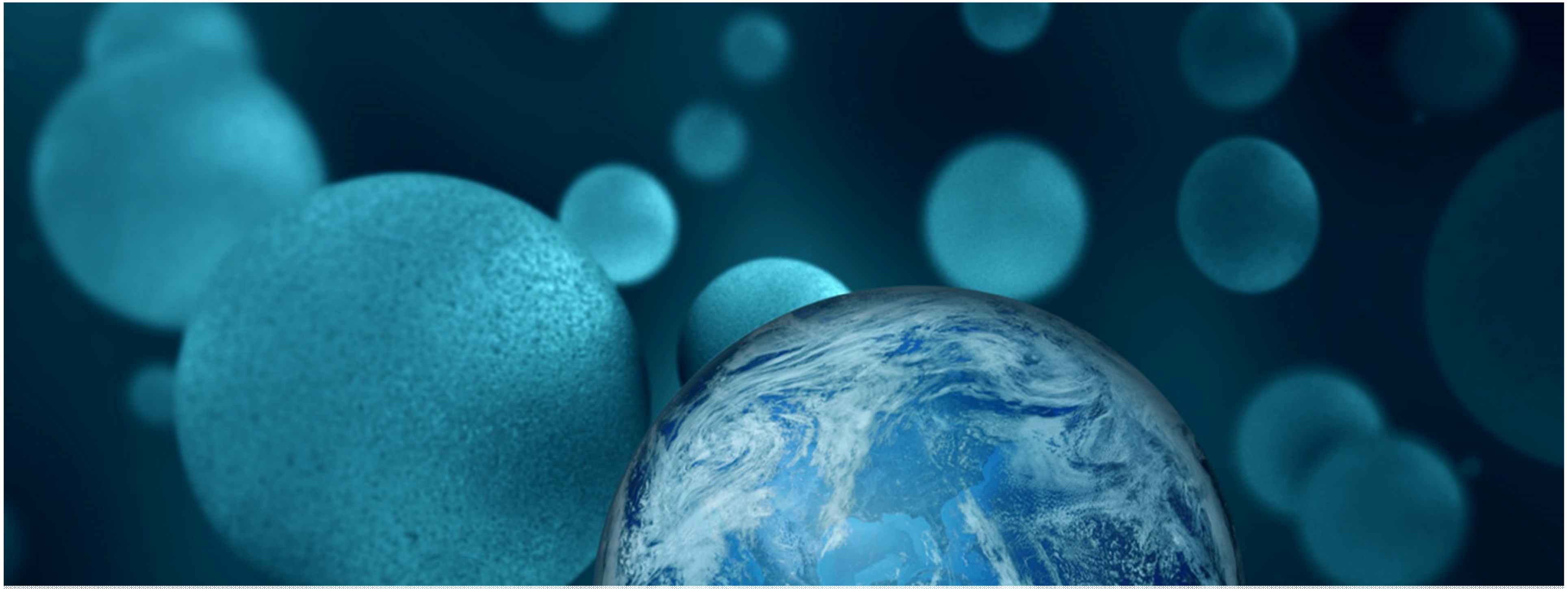


ThermoFisher SCIENTIFIC

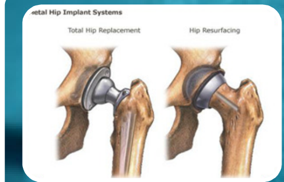
Clinical applications using triple quadrupole ICP-MS

Simon Lofthouse
Thermo Fisher Scientific

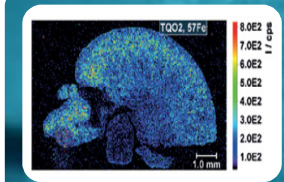
The world leader in serving science

Overview

Routine clinical measurements



Metal on metal hip replacements



Bio imaging

Summary

Testing for clinical applications

- Elemental analysis
  - Blood
  - Serum
  - Urine
  - Fluids
  - Tissue

Nutritional elements

- Nutritional status
- Cu, Zn, Se
- Mg, Mn
- Total parental nutrition
- Assessment after GI surgery

