Metal accumulation in brain, kidney, liver, bone, etc.
- Metals in plants
- Metal based chemotherapy cancer drugs (e.g. Ru and Pt)
- Impact of metal-on-metal implants in the body
- Nanoparticle accumulation in the cells/organs/body (e.g. Ti, Cu, Ag, Au, and Mn)

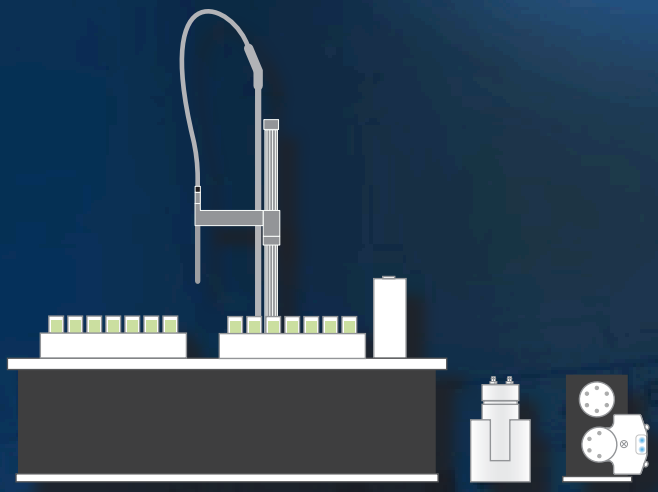
Elemental Scientific (ESI) provides sample introduction systems that increase laboratory productivity and make it possible to collect high-end scientific data with ICP or ICPMS instruments. The sample introduction technology provided by ESI offers wide-ranging solutions for both liquid and solid analyses. This technology includes nebulizers, basic sample introduction components, autosamplers, and complete systems for inline and offline sample preparation, laser ablation, and chromatography. These products are vital for research that falls into the realm of Metallomics.

ESI provides many sample introduction systems for ICP & ICPMS:

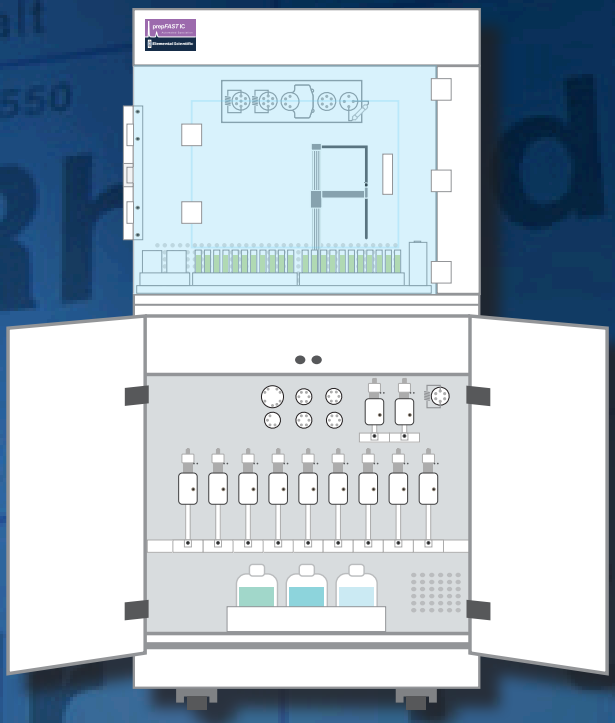
- Solid Sampling
  - imageBIO266
- Liquid Sampling
  - SampleSense *FAST* UHT-C
  - prep*FAST* IC (Clinical)
  - prep*FAST* IC UHT
  - **Dilution**Station (Offline)

Elemental Scientific

Sample Introduction Systems

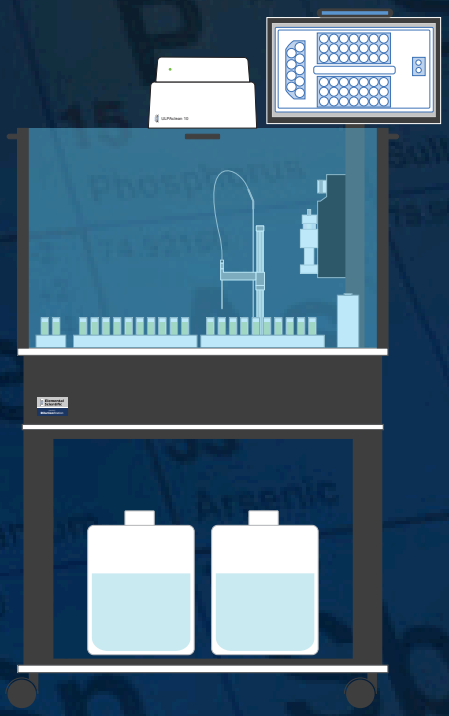


SampleSense *FAST* UHT-C



prep*FAST* IC (Clinical)

Elemental Scientific



DilutionStation

imageBIO266

imageBIO266

Laser Ablation

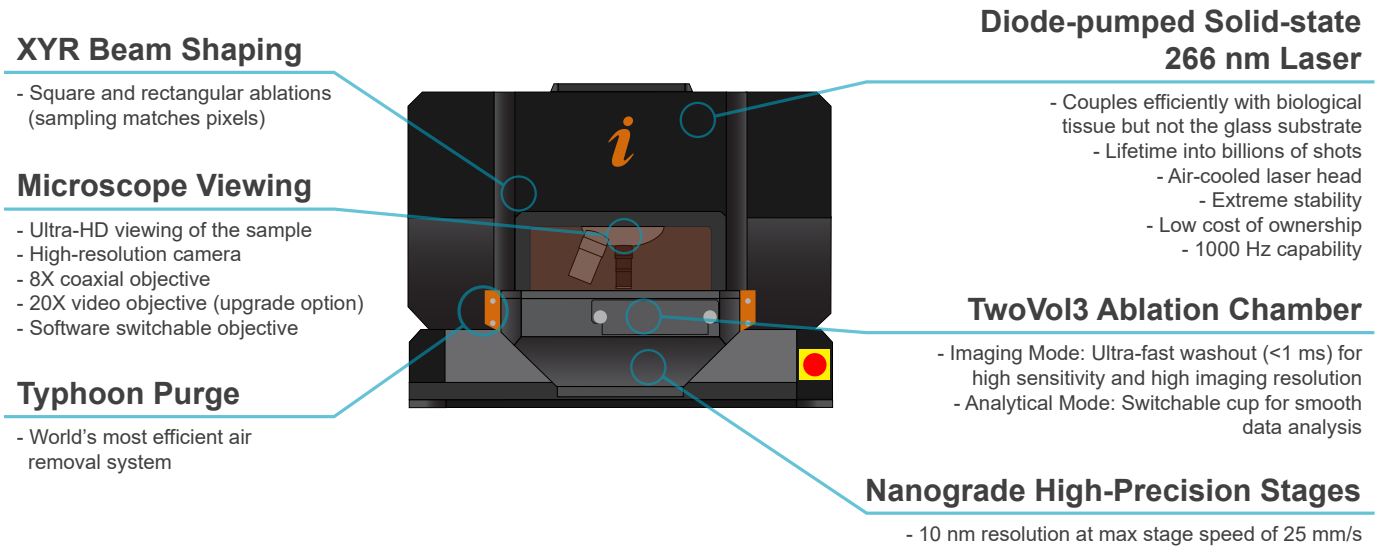
Laser Ablation-Inductively Coupled Plasma Mass Spectrometry (LA-ICPMS) offers the ability to remove and analyze microscopic quantities of material from solid samples without the need to solubilize the sample by acid digestion or other laborious wet chemistry techniques. Laser pulses interact with the surface of a sample, ejecting material as a small, extremely hot plasma in which the ablated material is vaporized and atomized. As the plasma cools, nanoparticles and agglomerates of particles form and are swept to the ICPMS torch by helium gas. This technique can be used to determine elemental information for bulk analysis, depth profiling, imaging, or localized (single location) analysis on scales ranging from sub-micron to centimeters.

imageBIO266

LA system designed solely for elemental imaging of biological matrices.

The imageBIO266 utilizes a 266 nm nanosecond laser to ablate biological samples that are fixed onto glass slides. There are a multitude of benefits for using a 266 nm laser:

- The laser beam couples efficiently with biological tissue and not the glass substrate. Unnecessary ablation of the glass substrate may lead to false interpretations of the elemental distribution within the biological sample.
- The lifetime of the laser (billions of laser shots) is longer than other laser options.
- It offers low cost of ownership.



imageBIO266

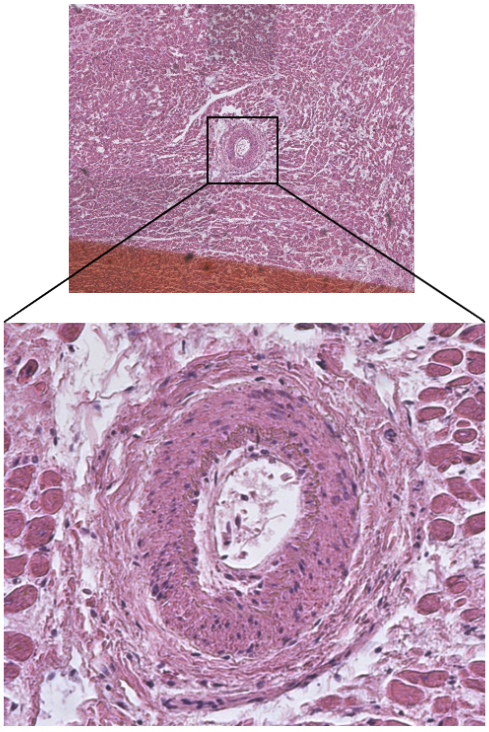
Spatially resolved information, generally in the nm–µm range, can be obtained using the TwoVol3 ablation chamber with ultra-fast washout in conjunction with high-precision stages to carefully move the sample in a controlled manner. Correlating the well-defined position on the sample with the ICPMS data allows for the creation of detailed elemental images in a technique known as bioimaging. This system is ideal for analyzing biological tissue sections to aid in the understanding of:

- Determining disease-related metal distributions within tumors, cells, or organs.
- Investigation of metal-based drug delivery within cells or tumors (e.g. cisplatin, chemotherapy drug).
- Understanding occupational/industrial exposure within the body (e.g. metal accumulation within the brain, liver, kidney, etc.).
- Simultaneously imaging multiple biomolecule distributions via metal-labelled monoclonal antibodies.

The particle delivery system is an extremely important aspect of the LA system, consisting of a two-volume laser ablation sample chamber and the dual concentric injector (DCI). The DCI allows for particles to be introduced directly into the ICP plasma, resulting in ideal transient peaks for elemental imaging and eliminating any potential washout issues. The latest two-volume chamber (TwoVol3) has been designed for fast, high-resolution imaging work ideal for clinically related applications.

Bioimaging examples:

- Determination of Gd-based contrast agents being retained in a rat exposed to Omniscan.
- Elemental distribution in a dragonfly wing to better understand pigmentation and resilin structure composition.
- Correlation of Pt distribution in the cochlea and ototoxicity (hearing loss) from cisplatin chemotherapy.
- Detection of asbestos in human mesothelioma cells.



