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Determination of ^{226}Ra in Urine Using Triple Quadrupole Inductively Coupled Plasma Mass Spectrometry

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Abstract

Measuring ^{226}Ra in urine at low levels is critical for both biomonitoring and radiological emergency response. Here we report a new analytical method to quantify ^{226}Ra, as developed and validated by a simple dilute-and-shoot procedure, followed by Inductively Coupled Plasma – triple quadrupole – mass spectrometry (ICP-QQQ-MS) detection using "No Gas MS-MS" mode. The method provides rapid and accurate results for ^{226}Ra with a limit of detection (LOD) down to 0.007 ng/L (0.26 Bq/L). This LOD is well below the recommended action levels for ^{226}Ra detection in children and pregnant women (C/P) set by the Clinical Decision Guide (CDG, NCRP Report #161). Results for ^{226}Ra obtained by this method are within +/−7.0% of the target values of Standard Reference Materials (SRM) spiked in urine.

Introduction

Radium (Ra) is a naturally occurring, silvery-white, radioactive metal found in uranium and thorium ores in trace amounts. As the heaviest alkaline earth metal, radium is partially soluble in natural water depending on the salinity of the water [1, 2]. Because radium is always present at very low levels in the surrounding environment, people are regularly exposed to small amounts via inhalation or ingestion. People may be exposed to higher levels of radium if they live in an area where radium is released into the air from burning coal or other fuels or if they drink water from a source that is high in natural radium, such as a deep well or a source near a radioactive waste disposal site [3]. When people breathe in radium, some of it may remain in their lungs for months, gradually entering the blood stream, and then carried to all parts of the body, especially the bones. For months post-exposure, very small amounts leave the body daily through the feces and urine. If radium is

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Conflict of interest

The authors declare that they have no conflict interest.

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swallowed in water or with food, most of it will promptly leave the body in the feces. As with inhalation exposure, the rest will enter the blood stream and be carried to all parts of the body, especially the bones. Some of this radium will also be excreted daily in feces and urine [4]. Because of its radioactivity and chemical reactivity, harmful health effects are likely when radium is incorporated into biochemical processes. Chronic exposure to higher levels of radium over a long period of time may result in increased incidence of anemia; cataracts; fractured teeth and bones; cancers of the liver, lung, breast, and especially bone; and even death.

^{226}Ra is also one of the priority radionuclides listed by the Health and Human Services Radiation Emergency Medical Management (REMM) web site because of its toxicity and potential use in a nuclear or radiological incident. These may include the detonation of a radiological dispersal device (dirty bomb) or a foreign radiological release. Hence, faster and more reliable methods are essential to evaluate ^{226}Ra contamination, not only for biomonitoring, but also for any emergency responses involving ^{226}Ra exposure.

Several radiometric approaches are available for measuring ^{226}Ra activity and mass concentrations in environmental samples and human biological samples [5–7]. Alpha spectrometry with PIPS detectors is the most sensitive technique used to determine ^{226}Ra because of its low background count, high sensitivity, and good spectral resolution [5–7]. Alpha spectrometry requires thorough separation of ^{226}Ra from the matrix and other radionuclides and correction of recovery loss by adding a tracer [6]. Labs have reported Limits of Detection (LODs) ranging from 0.2 to 0.5 mBq [5–15]. Liquid scintillation counting (LSC) is also a sensitive method to determine ^{226}Ra but generally requires a long wait time for the in-growth of ^{226}Ra daughters, as well as thorough radiochemical/ precipitation methodology [5–6, 16–18] to achieve precise and accurate measurements. Despite these limitations, as reported, LSC can still reach an LOD of 0.3 to 1.4 mBq in other studies [6]. All of these analytical protocols often require a large volume of sample (e.g. 1 L). Gamma spectromety is another analytical technique for ^{226}Ra analysis, however, it is also hindered by a long counting time and spectral interferences from other radionuclide isotope constituents in samples [5–6, 19–24]. In addition, the reported LOD varies from 0.08 to 1Bq, depending on the background level [6].

