Strategies for the determination of rare earth elements in biological tissues by inorganic mass spectrometry

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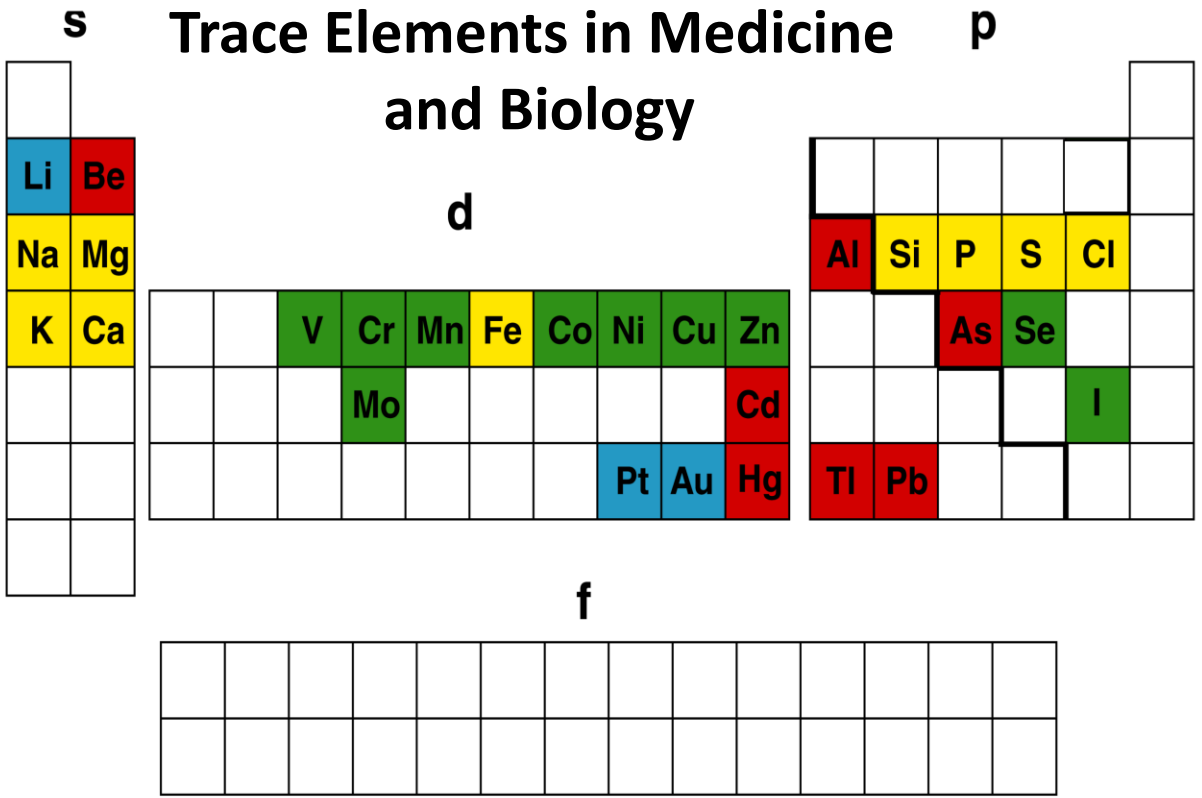
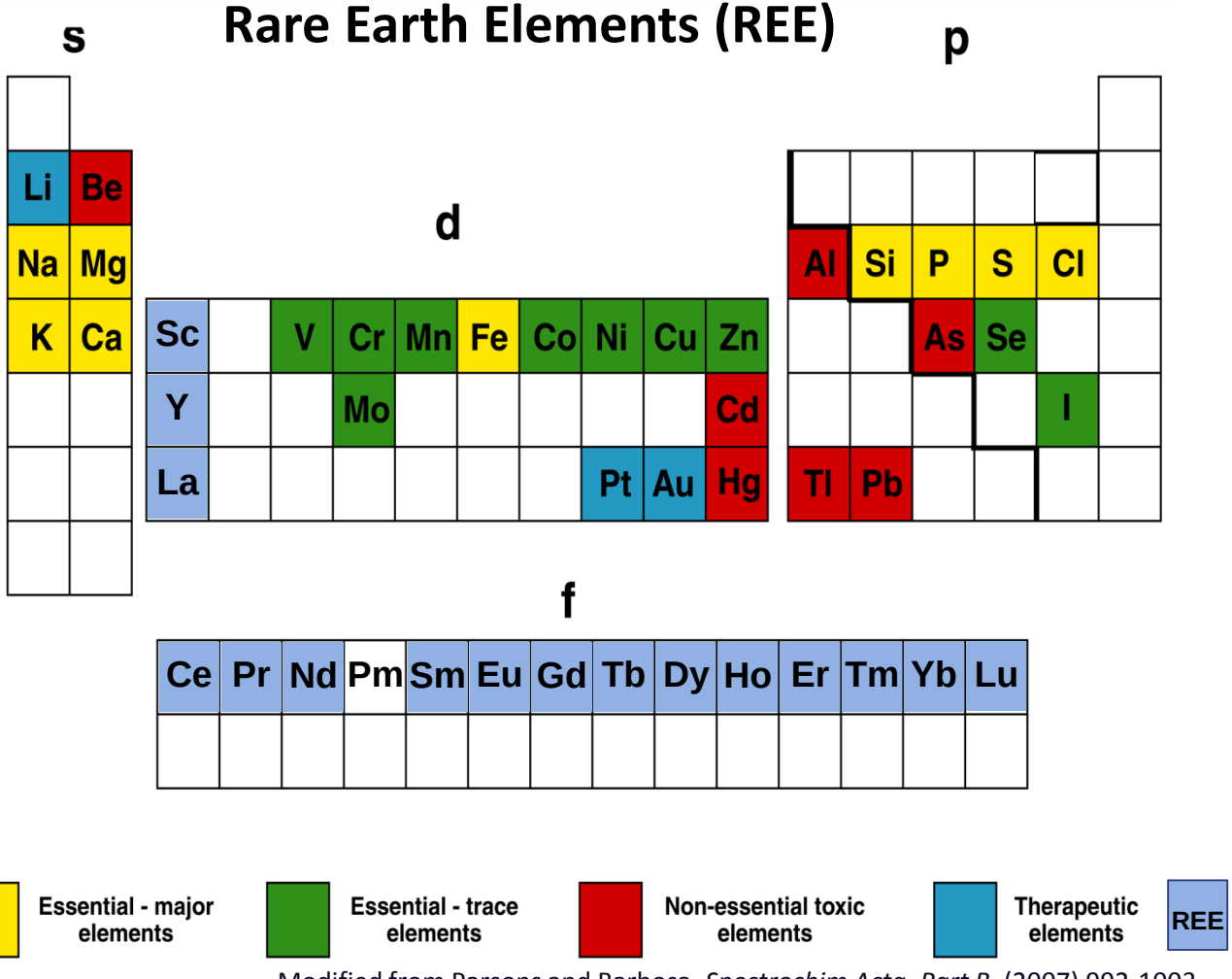
Outline