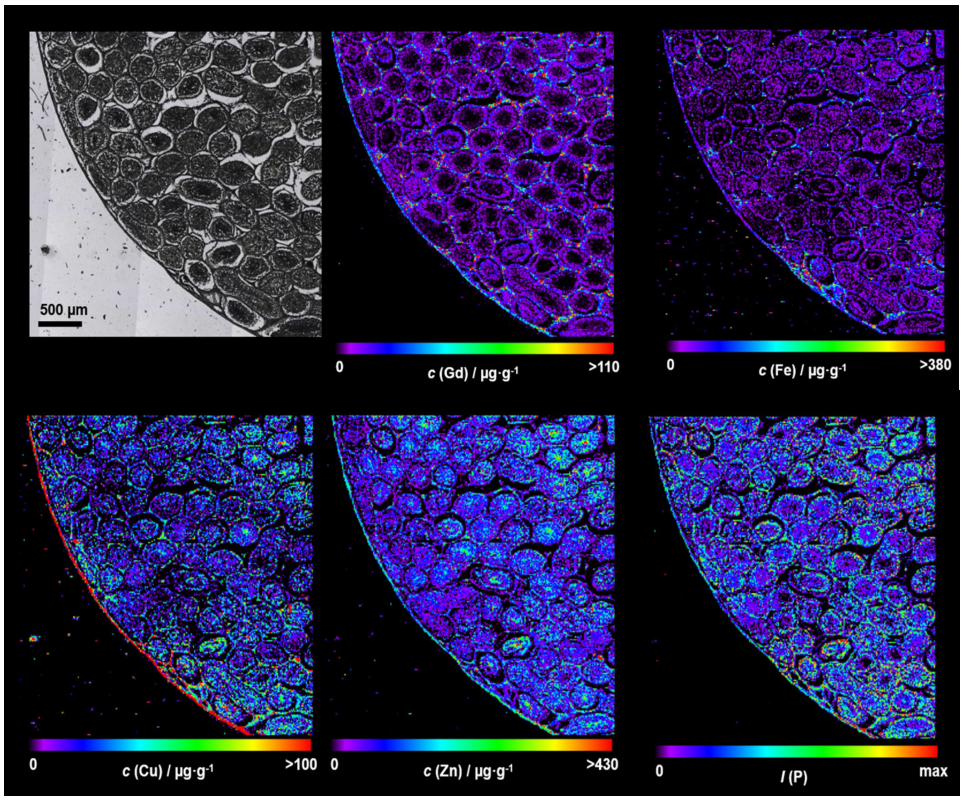
***See page 31 for ordering information**

imageBIO266

Gd-based MRI Contrast Agents

Magnetic resonance imaging (MRI) is a common non-invasive medical imaging technique. To increase the imaging quality, common practice is to administer Gd-based contrast agents. However, since Gd^{3+} is highly toxic and competes with Ca within the body, it is complexed in linear or macrocyclic chelating agents to reduce toxicity. These compounds were thought to excrete from the body within 12 h (~90%) and reach 99% excretion after one week. On the contrary, it was determined that certain forms of Gd remain in the body much longer than originally anticipated, with macrocyclic agents being more stable, and therefore more excretable and safer for medicinal applications, than the linear agents. In 2017, Europe suspended the use of two agents and limited the use of two others based on these findings.

A rat was administered 7.5 mM/kg Omniscan (suspended Gd-containing linear agent) and sacrificed 14 days later to determine if/where Gd was retained in the body. The example shown below is a 10 µm cross section of a rat testicle analyzed by LA-ICPMS using the imageBIO266 system.



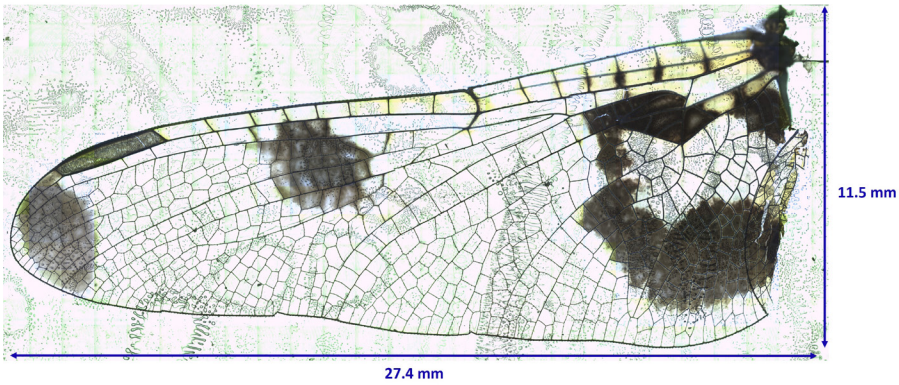
The Gd response ranges from a mean concentration of <10 µg/g with the seminiferous tubules up to locally very high concentrations (100s µg/g) with the interstitium.

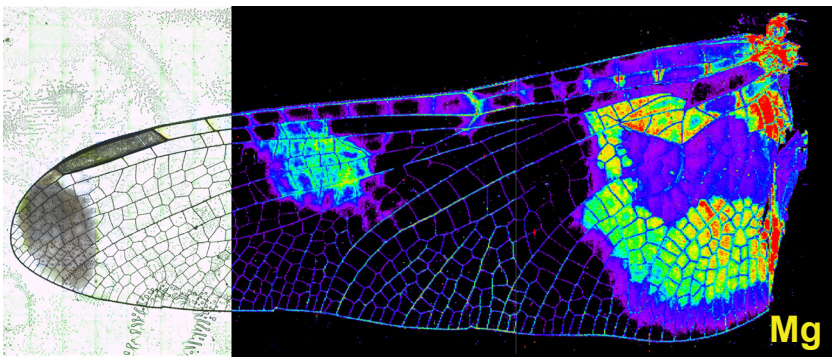
Data and images courtesy of Sabrina Funke and Uwe Karst, University of Muenster, Muenster, Germany.

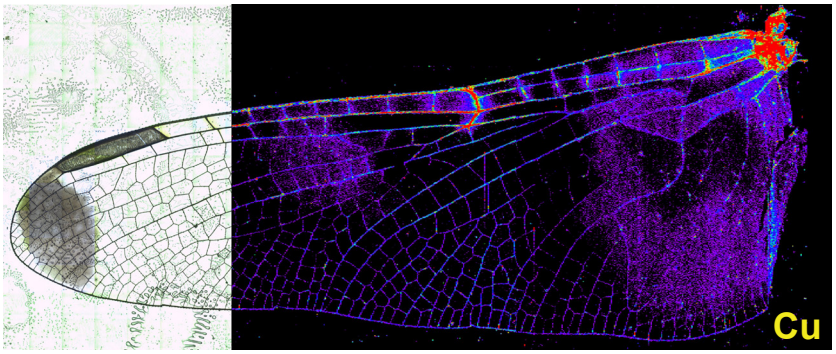
imageBIO266

Multi-Elemental Imaging – Dragonfly Wing

Dragonfly wings are of interest to medical research as well as military-related applications. The pivot joint and the tissue structure along the top of the wing are extremely flexible, lightweight, and strong, made from an elastomeric protein known as resilin. Medical researchers are interested in understanding resilin to aid in the development of new suture materials and prosthetic veins/arteries, and bioimaging with the imageBIO266 can provide insights into these structures at the elemental level. The speed of the imageBIO266 allows for large elemental maps to be constructed in a few hours, whereas, with other systems it could take over 24 h to collect the same type of data. In addition, dragonflies have unique markings and patterns that aid in camouflage and species identification. Understanding the elemental make-up of these pigments can help create natural pigmentation colors for military applications.



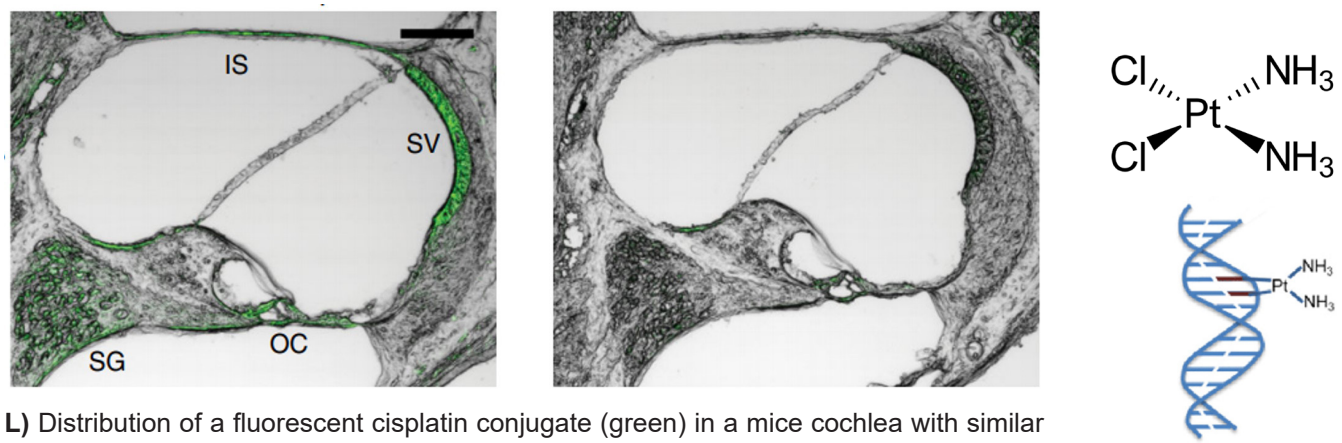




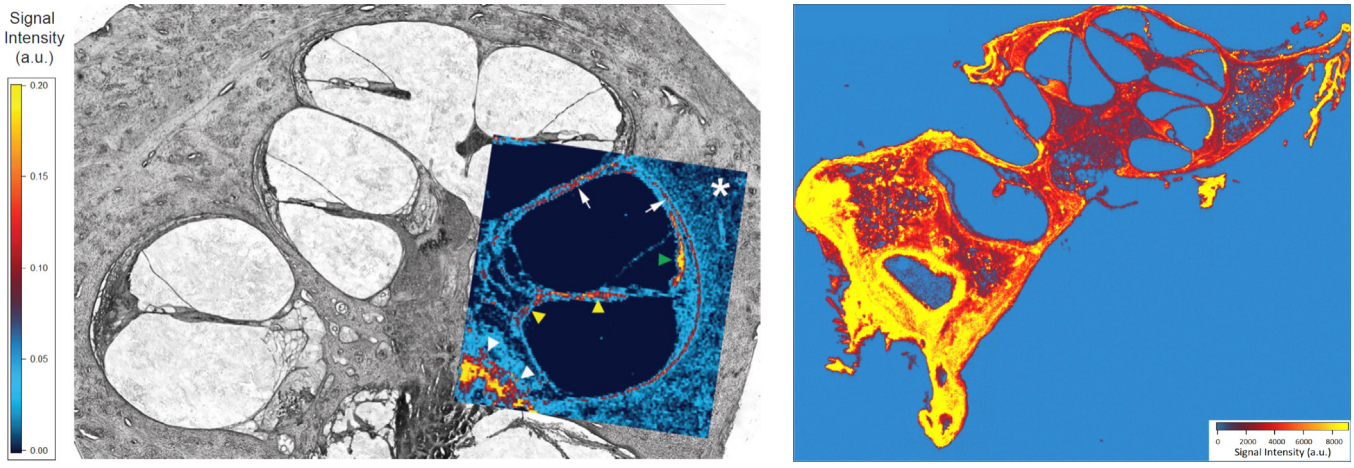
imageBIO266

Cisplatins

Cisplatin (cisplatinum) is a chemotherapeutic drug used commonly to treat ovarian, testicular, or bladder cancer. Chemotherapy drugs have commonly known side effects: nausea/vomiting, low blood count/lack of essential elements, kidney toxicity, ototoxicity, and/or hair loss. Ototoxicity (hearing loss) occurs in 40-80% of adults and 50% of children undergoing cisplatin chemotherapy. Breglio et al. predicted that ototoxicity was related to cisplatin accumulation within the cochlea, and using LA-ICPMS, they were able to confirm this theory by looking at the Pt response within a human cochlea and a mouse cochlea.[1]



