

Rapid Determination of Sr-90 in Urine by MS/MS Mode with O₂ as the Cell Gas on Triple Quadrupole Inductively Coupled Plasma Mass Spectrometry (ICP-MS/MS)

Ge Xiao

gax2@cdc.gov

Centers for Disease Control and Prevention

Jonathan Button

Centers for Disease Control and Prevention

Cynthia Ward-Momon

Centers for Disease Control and Prevention

Liza Valentin-Blasini

Centers for Disease Control and Prevention

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Abstract

A high-throughput ICP-MS/MS method was developed and validated for rapid determination of Sr-90 in urine to support radiological emergency response. Using an Agilent 8900 ICP-MS/MS with O₂ collision/reaction gas, isobaric interference from Zr-90 was reduced by > 99.999%, while remaining Ge and Se derived interferences in urine were well below the recommended action level of ~ 2.01 ng/L. The method achieved a LOD of 0.035 ng/L (176 Bq/L) with a simple dilution protocol requiring only 0.5 mL of urine. Validation demonstrated biases within ± 5% above 0.100 ng/L and performance comparable to liquid scintillation counting, providing a rapid, robust, and scalable alternative for emergency radiobioassay.

Introduction

Sr-90 is a high-yield byproduct of nuclear fission, produced during nuclear weapons testing and in nuclear reactors. Environmental Sr-90 originates primarily from atmospheric nuclear weapons testing in the 1950s–60s and from nuclear accidents such as those at Chernobyl and Fukushima [1–3]. A pure beta emitter with a half-life of 28.8 years, Sr-90 decays to yttrium-90 (Y-90), which subsequently undergoes beta decay to stable zirconium-90 (Zr-90) [4–6].

Sr-90 is considered one of the most hazardous radionuclides due to its persistence, biological uptake, and radiotoxicity [7, 8]. It is absorbed by plants through soil and transferred efficiently through the food chain to humans [9]. Ingestion is the primary exposure route. Following gastrointestinal absorption, 70–80% of ingested Sr-90 is excreted via urine, while the remainder accumulates in bone tissue, where it can persist for up to 13 years and expose surrounding tissues to beta radiation [10]. Long-term internal exposure increases the risk of bone cancer, soft tissue cancers, and leukemia. Noninvasive measurement of Sr-90 in urine provides an effective means for assessing internal contamination [11, 12].

Various analytical techniques have been developed for Sr-90 measurement in biological and environmental samples. CDC currently employs liquid scintillation counting (LSC) for low-concentration detection in urine. However, this method involves time-intensive chemical separation using costly Sr-specific resin and requires Sr-88 spike recovery analysis by ICP-MS [13]. Alternative mass spectrometric techniques—such as accelerator mass spectrometry, resonance ionization mass spectrometry, glow discharge mass spectrometry, and ICP-MS—offer reduced sample preparation and faster analysis [1–3, 5, 6, 14–16]. Among them, ICP-MS is widely preferred for its sensitivity, speed, low sample consumption, and minimal preparation. While isobaric interference from Zr-90 and tailing from Sr-88 complicate Sr-90 detection, next-generation ICP-MS platforms equipped with collision/reaction cell (CRC) technologies have greatly improved performance [17].

This study aimed to develop and validate a high-throughput method with simplified sample preparation for accurate determination of Sr-90 in urine with a target sensitivity of approximately 0.67 ng/L, an estimate of one-third of the Clinical Decision Guide (CDG) (2.01 ng/L) value for children and pregnant women (C/P) 5 days post exposure [18], as recommended by the National Council for Radiation Protection (NCRP). We employed the Agilent 8900 triple quadrupole ICP-MS/MS in tandem MS mode, which effectively mitigates the major interference, Zr-90, via oxygen reaction mode by converting Zr-90 to ZrO (mass 106) and ZrO₂ (mass 122).

The resulting method offers rapid, sensitive, and reliable quantification of Sr-90 in urine, suitable for emergency response scenarios, including accidental or deliberate releases, as well as for monitoring chronic environmental exposures. This work supports our laboratory's mission to develop scalable, transferable methods for rapid radiobioassay and public health preparedness.