Thermo Fisher SCIENTIFIC

Thermo Scientific iCAP RQ/TQ ICP-MS

Thermo Scientific
iCAP RQ ICP-MS

Thermo Scientific
iCAP TQ ICP-MS

Same Analyzer Quadrupole

Same QCell Collision/Reaction Cell

Additional Q1 Mass Filter

Additional Gases and Enhanced software

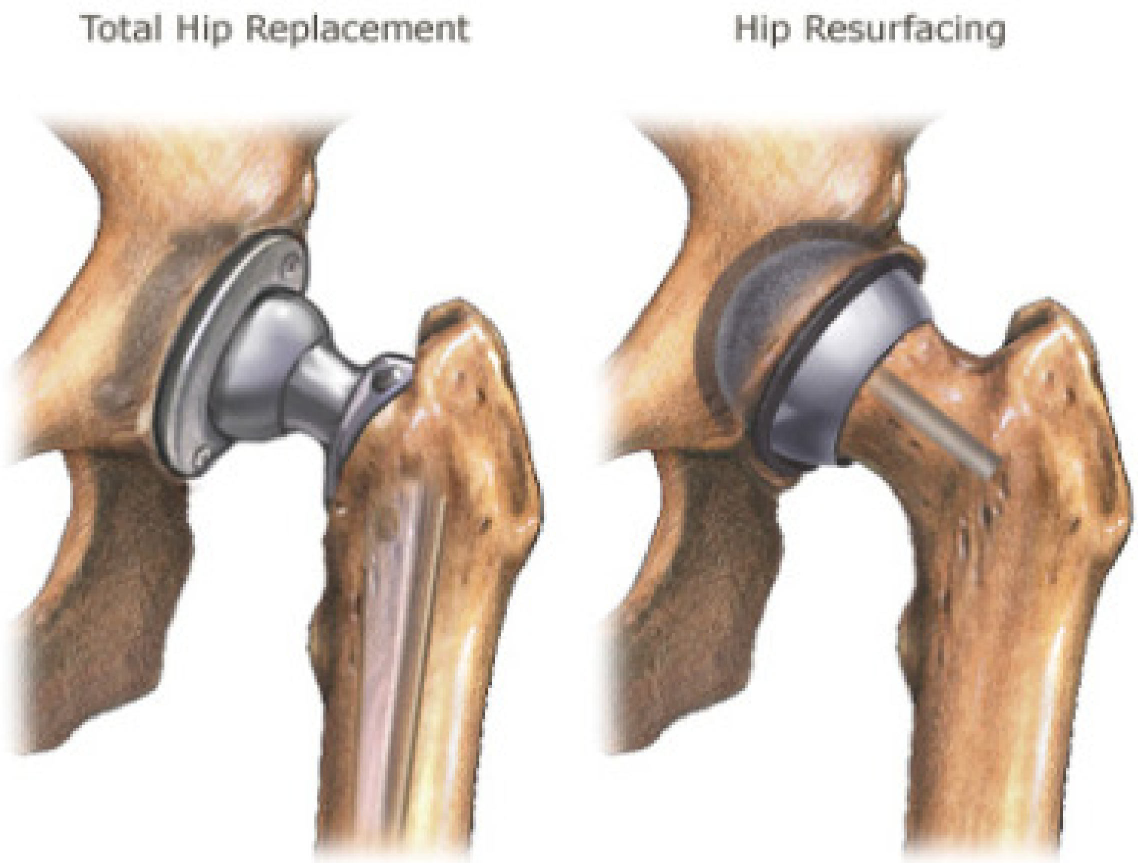
ThermoFisher SCIENTIFIC

Applications in Clinical Science

- Toxicology
  - High/accute Hg, Cd, Tl, Po
  - Medium/chronic As (speciation), Pb
  - Specific toxins Al (renal dialysis patients)

- Metal on Metal hip replacement patients
  - Co and Cr mainly also Ti, Mo, Ni for research
  - Indicative of poorly performing joints that may need replacement

Metal on metal hip replacements



Regulation

- April 2010 MHRA issued an advisory notice regarding MoM hip replacements:

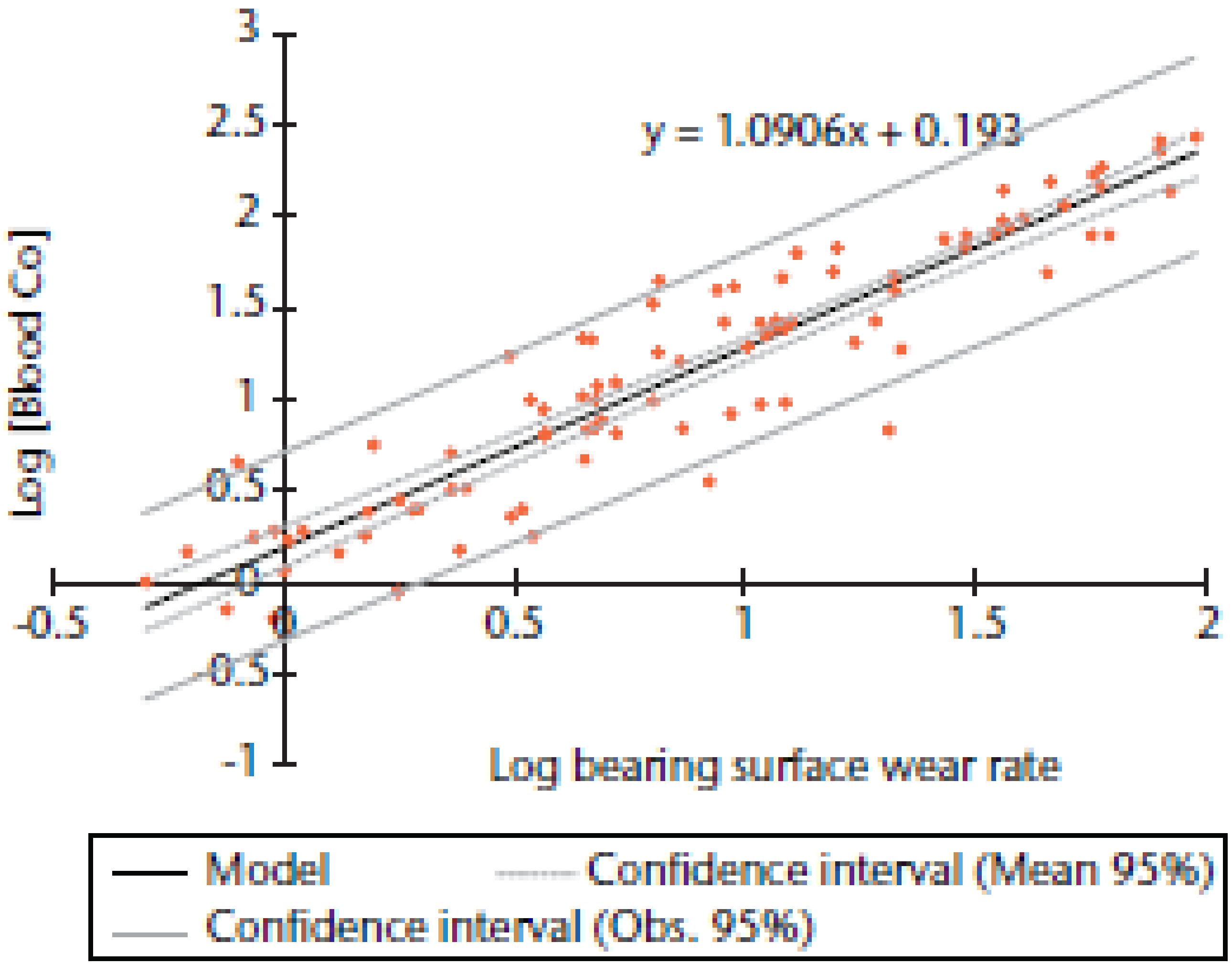
- “put in place systems for the follow up of patients receiving MoM hip replacements where appropriate blood metal ion measurements and sectional imaging”.