L) Distribution of a fluorescent cisplatin conjugate (green) in a mice cochlea with similar uptake to cisplatin. **R)** Control cochlea cross-section.[1]



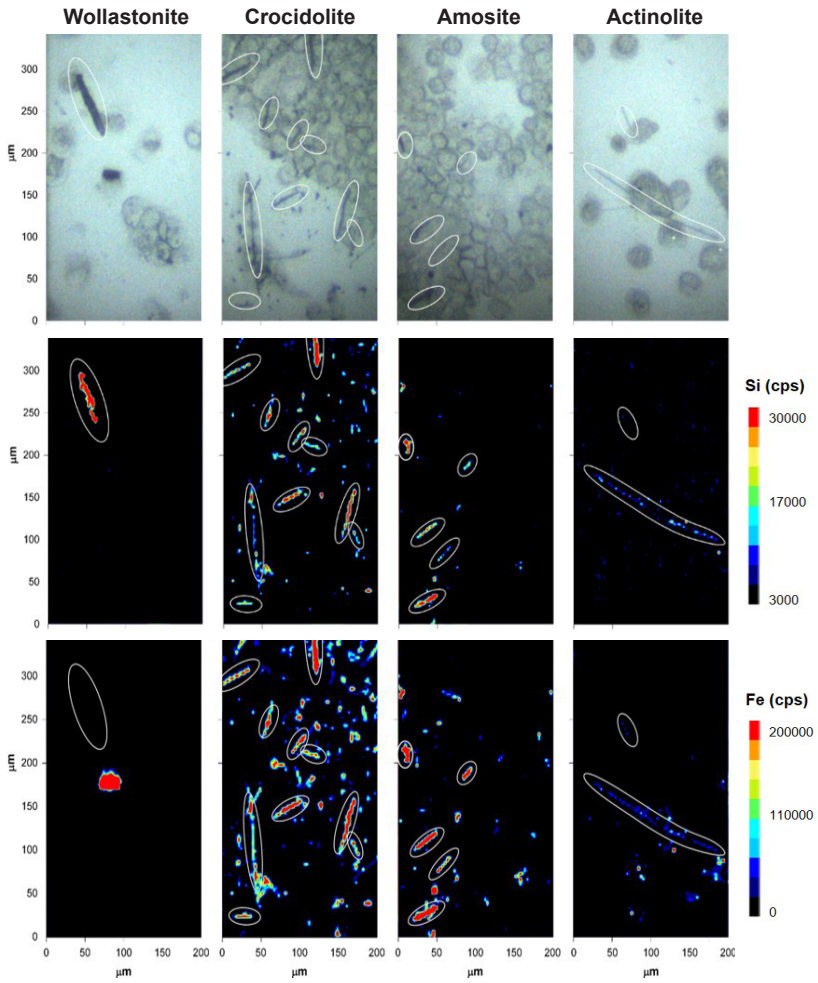
L) Distribution of Pt (cisplatin) in a cross-section of a human cochlea. Overlay of the LA-ICPMS elemental image was collected using a 25 µm laser spot. **R)** Distribution of Pt (cisplatin) in a cross-section of a mouse cochlea. LA-ICPMS elemental image was collected using a 2 µm laser spot.[1]

1. Breglio, Andrew M., et. al., Cisplatin is retained in the cochlea indefinitely following chemotherapy, *Nature Communications*, 2017, **8**, 1654, 1-9.

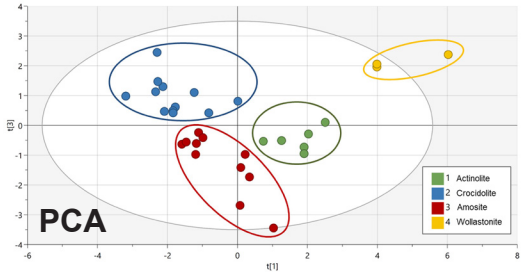
imageBIO266

In-Situ Identification of Asbestos Fibers in Tissue

Human mesothelioma cells (MSTO-211H) were cultured and spiked with 3 µg/mL asbestos, and the resulting suspension was cytospun onto microscope slides to mimic tissue conditions. Four different fibers were analyzed: 3 types of asbestos (crocidolite, amosite, actinolite) and 1 non-asbestos (wollastonite).



The four types of fibers can be observed by LA-ICPMS, but applying principle component analysis (PCA) clearly distinguishes between the fibers based on the responses of Na, Mg, Al, Si, P, K, Ca, Ti, Fe, and Mn. In addition, the control fiber (wollastonite) is distinctly different from the three asbestos samples.



Data and images courtesy of Amy Managh, Loughborough University, Loughborough, England.

Greenhalgh, C. J., et al., Needles in haystack: using fast-response LA chambers and ICP-TOF-MS to identify asbestos fibres in malignant mesothelioma models, JAAS, 2020, DOI: 10.1039/d0ja00268b.

prep*FAST* Station: **Dilution**Station

DilutionStation is a compact and highly configurable automation system used for preparing laboratory solutions including blood, urine, and serum samples. Flexible sample preparation methods stored on the integrated touchscreen controller make **Dilution**Station capable of automating several labor-intensive laboratory procedures including:

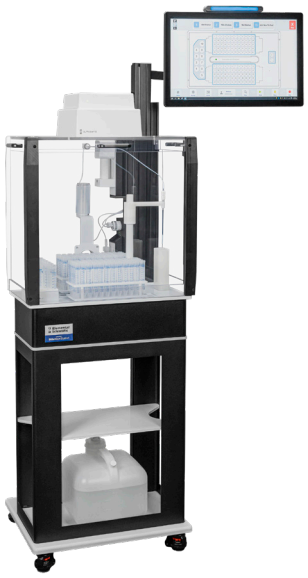
- Sample dilution
- Acidification
- Internal Standard Addition
- Sample mixing

DilutionStation can also prepare ICP/ICPMS calibration standards.

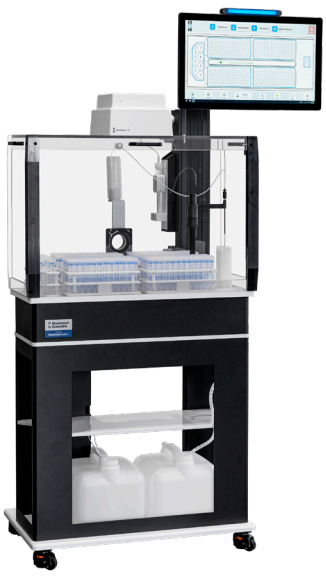
System Capacities

DilutionStation is available in four convenient capacities to fit the throughput requirements of your laboratory including 2, 4, 8, and 14-rack configurations. Specifically, the 4DX **Dilution**Station can be tailored for clinical purposes with a 9 microplate PTFE deck, enabling labs to enhance throughput using microplates.

Enclosure and ULPA filter options are available for all **Dilution**Station capacities.



2DX **Dilution**Station



4DX **Dilution**Station
*Also available in 9MT Clinical Configuration

8DX **Dilution**Station

14DX **Dilution**Station

prep*FAST* Station: **Dilution**Station

Clinical Features and Benefits

DilutionStation is equipped with several features that can be customized to automate tedious preparation tasks in clinical laboratories. An unlimited number of preparation procedures can be easily accessed on the main screen of the touchscreen controller, enabling **Dilution**Station to handle diverse sample types such as blood, urine, and serum efficiently. With just two clicks, daily sample preparation can be initiated: simply select your method from the main screen and click start..

In addition to the flexible software methods, **Dilution**Station features highly-configurable hardware components to better fit the specialized needs of clinical laboratories. The flexible sample deck can conform to racks of all shapes and sizes, and the 4DX **Dilution**Station can be altered with a PTFE deck capable of holding 9 microplates. The autosampler probe can also be altered to accommodate specialized clinical applications including septum piercing and micro-volume aliquots, and gas mixing.

DilutionStation Features

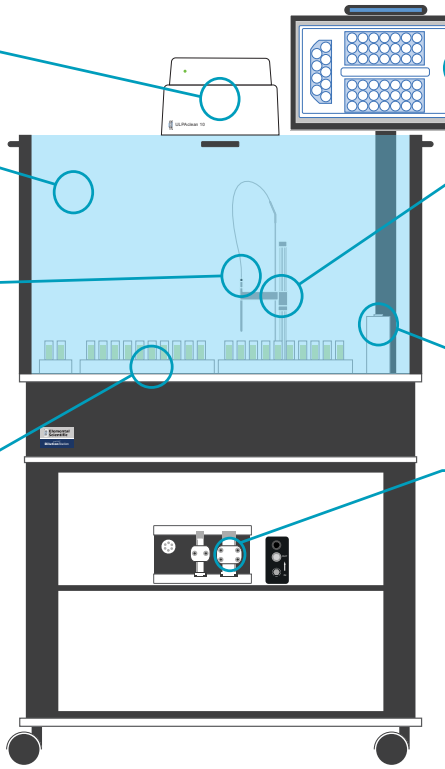
ULPAclean 10 Filter *(Optional)*
- Removes 99.9995% of airborne particles with size of 0.1 µm or larger

Clean3V Enclosure *(Optional)*
- Clean sample environment
- Protects lab from harmful fumes
- Includes three vertical sliding doors

Versatile Sample Probe

Several specialized probe options available including:
- Septum piercing probe
- Micro-volume needle probe
- Dual lumen probe – provides simultaneous gas mixing while dispensing

Flexible Sample Deck
- Accomodates vessels of all shapes and sizes
- Nine-microplate PTFE deck available for 4DX capacity



Integrated Touchscreen
- Easy-to-use software
- Stores an unlimited number of custom methods

AutoAlign Arm
- Self-aligns after encountering capped sample tube
- Metal-free fluoropolymer probe aligner
- Automatically goes to the right position every time

Dual Overflowing Rinse Stations
- Ultra-low cross-contamination
- Independently pumped for low rinse consumption

Syringe Autodilution
- More accurate and precise results
- Cleaner, more reproducible results

DilutionStation features diagram – several additional hardware options are available including enclosures, ULPA filter, leak sensor, septum piercing and fluoronetic rail.

SampleSense *FAST* UHT-C

Clinical laboratories support Medical/Healthcare facilities by providing rapid results needed to make medical decisions. These laboratories need to be able to handle many types of biological matrices, such as urine, blood, serum, hair, or nails, as well as perform high-throughput analysis for the most commonly requested tests, including Pb in blood, Cu in serum, or As in urine. In the case of Pb, a naturally occurring element used in many manufacturing processes and found in many products (e.g. paint, solder, batteries), toxicity is a major problem. Especially in children, lead competes with calcium in the body and is detrimental for the development of strong bones, teeth, muscles, and nervous system. Pb has a relatively long half-life of ~30 days in blood, so it is the preferred method for measuring Pb exposure. In the United States, the level of concern for children is set as 3.5 µg/dL Pb while medical treatment is recommended for levels exceeding 45 µg/dL Pb in blood.