- Introduction to the Rare Earth Elements (REEs)
- Challenges and Strategies for Measuring REEs
- Applications:
  - ICP-MS/MS to measure REEs in human bone samples
- Conclusions
- Q/A

Trace Elements in Medicine and Biology



Rare Earth Elements (REE)



Modified from Parsons and Barbosa, *Spectrochim Acta, Part B*, (2007) 992-1003

Introduction to REEs

Why do we measure REEs? Why in biological samples?

Gd-based Contrast Agents	REEs in catalytic converters
La-based phosphate binders	Ce-based topical antiseptics
REE-doped fertilizers	REEs in superconducters
Y-Mg-based implants	REEs in computers
Ce and La nanoparticles	REEs in food for livestock

Use of REEs in industry, agriculture, and medicine is escalating on a global scale, contributing to increased background levels in the environment, with the potential for human exposure and uncertain health effects.

Analytical Techniques for Measuring REEs

Atomic Absorption Spectrometry (Flame/Furnace AAS)

Atomic Emission Spectrometry (ICP-AES/OES)

X-ray Fluorescence Spectrometry (XRF)

Neutron Activation Analysis (NAA)

Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

Challenges for Measuring REEs in biological samples by ICP-MS

Selectivity	14 examples of REE isobars	All isotopes for 8/16 REEs can be affected by oxides of other REE
Sensitivity	Background levels may be <5 ng/g	Digestion = further dilution
Calibration Range	Natural abundance of REEs ranges from 0.32 µg/g (Lu) to 64 µg/g (Ce) in the upper crust	

Lack of Matrix-Matched Certified Reference Materials

Two materials with certified values: BCR 668 (Mussel Tissue) and BCR 670 (Aquatic Plant)

