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Ultra-trace analysis of ^{41}Ca in urine by accelerator mass spectrometry: an inter-laboratory comparison

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Abstract

A ^{41}Ca interlaboratory comparison between Lawrence Livermore National Laboratory (LLNL) and the Purdue Rare Isotope Laboratory (PRIME Lab) has been completed. Analysis of the ratios assayed by accelerator mass spectrometry (AMS) shows that there is no statistically significant difference in the ratios. Further, Bayesian analysis shows that the uncertainties reported by both facilities are correct with the possibility of a slight under-estimation by one laboratory. Finally, the chemistry procedures used by the two facilities to produce CaF_2 for the cesium sputter ion source are robust and don't yield any significant differences in the final result.

Keywords

^{41}Ca ; accelerator mass spectrometry; Bayesian statistics; interlaboratory comparison

1. Introduction

^{41}Ca has a long half-life ($T_{1/2} \sim 10^5$ years) when compared to the lifespan of an organism and decays with little energy deposition via pure electron capture. These features of ^{41}Ca , when coupled with the ability of accelerator mass spectrometry (AMS) to measure very small numbers of ^{41}Ca atoms, have led to an increasing number of applications of this nuclide in biomedical research. These applications include human health studies in osteoporosis [1-3] and other diseases [4, 5], and research into calcium metabolism [6-9]. This surge in applications has led to more demand being made at AMS facilities for ^{41}Ca assays. However, ^{41}Ca is a challenging AMS measurement; many interferences (i.e., ions other than ^{41}Ca) reach the detector, especially when samples come from a biological matrix which invariably contains ^{41}K , the most pernicious interference of all [10, 11]. The analytical challenge of the ^{41}Ca AMS measurement creates a natural need for laboratories that routinely measure this isotope to compare results.

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In this paper we report the results of an inter-laboratory ^{41}Ca comparison involving PRIME Lab and LLNL. Excess calcium purified from previously measured urine samples was used, allowing a robust test of laboratory methodology for $^{41}\text{Ca}/\text{Ca}$ measurement under realistic conditions. In order to test differences between both final chemical preparation (i.e., elemental purification, calcium fluoride production) and the AMS measurements, our study was divided into two different components: (1) a number of samples chemically prepared at PRIME Lab were measured at both PRIME Lab and at LLNL, to check AMS measurement consistency; (2) AMS samples from the same source material (calcium oxalate precipitate from urine) were prepared at both LLNL and at PRIME Lab, and then measured at LLNL. This part of the exercise focused on comparing the chemical preparation procedures in the two labs while minimizing any bias from AMS analysis.

This paper is organized as follows. In section 2 we discuss details of the chemistry and the AMS at LLNL and PRIME Lab. In section 3 we present a mathematical derivation, which will be used in the comparison. Section 4 presents the results of the different statistical methods that were brought to bear in the comparison. The main conclusion of our study is a positive one: the ^{41}Ca measurements from the two labs are in good agreement, which is encouraging for future use of this nuclide in biomedical research.

2. Materials and Methods

2.1 Samples

Samples were collected from the urine of ~40 post-menopausal subjects that were dosed with 50 or 100 nCi of ^{41}Ca (Argonne National Laboratories) in sterile saline by intravenous injection. Twenty four-hour urine collections were pooled until the approximate daily calcium excreted for each individual was established; then individual volume collections that provided the minimum calcium for analysis were requested (e.g., 500 ml or ml 1 l), up to a maximum of a 24-hour volume with the volume based on the typical calcium concentration of a particular subject's urine. Urine samples were collected in acid-washed containers and the volume was measured. Approximately 10 ml of ammonium hydroxide was added to every liter of urine and mixed to ensure that the pH was at least 10. Then, 50 ml of saturated ammonium oxalate was added and mixed to separate the calcium by precipitation as calcium oxalate (CaC_2O_4) by letting the sample stand overnight. The sample was then filtered and the wet oxalate air-dried on the filter. The filter and oxalate was then transferred to a 10 ml bottle for shipment to PRIME Lab and LLNL.