- If either Co or Cr levels are elevated above 7 ppb then further testing should be performed.

Medicines and Healthcare products Regulatory Agency
Government agency

Medicines & Healthcare products Regulatory Agency

Cobalt as a biomarker of wear



Methods for Ti analysis

- GF-AAS - titanium carbide formation is problematic
- Single quadrupole ICP-MS - the most abundant Ti isotope (73.80%) at m/z 48 suffers from Ca isobaric interference
- HR-ICP-MS - expensive hardware
- ICP-OES - offers a cost effective alternative, challenges to get required LOD
- Triple quadrupole ICP-MS can be used with NH_3 to form the cluster ion $Ti(NH_3)_3NH^+$

iCAP TQ

- Titanium in hip replacement samples
  - Lower LOQ possible using m/z 48
  - Use Ammonia as reaction gas

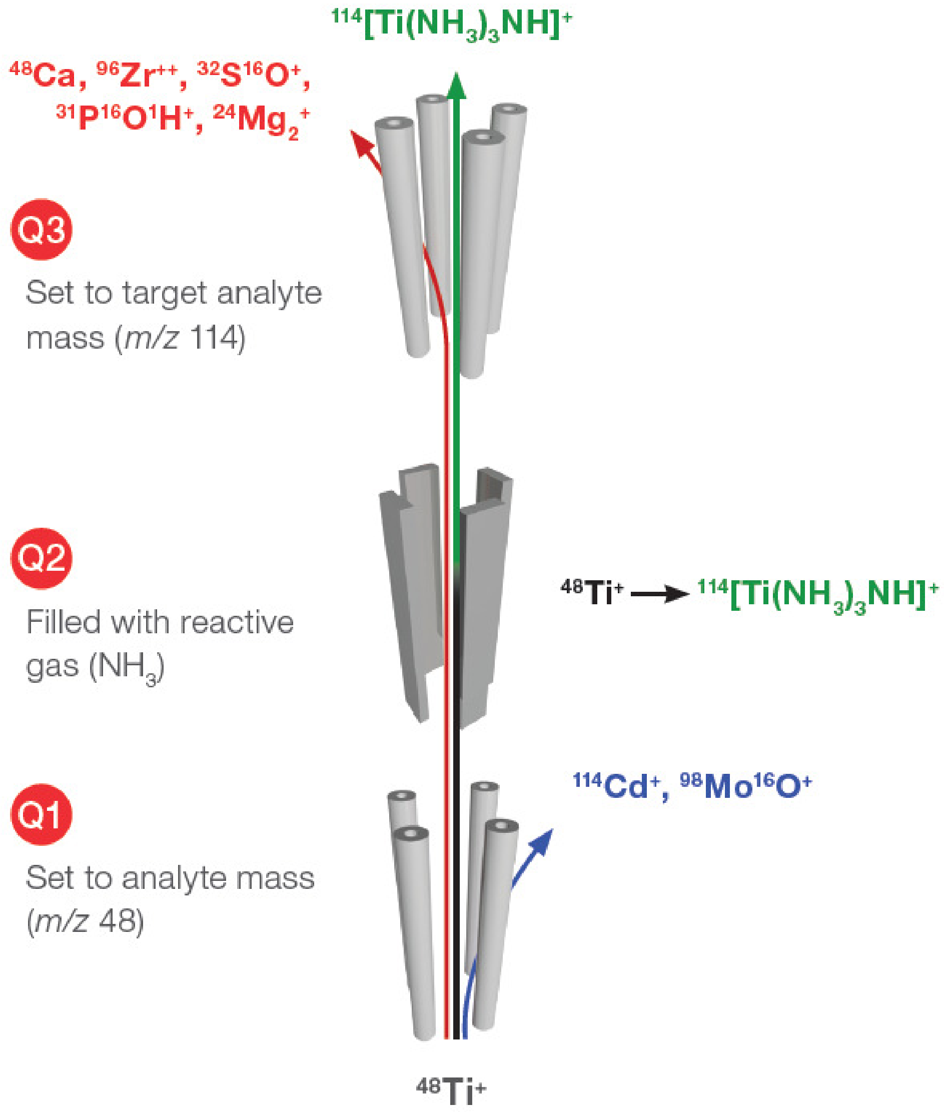
iCAP TQ measurement

Ti with NH_3 reaction gas:

Q1 – set to transmit Ti, potential interferents on the product ion (e.g. ^{114}Cd) and lower mass interference precursors (e.g. ^{31}P, ^{16}O) rejected.

Q2 – filled with NH_3. Ti collides and generates a range of adducts including $^{48}Ti(NH_3)_3NH^+$ at mass 114

Q3 – set to transmit mass 114, other masses rejected.