A laboratory may be required to analyze hundreds or even thousands of samples per day. For this type of throughput to be achieved, high-throughput methods with instrumentation capable of handling this extreme sample load must be maintained to provide fast, reliable, and accurate results. ESI offers the SampleSense *FAST* UHT-C system, which is an extremely fast sample-to-sample solution for ICP and ICPMS without compromising reliability or accuracy.

SampleSense *FAST* UHT-C

- Uses *FAST* technology to improve sample throughput.
- Includes the SampleSense valve with integrated optical sensors to automatically load, detect, and inject samples.
- Automatically triggers the instrument data acquisition, eliminating the need to change methods for changes in sample viscosity or injection loop volume.
- Ensures sample loading integrity by logging all failed sample loading events (e.g. not enough sample volume, missing vials, capped vials, or empty rinse station).
- Enhanced washout and reduction in sample volume.

Viscosity Differences

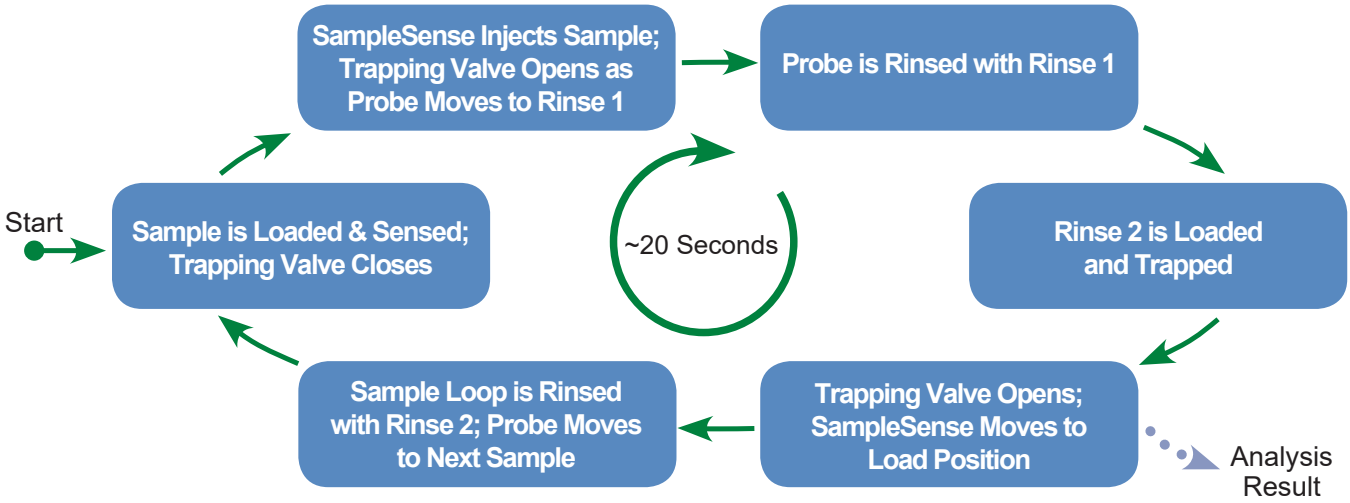
One valve, one loop and one method for multiple sample types. SampleSense accounts for viscosity and automatically adjusts timing.

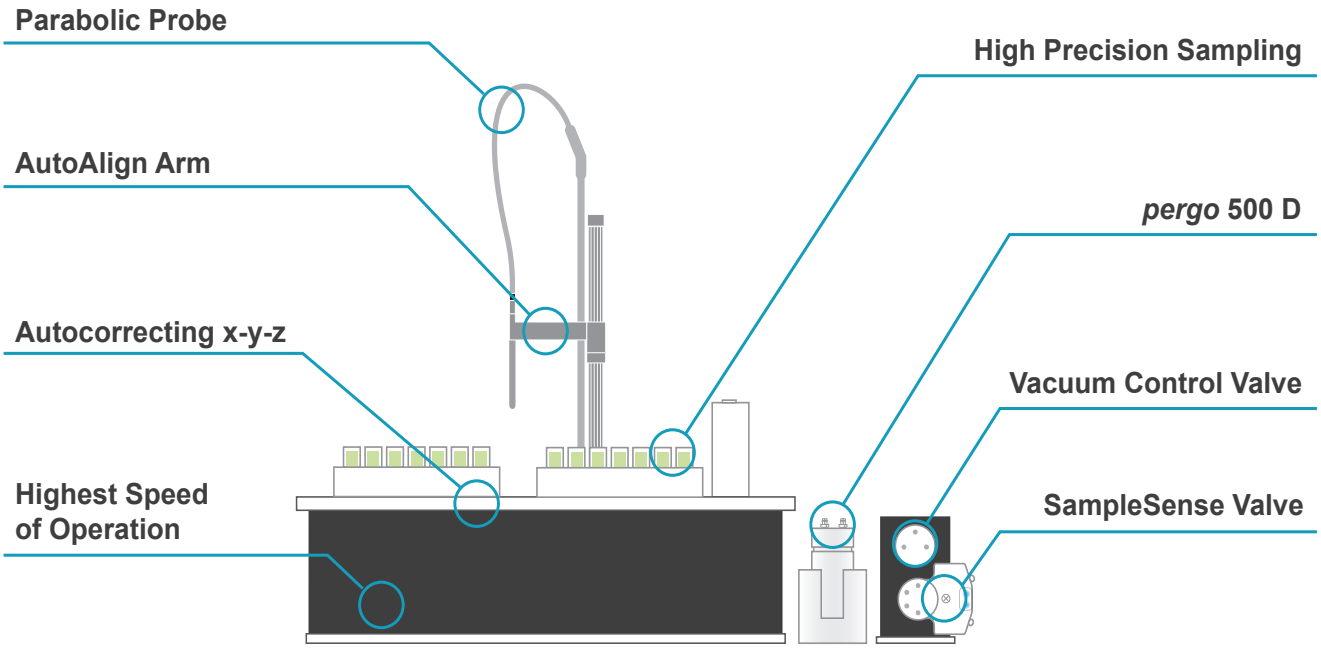
Time Savings

Operator time for sample introduction method development is eliminated. Just run samples.

SampleSense *FAST* UHT-C

SampleSense FAST UHT Analytical Cycle



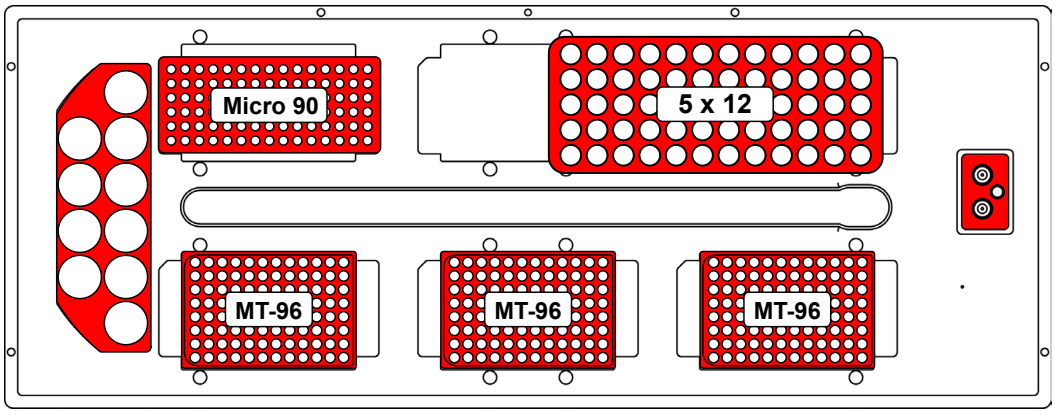


SampleSense *FAST* UHT-C

The SampleSense *FAST* UHT-C system includes an autosampler (available with 2, 4, 8, or 14-rack layouts), parabolic probe connected to an AutoAlign arm for autocorrecting abilities in the x, y, and z axis, trapping valve that reduces sample uptake and enhances washout, and *pergo* argon humidifier for improved long-term stability. The typical analytical workflow for a blood Pb analysis includes:

1. Start of analysis.
2. Sample is loaded/sensed, trapping valve closes.
3. SampleSense injects sample, trapping valve opens as probe moves to rinse 1.
4. Probe is rinsed with rinse 1.
5. Rinse 2 is loaded and trapped.
6. Analytical result is reported, trapping valve opens, SampleSense valve moves to load position.
7. Sample loop is rinsed with rinse 2, probe moves to next sample.
8. Next sample is started.

4DXCi



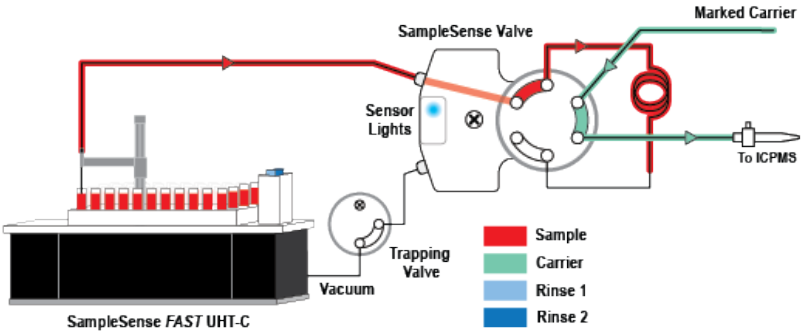
Micro 90 (P/N MR-90-08), 5x12 (P/N LR-60-16), MT-96 (P/N MT-96-2mL-02)

SampleSense *FAST* UHT-C Systems

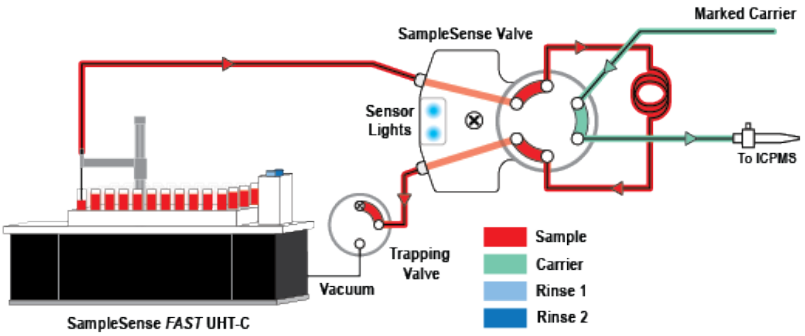
Autosampler Model	Part Numbers
2DXCi	2F-SS6-UHTC
4DXCi	4F-SS6-UHTC

*Autosampler model may be dependant on ICPMS. Contact your ESI representative for more information.

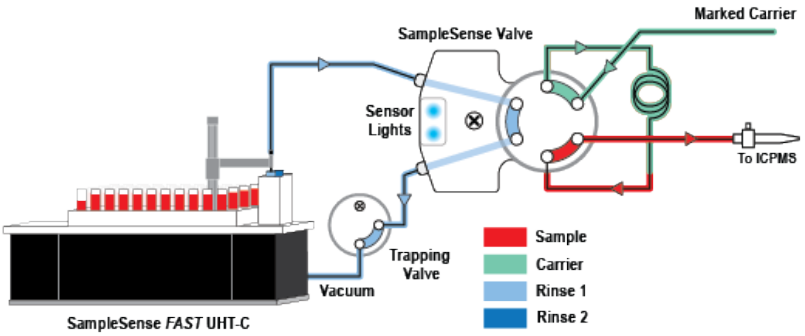
SampleSense *FAST* UHT-C



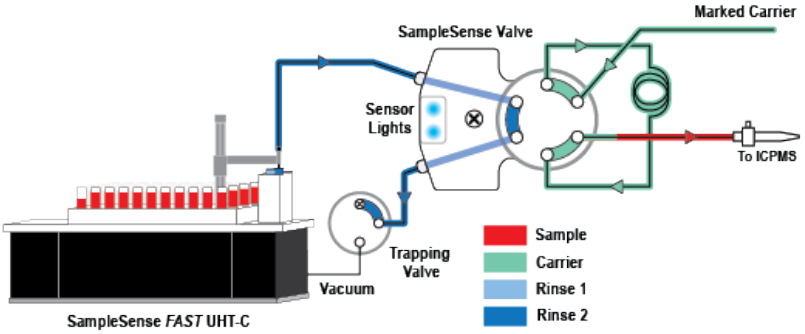
Step 1. Sample is loaded by vacuum, 1 of the 2 sensors is triggered (blue light).