The procedure for production of CaF_2 from calcium oxalate for PRIME Lab and LLNL will be described below. Both methods are based on chromatographic cleanup followed by precipitation of CaF_2 as originally developed by Freeman [10]. Samples were measured in several runs at PRIME Lab over the course of 4 years. In the summer of 2011, 47 of these samples were chosen at random and sent to LLNL for comparison purposes. This subset had already been chemically prepared at PRIME Lab. Further, thirteen more samples were chemically prepared at PRIME Lab and LLNL and AMS measurements for these two groups were made at LLNL. These samples were taken from a subset of 22 of the women that have taken place in multiple ^{41}Ca studies at Purdue [1, 2]. The Human Institutional Review Boards at Purdue University, Indiana University-Purdue University Indianapolis, and Clarian IRB approved the protocol in this study as part of larger intervention studies. The LLNL IRB approved the blind intercomparison as an exempt protocol.

2.1.1 Production of CaF_2 from CaC_2O_4 at PRIME Lab—First, 300-500 mg of the powder containing the oxalate is weighed out. If less than 300 mg was precipitated out, then the entire sample is used. The powder is then dissolved overnight in 5 ml of 4 M nitric acid. The sample is then diluted to 50 ml with 18 M water and centrifuged to remove insoluble

material. The sample is then poured over 4 ml of AG 50W-X8 cation exchange-resin (Bio-Rad, Hercules, CA). The resin is prepared with 12 ml of 4 M HNO₃ and then washed with 12 ml of 18 M water before addition of the sample. After the sample has been loaded onto the column, other metal ions (mostly monovalent interferences such as K) are removed with 18 ml of 0.4M HNO₃. Next, the calcium is eluted off of the column with 12 ml of 4 M HNO₃ and then diluted to 25 ml with 18 M water before precipitating out CaF₂ with 5 ml of 48% HF. The sample is left to sit for 48 hours before 3 rounds of centrifugation and washing with 18 M water followed by drying in a vacuum oven. Everything is disposable except for plastic funnels that are used to minimize sample loss from spilling during the chromatography step (they fit in the top of the disposable column). These are cleaned and rinsed 3 separate times in soapy ultrasonic baths before re-use.

2.1.2 Production of CaF₂ from CaC₂O₄ at LLNL—For the samples used in this paper, calcium oxalate (~50mg) was dissolved in nitric acid and then diluted to 0.1 M. The sample was then decanted over 1 ml resin prepared following the procedure of Freeman [10]. The resin was then washed with 15 ml of 0.1 M nitric and then extracted from the column with 6 ml of 5 M nitric. Next, 1.5 ml concentrated NH₄OH was added to the solution, which lowers the ionic strength. Then, 3 ml of 40% HF was added and the precipitate fell out of solution over a period of 24 hours. Next, the sample was spun down and the supernatant discarded. After this, ~2 mL of very dilute HF was added and the sample was transferred to a 2 ml centrifuge tube. This step kept a small amount of the CaF₂ from re-dissolving. The sample was then mixed and spun down and the supernatant was removed with a disposable pipet. Finally, the fluoride was dried overnight at 90 C (in air). Everything was disposable. The centrifuge tubes were cleaned with 10% nitric acid rinses before use.

2.2 Loading

The CaF₂ that was loaded into PRIME Lab cathodes was mixed with silver (Aldrich, 325 mesh) in equal volumes which is a 3 or 4/1 Ag/CaF₂ mass ratio. The CaF₂ that was loaded into LLNL cathodes was mixed with Nb (Alpha puratonic, 99.99%, ~325 mesh). The operators at LLNL observe a decrease in performance of the ionizer that is the heart of the ion source over time when they mix with Ag whereas this effect is not observed at Purdue.