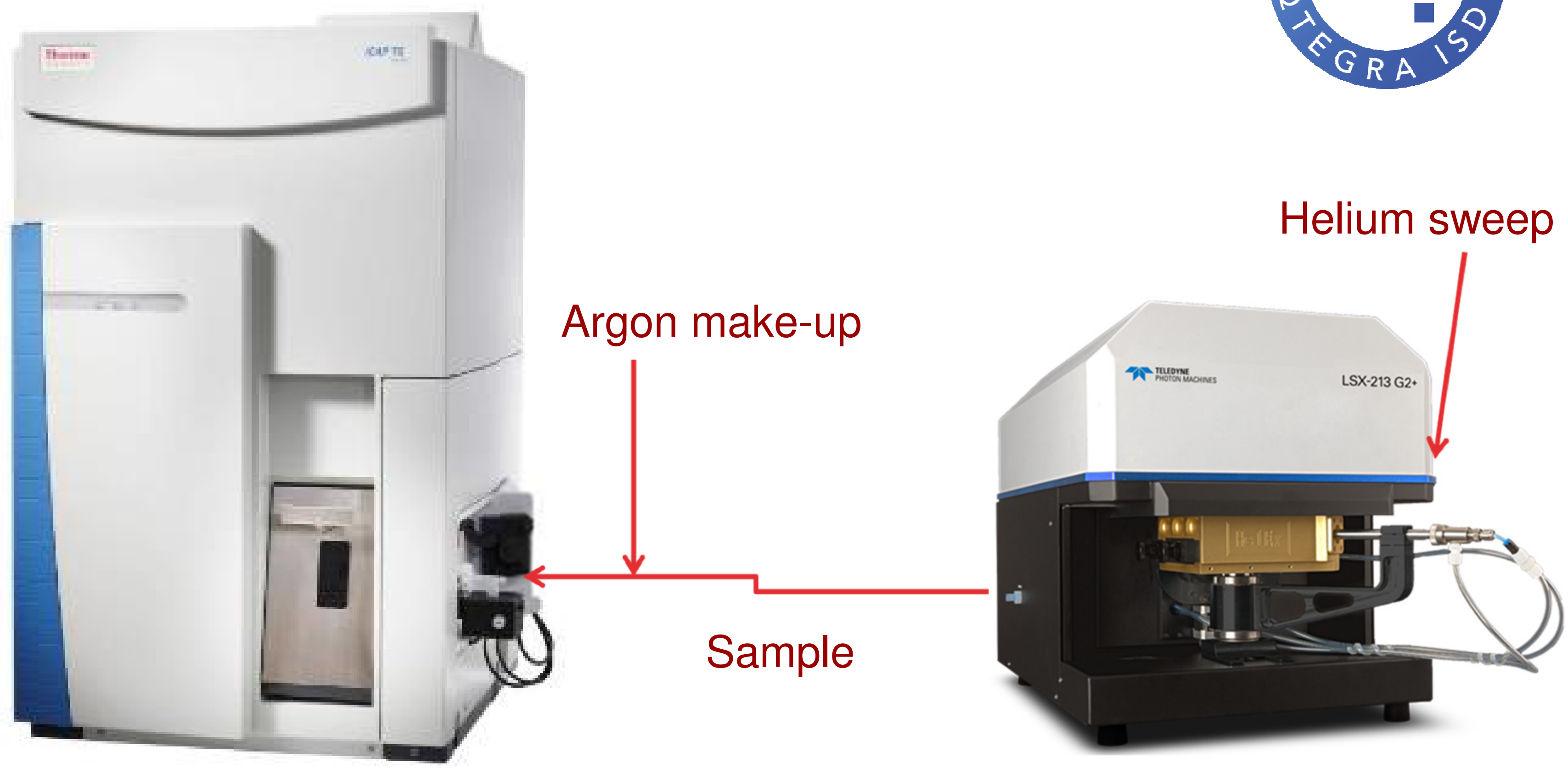
Multi-element analysis serum with iCAP TQ

	Measurement mode	Analyte/Product Ion mass	Internal standard
Na	SQ-KED	23	^{74}Ge
Mg	SQ-KED	24	^{74}Ge
P	SQ-KED	31	^{74}Ge
S	SQ-KED	34	^{74}Ge
K	SQ-KED	39	^{74}Ge
Ca	SQ-KED	44	^{74}Ge
Fe	SQ-KED	56	^{74}Ge
Li	SQ-KED	7	^{74}Ge
B	SQ-KED	11	^{74}Ge
Al	SQ-KED	27	^{74}Ge
V	SQ-KED	51	^{74}Ge
Cr	SQ-KED	52	^{74}Ge
Mn	SQ-KED	55	^{74}Ge
Co	SQ-KED	59	^{74}Ge
Ni	SQ-KED	60	^{89}Y
Zn	SQ-KED	66	^{74}Ge
As	SQ-KED	75	^{89}Y
Se	SQ-KED	78	^{74}Ge
Rb	SQ-KED	85	^{89}Y
Sr	SQ-KED	88	^{89}Y
Cd	SQ-KED	111	^{103}Rh
Ti	TQ-NH_3	114	^{74}Ge^{14}N^{1}H$_2$
Sb	SQ-KED	121	^{125}Te
[illegible]	[illegible]	[illegible]	[illegible]
Ba	SQ-KED	138	^{103}Rh
Pb	SQ-KED	208	^{209}Bi
U	SQ-KED	238	^{209}Bi