Step 2. Sample has been sensed (both lights blue), valve toggled to inject, trapping valve closes to reduce sample uptake volume.

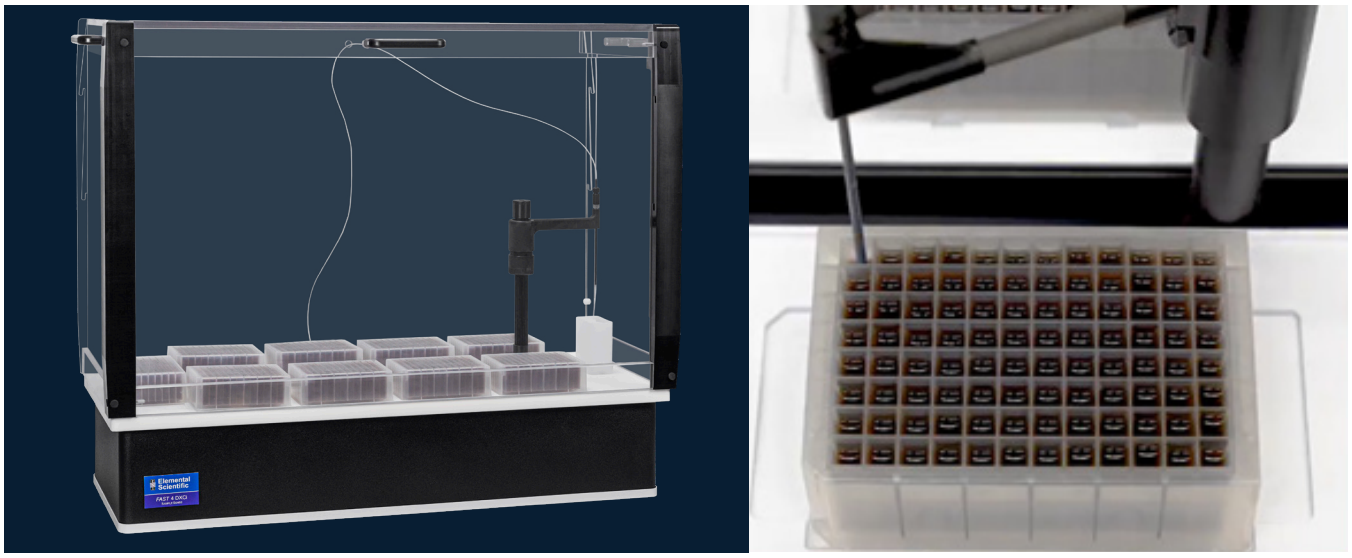


Step 3. SampleSense valve injects the sample to the ICPMS, and then rinse 1 flushes the probe.

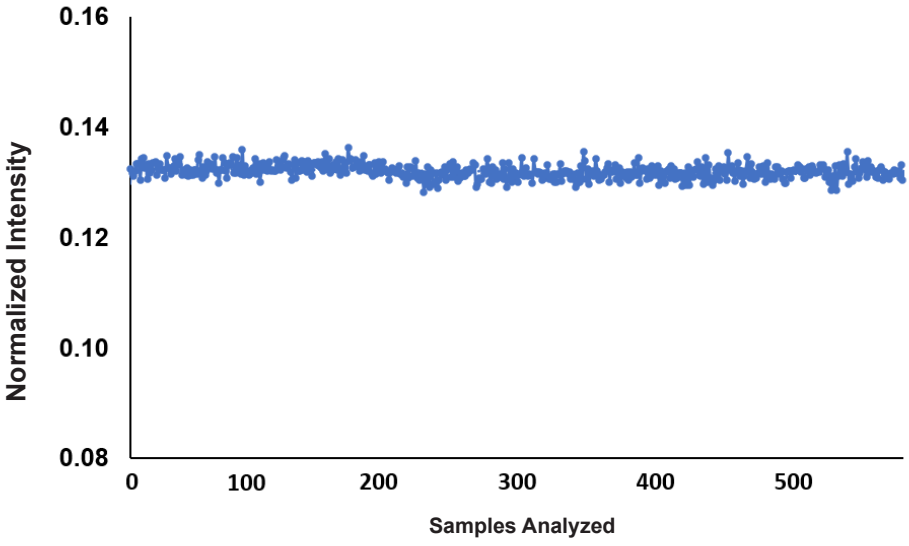


Step 4. Rinse 2 is loaded into the SampleSense valve (inject position) with the trapping valve closed. This rinse solution will sit there until the analysis is complete, once complete the rinse 2 solution is flushed through the sample loop (valve in load position). The rinse event is monitored by the sensor (both sensors lights are blue, meaning the rinse event was successful).

SampleSense *FAST* UHT-C



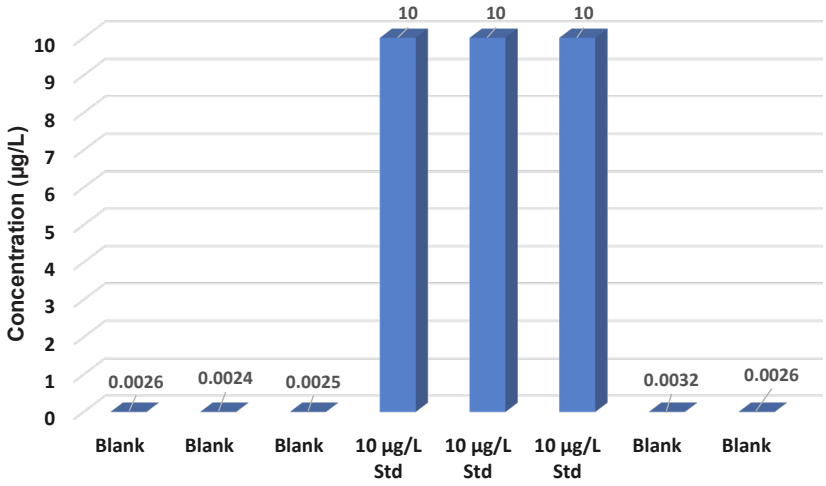
L) 4DXCi autosampler holds 4 traditional racks or 6 microtiter plates. **R)** Close up of the probe inserted into one of the wells of a 96 well microtiter plate with 2 mL of blood per location, enough to perform a repeat analysis if required.



Long-term stability for 50X diluted bovine blood analysis with SampleSense *FAST* UHT-C system (RSD = 0.96%).

Achieving rapid throughput without sacrificing stability requires excellent washout between samples. The SampleSense *FAST* UHT-C setup utilizes a trapping valve to enhance washout. This valve traps rinse solution in the probe and immediately rinses the loop after the ICPMS data acquisition is complete, using minimal rinse solution while still achieving >1000x washout after a 100 µg/dL Pb standard.

SampleSense *FAST* UHT-C



Pb washout after high calibration standard run 3x in a row. With SampleSense *FAST* UHT-C, washout after one blank is >1000x, and Pb returns fully to baseline after two blanks.

Sample integrity is an important consideration for high-throughput methods and cannot be ignored or compromised for speed. To that end, the SampleSense *FAST* UHT-C ensures the integrity of the sample results in two critical ways. First, every failed event (unsensed sample loading or rinse) is logged by the ESI software (in an Excel spreadsheet for easy exporting) and displayed on the computer screen for the analyst. Secondly, as additional confirmation of a missed sample in the raw ICPMS data, a marker component is added to the carrier solution (Tm in this work). If a sample fails to load correctly, SampleSense automatically responds by triggering the ICPMS analysis without injecting the sample loop contents, resulting in the analysis of the marked carrier solution. The presence of this marker, Tm, at a high-count rate in the ICPMS data provides additional confirmation to the analyst that a sample was not introduced successfully.

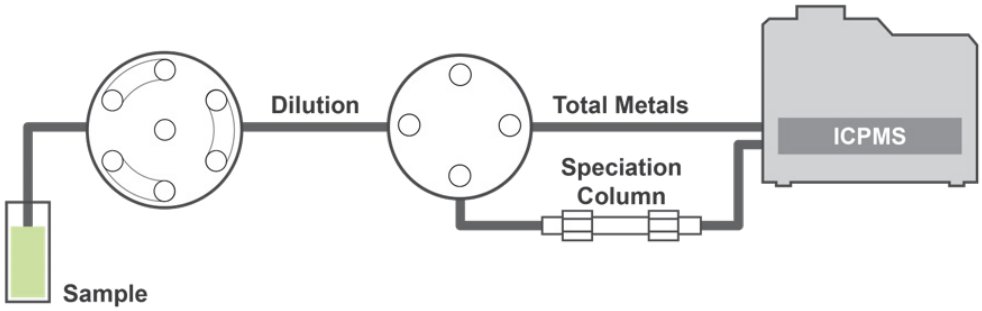
Sample Id	Acquisition Time	QC Status	Pb-1 208 (cps)	Bi 209 (IS) (cps)	Tm 169 (cps)
Blood Pb	10/17/2019 1:53:39 PM	Passed	17489.6	142851.4	93.3
Blood Pb	10/17/2019 1:54:19 PM	Passed	17524.9	141302.9	86.7
Blood Pb	10/17/2019 1:54:39 PM	Passed	17450.2	142313.4	126.7
Blood Pb	10/17/2019 1:55:18 PM	Passed	17426.2	142268.3	93.3
Blood Pb	10/17/2019 1:55:38 PM	Passed	17517.6	142268.3	80.0
Empty Vial	10/17/2019 1:55:57 PM	Failed	479.2	144139.6	321345.9
Capped Sample	10/17/2019 1:56:17 PM	Failed	445.8	143635.2	318745.5
Blood Pb	10/17/2019 1:56:37 PM	Passed	17570.3	142044.8	73.3
Blood Pb	10/17/2019 1:56:56 PM	Passed	17556.9	142044.8	80.0

Example of sample results for an experiment that includes an empty vial and capped sample. The QC functions monitor the carrier marker (Tm in this case) and flag the sample if it exceeds a set value (e.g. 1000 cps), meaning no sample is present at time of measurement.

prep*FAST* IC (Clinical)

For some elements, such as arsenic, an elevated patient result may not require a medical course of action. For example, inorganic arsenic (As III and As V) is more toxic than organic arsenic (AsB, AsC, DMA, and MMA). If elevated levels are found to be AsB, it may have resulted from a seafood diet whereas elevated inorganic As could be caused by consuming contaminated drinking water. LC-ICPMS is the most common technique used to determine patient arsenic species exposure. However, dedicating an ICPMS for just speciation may not be practical for many labs. Thus, ESI developed a more versatile and flexible system for elemental speciation that is also capable of doing routine total metals analyses.