2.3 AMS Measurement

We will now discuss the basics of the AMS measurement and analysis of the data, the details of which can be found elsewhere [12, 13]. AMS measures very rare (often radioactive) isotopes in quick succession with a more abundant stable isotope of the same element, providing a ratio of the two: essentially, AMS is a very sensitive type of isotope ratio mass spectrometer. There are other analytical methods with similar sensitivity, such as resonant ionization mass spectrometry [14, 15] and atom trap trace analysis [16, 17], but these lack development as high throughput platforms needed for biomedical tracing research and are not as available as AMS facilities. Values obtained from this assay are in units of ⁴¹Ca/Ca or the ratio of ⁴¹Ca to total calcium, the sum of all the other calcium isotopes, can be converted to a ratio of ⁴¹Ca/⁴⁰Ca using the cosmic abundance of ⁴⁰Ca with no loss in information [18]. At PRIME Lab, the background due to chemical processing is regularly checked by running chemical process blanks over the chromatography columns, one a calcium solution and the other a urine specimen. The Purdue ion source generates CaF₃⁻ ion currents of 50-500 nA with the corresponding ⁴¹Ca⁸⁺ ion detection rates of about 1 s⁻¹ for a sample ⁴¹Ca-enrichment of about 2×10⁻¹⁰ of total calcium. A background of 5×10⁻¹³ is routinely achievable with samples collected prior to tracer administration. Analytical performance at LLNL is similar.

Samples assayed at PRIME lab had their $^{41}\text{Ca}/\text{Ca}$ determined by normalizing the measured value against the value of two standards, one measured before and one measured after each unknown. Typically, these standards have the same isotope ratio, but not always. At LLNL, the analyst can decide how many standards are used in the normalization, typically using 4-6 standards that are measured nearest in time to each unknown. Each sample was measured multiple times. For the uncertainty calculation each lab takes the larger of the internal (the $\frac{1}{\sqrt{N}}$ uncertainty that arises from counting statistics where N is the number of counts) and external uncertainty (uncertainty that arises from the scatter of the data). For more information about how the uncertainty for the cycle is determined, refer to Elmore *et al.*, 1984 [19].

3. Theory/Calculation

Later in this paper, we will discuss whether or not either lab is over or under-estimating its reported uncertainty. The theory behind this analysis follows. The derivation follows the approach outlined in section 5.1 of the paper by Dose [20]; our problem is somewhat different from that of Dose, but the basic method is the same.

Let $\{x_i, \sigma_{Li}\}$ be the LLNL data points and their quoted uncertainties, and $\{y_i, \sigma_{Pi}\}$ be the corresponding PRIME Lab results. We introduce two multipliers, v and w , such that the true uncertainties in the data should be $v \sigma_{Li}$ and $w \sigma_{Pi}$. Our goal is to derive a joint probability density for v and w ; this density will summarize what the data from the two laboratories imply about the likely range of values for v and w .

We start with Bayes theorem [21]:

$$p(v, w | \text{Data}) p(\text{Data}) = p(\text{Data} | v, w) p(v, w) \quad (1)$$

or

$$p(v, w | \text{Data}) = c p(\text{Data} | v, w) p(v, w) \quad (2)$$

with

$$1 = \int dv \int dw p(v, w | \text{Data}) \quad (3)$$

Here, $p(v, w | \text{data})$ is the function we want – the probability density for v and w given the data. $p(\text{data} | v, w)$, also known as the likelihood, is the probability of obtaining our data, given v and w ; we will derive a useful expression for this function. $p(\text{data})$ does not depend on v and w , and can be omitted if we normalize our formula for $p(v, w | \text{data})$ (as we did in equation (3) above). $p(v, w)$ is called the prior – it incorporates the knowledge we have concerning v and w before we obtained the data.

To derive an expression for $p(\text{data} | v, w)$ we proceed as follows. Let z_i be the (unknown) true value for sample i . Then we have

$$p(\text{Data} | v, w) = \prod_i p(x_i y_i | v, w) \quad (4)$$

$$p(x_i y_i | v, w) = \int dz_i p(x_i y_i | v, w, z_i) p(z_i | v, w) \quad (5)$$

$$p(x_i y_i | v, w) \propto \left(\frac{e^{-\left(\frac{(x_i - z_i)^2}{2v^2 \sigma_{Li}^2}\right)}}{\sqrt{v^2 \sigma_{Li}^2}} \right) \left(\frac{e^{-\left(\frac{(y_i - z_i)^2}{2w^2 \sigma_{Pi}^2}\right)}}{\sqrt{w^2 \sigma_{Pi}^2}} \right) p(z_i | v, w) \quad (6)$$

If we take $p(z_i | v, w)$ to be a constant, then we have

$$p(x_i y_i | v, w) \propto \frac{e^{-\left(\frac{(x_i - y_i)^2}{2(v^2 \sigma_{Li}^2 + w^2 \sigma_{Pi}^2)}\right)}}{\sqrt{v^2 \sigma_{Li}^2 + w^2 \sigma_{Pi}^2}} \quad (7)$$