Mass spectrometric measurement using atomic mass spectrometry (AMS), thermal ionization mass spectrometry (TIMS), and inductively coupled plasma-mass spectrometry (ICP-MS) have been reported to assess ^{226}Ra content in environmental and human samples [6]. Both AMS and TIMS are sensitive with LODs of 0.1mBq and 0.037mBq were reported, respectively, for environmental samples. However, both require lengthy sample preparation procedures, and the daily sample throughput is very low [6]. ICP-MS offers considerable benefits over other mass spectrometric techniques and has been used over the last 20 years to analyze many long-lived radionuclides in various sample types. It has proven to be one of the fastest, highest throughput methods for determining ^{226}Ra. There are no isobaric interferences to ^{226}Ra on ICP-MS. The main analytical issue of ICP-MS for ^{226}Ra is from potential polyatomic interferences that affect directly the isotope 226 (e.g. $^{138}Ba^{88}Sr^{+}$, $^{186}Os^{40}Ar^{+}$, $^{186}W^{40}Ar^{+}$, $^{188}Os^{38}Ar^{+}$, $^{190}Os^{36}Ar^{+}$, $^{189}Os^{37}Cl^{+}$, $^{194}Pt^{16}O_2^{+}$, $^{208}Pb^{18}O^{+}$, $^{209}Bi^{17}O^{+}$, $^{207}Pb^{18}O^{1}H^{+}$, $^{208}Pb^{17}O^{1}H^{+}$, $^{209}Bi^{16}O^{1}H^{+}$, $^{207}Pb^{18}O^{1}H^{+}$, $^{191}Ir^{35}Cl^{+}$) though can

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be corrected by many instrumental strategy such as ICP-MS instruments with reaction and collision cell technologies (ICP-DRC-MS) which polyatomic ions can be eliminated by reaction with gases (monitoring the new isotope formed by the sum of analyte mass-charge and gas mass-charge) and collision with inert gases (Kinetic energy discrimination, ICP-KED-MS) [25], however, for trace amount of ^{226}Ra determination at pg/L level, requiring chemical separation before the ICP-MS measurement [26–31]. A LOD of 0.02 to 0.5mBq for ^{226}Ra has been reported on SF-ICP-MS [6, 32], which is comparable to that of alpha spectromety. Nonetheless, SF-ICP-MS at LR/MR is still not practical for a rapid ^{226}Ra measurement because a long half-life radium isotope is unavailable to use as a tracer to correct for recovery during sample purification procedures.

Centers for Disease Control and Prevention (CDC)'s emergency preparedness and response programs include planning for and managing emergencies involving radioactive materials. Therefore, developing methods to determine exposure to ^{226}Ra is a crucial part of CDC's public health mission. The Inorganic and Radiation Analytical Toxicology (IRAT) branch within CDC has a long history of and extensive experience with determining levels of environmental exposure to chemicals through direct measurement of the heavy metals in human specimens such as urine on ICP-MS. Quantitative analysis of ^{226}Ra in urine is considered a convenient, non-intrusive way to assess levels of internal contamination; therefore, we decided to develop a novel and more practical emergency radiobioassay of ^{226}Ra using a small volume urine sample via ICP-MS. CDC's emergency response analytical goal is to detect priority threat radionuclides in urine at levels well below (i.e., 1/3 or lower) the action levels for the general population or for special subgroups, such as children or pregnant women (C/P), as set by the National Council on Radiation Protection and Measurements (NCRP) [33, 34]. This action level is 0.046 ng/L (1.68 Bq/L) for ^{226}Ra (urine output expected at 5 days post-intake). As ^{226}Ra is one of the radionuclides likely to be present after possible radiological accidents or incidents involving a radiological dispersal device, rapid identification and quantification for those radionuclides (e.g. ^{226}Ra) is important in determining who has been contaminated, as well as which radionuclides they had contact with and the level of contamination. Having a rapid and high throughput analytical method that provides crucial information for rapid medical management and treatment decisions, and follow-up for possible victims of radiological contamination is critical for a large-scale public health emergency response. The bioassay analytical results give the medical community an assessment of the victims' short- and long-term health risks from exposure to this toxic radionuclide.