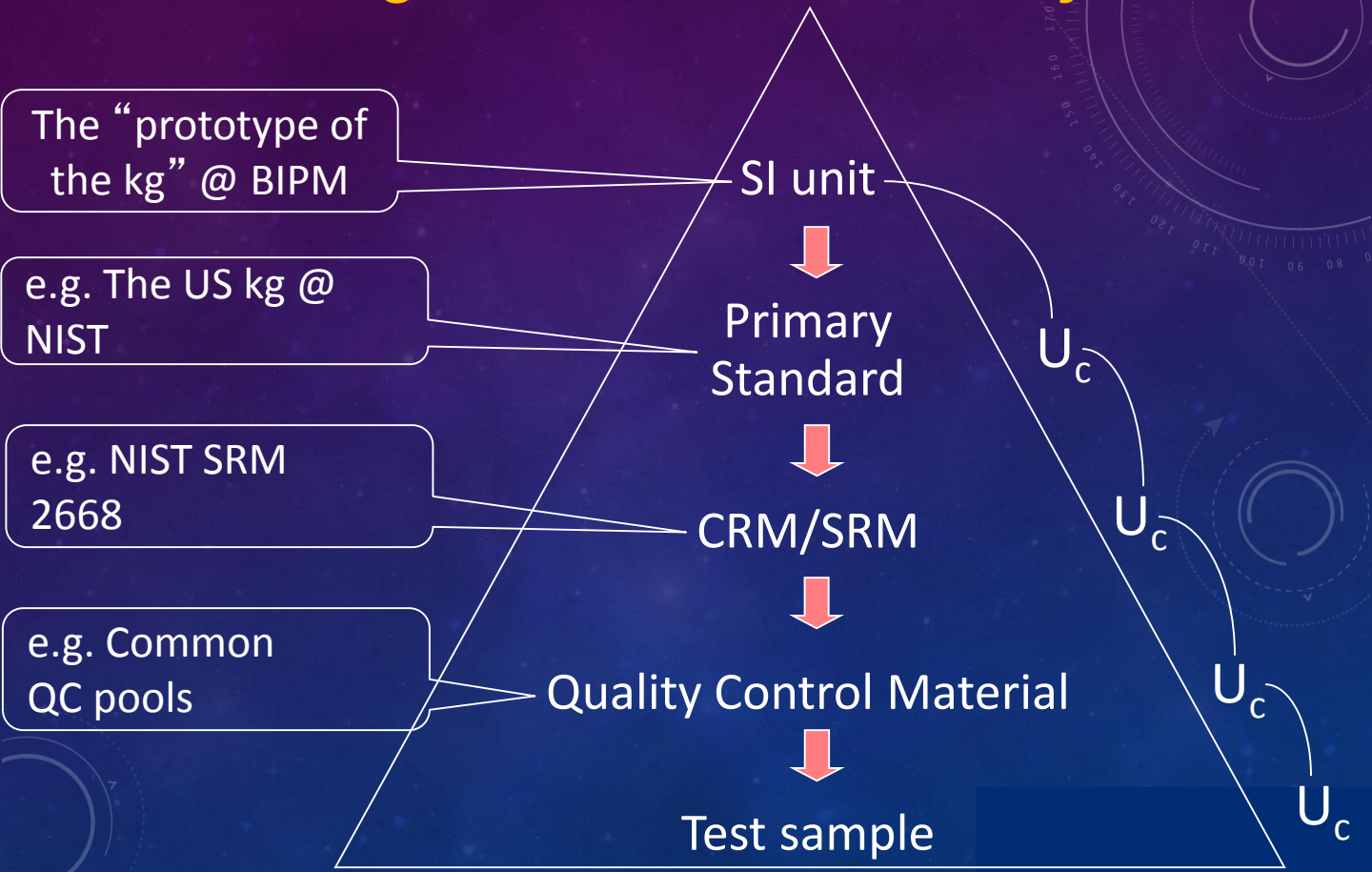
Strategies for Measuring REEs in biological samples by ICP-MS

Selectivity	Reaction/Collision Cells	Desolvation/ Electrothermal Vaporization
Sensitivity	High Resolution ICP-MS Extractions	
Calibration Range	Carefully thought out	

Lack of Matrix-Matched Certified Reference Materials

Strategies for establishing traceability?