Our final formula for $p(v, w | \text{data})$ is then

$$p(v, w | \text{Data}) = c \left(\prod_i G_i \right) p(v, w) \quad (8)$$

$$G_i = \frac{e^{-\left(\frac{(x_i - y_i)^2}{2(v^2 \sigma_{Li}^2 + w^2 \sigma_{Pi}^2)}\right)}}{\sqrt{v^2 \sigma_{Li}^2 + w^2 \sigma_{Pi}^2}}$$

Where

The prior $p(v, w)$ can be used to input any additional information, such as constraints on the values of v and w . For example, we may set the prior equal to zero if v or w is less than 0.5; we would then be ruling out the possibility that the true uncertainties were less than half the quoted values.

4. Results/Discussion

In this section, multiple statistical methods are used to compare the two data sets, and to explore the possibility of under or over-estimation of the uncertainty as reported by either laboratory. First, we plotted the ratios against each other and performed a linear regression that took into account the uncertainty of each data set. Next, we examined the data to determine that the data set as a whole is not normally distributed. Thus, a paired t-test was done on two sub-sets of data that were normally distributed. The highest ratios could not be included in any analysis that relied on normality of the data, so a non-parametric test (the Wilcoxon rank test) was used to analyze the entire data set. Finally, we examined the magnitude of the reported uncertainties by 1) determining if we had close to the expected distribution and 2) performing a Bayesian analysis to rigorously explore whether or not the uncertainty was being over or under-estimated.

4.1 Samples prepared at PRIME Lab and measured at LLNL and PRIME Lab

As a first step in our analysis, we plotted the ratios measured at each laboratory against each other (Figure 1). We'll report the results of a linear regression performed using the methodology of York which takes into account the x (LLNL) and y (PRIME Lab) uncertainty when determining the uncertainty associated with the fit parameters [22]. The slope of the fit is 1.027 ± 0.011 , with a y -intercept of $-1.53 \times 10^{-12} \pm 1.94 \times 10^{-12}$ ($\sim 1.5\%$ of a

1×10^{-10} ratio). The fitting was done with Origin Pro 8.6 (OriginLab Corporation, Northampton, Massachusetts). A slope of one is almost, but not included in a 95% confidence interval. A y-intercept of 0 is within 95% confidence bands. So, we can conclude that perhaps uncertainty is being under-estimated by a small amount, but there is no significant offset. We will use the Bayesian analysis we derived in the Theory and Calculation section to discuss uncertainty in greater detail later in this section.

Our overall goal was to determine if the $^{41}\text{Ca}/\text{Ca}$ measurement was robust between LLNL and PRIME Lab. We took 47 samples that had been assayed at PRIME Lab and sent excess CaF_2 to LLNL for comparison. The results are shown in Table 1. Once each laboratory had reported ratios, we took the difference between the ratios measured at each laboratory. This is shown in the next to last column of Table 1. The last column of Table 1, $D/$ (Difference/uncertainty) gives the reader a chance to assess the quality of each pair of measurements and the whole data set at a glance.

We would like to apply a paired t-test to see if there were any statistically significant differences between the two sets of ratios. However, this test should be applied to data that follows a normal distribution. Our test for normality was the D'Agostino-Pearson K^2 test [23]. This test uses standardized z-scores derived from the skew (Z_{skew}) and the kurtosis (Z_{kurt}). The z-score is a standard score that shows how many standard deviations an observation is above or below the mean. Skewness is a measure of the asymmetry of a probability distribution and kurtosis is a measure of how similar the shape of a probability curve is to a normal distribution. The K^2 statistic is $K^2 = Z_{\text{skew}}^2 + Z_{\text{kurt}}^2$, with the K^2 statistic assumed to have the chi-squared distribution with 2 degrees of freedom. The null hypothesis for this test is the normality of the data set for $p > 0.05$.