Experimental

Reagents and solutions

All nitric acid (HNO₃) solutions were prepared using double-distilled acid (GFS Chemicals Inc., Columbus, OH). Ultrapure deionized water (resistivity ≥ 18 MΩ·cm) was obtained from an Aqua Solutions Ultrapure Water System (Aqua Solutions, Inc., Jasper, GA) and used in all solution preparations. Urine samples were collected anonymously in accordance with the Division of Laboratory Sciences' protocol, pooled and then acidified to 1% (v/v) HNO₃ to serve as the base urine matrix.

Certified reference materials (CRMs) of Sr-90 (Eckert & Ziegler Analytics, Inc., Atlanta, GA), traceable to the National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA), were used for spiking experiments. Urine pools for LOD studies and additional urine solutions for accuracy assessments were prepared by spiking base urine volumetrically with Sr-90 CRM. Iridium-193 (Ir-193) was used as the internal standard (High-Purity Standards, Charleston, SC).

To evaluate potential spectral interferences, single-element standards were spiked into the base urine to confirm the efficacy of the simple dilution procedure for minimizing isobaric and polyatomic interferences. These standards included zirconium (Zr), strontium (Sr), yttrium (Y),

chromium (Cr), iron (Fe), titanium (Ti), vanadium (V), germanium (Ge), selenium (Se), tungsten (W), hafnium (Hf), tantalum (Ta), and manganese (Mn), all sourced from Inorganic Ventures (Christiansburg, VA).

Two independent sets of external aqueous-based stock calibrators were prepared by serial dilution of two different lots of the Sr-90 CRM in 2% (v/v) HNO₃. Calibration levels included a blank (0.000) and six spiked concentrations: 0.030, 0.100, 0.300, 1.00, 3.00, and 10.0 ng/L. The sample diluent consisted of 2% (v/v) HNO₃ containing 100 ng/L of Ir-193. The rinse solution for the sample introduction system was composed of 5% (v/v) HNO₃.

Quality control (QC) and reference materials

Three levels of urine-based bench QC materials were prepared by spiking Sr-90 CRM into base urine at low, medium, and high concentrations—0.600, 2.000, and 6.000 ng/L—covering the full calibration range. QC materials were analyzed at both the beginning and end of each analytical run to evaluate the quality of the analytical process. Run acceptance was determined using standard statistical criteria outlined in the DLS policies and procedures manual [19]. These criteria were used to classify analytical runs as either in-control or out-of-control. Method precision, accuracy, and analyte recovery were evaluated using the prepared QC materials and multiple urine samples spiked with Sr-90 CRM in base urine. These assessments confirmed the method’s robustness and suitability for routine analysis.

Sample preparation

All samples, calibrators, and blanks were prepared using a 10× dilution in 15 mL polypropylene conical tubes. Matrix-matched working calibrators were generated by combining aliquots of each stock calibrator with base urine and sample diluent. Urine samples, including QC samples, were prepared using the same procedure. The aqueous (reagent) blank was prepared

using the same procedure but substituting the urine volume with deionized water. This reagent blank served as the baseline for all patient samples, urine QC samples, and reference materials. The composition of all sample types is summarized in Table 1.

Table 1 Sample preparation procedure and volumes used (mL)						
Calibration standard	Diluent*	2% v/v HNO ₃	Water	Base urine	Patient sample/QC	Calibrator stock
	4.00			0.500		0.500
Urine blank	4.00	0.500		0.500		
Aqueous blank	4.00	0.500	0.500			
Urine/QC sample	4.00	0.500			0.500	
*100 ng/L of Ir-193 in 2% v/v HNO ₃						

All dilution procedures were previously validated to ensure accuracy and reliability. For samples with Sr-90 concentrations exceeding the calibration range, additional dilutions—up to 10× with 2% (v/v) HNO₃—were performed to bring concentrations within the validated calibration range.

Instrumentation

Sr-90 concentrations were determined using an Agilent 8900 Triple Quadrupole ICP-MS/MS (Agilent Technologies, Wilmington, DE). The system was equipped with a Micro Mist nebulizer, double-pass quartz spray chamber, quartz injector, nickel/platinum sampler cone, and nickel/platinum skimmer cone for all measurements. Diluted urine samples were introduced via an ASX-520 autosampler (Elemental Scientific Inc., Omaha, NE).