	LOD	MDL	*Serum L-1*		*Serum L-2*		*Urine*
			Measured	Reference or reported value	Measured	Reference or reported value	Measured
Na*	0.0027	0.027	2743	2330-3504	3255	2820-4241	2977
Mg*	0.0001	0.0010	21.0	13.4-20.1	39.7	27.1-40.7	85.6
P*	0.0008	0.08	52.3	43.3-65.1	120	88-132	710
S*	0.145	1.3800	1100	1008	1495	1335	476
K*	0.0021	0.02	150	101-153	260	176-265	1946
Ca*	0.002	0.0200	90.1	69-104	124	95-143	99.8
Fe*	0.00002	0.00023	1.64	1.17-1.77	2.18	1.72-2.58	0.005
Li	1.13	11.2920	5778	4202-6320	10806	7739-11639	22.4
B	0.67	6.746	70.1	79.4	87	82.1	1548
Al	0.20	1.9670	54.2	25.2-75.7	122	96-144	13.7
V	0.002	0.022	1.04	1.10	1.26	1.10	0.229
Cr	0.008	0.0800	1.70	1.30-3.05	5.20	4.00-7.50	0.838
Mn	0.008	0.084	10.7	7.9-11.9	14.2	11.6-17.4	0.914
Co	0.0001	0.0010	1.38	0.67-1.57	2.16	2.13-3.97	0.027
Ni	0.006	0.055	6.26	3.38-7.9	9.41	7.9-11.9	1.45
Zn	0.051	0.5130	1052	844-1269	1527	1404-1831	359
As	0.002	0.018	0.383	0.400	0.374	0.380	1.31
Se	0.010	0.1000	80.8	51-120	124	95-176	7.31
Rb	0.004	0.035	4.20	4.40	8.70	8.70	812
Sr	0.006	0.0570	95.7	95.0	106	110	89.2
Mo	0.005	0.048	0.710	0.760	1.20	1.21	7.62
[illegible]	[illegible]001	0.0100	0.130	0.130	0.140	0.140	0.229
[illegible]	[illegible]002	0.02	6.64	6.80	6.38	6.80	0.151
[illegible]	[illegible]006	0.0600	11.6	10.4	16.1	15.0	0.040
[illegible]	[illegible]022	0.219	75.5	71.8	69.9	60.9	82.8
[illegible]	[illegible]003	0.0300	172	190	133	139	2.09
Pb	0.0007	0.007	0.370	0.400	0.666	0.660	0.446
U	0.0001	0.0010	0.288	0.302	0.357	0.359	0.020

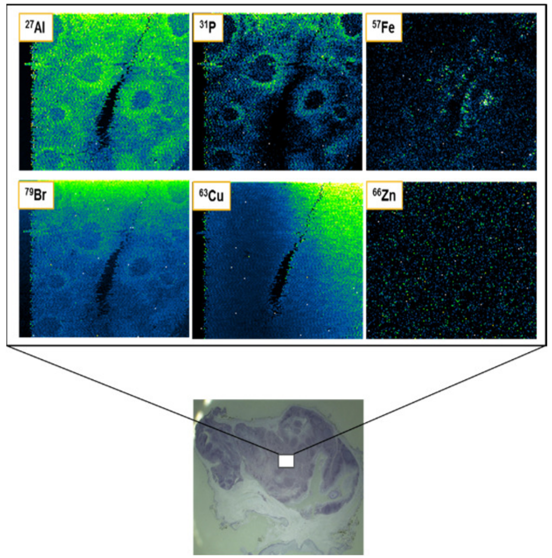
ThermoFisher SCIENTIFIC

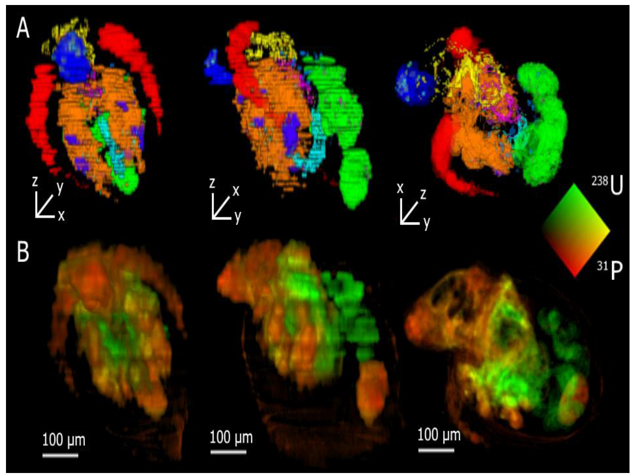
Bio imaging with LA-ICP-MS



Bio-Imaging with Laser Ablation ICP-MS

- An increasing number of studies in the field of Life Sciences employ different imaging techniques
- Trace elements are involved in many biological functions, for example:
  - Cu, Fe, Zn are all enzyme cofactors, and accumulation/deficiency are currently being investigated for links to neurological disease
  - P is present in DNA, and phosphorylated proteins and peptides are 'activated' states in biological functions
  - S is present in thiol groups, e.g. cysteine
  - Na and K are present in Na/K channels, which regulate cellular transport functions
  - Ca and Mg are used in signal transduction, esp. in nerve cells.
  - Se deficiency is being investigated for links with neurological disorders

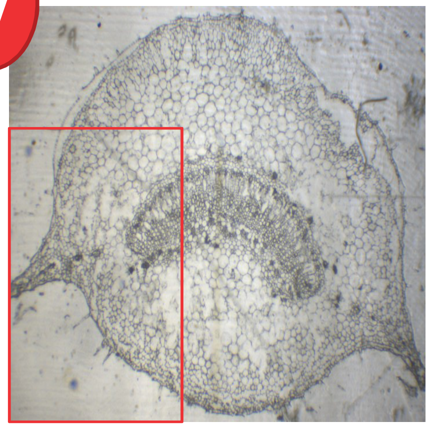




Bio-Imaging Technique: Balance between spatial resolution and speed

- Highest resolution can be achieved by mapping point-by-point, which leads very long analysis times. The best balance between speed and resolution is so-called 'line-mapping':