In the method described here, ^{226}Ra is measured using an Agilent 8800 Triple Quad inductively coupled plasma-mass spectrometer (ICP-QQQ-MS) to count ^{226}Ra ions from urine samples after a simple dilution sample preparation step. This is a prompt method for determining ^{226}Ra in urine samples and can be used either to screen urine when acute contamination of ^{226}Ra is possible or to evaluate chronic environmental or other non-occupational contamination. Although this method is not designed to determine the normal background level of ^{226}Ra in the non-occupationally contaminated people, this approach has a LOD that is well below the indicated NCRP guidance for medical follow-up. Therefore, it swiftly detects adults and children who have been internally contaminated with ^{226}Ra and may require medical treatment and/or follow-up.

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Experimental

Reagents and solutions

All nitric acid (HNO_3) solutions were prepared from double-distilled acids (GFS Chemicals Inc. Columbus, OH). Deionized water was used for all solutions (18 MΩ·cm, from an Aqua Solutions Ultrapure Water System, Aqua Solutions, Inc., Jasper, GA). “Base urine” was collected through anonymous human donations (following CDC IRB protocol 3994) and acidified to 1% v/v HNO_3 to be used as the base matrix. All radioactive source solutions were traceable to the National Institute for Standards and Technology (NIST) (Gaithersburg, MD, USA). We prepared urine pools for LOD determinations, as well as other urine solutions for accuracy testing, by spiking (volumetric determinations) base urine with dilutions of ^{226}Ra isotope standard reference materials (SRM) from NIST 4967A. We used NIST traceable ^{193}Ir as an internal standard (High-Purity Standards, Charleston, SC). Serial dilutions of Pt, W, Pb, Ba, Sr, Bi, Os, and Ir single-element stock standards (Inorganic Ventures, Christiansburg, VA) were spiked into the base urine to verify high elimination factors for elements forming polyatomic interference by using the simple dilute and shoot sample procedure and analyzing them on ICP-QQQ-MS. We prepared different sets of external, aqueous-based stock calibrators from dilutions of ^{226}Ra isotope SRM from the NIST and certified reference material (CRM) from Eckert & Ziegler Analytics, Inc. (Atlanta, GA) and Eckert & Ziegler Isotope Products (Valencia, CA). They were prepared by spiking 5% v/v HNO_3 with dilutions of ^{226}Ra isotope SRM and CRM (7 calibration standards (S0–S6) with concentrations of 0.000, 0.006, 0.020, 0.060, 0.200, 0.600 and 2.00 ng/L). The sample diluent consisted of 2% v/v HNO_3 and 100 ng/L of ^{193}Ir, while the sample introduction system rinse solution consisted of 5% v/v HNO_3.

Sample and sample preparation

All samples, calibrators, and blanks were prepared at a 10x dilution into 15 mL polypropylene conical tubes. Matrix matched working calibrators were prepared by mixing an aliquot of each stock calibrator with base urine and sample diluent (0.5 mL of stock calibrator, 0.5 mL of base urine, and 4.0 mL of sample diluent). Urine samples (including quality control samples) were prepared in the same manner (0.5 mL of urine sample, 0.5 mL of 5% v/v HNO_3, and 4.0 mL of sample diluent). The aqueous blank (Reagent blank) was prepared similarly, replacing the urine volume with 18.2 MΩ·cm water (0.5 mL of 5% v/v HNO_3, 0.5 mL of water, and 4.0 mL of sample diluent), and was used as the blank for all patient samples, urine quality controls, and reference materials.

When detected results were greater than the calibration range verified by calibrators, we performed up to a 100x additional sample dilution with 5% v/v HNO_3 to dilute to bring the concentration within the calibration range. All dilutions have been validated.

Quality Control (QC) and Reference Materials

Three levels of urine-based bench QC materials were prepared by spiking base urine with ^{226}Ra at low, medium, and high concentrations (0.050, 0.450 and 1.50 ng/L), which are within the calibration range, by using NIST SRM 4967A in base urine. They were analyzed at the beginning and again at the end of each run. Modified Westgard rules as detailed in the

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Division of Laboratory Sciences Policies and Procedures Manual, NCEH, CDC were used to establish/determine whether runs were in control. Method precision, accuracy, and recovery were assessed using above prepared QC materials as well as urine samples spiked with NIST SRM 4967A in base urine.