When we applied this test to our complete data set, we found that the differences yielded a K^2 value of ~ 44 which yields a p-value $\lll 0.001$. The differences in Table 1 are clearly not normally distributed. The reason for this is shown in Figure 2. As the ratio increases, so does the magnitude of the difference. This is caused by the uncertainties increasing with increasing ratio. We'll discuss this effect in more detail later in this section. For now, we'll use our knowledge to find a subset of data that is normal and perform a paired t-test on the subset in question. Examination of Figure 2 reveals that the most straightforward approach is to limit the range of ratios studied. We found that the smallest 23 ratios as measured by PRIME Lab, yielded a normal data set ($Z_{\text{skew}} = 0.67$, $Z_{\text{kurt}} = 0.99$, $K^2 = 1.43$, $p = 0.49$) for the differences. A paired t-test on this subset of data produced t-statistic of 0.69 and $p = 0.49$. Thus, the population means are not significantly different. We found that next 18 smallest ratios as measured by PRIME Lab also yielded a normal data set ($Z_{\text{skew}} = -0.81$, $Z_{\text{kurt}} = -0.69$, $K^2 = 1.13$, $p = 0.57$). This subset of data produced a t-statistic of 0.53 and $p = 0.60$. This also implies that the difference in population means is not statistically significant.

Including the last 6 sets of paired data points made any test of normality with a large enough N difficult since the last 6 pairs span a factor of 3 in isotope ratios. However, we did a non-parametric test with all 47 data points, the Wilcoxon rank test [24]. This test provides a procedure to generate a z-score by ranking the differences based on their magnitudes. This analysis yields a z-score of 1.09 and $p = 0.28$. Once again, these results indicate that the ratios measured at each laboratory are not considered significantly different. The results are summarized in Table 2.

If we go by these traditional statistical tests these two data sets appear equivalent. However, AMS labs assign uncertainty values to each measurement. In this case, most of the uncertainties are the "external error" as discussed in the Materials and Methods section. The reason for this is unclear. Many of these samples provide enough counts to have

uncertainties well below 1% if counting statistics were dominant. In particular, one may wonder if PRIME Lab is over-estimating its uncertainty. This may be suggested by the fact that very similar methodologies on equivalent samples at the two laboratories result in disparate average uncertainties: 4.4% for PRIME Lab, and 1.8% for LLNL. However, there are some key analytical differences in the assays that undoubtedly explain this difference. Most notably, PRIME Lab switches between rare and stable isotopes by shifting the magnet field to sequentially inject each species through the accelerator and to their respective detector. Although the use of a laminated magnet enables relatively fast changes in magnetic field, this is a much slower process than the electrostatic “bouncing” used by LLNL. We hypothesize that changes in ion source output and other beamline components during the time it takes to switch the magnet causes increased uncertainty in $^{41}\text{Ca}/\text{Ca}$ measurements [25, 26]. Furthermore, PRIME Lab is using an ion source that features a rod for sample insertion and an immersion lens that was attached to its own power supply [27]. It was recently found that grounding the lens to the rod increased the reproducibility of the measurements made on our primary standard. This change in setup may have a long-term meritorious effect on the uncertainty. LLNL does not have equivalent issues, but many of the ratios measured at LLNL have an external uncertainty that is larger than the internal uncertainty, even though some results do have the uncertainty expected from counting statistics. It is likely that these issues, similarly, arise from performance of calcium fluoride as the AMS ion source material: versus all other AMS isotopes measured at LLNL, CaF_3^- ion beams are lower in magnitude and higher in relative inter and intra sample variability. Further work in sample production and analysis would likely minimize these sources of variability, but for most biomedical ^{41}Ca research projects the biological variability exceeds the analytical variability, and such efforts are not warranted. Additionally, both labs have to deal with numerous interferences – frequently with much higher count rates than ^{41}Ca in the detector. The absence of an easily explainable physical cause as to why counting statistics are not the only contributor to the uncertainty makes this analysis more important.

Our first step in examining the uncertainties was to combine the uncertainty reported by each laboratory in quadrature and make this our 1σ . The results of this analysis were close to the expected distribution with 29/47 samples agreeing within one 1σ (62%), 41/47 samples agreeing within 2σ (87%), and 46 of 47 measurements agreeing within 3σ (98%) with one sample being slightly over 3σ (see D/ in Table 1) In fact a normality check of the differences divided by combined uncertainty (the last column in Table 1) yield $p = 0.73$. This isn't very surprising since our simple analysis yielded results that were very close to what one would expect from a Gaussian distribution.