1 Choose an area to image

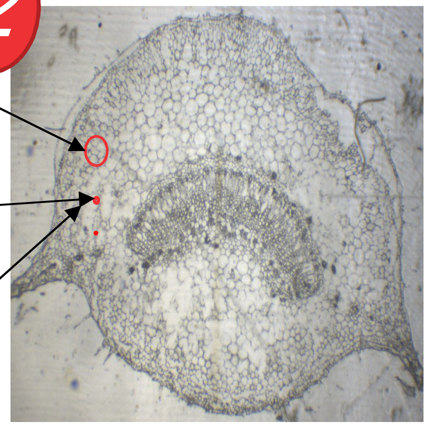


2 Choose an appropriate spot size

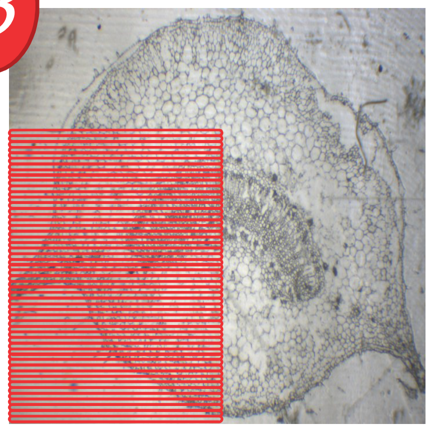
Large Spots = low spatial resolution

Balance between resolution and sensitivity

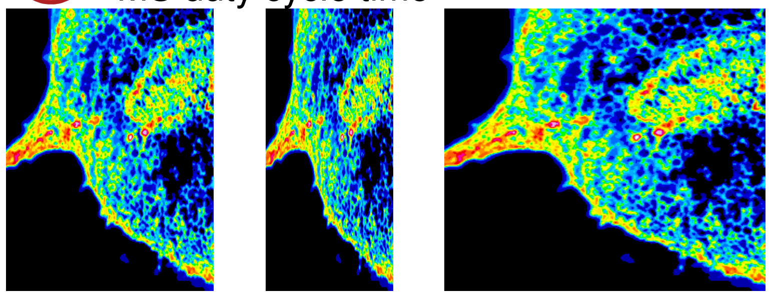
Very Small Spots = low signal



3 Draw lines with the chosen spot size (*x* µm)



4 Acquire data at a constant line scan rate (*s* µm s^{-1}) according to the ICP-MS duty cycle time



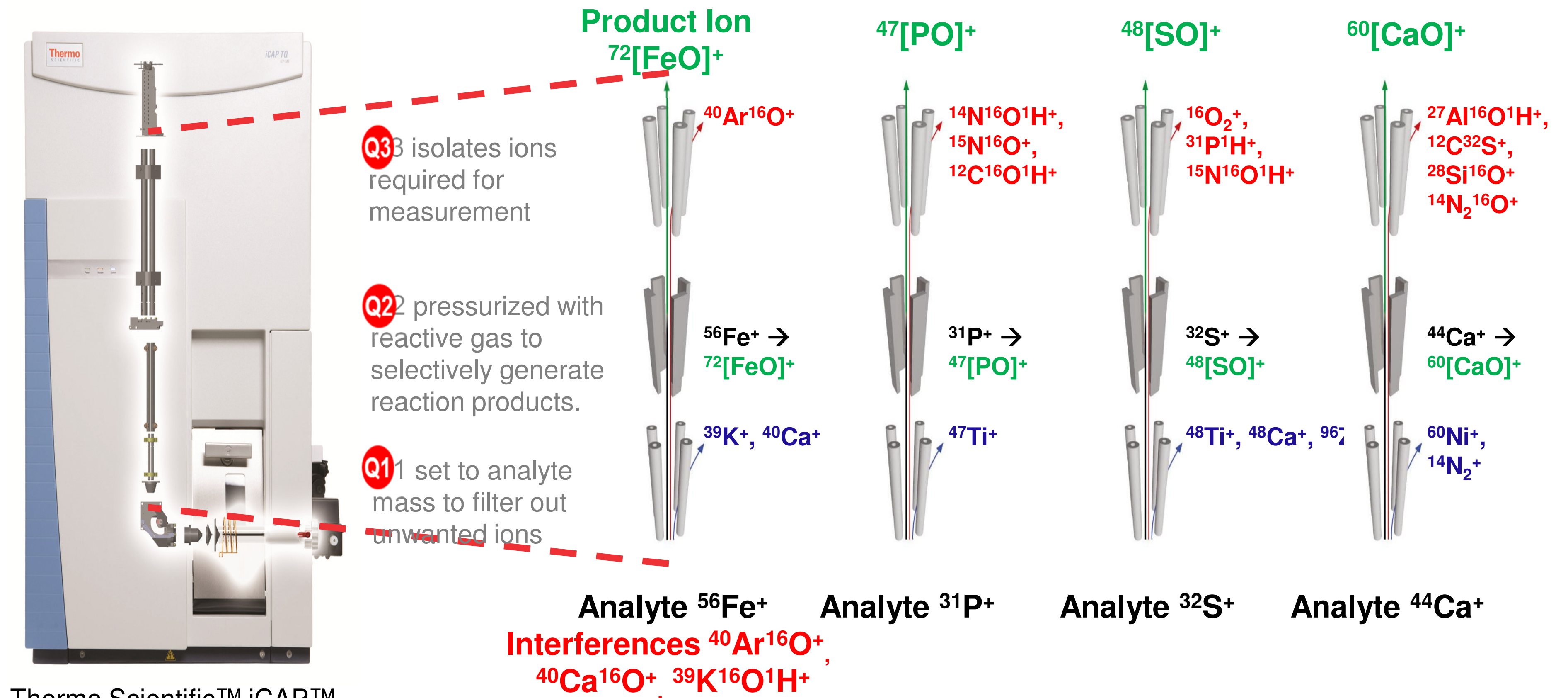
Convert data and image to 2D or 3D plot

Typical interferences in LA-ICP-MS based bio-imaging

Isotope	Abundance [%]	Possible interferences
31P	100	$^{16}O^{1}H^{14}N^{+}$, $^{16}O^{15}N^{+}$, $^{12}C^{16}O^{1}H^{+}$, $^{63}Cu^{++}$
32S	95.0	$^{16}O_2^{+}$, $^{31}P^{1}H^{+}$, $^{12}C^{20}Ne^{+}$, $^{16}O^{1}H^{15}N^{+}$
34S	4.3	$^{16}O^{18}O^{+}$
40Ca	96.9	$^{40}Ar^{+}$, $^{39}K^{1}H^{+}$
44Ca	2.1	$^{16}O^{1}H^{27}Al^{+}$, $^{40}Ar^{4}He^{+}$, $^{12}C^{32}S^{+}$, $^{16}O^{28}Si^{+}$