High-purity argon gas (> 99.999%, Specialty Gases Southeast, Atlanta, GA) was used for both the plasma and nebulizer gases. The instrument was operated in MS/MS mode with oxygen reaction gas (> 99.997%, Specialty Gases Southeast, Atlanta, GA) introduced independently into the CRC gas line. All method parameters were carefully optimized for maximum performance.

The instrument demonstrated sensitivity of approximately 300–400 counts per second (cps) per ng/L of Sr-90, with a sample flow rate of ~ 0.8 mL/min. Major operating conditions and optimized method parameters are summarized in Tables 2a and 2b.

Table 2
a. Typical operating parameters for Sr-90 measurements
using ICP-MS/MS

Plasma Parameters	Setting (optimize as needed)
RF power	1550 W
RF matching	1.80 V
Nebulizer pump	0.30 rps
S/C temperature	2° C
Nebulizer gas	1.05 L/min
Lenses Parameters	
Extract 1	0
Extract 2	-190 V
Cell Parameters	
Use gas 4th gas flow [O ₂]	50% (0.75 mL/min)
OctP bias	-5.0 V
Axial acceleration	1.5 V
OctP RF	180 V
Energy discrimination	-13.0 V
Wait time offset	2 msec

Table 2
b Method parameters and data acquisition settings for Sr-90 analysis by ICP-MS/MS

Scan type	MS/MS
Q1/Q2 (Ir -ISTD)	193/193
Q1/Q2 (Sr - Analyte)	90/90
Q1/Q2 (ZrO - Analyte)	90/106 (informational, not calibrated)
Q1/Q2 (ZrO ₂ - Analyte)	90/122 (informational, not calibrated)
Acquisition mode	Spectrum
Q2 peak pattern	3 points
Replicates	5
Sweeps/Replicates	500
Data analysis method	FullQuant analysis
Calibration method	External calibration
Curve fit	Linear
Origin	Ignore
Weight	1/x
Minimum concentration	None
Calibration level (ng/L)	0.000, 0.030, 0.100, 0.300, 1.00, 3.00, 10.0
Stabilization time (sec)	30
Integ time/mass (sec) - Ir	1.0
Integ time/mass (sec) - Sr	20.0
Integ time/mass (sec) – ZrO	1.0
Integ time/mass (sec) – ZrO ₂	1.0
Total acquisition time (min)	2:35

Validation test, results, and discussion

Removal of potential spectral interferences

Isobaric Zr-90 removal

To accurately determine Sr-90 (atomic mass 89.9077 u), we optimized method parameters and oxygen (O₂) reaction gas conditions to overcome isobaric interference from Zr-90 (atomic mass 89.9047 u). Zr-90 is commonly found in human urine at concentrations approximately three orders of magnitude higher than the recommended Sr-90 action level of 2.01 ng/L [18]. Stable Zr-90 and Sr-88 standards were spiked into 5% HNO₃ to evaluate the efficiency of mass-shift mode in separating Zr and Sr at mass 90. Results demonstrated that Zr-90 was effectively separated from Sr-90 via reaction with O₂ in the CRC of the ICP-MS/MS, forming ZrO and ZrO₂ species (Fig. 1a). Optimization plots indicated that approximately 99.999% of Zr-90 was removed at 50% O₂ gas flow, while only approximately 5% of Sr underwent reaction across the O₂ flow rate range under the current instrument settings (Fig. 1b).

Sr-88 peak tailing effect

A critical challenge in Sr-90 measurement using previous-generation ICP-MS platforms is mitigating peak tailing from abundant Sr-88 and its hydride formation, which can interfere at mass 90. To evaluate our method's robustness, Sr-88 was spiked into several aliquots of base urine at concentrations up to 600 µg/L, significantly exceeding the 95th percentile concentration for strontium (299 µg/L) for the total population in the 2015–2016 cycle of the National Health and Nutrition Examination Survey (NHANES) [20]. Despite this high-level of spiked Sr-88, the signals were not significant as they were below our LOD of 0.035 ng/L at m/z 90 relative to base urine when the spiked samples were analyzed using the optimized method parameters (Fig. 3a), demonstrating effective suppression of Sr-88 tailing.