In the Theory and Calculation section, we derived a formula based on Bayesian statistics to check if PRIME Lab or LLNL are over or under-estimating the uncertainty. If w (the uncertainty multiplier for PRIME Lab) and v (the uncertainty multiplier for LLNL) are 1, then that would indicate both labs were estimating the uncertainty perfectly. A value more than 1 indicates that the uncertainty needs to be multiplied by that amount to take into account all sources of uncertainty whereas a value of less than one would indicate that a facility was over-estimating its uncertainty.

First, let us allow w and v to vary. We can use the probability density $p(w,v|\text{data})$ to calculate averages and standard deviations for w and v . We set the prior equal to a constant so all values of w and v are allowed. We find that the multiplier for PRIME Lab (w) is 1.32 ± 0.20 , whereas the multiplier for LLNL (v) is 1.15 ± 0.69 . A contour plot of $p(w,v|\text{data})$ is shown in Figure 3 demonstrating the joint probability of w and v . We see that there is a peak near the point $w = 1.3$, $v = 1.1$. The solution of the uncertainty multipliers was performed in both Matlab (The MathWorks, Natick, Massachusetts) and Maple (Maplesoft, Waterloo, Ontario).

PRIME Lab's multiplier is a bit bigger than one, but is not indicative of a gross miscalculation. LLNL's multiplier includes one. The PRIME Lab multiplier does include one within 2 . Thus, one could conclude that both laboratories do a good job estimating their uncertainty and there is some evidence for a slight under-estimation. One contributing factor is that AMS facilities tend to take the larger of the uncertainties attributable to scatter or counting statistics. When these two values are equal, they probably should be combined in quadrature. This isn't the typical case, but it could partly explain why w is a bit larger than one. However, this analysis shows that both facilities are very close with respect to the magnitude of their quoted uncertainties.

We may do a slightly different calculation; rather than averaging over both w and v , we can set $v=1$, and then average over w . This assumes that the quoted LLNL uncertainty is correct. Using this approach, the value for the PRIME Lab multiplier (w) is 1.34 ± 0.16 , which is essentially no different than the result obtained when both are allowed to vary. Since one is almost included within 2 this is further indication that there may be a slight under-estimation of the uncertainty.

4.2 Samples measured at LLNL and prepared at LLNL and PRIME Lab

Though the differences between the chemistry procedures at the two facilities appear to be minor, it was decided that measuring a set of samples at one lab that were prepared at each facility would be worthwhile. Since the unknowns for this experiment were all measured at LLNL, they were all mixed with Nb and loaded using the LLNL procedure. The results are shown in Table 3 and plotted in Figure 4. The fit was performed with the previously mentioned method outlined by York [22]. The fit to the line has a slope of 1.00 ± 0.02 , so a slope of one is included. Further, the y-intercept is -1.58×10^{-12} with a standard error of 2.66×10^{-12} so a value of 0 is included. The high quality fit obtained with only 13 data points indicate that no other statistical tests are required. However, examination of the measurement data reveals several interesting trends. First, the samples prepared at PRIME Lab had ^{40}Ca currents that were 45% higher on average ($45\% \pm 33\%$). This could be the result of some subtle difference in the chemistry or just statistical noise since it's barely more than 1 . However, this seems unlikely since only one of the 13 samples prepared at LLNL had more source output. Yet, it is challenging to proffer a reason for this discrepancy. One difference in the sample processing is that the samples are dried in a vacuum oven at PRIME Lab before loading. The next difference was that the ^{41}K interference in the PRIME lab prepared samples had a significantly higher count rate by an order of magnitude. The LLNL prepared samples had ^{41}K count rates ranging from 10-1000 counts per minute (average = 400 ± 300), whereas the PRIME Lab prepared samples ranged from 700-10,000 counts per minute (average = 4000 ± 2000). The ratio of acid to resin used to remove interferences is essentially the same for both procedures with PRIME lab using 18 ml of 0.4 M nitric for 4 ml of resin, whilst LLNL uses 15 ml of 0.1 M nitric for 1ml of resin. However, PRIME Lab uses 6-10 times as much sample so this may be the source of the problem. PRIME Lab could modify the procedure slightly and use 200 mg of calcium oxalate. If the focus of the ion source at PRIME Lab improves, it may be possible to replicate the LLNL procedure and use 50 mg of oxalate powder. In PRIME Lab's present ion source configuration it is very challenging to get ratios with small uncertainties with small samples since the cesium beam is not well enough focused to sputter material in the bottom of the cathode. Another possibility would be to discard the first 1 ml of eluant during sample elution [11], since this ml contains most of the interference. The additional interference counts may also explain why there is a small offset on the order of 1% between the two measurement sets with the samples prepared at PRIME Lab having generally higher ratios.