56Fe	91.8	$^{40}Ar^{16}O^{+}$, $^{1}H^{55}Mn^{+}$, $^{16}O^{40}Ca^{+}$, $^{16}O^{1}H^{39}K^{+}$
57Fe	2.1	$^{16}O^{1}H^{40}Ar^{+}$, $^{16}O^{1}H^{40}Ca^{+}$, $^{16}O^{41}K^{+}$
63Cu	69.2	$^{40}Ar^{23}Na^{+}$, $^{31}P^{16}O_2^{+}$, $^{47}Ti^{16}O^{+}$, $^{23}Na^{40}Ca^{+}$, $^{46}Ca^{16}O^{1}H^{+}$
66Zn	27.9	$^{32}S^{17}O_2^{+}$, $^{33}S^{16}O^{17}O^{+}$, $^{32}S^{34}S^{+}$, $^{33}S_2^{+}$
78Se	23.8	$^{40}Ar^{38}Ar^{+}$, $^{38}Ar^{40}Ca^{+}$
80Se	49.6	$^{40}Ar_2^{+}$, $^{40}Ar^{40}Ca^{+}$, $^{16}O^{1}H^{63}Cu^{+}$

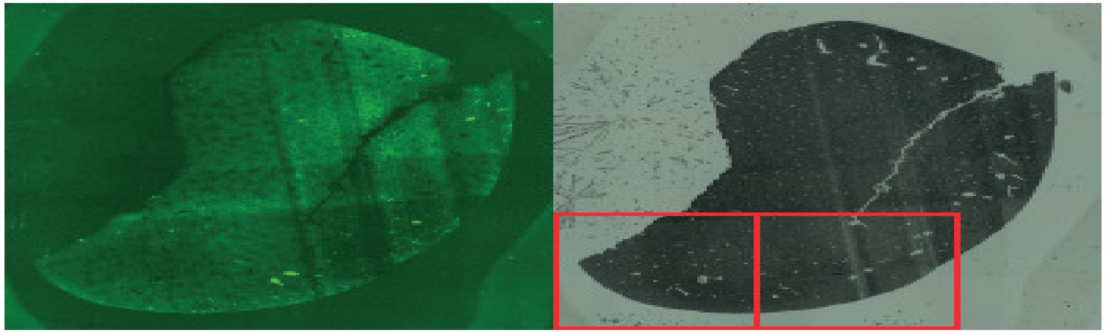
- Isobaric and polyatomic interferences caused by complex bio matrices leading to false positive results
  - P and S difficult to access due to presence of interferences from background (gas) species
  - Ca and Fe is complicated by both background gas interferences and by the sample

Bio-imaging using the iCAP TQ ICP-MS

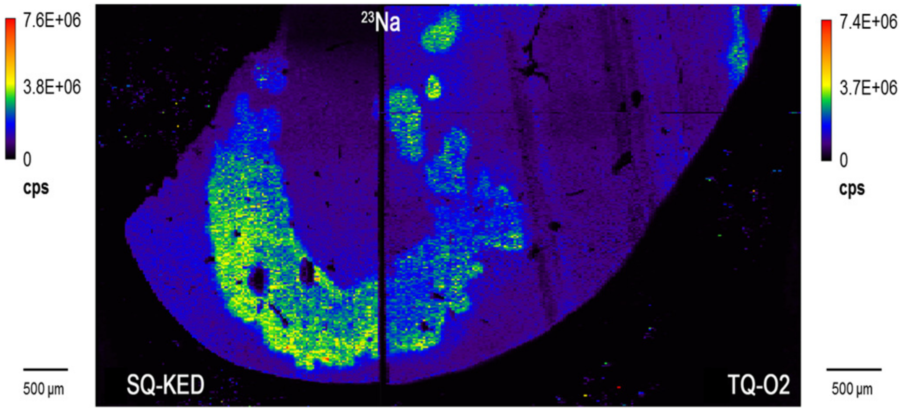


Thermo Scientific™ iCAP™ TQ ICP-MS

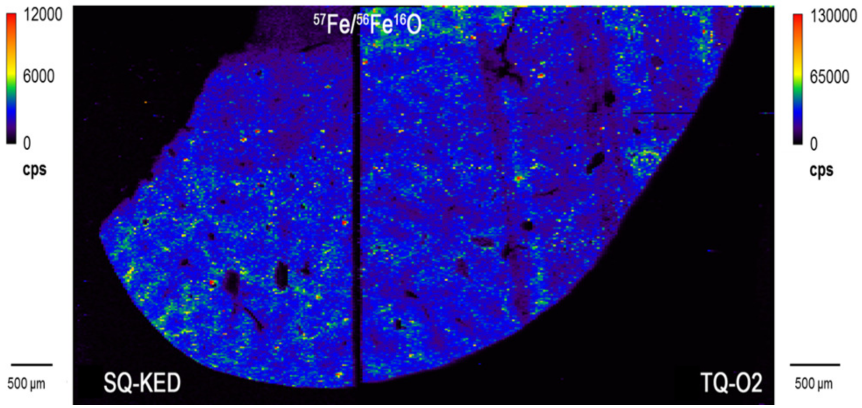
SQ-KED vs TQ-O_2 analysis of liver thin sections