Instrumentation

For this rapid method, we used the Agilent 8800 Triple Quadrupole ICP-QQQ-MS (Agilent Technologies, Wilmington, DE) instrument to determine ^{226}Ra concentrations. This device was the world's first ICP Triple Quad meaning that it is a tandem MS that uses two hyperbolic profile quadrupoles separated by the octupole reaction system (ORS cell). Allowing operation in MS/MS, the distinctive tandem MS construction allows superlative control of interferences in reaction mode, providing extremely low background, greater accuracy and more consistent results [35–37]. A Micro Mist nebulizer, a quartz spray chamber double pass, quartz injector, nickel sampler cone, and nickel skimmer cone were used for all experiments (instrument and method parameters are listed in Table 1).

An ASX-520 autosampler (Elemental Scientific Inc., Omaha, NE) was used to access diluted urine samples for analysis. We used > 99.999% argon for the plasma and nebulizer gas (Specialty Gases Southeast, Atlanta, GA). All experimental on ICP-QQQ-MS instrument parameters are optimized to determine ^{226}Ra concentrations by maximizing Tl ion intensity and minimizing the oxide formation rate using a 1 μg/L tuning solution (Agilent Technologies, Wilmington, DE). The method parameters were optimized with minimum relative standard deviations for ^{226}Ra in a trade-off with minimal analysis time. The instrument sensitivity is ~0.26 cps per pg/L for ^{226}Ra and the sample flow rate is ~0.8 mL/min. Table 1a and Table 1b summarize the optimized operating conditions and method parameters.

Results and discussion

Evaluation of potential spectral interferences on ^{226}Ra

The determination of ^{226}Ra by ICP-MS can be affected by spectral interferences caused by polyatomic species. The method we report here used a unique MS/MS function of Agilent 8800 to successfully eliminate these interferences. In MS/MS mode, Q1 of the Agilent 8800 operates as a mass filter, allowing only the target analyte mass to enter the cell and rejecting all other masses. Q2 is the second high-frequency hyperbolic quadrupole that filters the ions emerging from the cell exit, passing only the target analyte/product ions to the detector [35–37]. Interference removal experiments were performed using solutions containing the elements Pt, W, Pb, Ba and Sr at five concentration levels: 0.5 μg/L, 1.5 μg/L, 5.0 μg/L, 15 μg/L and 650 μg/L. These potential elements (Pt, W, Pb, Ba and Sr) along with argon and other elements from sample preparation (e.g., oxygen and hydrogen) can form polyatomic interferences in mass-charge 226. These spiked urine sample concentrations were well above the National Health and Nutrition Examination Survey (NHANES) 95th percentile of urine Pt, W, Pb, Ba and Sr concentrations [38]. Although NHANES survey data is not available for Bi, Os and Ir, analysis of what were otherwise determined [39] to be high urine concentrations at 0.5 μg/L of Bi, 0.5 μg/L of Os and 1 μg/L of Ir did not implied in positive

recoveries at mass-charge 226. On the other hand, when single-quad mode was chosen on Agilent 8800, though we obtained increased ^{226}Ra sensitivity, high background on mass of 226 was observed for urine blank samples.

Limit of detection

The LOD determination for ^{226}Ra in urine specimens with this method is validated on an approach of considering both Type I and Type II error recommended by Clinical Laboratory Standards Institute (CLSI) [40], which is required by our Division of Laboratory Sciences in CDC. Based on 20 analytical runs, 0.5 mL of urine matrix-matched samples from four different low concentration pools that were spiked at concentrations close to the LOD - roughly the measured blank concentration plus 3 times the standard deviation (SD) of the measured blank concentration.

The LODs were calculated according to the following formula:

$$Conc_{LOD} = [mean_b + 1.645(S_b + int)]/[1 - 1.645(slope)]$$

Where

$mean_b$ = blank average

S_b = SD of blank average

int = intercept of the equation of SD versus concentration for LOD samples analyzed, and

slope = slope of the equation of SD versus concentration.