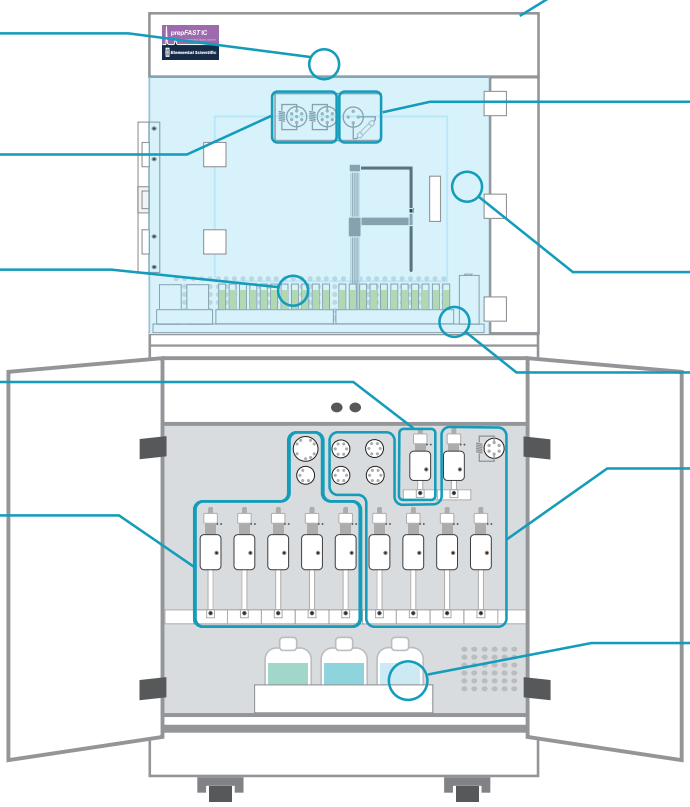
The prep*FAST* IC is a fully automated sample introduction system that can perform both elemental speciation and total metals analysis. This system takes advantage of the prep*FAST* functionality that allows for autocalibration from a single standard and inline sample dilutions, eliminating tedious manual standard and sample preparation.



Highlighted features of the prep*FAST* IC:

- Total Metals and Speciation analysis performed within a single instrument.
- Completely metal-free system with gradient elution.
- Utilizes the prep*FAST* functions for autocalibration and inline dilutions of samples.
  - Autocalibration – system prepares calibration from a single stock standard.
- Xceleri data analysis software.
  - Re-analyze samples when over-range.
  - Analyze sample at a higher dilution factor within calibration curve.
  - Automatically run speciation method on sample when total result is over specified value.

prep*FAST* IC (Clinical)



Optional ULPA Filter

Autodilution Valves

Inline automated calibration and dilution system

Sample Containers

<1 mL up to 500 mL

Autotuning

Autodilution Syringe Module

- Sample autodilution at time of analysis
- Species-specific autocalibration capability
- Micro-volume sample syringe-loading
- Calibration matrix matching
- Inline sample chemical reactions
- Inline sample derivatization

Electronics in Rear Plenum

Speciation/Total Metals Selection Valve

Auto switching of total metals or speciation (chromatography mode)

Exhausted Enclosure

High-precision DX Autosampler

High-pressure Speciation Module

-Ultra-high-purity, metal free pump
-Gradient elution
-Post-column internal standard
-Post-column dilution
-Post-column derivatization

Reagent Reservoirs

For autodilution and elution reagents.

The prep*FAST* IC offers ultimate flexibility for end-users who need one sample introduction system capable of many applications. For example, these applications have direct clinical relevance:

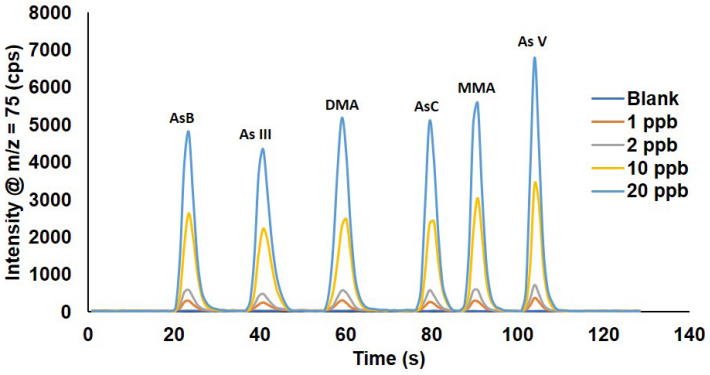
- Determination of arsenic species in urine for clinical testing.
- Determination of Gd-based MRI contrast agents and “free Gd^{3+}” in urine or tissue biopsies.
- Direct determination of bound and free Cu in serum, diagnostic tool for copper-related diseases, such as Wilson disease.
- All-in-one clinical system for undiluted blood, serum/plasma, urine, hair, nails.
- Other applications of interest include speciation methods for Hg, Se, P, Cr, Br, Cl, and I.

***See page 31 for ordering information**

prep*FAST* IC

As Speciation

Arsenic is a naturally occurring element that can leach into water systems, contaminating them. In addition, arsenic contamination can occur from industrial exposures or during mining processes. Human consumption of contaminated drinking water or arsenic-containing foods can lead to increased arsenic levels within the body. Inorganic arsenic has a higher bioavailability than organic arsenic, making inorganic arsenic the more toxic type. For example, the LD50 for As III and As V is 14 mg/kg and 20 mg/kg, respectively, whereas the LD50 for AsB and MMA is ~5,000 mg/kg and 2,000 mg/kg, respectively. Since arsenic is excreted in urine within 6-8 h of consumption/exposure, the preferred testing method is urine analysis.



Stock Standard Prepared	Dilution Factor	Concentration at ICPMS (ppb)
100 ppb	100	1
	50	2
	20	5
	10	10
	5	20
	2	30

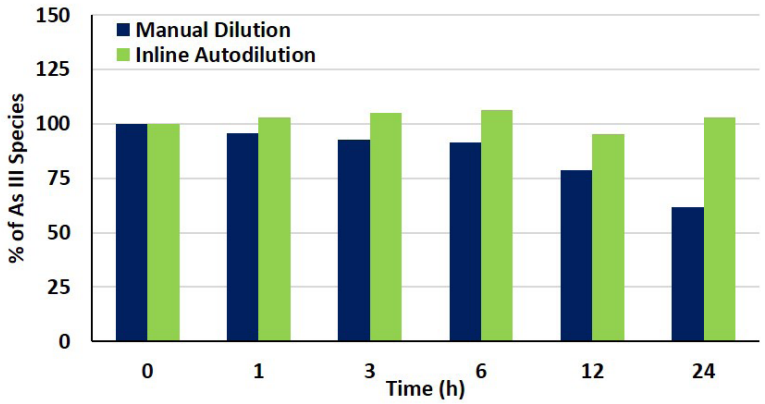
Example chromatogram prepared using a single stock arsenic species standard. The Typical LODs for each arsenic species is ~1 ppt using an ICPMS with collision or reaction cell technology.

Arsenic, as well as other elemental species, can convert to other forms if the native conditions are altered. Thus, it is important to maintain the sample conditions prior to analysis. To explore the advantages of inline dilutions, two urine samples were placed on the autosampler deck and analyzed over a 24 h time period – one with 30X manual dilution (with DI water to maintain the sample pH as close as possible to the original sample) and the other undiluted. The results show that some As III converts to As V in the manually diluted sample, but the arsenic species do not significantly change using the inline dilution method. By performing the dilution just prior to the analysis, the prep*FAST* IC maintains sample integrity by eliminating conditions that promote species conversion.

prep*FAST* IC

As Speciation

An experiment involving seafood consumption was designed to demonstrate the importance of differentiating between different arsenic species in urine samples. Three individuals donated urine samples (baseline) immediately prior to consuming tuna or salmon sashimi. After lunch, urine samples were collected at various intervals throughout the next 24 h. All of these urine samples were analyzed for As species to compare the sources and species of As. Subject A and C ate tuna, while subject B had salmon. With the aid of speciation analysis, the high levels of arsenic were identified as organic arsenic species, which are not as harmful as the inorganic species.



		µg/L				
	Time	**AsB**	**AsIII**	**DMA**	**MMA**	**As V**
Subject A	Before Sushi	94	<DL	6	0.3	<DL
	+2 h After Sushi	129	<DL	7	0.8	<DL
	+8 h After Sushi	271	<DL	13	0.8	<DL
	+24 h After Sushi	97	<DL	6	0.3	<DL

		µg/L				
	Time	**AsB**	**As III**	**DMA**	**MMA**	**As V**
Subject B	Before Sushi	2	<DL	4	0.0	<DL
	+8 h After Sushi	18	<DL	6	1.2	<DL
	+20 h After Sushi	22	<DL	17	4.5	<DL
	+24 h After Sushi	4	<DL	4	0.5	<DL

		µg/L				
	Time	**AsB**	**As III**	**DMA**	**MMA**	**As V**
Subject C	Before Sushi	110	<DL	8	0.8	<DL
	+2 h After Sushi	231	<DL	10	1.1	<DL
	+8 h After Sushi	158	<DL	11	1.5	<DL
	+20 h After Sushi	84	<DL	8	0.7	<DL

Gd-based Contrast Agents

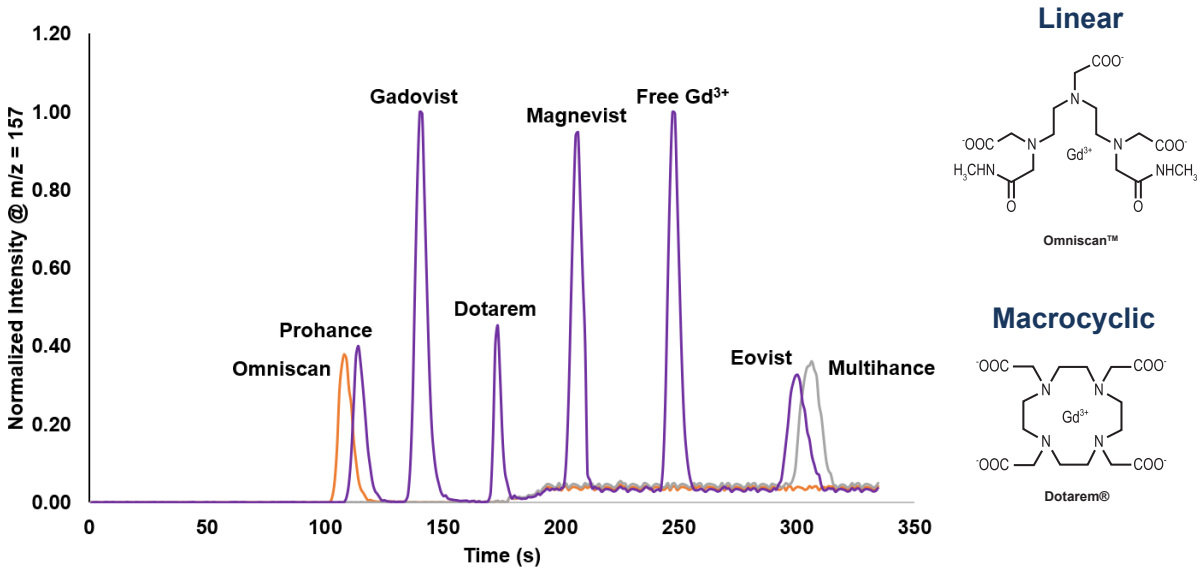
Magnetic resonance imaging (MRI) is a common non-invasive medical imaging technique. The table below is a list of the compounds approved or recommended on in Europe and the USA (data up to date as of May 2020).