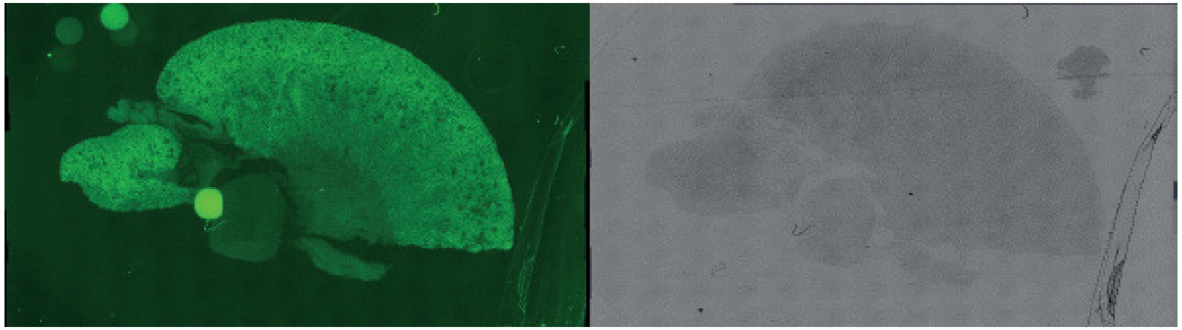
SQ-KED vs TQ-O_2: ^{23}Na
Na distribution is clearly visible in both modes. TQ-O_2 is a good compromise when several elements have to be analyzed at the same time, even if not all of them benefit from the interference correction.

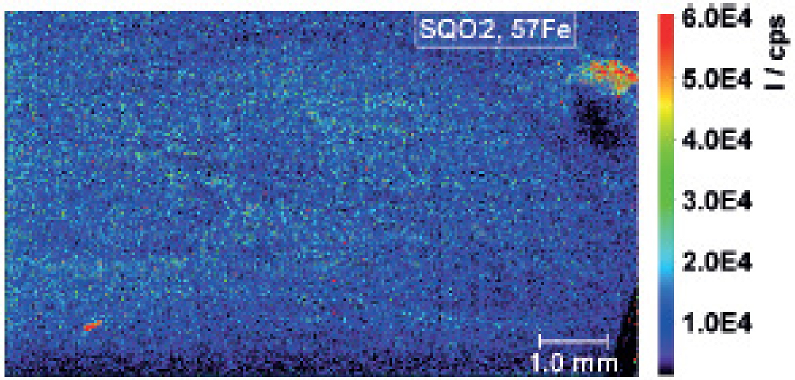


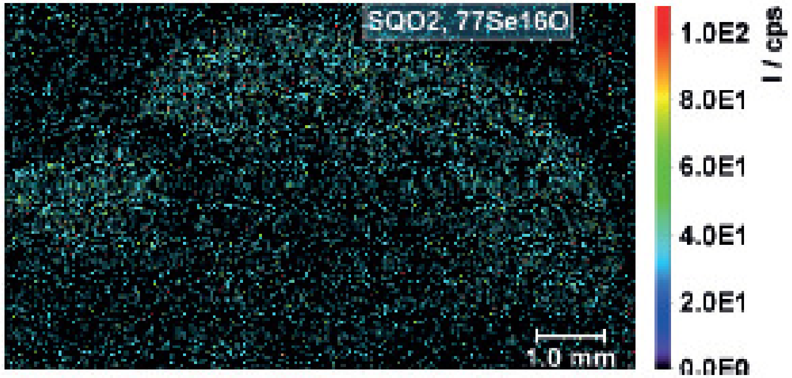
SQ-KED vs TQ-O_2: ^{56}Fe vs ^{56}Fe^{16}O
Fe distribution is shown similarly in SQ-KED and TQ-O_2 mode;

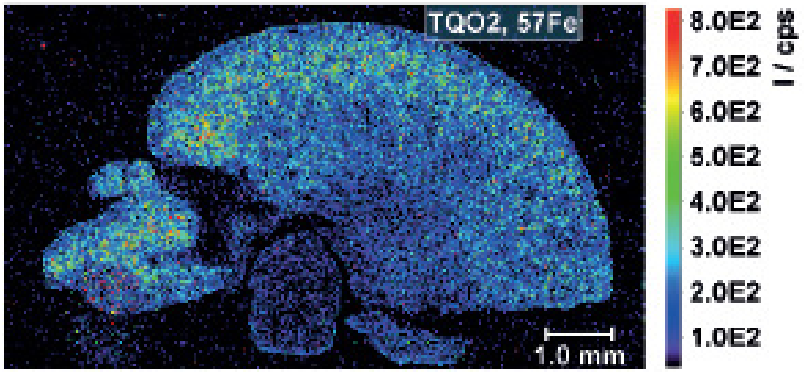


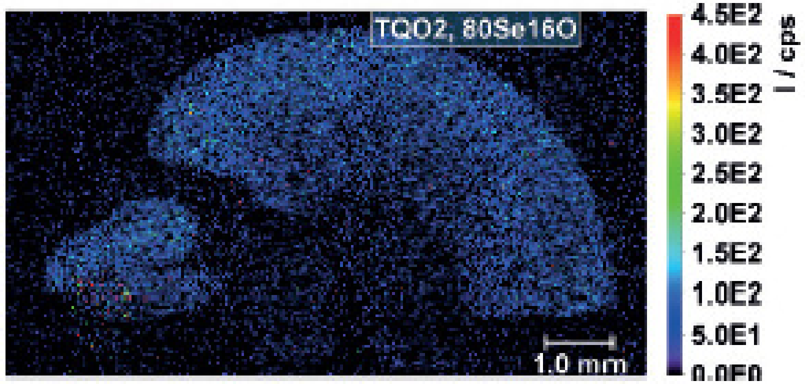
LA-ICP-MS kidney thin sections











Summary

- Triple quadrupole ICP-MS can be used effectively for clinical measurements
- iCAP TQ measurements for routine clinical measurements compares well to routine single quadrupole measurements
- Triple quadrupole ICP-MS shown to provide excellent performance for the determination of trace element analysis in biological research samples
    - TQ-ICP-MS provides accurate results for Ti in serum samples
- TQ-ICP-MS can be effectively used for imaging of biological samples when coupled with a laser ablation system

Questions