The LOD of this method was determined to be 0.007 ng/L (0.26 Bq/L) for ^{226}Ra (Figure 1, Table 2, Spike 1 to Spike 4 were used for LOD determination). This LOD is well below 1/3 of the C/P CDG level (0.046 ng/L for ^{226}Ra), and therefore acceptable for an emergency radiobioassay method to determine the concentration of ^{226}Ra in urine collected at 5 days post-exposure.

Linearity and carryover

We use linear calibration model for this method, which exhibits good linear regression signal response between concentrations of 0.006 ng/L and 2.00 ng/L (S1–S6) of ^{226}Ra, with a linear fit coefficient >0.999 by using 1/x weighting for quantitation. If an assessed urine ^{226}Ra concentration is above the concentration of the highest calibrator, the urine sample is diluted with 5% v/v HNO_3 to bring the concentration within the validated calibration range. Accuracy tests of diluted reference materials spiked in base urine show that ^{226}Ra can be analyzed at up to a 100x extra dilution without significant effect ($< \pm 10\%$ error) on the target values (Table 3).

We evaluated the analyte of ^{226}Ra carryover by alternating the analysis of spiked urine samples (3 times the highest calibrator's concentration) containing approximately 6.0 ng/L of analyte ^{226}Ra and urine blanks over the period of ~ 2 hours (analysis time of 4.5 minutes

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per sample with 30 samples analyzed). The data showed no observed intensities or resulting concentration spikes of ^{226}Ra in the urine blanks following high spiked urine samples.

Precision, accuracy and recovery

To ensure the method's run-to-run reproducibility, we evaluated in-house CDC QC samples spiked at desired concentrations as described above. Table 4 shows the calculated long-term precision observed among daily QCs analyzed at the beginning and at the end of each analytical run. The precision for the low, medium, and high QCs was within ±14% over 30 analytical runs, spanning a period of ~ 2 months, by using different sets of calibrators prepared from ^{226}Ra stock solutions from different vendors. Compared to the spiking target values, the bias for these samples was in a range of −0.08% to 3.9%. Evaluation of the method's accuracy was achieved by analyzing 18 urine samples prepared by using NIST SRM 4967A and using NIST traceable CRM from Eckert and Ziegler Analytics (EZA) spiked into base urine. These spiked samples were analyzed in 10 to 20 analytical runs spanning roughly one month by using different sets of calibrators prepared from ^{226}Ra stock solutions from different vendors. ^{226}Ra results for these samples analyzed on ICP-QQQ-MS are listed in Table 2. Compared to the spiking target values, results showed a bias of −4.7% to 6.2% for ^{226}Ra. Additionally, 24 urine samples were prepared /spiked at 6 concentration levels using NIST traceable CRM from Eckert and Ziegler Isotope Products (EZIP) in order to evaluate the accuracy using spike recovery. Urine samples spiked with 0.060, 0.200, 0.600, 0.400, 1.00 and 1.60 ng/L had recoveries ranging from 93.3 to 102% for ^{226}Ra in two analytical runs (Table 5) on two different days. The mean recovery was 99.7% with a SD of 3.3%.

Stability

To ascertain that the determined concentration of ^{226}Ra in a urine sample was not altered by other factors during analysis, stability tests were conducted with QC materials to evaluate for conditions it would experience when the method is employed. These include sample collection and handling, short-term room temperature storage, long-term freezer storage at a specified temperature, and three freeze/thaw cycles. The results are shown in Table 6. The mean values from the replicates in stability testing results are within ± 11% of the values of initial measurement for each QC material.

Sample throughput and turnaround time

In addition to high quality results, sample throughput is one of the most essential considerations in a radiological emergency response. For this method, the preparation of urine samples by simple dilution for a batch of 20 patient urine specimens, calibrators, blanks and QC samples, took ~30 minutes. The analysis run time for the above 20 samples was 2.5 hours (the average analysis time for each sample is ~4.5 minutes including rinsing). Samples may be prepared simultaneously with final ICP-QQQ-MS analysis, leading to a daily throughput of about 180 samples per day (24 hours) per instrument.