The Metrological Order - Traceability



Application – Measuring REEs in human bone by ICP-MS/MS

ICP-MS/MS

Sample preparation

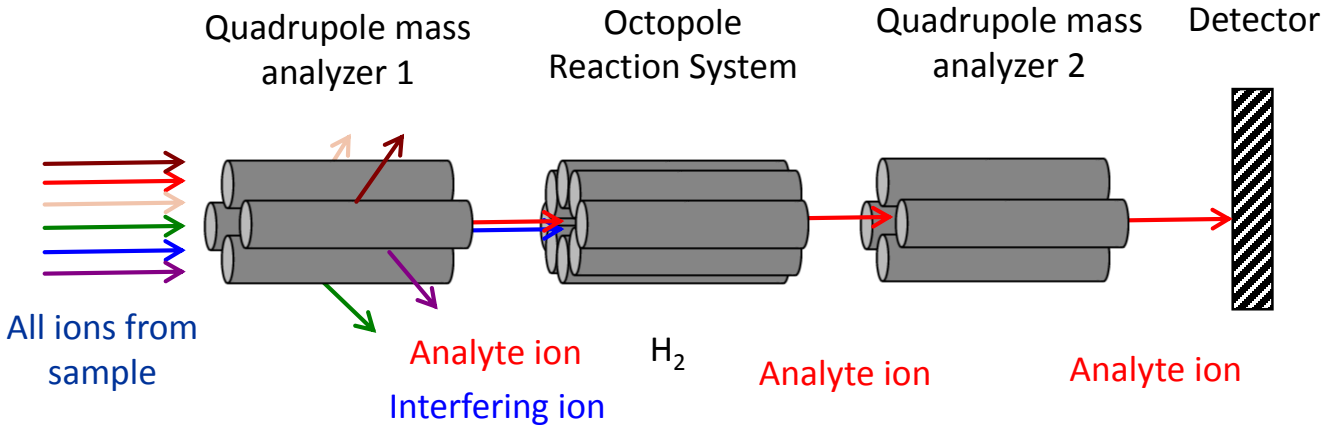
Approach

Internal Standard Selection

Gas flow optimization

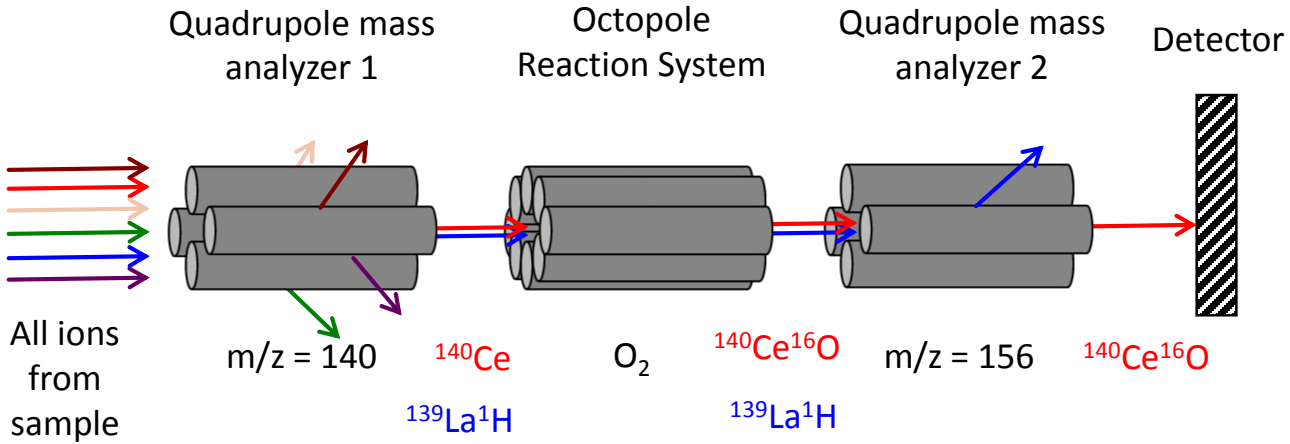
Accuracy/traceability

ICP-MS/MS "tandem ICP-MS"



The ORS can be used with various gases (e.g., H_2, He) to remove polyatomic interferences.

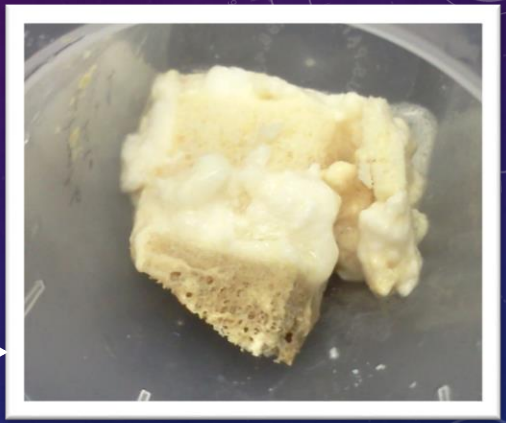
ICP-MS/MS "tandem ICP-MS"



Or, the ORS can be used with gases (e.g., O_2, NH_3) to achieve a mass shift for the analyte thereby avoiding polyatomic interferences.