	Chemical Structure	EMA*	FDA
Dotarem	Macrocyclic	Approved	Approved**
Gadovist	Macrocyclic	Approved	Approved**
Magnevist	Linear	Injection into the joints only	Approved
Multihance	Linear	Liver scans only	Approved
Omniscan	Linear	Suspend	Approved/Highest retention
Optimark	Linear	Suspend	Approved/Highest retention
Primovost or Eovist	Linear	Approved	Approved
Prohance	Macrocyclic	Approved	Approved**

* Based on 2017 report from European Medicines Agency (EMA).

** Levels remaining in body are the lowest (2018 FDA report).

When investigating the amount of Gd-based contrast agent or free Gd^{3+} that remains in the body, there are two options: tissue biopsy or urine analysis. In either case, if the form of Gd needs to be known (compound vs free Gd^{3+}) , it must be determined by LC-ICPMS. The figure below is an example separation of commonly used Gd-based contrast agents. Some compounds co-elute, but the likelihood of a patient sample having more than one compound is slim.



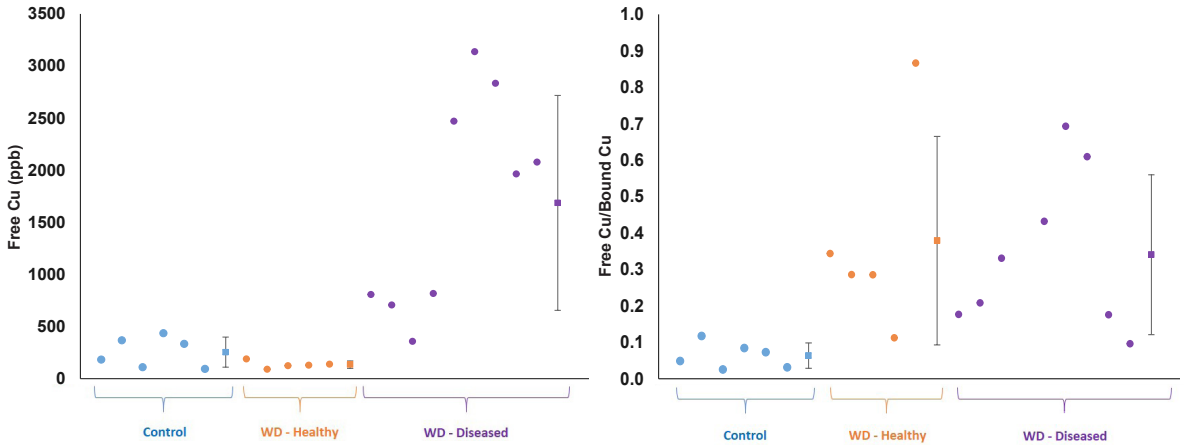
Wilson Disease

Copper is an essential element as it acts as a cofactor for many proteins, such as ceruloplasmin, cytochrome oxidase, and superoxide dismutase. The main source for Cu is dietary intake; deficient or excess amounts of Cu can be detrimental to human development and normal human cellular functions.

There are two well-known disease associated with Cu:

1. **Menkes disease** is caused by a genetic mutation in *ATP7A*, which results in low serum Cu and ceruloplasmin levels. Patients with this disease normally do not live past the age of 3. 1 in 100,000-250,000 are diagnosed with this disease.
2. **Wilson disease** is caused by a genetic mutation in *ATP7B*, which is responsible for production of ATPase. ATPase is the copper-transporting P-type adenosine triphosphate, which incorporates Cu into ceruloplasmin and aids in the excretion of Cu into bile. Ceruloplasmin is the copper-transporting protein in blood and is responsible for ~85-95% of the circulating copper in normal individuals. 1 in 90 people carry the gene for the disease, and one in 30,000 are diagnosed with it.

ESI has developed a direct method for the determination of free Cu in serum. This method allows for the detection of bound and free Cu in serum and can be used for diagnostic purposes to detect Wilson's disease in patients. Free Cu alone can help identify disease-state patients, but taking into account the [free Cu]/[bound Cu] ratio allows for the diagnosis of patients who are not yet symptomatic. This may prevent liver damage that can occur in patients who are not diagnosed early enough.



Quarles, C. D, et al., LC-ICP-MS method for the determination of "extractable copper" in serum, *Metallomics*, 2020, **12**, 1348-1355.

prep*FAST* IC

Clinical

Many prep*FAST* IC features make it an ideal system for the analysis of biological samples (blood, serum, urine, etc.). Not only can it be used for both total metals and elemental speciation, but utilizing the prep*FAST* functionality of the system, samples can be placed directly onto the autosampler deck and prepared automatically. As biological samples are prone to settling, sample stirring may be implemented prior to syringe or vacuum loading to ensure the samples are mixed properly prior to inline sample dilution. Since sample volume is limited for many types of clinical samples, the system can handle biological samples as small as 50 µL. Lastly, matrix matching of standards and blanks using ESI's clinical matrix (P/N CLIN-0500) is simple and requires no real biological samples, providing the lowest blanks and minimizing handling of potentially hazardous biological matrices.

P/N CLIN-0500

	Sample Loading	Sample Uptake Volume
Urine	Vacuum* or Syringe	≥50 µL
Urine As Speciation	Vacuum* or Syringe	≥50 µL
Blood	Syringe	≥50 µL
Serum, Plasma	Syringe	≥50 µL
Hair, Nails	Syringe	≥50 µL

* When plenty of urine sample is available vacuum loading is an option.

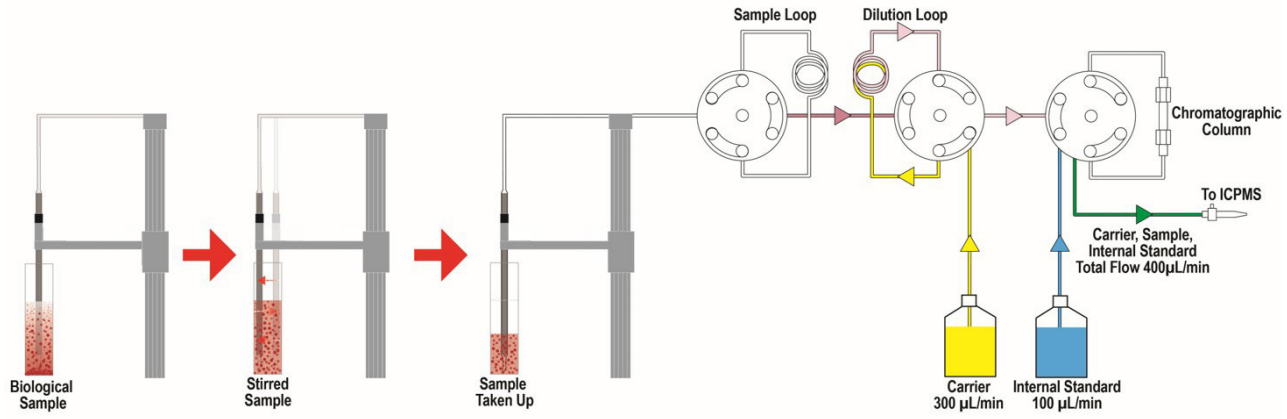


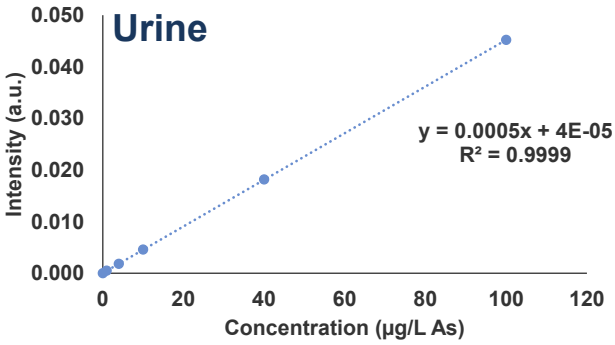
Illustration of undiluted biological sample being stirred and syringe-loaded followed by inline dilution using an appropriate diluent. Carrier is typically the same as the diluent. The column valve is bypassed for total-metals mode since chromatography is not needed for this type of application.

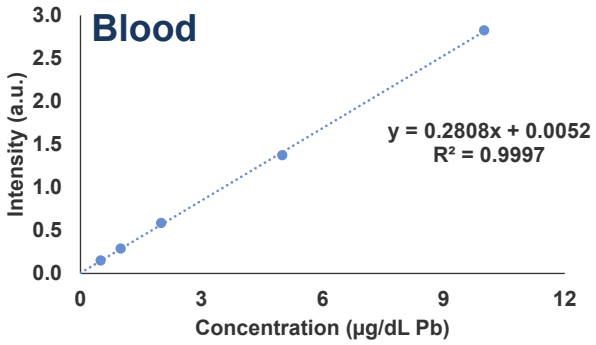
prep*FAST* IC

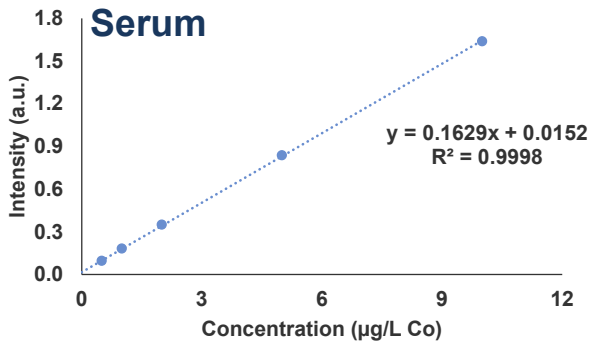
Clinical

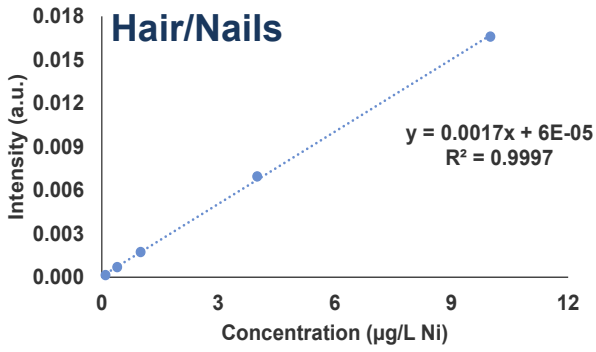
Typical elements for each biological matrix. The ideal method conditions, sample preparation procedures, and recommended quality control protocols are included in the method guide. The calibration ranges are based on expected normal and elevated biological levels.