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Conclusions

We introduced a method for rapidly determining ^{226}Ra in urine samples using a new generation of Agilent 8800 ICP-QQQ-MS. Polyatomic interferences were removed by running the MS/MS in no gas On-Mass mode. This method provides for analysis of ^{226}Ra at very low levels, with a LOD of 0.007 ng/L (0.26 Bq/L, well below the 1/3 of C/P NCRP guidance level) and allows rapid throughput of samples by a simple dilute and shoot approach. We obtained good agreement on this method (with a bias of −4.7% to 6.2%), compared to the target values of spiked SRM in urine samples. The triple quadrupole-based method provides an easier and more robust platform to operate than alpha spectrometry and other techniques. Performing the analysis requires only a small volume 0.5 mL of each urine sample, making the method suitable for a wider range of individuals, especially for young children and infants that excrete smaller urine volumes.

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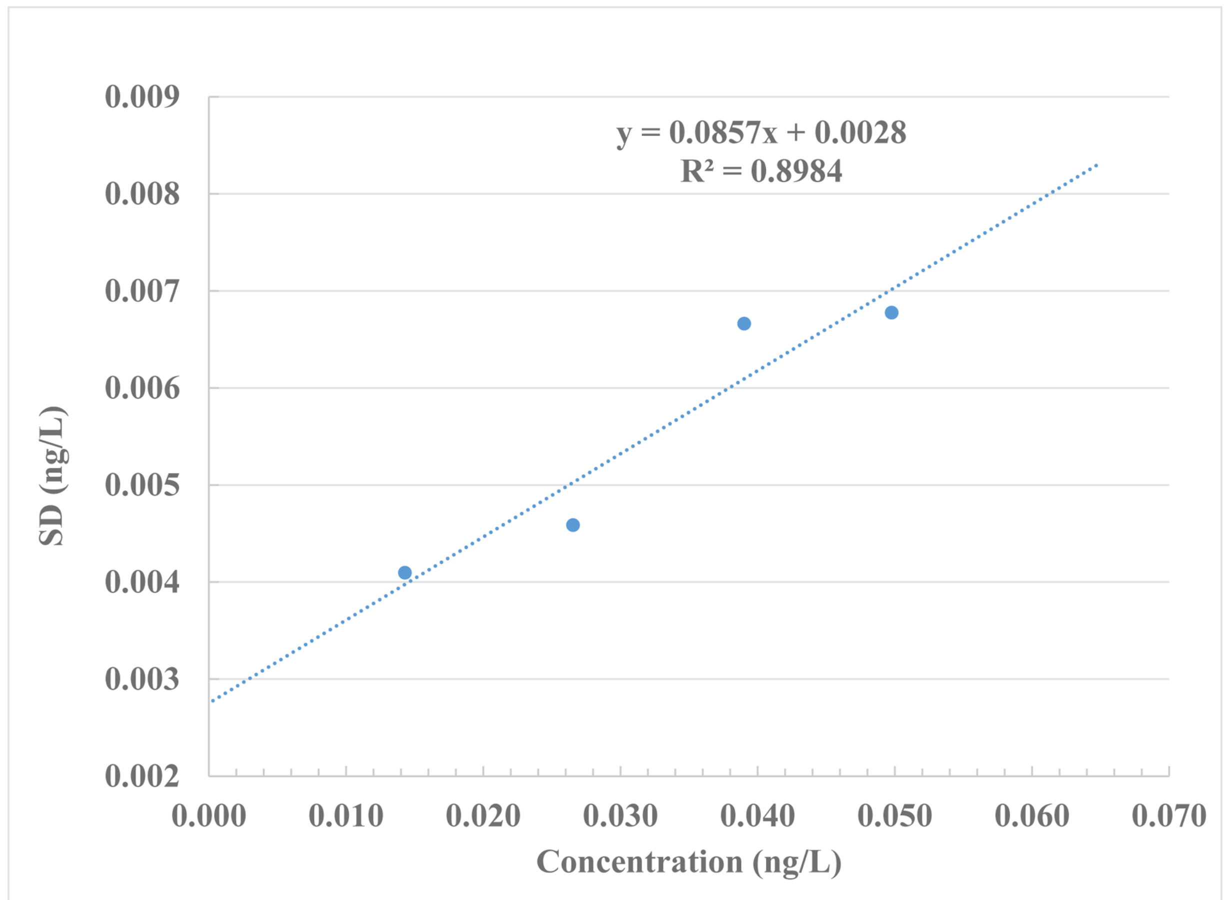

Fig. 1.
Plot for ^{226}Ra LOD determination (20 runs per point).

