Inductively Coupled Plasma Mass Spectrometry (ICP-MS) Method Portability Assessment Across Instrument Platforms

Skoworodko, L., Bennett, M., Bitcon, R., Molina, A., Granley, C., Gillson, G.

Rocky Mountain Analytical Division of LifeLabs LP, Calgary, Alberta, Canada

skoworodko@rmalab.com

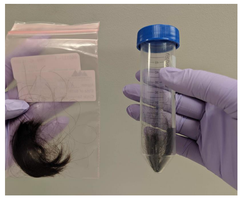
Overview:

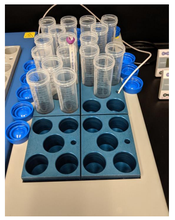
Our objective was to determine the portability of our existing hair element method from a PerkinElmer ELAN DRC II ICP-MS (ELAN) to an Agilent 8900 Triple Quadrupole ICP-MS (Agilent 8900). The intention of the switch in ICP-MS instruments was to reduce the amount of interferences seen in elemental analysis results from the ELAN which used only a single quadrupole, while also improving the accuracy of the method. In the end, the method was found to be portable to the newer ICP-MS model, the Agilent 8900 and the amount of interferences reduced due to the triple quadrupole upgrade that is used in the Agilent 8900.

Introduction:

Rocky Mountain Analytical first purchased the ELAN, used, in 2008. With the advancement of ICP-MS technology, it was decided in 2016 that the ELAN would be replaced with an Agilent 8900 with the hope of increasing precision and accuracy, decreasing sampling time, and the option of a triple quadrupole that could utilize up to 5 different gas modes.

One of the assays that was being run on the ELAN was the Hair Element Analysis method. In this method, hair samples are weighed, washed, digested in HNO_3, diluted, and analyzed on an ICP-MS measuring 45 different elements, which are both toxic and essential to the health of the individual depending on the concentrations present.





Methods:

Portability of the hair element method across the two instrument platforms was assessed by a number of quality metrics, including limit of quantitation (LoQ), precision, accuracy, and linearity on the Agilent 8900.

The Agilent 8900 comes equipped with a triple quadrupole (QQQ) and five different gas modes: No gas, He, H_2, O_2, and NH_3. This is compared to the ELAN, which had a single quadrupole and 3 gas modes (No gas, O_2, and NH_3). These upgraded capabilities aid in removing elemental interferences found in the samples.

Results:

I. Correlation to ELAN DRC II

The first task of assessing portability was to select the optimal gas mode and mass for each of the 45 elements being tested. 249 samples and 3 different controls were run on 6 different mirror runs between the Agilent 8900 and the ELAN. These results from the Agilent 8900 were plotted against the ELAN and analyzed to find slope, R^2 , and offset data were initially collected from multiple gas modes for the different elements.

I. Correlation to ELAN DRC II (Continued)

These values were used to determine the optimal gas mode to be used going forward with the Agilent 8900. Examples of the slope, R^2 and offset of several gas modes selected for a few elements are presented in Table 1 below.

Element [gas mode]	Comparison Slope	Comparison R^2	Comparison Offset
23 Na [He]	0.93	0.99	3.593
24 Mg [He]	0.92	0.98	2.753
32 -> 48 S [O2]	1.02	0.99	293.150
39 -> 39 K [O2]	1.03	1.00	-0.032
63 Cu [He]	1.00	1.00	-1.033
107 Ag [He]	1.01	1.00	-0.011
195 Pt [He]	1.05	1.00	-0.001
200 Hg [He]	1.56	0.99	0.007
208 Pb [He]	1.02	1.00	-0.004
238 U [He]	0.98	0.99	0.003

Table 1: Comparison slope, R^2 and offset calculated from six different mirror runs consisting of a total of 249 different patient hair samples. Ten examples of elements analyzed at Rocky Mountain Analytical show that the Hair Element Analysis method is statistically similar whether the method is run on the ELAN or Agilent 8900.

For the most part, the slopes of the scatterplots were within 0.9 to 1.1 which was deemed an acceptable range for the portability of the method.

One exception is Hg. In this dataset, the slope of the scatterplot for Hg (Agilent) vs Hg (ELAN) was 1.56. However, there was previously a scaling factor of 1.5 being applied to Hg results when reported from the ELAN in order to align with external QA samples. With a slope of 1.56, it was determined that the ELAN scaling factor could be removed when testing switched to the Agilent 8900 as it reported accurate Hg results.

In general, the correlations between the two instruments were excellent, with the R^2 values being greater than 0.97, and in most cases being 0.99.

Not all of the elements, however, correlated well with the ELAN. Upon review of the 249 mirror data, it was decided that the reference ranges for six elements (Si, V, Cr, As, Fe and Zr) would need to be re-established as there was significant discrepancy between the Agilent and the ELAN values. This arises from the Agilent 8900's superior ability to reduce molecular interferences.