Bone Sample Preparation

Removal of excess tissue



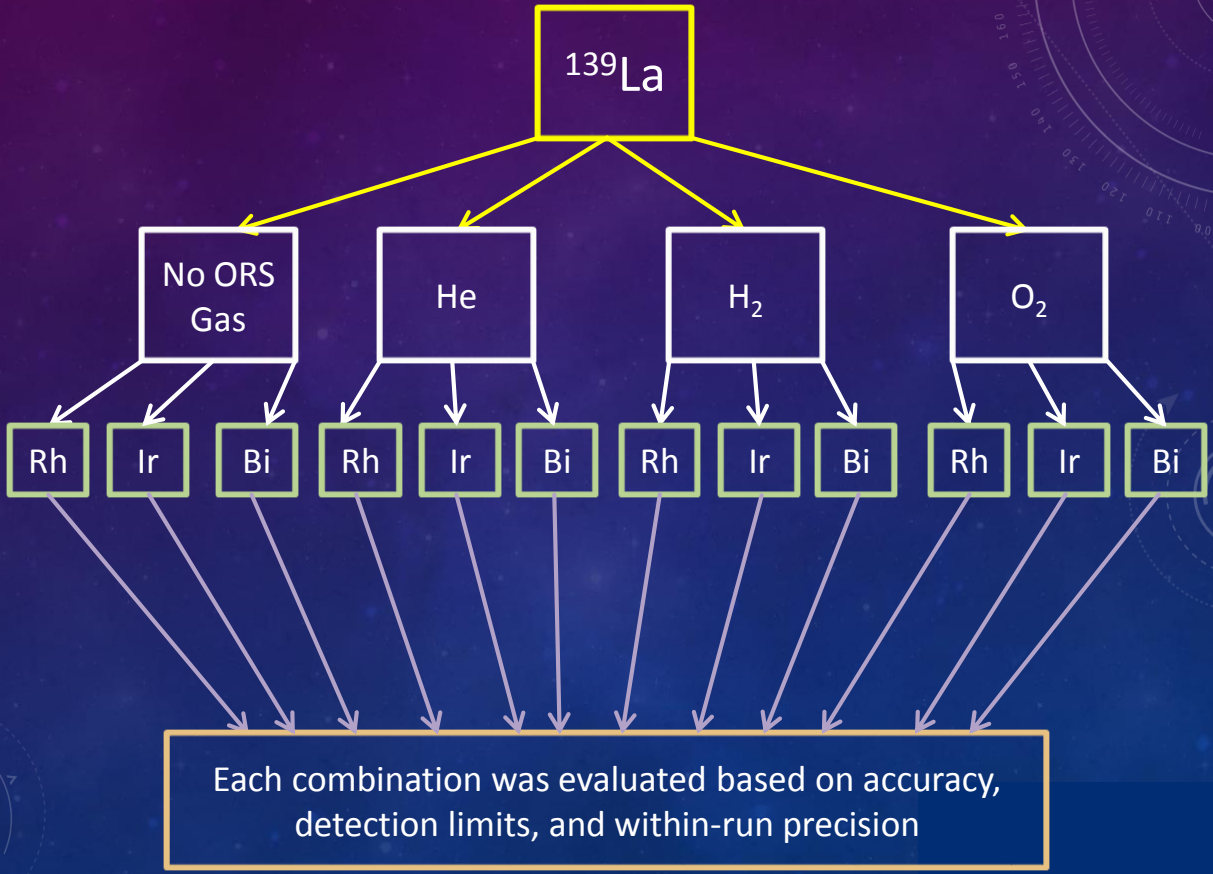
Cleaned, defatted, freeze dried

Sectioned, digested

Approach

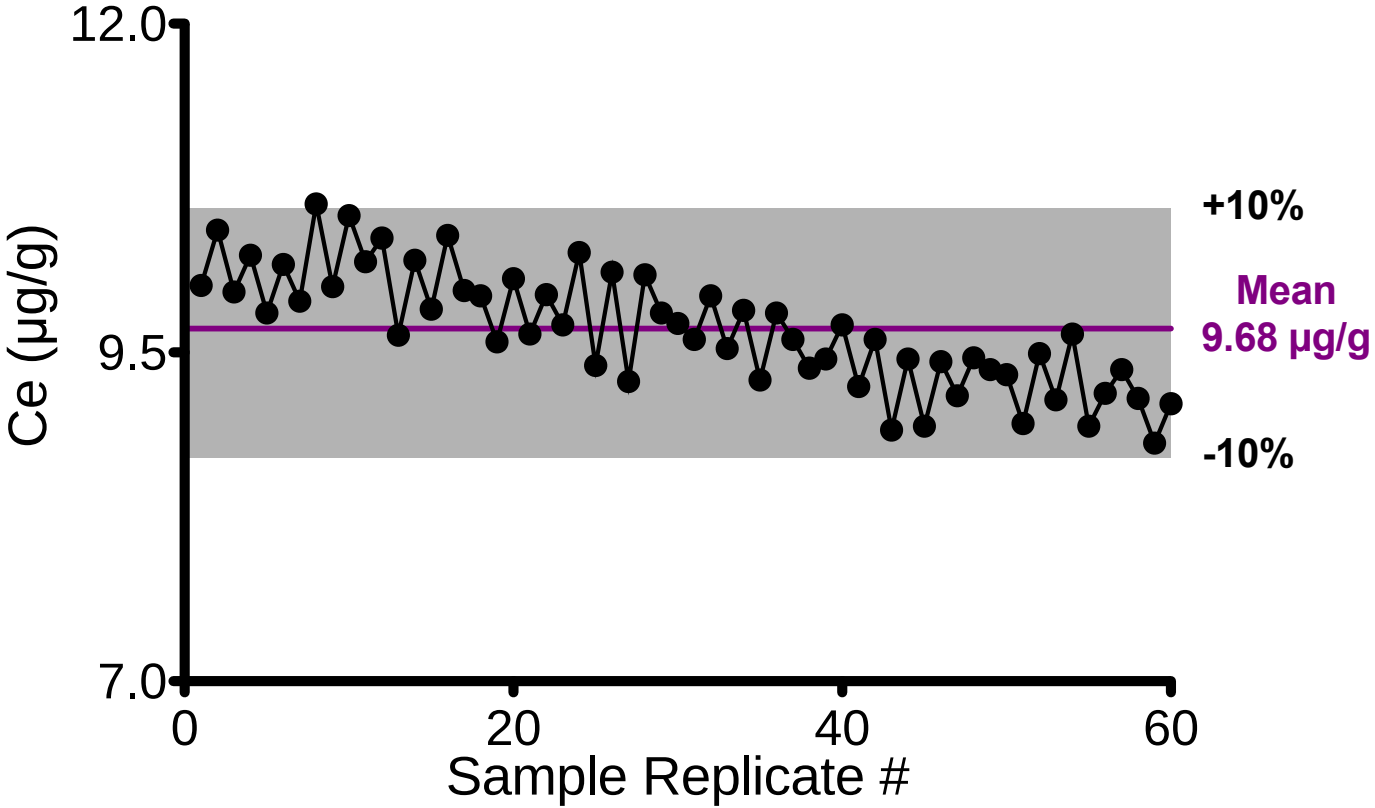
- 31 different isotopes investigated for 16 REEs
- Each REE isotope evaluated with 4 ORS gas modes: no gas, He, H_2, and O_2
- 3 different internal standards evaluated: Rh, Ir, Bi