Potential polyatomic interferences

Other potential interferences may arise from compounds formed by urine constituents such as Ge, V, Cr, Mn, Ti, Se, Fe, Co, Ga, Y, Ni, and As in combination with elements including Ar, Cl, P, S, F, N, H, and O. These can produce polyatomic ions overlapping Sr-90 at m/z 90, including species such as $^{74}\text{Ge}^{16}\text{O}$, $^{72}\text{Ge}^{18}\text{O}$, $^{50}\text{V}^{40}\text{Ar}$, $^{52}\text{Cr}^{38}\text{Ar}$, $^{54}\text{Cr}^{36}\text{Ar}$, $^{50}\text{Cr}^{40}\text{Ar}$, $^{53}\text{Cr}^{37}\text{Cl}$, $^{55}\text{Mn}^{35}\text{Cl}$, $^{50}\text{Ti}^{40}\text{Ar}$, $^{74}\text{Se}^{16}\text{O}$, $^{54}\text{Fe}^{36}\text{Ar}$, $^{59}\text{Co}^{31}\text{P}$, $^{71}\text{Ga}^{19}\text{F}$, $^{71}\text{Ga}^{18}\text{O}^{1}\text{H}$, $^{89}\text{Y}^{1}\text{H}$, $^{58}\text{Ni}^{32}\text{S}$, $^{75}\text{As}^{15}\text{N}$, as well as doubly charged ions such as $^{180}\text{Ta}^{2+}$, $^{180}\text{Hf}^{2+}$, and $^{180}\text{W}^{2+}$.

To evaluate their contribution to the Sr-90 signal in urine, these elements were spiked into base urine at concentrations significantly exceeding the 95th percentile levels for the total population in the 2015–2016 cycle reported by the National Health and Nutrition Examination Survey (NHANES) [20]. Where NHANES data were unavailable, concentrations were selected based on potential maximum levels from prior studies [21–28], concentrations for other listed below: 5 µg/L for Ge, V, Cr, Ta, Ga, Y, W, and Hf; 50 µg/L for Ti and Ni; and 200 µg/L for Se and Fe.

No measurable signal at m/z 90 was observed for most elements except Ge and Se. Using O₂ as the CRC gas, $^{74}\text{Ge}^{16}\text{O}$, $^{72}\text{Ge}^{18}\text{O}$, and $^{74}\text{Se}^{16}\text{O}$ species formed at m/z 90 generated false-positive signals corresponding to 0.093 ng/L (N = 3) for Ge and 0.069 ng/L (N = 3) for Se, when spiked at concentrations of 5 µg/L Ge and 200 µg/L Se.

Typically, urine Ge concentrations previously reported in general population are below the method's LOD of 0.25 µg/L, and occupational exposure studies have shown the Ge levels generally remain below 1 µg/L [24]. Therefore, interference from Ge is expected to be negligible.

Urinary Se, investigated as a biomarker of selenium status [28], typically has population means below 32 µg/L, substantially lower than the tested 200 µg/L. However, individual Se concentrations can vary widely from 0.8 µg/L to 563 µg/L [28]. Interference testing with Se concentrations spiked up to 800 µg/L yielded a maximum contribution Sr-90 signal of < 0.160 ng/L (Fig. 3b), more than 10-fold below the clinical/pregnancy decision guide (C/P CDG) threshold of 2.01 ng/L five days post-exposure. Therefore, the observed Se related interference is unlikely to affect clinical interpretation, patient triage, or medical countermeasure decisions. Consequently, these interference levels are considered acceptable for emergency Sr-90 determination.

Analytical specificity was further confirmed by assessing potential interferences in urine samples from 50 anonymous donors. The mean false positive Sr-90 concentration was 0.008 ± 0.007 ng/L (average $\pm$ 1 SD), indicating no interfering substances producing signals above the LOD.

LOD determination

The LOD in this study was calculated by evaluating false positive and false negative rates, following guidelines recommended by the Clinical Laboratory Standards Institute (CLSI) [29] and requirements established by the DLS [19, 30–32]. These guidelines uniformly characterize the relationship between the standard deviation of measurements and analyte concentration at low levels.