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Table 1a

Typical instrumental parameters for ICP-QQQ-MS measurements

Plasma Parameters	Setting (optimize as needed)
RF power	1550W
RF matching	1.80 V
Smpl Depth	5.5 – 6.0 mm
Nebulizer pump	0.30 rps
S/C Temp	2 °C
Gas switch	Dilution Gas
Carrier Gas	0.75 – 0.80 L/min
Makeup/Dilution Gas	0.26 – 0.30 L/min
Option Gas	0.0%
Lenses Parameters	**Setting (optimize as needed)**
Extract 1	−5.0 V
Extract 2	−200.0 V
Omega Bias	−100 V
Omega Lens	10.2 V
Q1 Entrance	1 V
Q1 Exit	2 V
Cell Focus	−3.0 V
Cell Entrance	−50 V
Cell Exit	−70 V
Deflect	15.8 V
Plate Bias	−60 V
Q1 Parameters	**Setting (optimize as needed)**
Q1 bias	0.0 V
Q1 Prefilter Bias	−14.0 V
Q1 Postfilter Bias	−22 V
Cell Parameters	**Setting (optimize as needed)**
Use Gas	false
OctP Bias	−8.0 V
OctP RF	180 V
Energy Discrimination	2.0 V

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Table 1b

Method parameters (data acquisition settings) for ICP-QQQ-MS measurements

Tune Mode	**No Gas MS/MS**
Scan Type	**MS/MS**
Q1/Q2 (Ir -ISTD)	193/193
Q1/Q2 (Ra - Analyte)	226/226
Q2 Peak Pattern	1 Point
Replicates	5
Sweeps/Replicates	600
Data Analysis Method	FullQuant Analysis
Calibration Method	External Calibration
Curve Fit	Linear
Origin	Ignore
Weight	1/x
Min Conc	None
Level (ng/L)	0.000, 0.006, 0.02, 0.06, 0.2, 0.6, 2
Stabilization Time (sec)	5
Resolution	Standard
Integ Time/Mass (sec) - Ir	0.10
Integ Time/Mass (sec) - Ra	16.00

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Table 2

Accuracy for NIST SRM 4967A (Spike1 to Spike 9) and NIST traceable CRM from Eckert and Ziegler Analytics (Spike 9 to Spike 18) spiked into base urine (ng/L)

Sample ID	N	Observed Average Results	SD	RSD (%)	Spiking Target Value (NIST)	Bias (%)
Spike 1	20	0.014	0.0041	28.6	0.015	–4.7
Spike 2	20	0.027	0.0046	17.3	0.025	6.2
Spike 3	20	0.039	0.0067	17.1	0.040	–2.4
Spike 4	20	0.050	0.0068	13.6	0.050	–0.45
Spike 5	20	0.062	0.0069	11.2	0.060	3.3
Spike 6	20	0.070	0.0083	11.9	0.070	–0.45
Spike 7	20	0.078	0.0058	7.42	0.080	–2.8
Spike 8	20	0.162	0.013	8.31	0.160	0.95
Spike 9	20	0.321	0.025	7.79	0.320	0.24
Spike 10	10	0.281	0.016	5.70	0.280	0.48
Spike 11	10	0.303	0.028	9.13	0.300	1.1
Spike 12	10	0.325	0.027	8.39	0.320	1.7
Spike 13	10	0.935	0.049	5.22	0.950	–1.6
Spike 14	10	0.997	0.075	7.52	1.00	–0.33
Spike 15	10	1.08	0.088	8.09	1.05	3.2
Spike 16	10	1.44	0.090	6.26	1.43	0.86
Spike 17	10	1.53	0.12	7.57	1.50	2.0
Spike 18	10	1.58	0.085	5.39	1.57	0.46