Approach

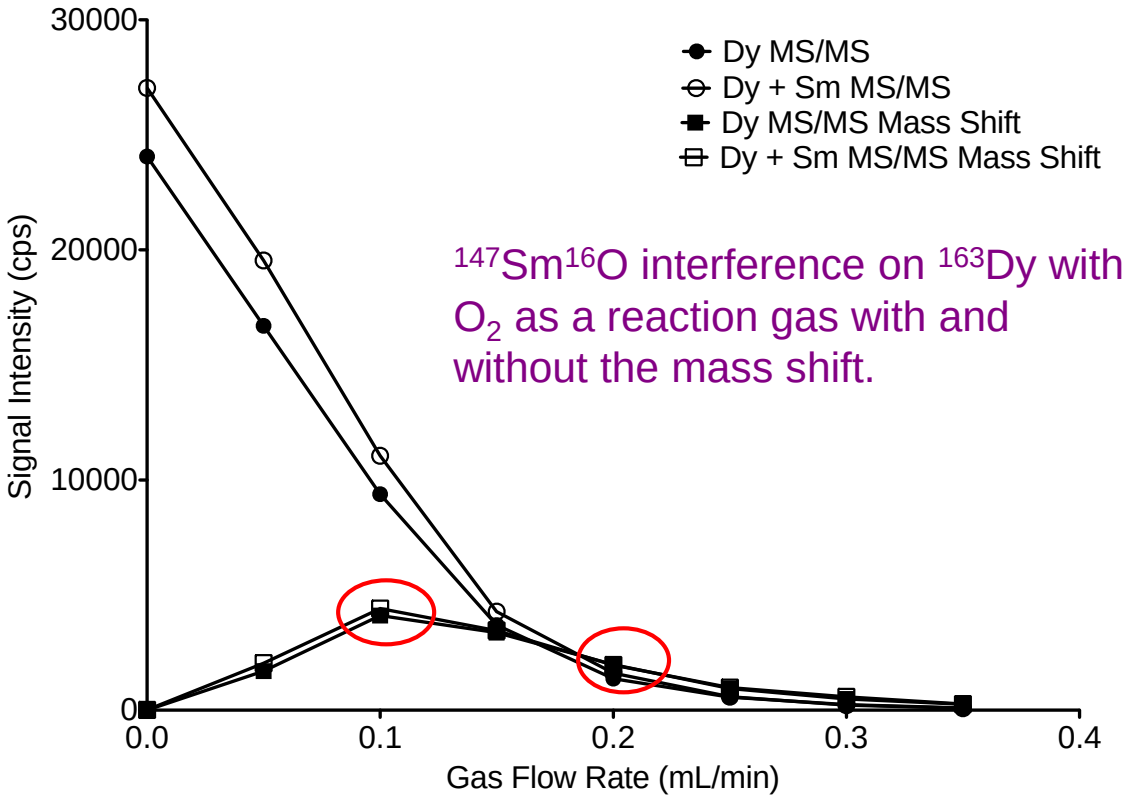

^{139}La
No ORS Gas
He
H_2
O_2
Rh
Ir
Bi
Rh
Ir
Bi
Rh
Ir
Bi
Rh
Ir
Bi
Each combination was evaluated based on accuracy, detection limits, and within-run precision

Rare Earth Element	m/z of Isotope(s) Monitored
Sc	45
Y	89
La	139
Ce	140
Pr	141
Nd	142, 144, 146
Sm	147, 149, 152, 154
Eu	151, 153
Gd	155, 156, 157, 158, 160
Tb	159
Dy	162, 163, 164
Ho	165
Er	166, 167, 168
Tm	169
Yb	172, 174
Lu	175

Internal Standard – Evaluation of Cerium



ORS Gas Flow Optimization



Accuracy

In the absence of bone materials certified for REEs, 7 biological CRMs were analyzed:

BCR 668 Mussel Tissue

BCR 670 Aquatic Plant

NIST SRM 1515 Apple Leaves

NIST SRM 1547 Peach Leaves

NIST SRM 1570a Spinach Leaves

NIST SRM 1573a Tomato Leaves

NIST SRM 2976 Mussel Tissue

Accuracy

…and 6 bone reference materials:

NIST SRM 1400 Bone Ash

NIST SRM 1486 Bone Meal

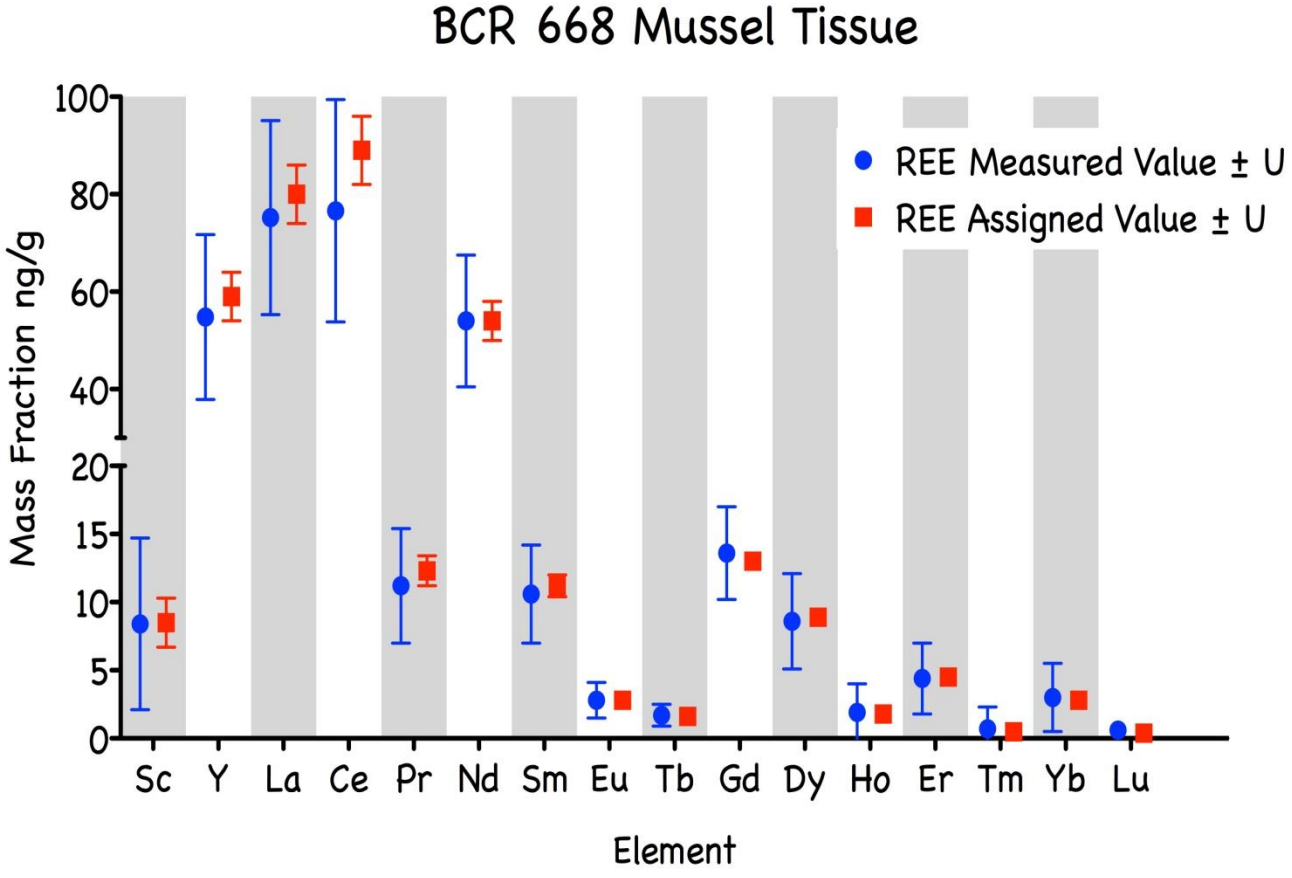
NYS RM 05-01 Lead in Bovine Bone

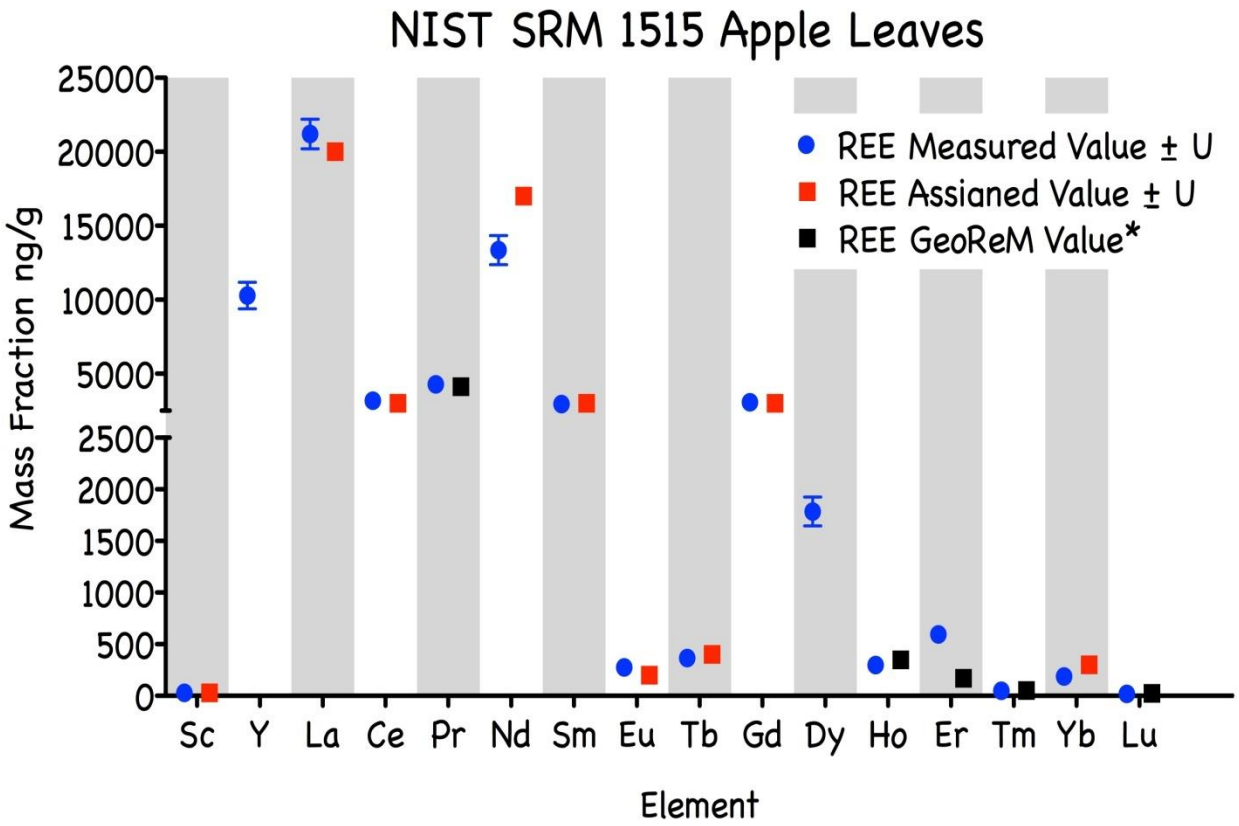
NYS RM 05-02 Lead in Bovine Bone

NYS RM 05-03 Lead in Caprine Bone

NYS RM 05-04 Lead in Caprine Bone

Plus sample spikes…


BCR 668 Mussel Tissue
REE Measured Value ± U
REE Assigned Value ± U
Mass Fraction ng/g
100
80
60
40
20
15
10
5
0
Sc
Y
La
Ce
Pr
Nd
Sm
Eu
Tb
Gd
Dy
Ho
Er
Tm
Yb
Lu
Element



*GeoReM values obtained from the Geological Reference Materials Database, http://georem.mpch-mainz.gwdg.de

NIST SRM 1486 Bone Meal

Technique	Q-ICP-MS [1]	Q-ICP-MS [2]	ICP-MS/MS
	Zaichick et al. 2011	Darrah et al. 2009	Galusha 2015
Y	21.9 ± 6.9	NR	37 ± 5
La	21.1 ± 5.8	23.02	25 ± 7
Ce	27.2 ± 5.6	32.99	22 ± 3
Pr	3.5 ± 0.6	8.65	3.4 ± 0.9
Nd	15.9 ± 2.8	23.2	16 ± 2
Sm	5.9 ± 1.6	10.57 ± 0.11	4 ± 2
Eu	<0.7	36.12	4 ± 2
Gd	6.4 ± 1.2	10.44 ± 0.11	6 ± 2
Tb	1.3 ± 0.2	6.12 ± 0.07	<1.1
Dy	4.6 ± 0.8	9.78	4 ± 2
Ho	<1.0	6.02	<2.7
Er	2.2 ± 0.9	7.94	2.3 ± 0.9
Tm	<0.33	4.94	<0.9
Yb	1.9 ± 0.6	7.91	2 ± 1
Lu	<0.67	6.19	<1.6

1. S. Zaichick, V. Zaichick, V. Karandashev and S. Nosenko, *Metallomics*, 2011, **3**, 186-194.
2. T. H. Darrah, J. J. Prutsman-Pfeiffer, R. J. Poreda, M. E. Campbell, P. V. Hauschka and R. E. Hannigan, *Metallomics*, 2009, **1**, 479-488.

Conclusions

REEs are challenging elements to measure with good selectivity, sensitivity and accuracy

Analyzing biological samples presents unique challenges:

- Sample complexity and analyte heterogeneity
- Long-term signal drift
- Lack of matrix-specific CRMs certified for REEs

Conclusions

Leveraging the mass shift option with ICP-MS/MS is one viable option for selective determination of REEs

Sensitivity can be optimized further

Accuracy is best assessed with matrix-based CRMs, but comparability with other databases may also be acceptable.

Long term signal drift partially attenuated with internal standard

Multiple sub-sections of solid tissues to estimate biological variability

Q & A

What other approaches apart from ICP-MS/MS have you used to determine REEs in biological samples?

Q & A

What other gases besides oxygen can be used for selective determination of REEs?

Q & A

Are there other interfering elements from the matrix (i.e. non-REE)?