5. Conclusion

Our inter-laboratory comparison has shown conclusively that $^{41}\text{Ca}/\text{Ca}$ ratios are in agreement between LLNL and PRIME Lab. Neither chemistry nor the AMS measurement has a significant impact on results. There may be a slight under-estimation of uncertainty by one or both labs but it is not significant at the 95% level.

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Figure 1.
Plot of PRIME Lab vs. LLNL $^{41}\text{Ca}/\text{Ca}$. All of the samples were chemically prepared at PRIME Lab.

Figure 2.

Plot of the $^{41}\text{Ca}/\text{Ca}$ ratio measured at PRIME Lab versus the absolute value of the difference between the PRIME Lab and LLNL ratios. This plot shows that the magnitude of the difference is dependent on the magnitude of the ratio.

Figure 3. Contour plot of the probability density given by equation (1). The LLNL multiplier (v) is on the y-axis and the PRIME Lab multiplier (w) is on the x-axis.

Figure 4.

Plot of PRIME Lab vs. LLNL chemistry samples, $^{41}\text{Ca}/\text{Ca}$. All of the measurements were made at LLNL. The error margins are small and with the exception of the last data point are obscured by the data points.

Table 1

$^{41}\text{Ca}/\text{Ca}$ ratios from samples measured at Berkeley and PRIME Lab. All the samples were chemically prepared at PRIME Lab.

USER ID	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}). LLNL	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}). Prime Lab	Difference (PRIME Lab-LLNL, 10^{-10})	$\frac{D}{\sigma}$
B2_1076_CB	22.4±0.3	23.6±1.0	1.2±1.0	1.2
B2 1478 CB	15.5±0.2	15±1	-0.5±1.0	-0.5
B2 1168 CL	5.07±0.06	4.4±0.2	-0.7±0.2	-3.5
B2 1192 CL	4.50±0.06	4.8±0.2	0.3±0.2	1.5
B2 1204 CL	4.62±0.05	5.2±0.2	0.5±0.2	2.5
B2 1219 CL	4.49±0.06	4.2±0.3	-0.3 ±0.3	-1.0
B2 1240 CL	4.70±0.08	5.3±0.3	0.6±0.3	2.0
B2 1259 CL	4.00±0.05	4.2±0.2	0.2±0.2	1.0
B2 1295 CL	4.37±0.06	3.9±0.3	-0.4±0.3	-1.3
B2 1338 CL	4.86±0.06	4.9±0.3	0.0±0.3	0.0
B2_1371_CL	5.3±0.1	5.5±0.4	0.2±0.4	0.5
B2_1217_MJO	24.8±0.2	24±1	-1±1	-1
B2_1043_NC	15.4±0.3	16.4±0.8	1.0±0.8	1.3
B2_1111_NC	13.5±0.2	13.1±0.6	-0.4±0.6	-0.7
B3-005-307	36.2±0.5	36±2	0±2	0
B3-011-301	6.61±0.09	6.3±0.3	-0.3±0.3	-1
B3-017-301	3.33±0.05	3.3±0.1	-0.0±0.16	0.0
B3-260-328	1.33±0.03	1.32±0.07	-0.01±0.08	-0.07
B3-241-301	1.07±0.03	1.07±0.05	0.00±0.06	0.00
B3-276-314	1.07±0.02	1.21±0.05	0.14±0.06	2.46
B3-369-339	25.3±0.6	24.8±0.7	-0.5±0.9	-0.5
B3-298-325	9.9±0.2	10.3±0.4	0.4±0.5	0.8
B3-342-301	0.88±0.02	0.91±0.04	0.03±0.05	0.72
B3-412-333	9.19±0.09	9.9±0.3	0.7±0.31	2.3
B3-422-331	2.63±0.06	2.7±0.1	0.1±0.1	1
B3-442-333	4.79±0.07	5.0±0.1	0.2±0.1	2.0
B3-443-339	3.58±0.07	3.7±0.1	0.1±0.1	1.0
B3-484-333	3.32±0.08	3.60±0.09	0.28±0.12	2.33
B3-560-325	2.44±0.04	2.5±0.1	0.1±0.1	1.0
B3-657-330	1.35±0.03	1.41±0.04	0.06±0.05	1.15
B3-663-310	2.51±0.06	2.59±0.09	0.08±0.11	0.74
B3-691-343	1.60±0.03	1.62±0.06	0.02±0.07	0.29
B3-735-355	33.7±0.6	36±1	2.6±1.16	2.2
B3-769-335	1.61±0.03	1.56±0.05	-0.05±0.06	-0.80
B3-770-349	2.90±0.04	2.8±0.1	-0.1±0.1	-1.0
B3-904-307	1.07±0.02	1.00±0.03	-0.07±0.04	-1.75
B3-895-355	3.18±0.05	3.3±0.1	0.1±0.1	1.0