Biological Matrices	Elements Included
Urine	Be, Al, Cr, Mn, Co, Ni, Cu, Zn, As, Sr, Mo, Cd, Sn, Sb, Cs, Ba, Gd, W, Pt, Tl, Hg, Pb, Bi, and U
Blood	Cr, Mn, Co, As, Se, Mo, Cd, Sb, Tl, Hg, and Pb
Serum, Plasma	Se, Al, Cr, Mn, Co, Fe, Cu, Zn, Pt, Hg, and Mg
Hair, Nails	As, Cd, Cu, Hg, Pb, Se, Zn, Ni, and Mn









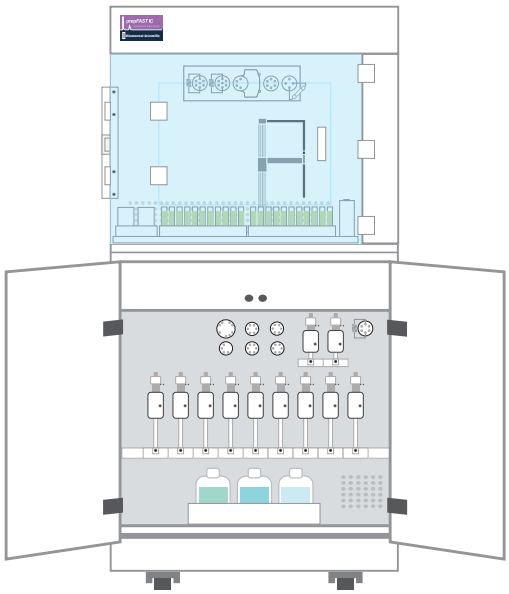
Typical calibration curves for As in urine (10X DF), Pb in blood (50X DF), Co in serum (25X DF), and Ni in hair or nails (5X DF), prepared using ESI's synthetic clinical matrix.

prep*FAST* IC

There are two main options for the prep*FAST* IC:

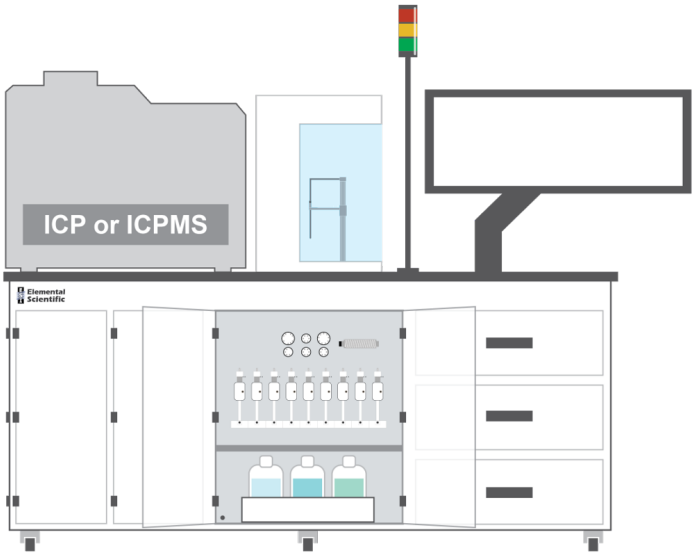
1. **Enclosed Mobile Station**

   Polypropylene cabinet with wheels: includes high precision autosampler; autodilution, speciation, and autotuning modules; reagent reservoir base; exhaust for autosampler and reagent decks; and optional ULPA filter. Door configuration is customizable depending on ICPMS model.



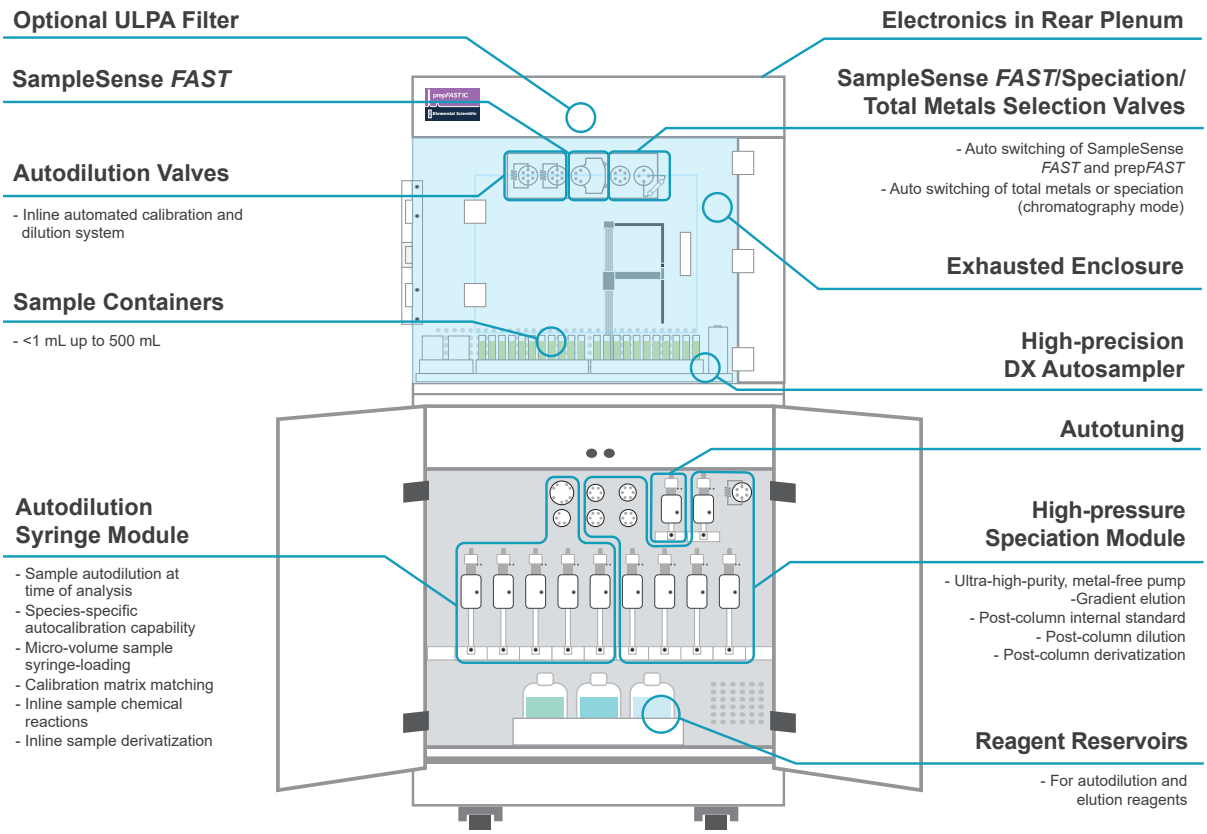
2. **Integrated Bench**

   Includes prep*FAST* IC components plus built in computer monitor, storage drawers, status indicator lights (for leaks, full waste, etc.), waste sensors, leak sensors, waste reservoir cabinet, rinse bottle cabinet, and inert/acid resistant countertop. Table configuration is customizable depending on ICPMS model.



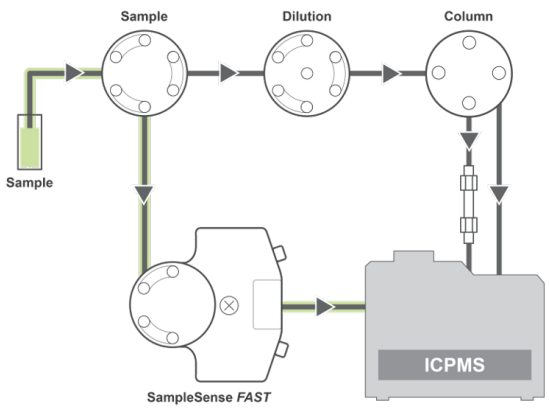
The prep*FAST* IC is a versatile instrument that can be customized to meet the automation needs of the laboratory. The aforementioned SampleSense *FAST* UHT-C is one possible upgrade that adds high-throughput analysis to the speciation and total metals capabilities of the prep*FAST* IC.

prep*FAST* IC

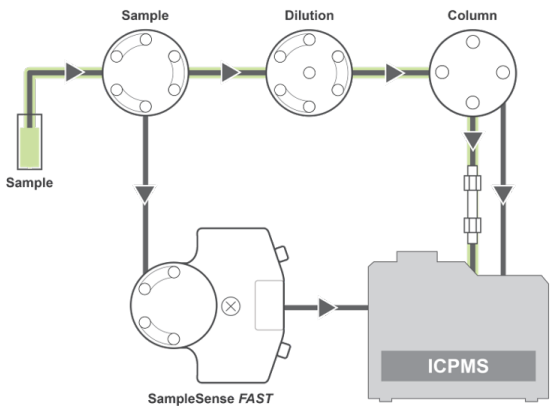


The prep*FAST* IC UHT system allows for a total of 3 different methods to be automated in an ICPMS sequence. For example, the following three methods could be run in sequence, all without user interaction with the autosampler or ICPMS: a blood Pb method using SampleSense *FAST* UHT, a urine total metals method with inline sample dilution, and a urine arsenic speciation method with inline sample dilution.

prep*FAST* IC UHT – SampleSense *FAST* UHT Mode



prep*FAST* IC UHT – Speciation Mode



Product Summary

imageBIO266

Laser ablation instrument designed solely for elemental imaging of biological matrices. Utilizes a 266 nm ns laser for ideal tissue sampling and lower cost of ownership. Includes DCI torch, trigger cable, and TwoVol2 chamber. Optional upgrades include TwoVol3 chamber, 20X video objective, and Iolite V4 research license.

DilutionStation

Automated, compact, and highly configurable system for preparing laboratory solutions including blood, serum, and urine. Autosampler available in 4 sizes (2DX, 4DX, 8DX, and 14DX).

SampleSense *FAST* UHT-C

Automated high-throughput valve injection system with optically-sensed sample loading and triggered analysis. Includes *pergo*, PFA-ICN nebulizer, DXCi autocorrecting autosampler, and rinse trapping valve. Autosampler available in 4 sizes (2DX, 4DX, 8DX, and 14DX).

prep*FAST* IC

Single platform automation system capable of elemental speciation and total metals, with inline sample preparation and autocalibration. The system in enclosed in a polypropylene cart and includes a 4DXCi autosampler. Optional items include Xceleri (data anlaysis software) and elemental speciation kits (includes chromatographic column, speciation standards, and method guide).

prep*FAST* IC UHT

Upgrade option that includes SampleSense *FAST* UHT-C and prep*FAST* IC into a single system.

Ordering

Laser Ablation

Description	Part Number
imageBIO 266 core system	300212
DCI torch	**
Trigger cable	**
20X objective	300723
TwoVol3 ablation chamber	300725
iolite V4 license	254407

** Part number dependent on ICPMS mode.

SampleSense

SampleSense *FAST* UHT-C Autosampler	Part Number
2DXCi	2F-SS6-UHTC
4DXCi	4F-SS6-UHTC

DilutionStation

Description	Part Number
4DX **Dilution**Station with 9MT PTFE deck and septum-piercing probe	PFSTNS-007
Clean3V Enclosure for 4DX Autosampler	C3V4
ULPAclean-10 ULPA filter	ULPA10

prep*FAST* IC

Configuration	prep*FAST* IC Clinical Part Numbers
Total metals only	IC-0101, IC-0103, IC-0104, IC-0106
Total metals & speciation	IC-0101, IC-0109, IC-0103, IC-0104, IC-0106
Autotune add-on	IC-0105
SampleSense high-throughput module add-on	IC-0107
Xceleri software	IC-0201

prep*FAST* IC Speciation Kits (includes method guide)	Part Number
As speciation kit. CF-As-01 column. AsB, DMA, MMA, As(III), As(V) included.	ICX-As35
As speciation kit. CF-As-01 & CF-As-02 columns. AsB, DMA, MMA, As(III), As(V) included.	ICX-AsTMAO
Se speciation kit. CF-Se-01 column. Se (IV), Se(VI) included.	ICX-Se46
Hg speciation kit. CF-Hg-02 column. Inorganic Hg included.	ICX-Hg
Gd-based MRI Imaging speciation kit. CF-Gd-01 column. Inorganic Gd included.	ICX-Gd
Bound and Free Cu speciation kit. CF-Cu-01 column.	ICX-Cu

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