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Table 3

SRM spiked in base urine shows that ^{226}Ra can be analyzed at up to a 100x extra dilution (ng/L)

Sample ID	N	Spiking Target Value (NIST)	Observed Average Results (on instrument)	Dilution Factor	Final Results (Calculated)	RSD (%)	Bias (%)
Spike a	8	15.0	1.50	10	15.0	5.41	–0.21
Spike b	8	30.0	1.45	20	29.1	7.46	–3.1
Spike c	8	75.0	1.53	50	76.6	5.82	2.2
Spike d	8	150	1.51	100	151	4.68	0.88

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Table 4

Observed ^{226}Ra among-run precision for internal quality control material (ng/L)

Sample ID	N	Average	SD	RSD (%)	Target Value	Bias (%)
Low QC*	60	0.052	0.007	13.6	0.050	3.9
Med QC*	60	0.453	0.034	7.42	0.450	0.65
High QC*	60	1.50	0.09	6.07	1.50	–0.08

*Internal quality control materials made at CDC by spiking SRM 4967A in pooled urine collected anonymously. N = 60 (30 beginning analytical results + 30 ending analytical results)

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Table 5

Accuracy of ^{226}Ra using spike recovery by NIST traceable CRM from Eckert and Ziegler Isotope Products (EZIP) (ng/L)

		Sample 1					Sample 2				
			Measured concentration					Measured concentration			
	Replicate	Spike concentration	Day 1	Day 2	Mean	Recovery (%)	Spike concentration	Day 1	Day 2	Mean	Recovery (%)
Sample	1	0.000	<LOD	<LOD	<LOD		0.000	<LOD	<LOD	<LOD	
	2		<LOD	<LOD				<LOD	<LOD		
	3		<LOD	<LOD				<LOD	<LOD		
Sample + Spike 1	1	0.060	0.047	0.054	0.057	93.3	0.400	0.430	0.393	0.402	101
	2		0.062	0.050				0.422	0.385		
	3		0.063	0.065				0.389	0.395		
Sample + Spike 2	1	0.200	0.226	0.180	0.205	102	1.00	1.03	0.947	0.998	99.9
	2		0.238	0.191				1.07	0.946		
	3		0.211	0.186				1.03	0.971		
Sample + Spike 3	1	0.600	0.655	0.553	0.614	102	1.60	1.63	1.56	1.60	100
	2		0.663	0.592				1.69	1.57		
	3		0.629	0.595				1.62	1.55		

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Table 6

Stability test (ng/L)

Med QC	Initial measurement	Three freeze-thaw cycles[1]	Bench-top stability[2]	Processed sample stability[3]	Long-term stability[4]	Long-term stability[5]
Replicate 1	0.492	0.427	0.430	0.404	0.456	0.440
Replicate 2	0.448	0.429	0.417	0.424	0.521	0.407
Replicate 3	0.419	0.468	0.443	0.387	0.475	0.457
Mean	0.453	0.441	0.430	0.405	0.484	0.435
% difference from initial measurement		**−2.6**	**−5.0**	**−11**	**6.8**	**−4.0**
High QC						
Replicate 1	1.52	1.42	1.44	1.40	1.55	1.54
Replicate 2	1.48	1.46	1.38	1.35	1.68	1.48
Replicate 3	1.43	1.53	1.39	1.36	1.66	1.42
Mean	1.48	1.47	1.40	1.37	1.63	1.48
% difference from initial measurement		**−0.4**	**−4.9**	**−7.1**	**11**	**0.2**

1. Three times frozen at −70°C and then thawed (3 freeze-thaw cycles)

2. Original samples (not yet prepared for instrument analysis) stored at room temperature for 1 day

3. Processed samples (ready for instrument analysis) stored at room temperature for 1 day

4. Samples stored at 4°- 6°C for 13 months, freeze-thaw three cycles, left at room temp for more than 24 hours, then processed and left in room temp > 3 days.

5. Samples stored at 4°- 6°C for more than 2 years.