USER ID	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}), LLNL	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}), Prime Lab	Difference (PRIME Lab-LLNL, 10^{-10})	$\frac{D}{\sigma}$
B3-959-128	1.23±0.05	1.20±0.04	-0.03±0.06	-0.48
B3-1031-128	1.40±0.03	1.42±0.06	0.02±0.07	0.27
B3-1044-328	1.14±0.02	1.15±0.06	0.01±0.06	0.16
B3-1049-128	1.44±0.03	1.45±0.06	0.01±0.06	0.11
B3-1050-328	0.81±0.02	0.80±0.03	-0.01±0.04	-0.38
B3-1056-355	1.93±0.03	1.90±0.08	-0.03±0.09	-0.38
B3-1089-355	1.89±0.03	1.86±0.08	-0.03±0.08	-0.31
B3-1125-333	1.37±0.03	1.55±0.08	0.18±0.09	2.00
B3-1169-328	0.89±0.02	0.81±0.04	-0.08±0.04	-1.90
B3-1240-328	0.81±0.03	0.87±0.03	0.06±0.05	1.23

Table 2

Statistical results for the difference between the LLNL and PRIME Lab results.

analysis	N	t-statistic	p
Paired t-test	23 ^a	0.69	0.49
Paired t-test	18 ^b	0.53	0.60
Wilcoxon	47	1.09 ^c	0.28

^aThe subset of data consists of the 23 smallest ratios as measured by PRIME Lab.

^bThe next 18 smallest ratios as measured by PRIME Lab.

^cThe value is actually a z-score and not a t-statistic.

Table 3

$^{41}\text{Ca}:\text{Ca}$ ratios from samples measured at LLNL. An aliquot was chemically prepared at LLNL and an aliquot was chemically prepared at PRIME Lab.

USER ID	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}), LLNL chemistry	$^{41}\text{Ca}/\text{Ca}$ (10^{-10}), PRIME Lab chemistry	Difference (PRIME Lab-LLNL, 10^{-12})
B3_422_331	2.63±0.06	2.54±0.05	-9.04±7.34
B3_442_333	4.79±0.07	4.91±0.06	12.4±9.1
B3_560_325	2.44±0.04	2.47±0.04	3.07±6.03
B3_657_330	1.35±0.02	1.41±0.03	5.75±3.58
B3_769_335	1.61±0.03	1.61±0.02	0.42±3.78
B3_904_307	1.07±0.02	1.07±0.02	0.38±2.91
B3_895_355	3.18±0.05	3.20±0.05	1.42±7.18
B3_1031_128	1.40±0.03	1.42±0.03	1.81±4.07
B3_1056_355	1.93±0.03	1.94±0.03	0.61±4.39
B3_1089_355	1.89±0.02	1.87±0.03	-1.19±4.27
B3_1125_333	1.37±0.03	1.40±0.02	3.05±3.51
B3_1169_328	0.89±0.02	0.89±0.02	0.48±2.59
B3_1240_328	0.81±0.03	0.88±0.02	6.72±3.78