II. Limit of Quantification

Ideally, the Limit of Quantification (LoQ) should be determined by examining the recovery of successively lower concentrations of each analyte in a matrix identical to that of the patient samples. Unfortunately this approach is not possible for all analytes in human hair, as no truly "blank" or close-to-blank hair exists. For the purposes of this validation, a two-pronged approach was taken.

a) For elements that are either not typically present or present in very low concentrations in hair, various dilutions of our calibration standards were used to spike patient hair digestates to determine the LoQ.

b) For elements that are typically present in human hair at detectable levels, the spikes of increasing amounts of calibration standards were added to a 6% nitric acid solution, rather than patient samples, in order to match the acid content of digested patient samples. Each spike concentration was run a minimum of 7 times and the variation amongst these replicates was used to determine the LoQ.

For the purpose of this validation, the LoQ was defined as 3 times the standard deviation once a coefficient of variation (CV) of ≤15% for the 7 replicates was achieved. For most elements, the LoQ was significantly lower run on the Agilent 8900 compared to the ELAN, therefore demonstrating improved sensitivity. 36 of the 45 elements had lower LoQ. The other 9 elements were only slightly higher. A sample list of the current LoQ for the Agilent 8900 instrument, as well as the original ELAN LoQ, is shown in Table 2.

Element	ELAN LoQ (µg/g Dry Hair) (ppm)	Agilent 8900 LoQ (µg/g Dry Hair) (ppm)
Sodium (Na)	1.0000	0.2986
Magnesium (Mg)	1.0000	0.1010
Sulfur (S)	300.0000	1.6725
Potassium (K)	0.5000	0.3000
Copper (Cu)	0.5000	0.0031
Silver (Ag)	0.1500	0.0002
Platinum (Pt)*	0.0040	0.0016
Mercury (Hg)	0.0100	0.0005
Lead (Pb)	0.0100	0.0007
Uranium (U)	0.0006	0.0001

Table 2: Comparison of the Agilent 8900 Limit of Quantitation for 10 elements to the ELAN's Limit of Quantitation. The LOQ of these ten elements decreases when the Agilent 8900 is used, due to its superior sensitivity. LoQs determined via spiking digested hair sample s are marked with an asterisk.

III. Precision

Three control samples (Low Pool 4, High Pool 6, and 7601a) were run a minimum of 20 times total, with a maximum of two runs per day. Below are the tables representing the mean, standard deviation and %CV for each of the three controls. For each element in each control, outliers were statistically calculated using the program "Analyse it" with a 2-sided plot and a 90% confidence interval. The far outliers were removed from the mean, standard deviation and %CV calculations.

For some elements, precision actually decreased when the samples were run on the Agilent, but it was determined that the difference was statistically not significant.

The table below lists the precision, measured as %CV, in the ELAN vs. the Agilent 8900 for the 7601a control.

Table 3: Comparison of the Agilent 8900 %CV to the ELAN's %CV. All of the elements except for platinum (Pt) listed in the chart have lower CV% when run on the Agilent 8900, which is mainly due to the successful removal of interferences when a triple quadrupole is used.
The %CV for Pt appears to have increased in the Agilent 8900, however, the results were all below detectable ranges on both instruments as it is not present in the control sample.

Element	%CV ELAN	%CV Agilent 8900
Sodium (Na)	11.828	9.076
Magnesium (Mg)	18.086	12.538
Sulfur (S)	11.501	4.692
Potassium (K)	11.981	12.995
Copper (Cu)	45.530	6.764
Silver (Ag)	20.325	6.484
Platinum (Pt)	27.448	39.047
Mercury (Hg)	11.446	6.407
Lead (Pb)	10.441	6.771
Uranium (U)	8.999	4.426

IV. Accuracy

The accuracy of patient results are measured using a Certified Reference Material (CRM), two in-house controls, as well as by participation in an external proficiency program. The CRM used is called GBW07601a, a powdered hair sample from the Institute of Geophysical and Geochemical Exploration. This CRM is weighed, digested, and analyzed with each hair run. The two in-house controls consist of one high patient pool and one low patient pool which have established acceptable ranges based on a minimum of 20 digestates over 10 hair element runs. These patient pools are finely cut and homogenized and are weighed, washed, digested and analyzed with each run. The external proficiency scheme that is used to assess the hair element method is provided by an ISO accredited source called Quebec Multielement External Quality Assessment Scheme (QMEQAS), which is a hair matrix. There have been two rounds of QMEQAS that have been submitted from the Agilent 8900, both rounds easily passed according to their criteria.

V. Linearity

Linearity of each element is measured in each analytical run using calibration standards. The acceptable criteria of the calibration curve is a slope value greater than 0.995. The actual measured curves are often greater than 0.999.

For elements which occasionally exceed the concentration of our calibration standards in patient samples, linearity was proven to these higher concentrations. To determine the concentration at which linearity needed to be proven, we evaluated the last six month of patient data to find each element's highest measured value. All of the extended calibration concentrations measured came back with a slope greater than 0.995.

Conclusions:

In conclusion, it was determined that the existing ICP-MS hair method was portable from the ELAN DRC II to the Agilent 8900. Not only was the method successfully transferred to the Agilent 8900, the new triple quadrupole ICP-MS also improved the precision and accuracy of the method, with greater sensitivity and dramatically reduced sampling time. Two further improvements were the significant reduction in sample volume required to perform the Hair Element Analysis, and a reduction in all solutions utilized by this method.