To determine the LOD, 36 analytical runs were performed using urine matrix-matched samples spanning a concentration range expected to encompass the LOD. Samples included urine blanks, five low-concentration pools, and the initial low QC pool (Table 3). LOD estimates were generated using statistical tests based on both linear and quadratic models. The linear model provided a superior fit for this method, evidenced by a P value of 0.0005. The LOD was then calculated using the following formula:

Table 3
Among-run precision of Sr-90 measurements for internal QC materials and LOD determination samples (ng/L)

QC materials	N	Mean ± 2SD	CV (%)	Target value	Bias (%)
Low QC	72	0.595 ± 0.057	4.83	0.600	-0.80
Med QC	72	2.01 ± 0.14	3.48	2.00	0.64
High QC	72	6.01 ± 0.34	2.81	6.00	0.17
Samples used for LOD determination					
Base urine	36	0.008 ± 0.014	—	0.000	—
LOD1	36	0.040 ± 0.017	21.0	0.030	34.4
LOD2	36	0.058 ± 0.019	16.1	0.050	16.3
LOD3	36	0.105 ± 0.023	10.8	0.100	4.78
LOD4	36	0.206 ± 0.031	7.43	0.200	3.00
LOD5	36	0.301 ± 0.032	5.36	0.300	0.41
Low QC (beginning)	36	0.602 ± 0.044	3.64	0.600	0.35
*QC and LOD samples were prepared at the CDC by spiking NIST traceable Sr-90 CRM in pooled urine collected anonymously.					
All measured results were not urine blank corrected.					

$$conc_{LOD} = \frac{\mu_{blank} + 1.645(\sigma_{blank} + b)}{1 - 1.645a}$$

Where, μ_{blank} and σ_{blank} represent the mean and standard deviation of blank sample measurements, respectively. Following this procedure, results at the LOD correspond to a maximum false negative rate of 5%. Results above the LOD exhibit even lower false negative rates. The LOD for Sr-90 in this method was determined to be 0.035 ng/L (Fig. 2), which is more than 10-fold below one-third of the C/P CDG level of 2.01ng/L, at 0.67 ng/L. This sensitivity is therefore suitable for emergency radiobioassay applications, enabling accurate determination of Sr-90 concentrations in urine collected five days post-exposure.

Linearity and carryover

A 1/x weighted linear regression model was applied to six calibration standards ranging from 0.030 to 10.0 ng/L (S1–S6) of Sr-90, demonstrating excellent linearity with correlation coefficients (R^2) exceeding 0.9999 across all 36 analytical runs. For urine samples with Sr-90 concentrations exceeding the calibration range, dilution with 2% v/v HNO_3 is recommended to bring concentrations within the validated range. Accuracy testing with reference materials spiked into base urine confirmed that Sr-90 concentrations could be diluted up to 10-fold beyond the normal sample preparation without significant bias, ranging from -1.27% to -7.88% relative to target values (Table 4), effectively expanding the quantification range up to 100 ng/L.

Table 4
Urine sample dilution study for Sr-90: mean concentrations and normalized results (ng/L)

Dilution factor	N	Mean observed ± 2SD	Mean final ± 2SD	CRM spiking T. V.	Bias (%)	Normalized extra dilution result
1×	6	7.41 ± 0.89	7.41 ± 0.89	7.50	-1.27	1.00
2×	6	7.38 ± 0.90	14.8 ± 1.8	15.0	-1.58	0.997
5×	6	7.03 ± 0.78	35.2 ± 3.9	37.5	-6.21	0.950
10×	6	6.91 ± 0.92	69.1 ± 9.1	75.0	-7.88	0.933

Carryover was evaluated by alternating the analysis of urine samples spiked with 10.0 ng/L Sr-90 with the analysis of urine blanks. Five blanks were measured before and after the spiked samples to establish baseline levels. No significant carryover was observed, as no increase in Sr-90 concentration was detected in the blanks following high-concentration samples (Fig. 4).

Precision, accuracy, and recovery

The precision of the method was evaluated through run-to-run reproducibility of bench QC materials. As shown in Table 3, QC samples were analyzed at the beginning and end of each of the 36 analytical runs conducted over a period of approximately nine months. The precision for the low, medium, and high QC levels remained within 5% throughout the study.

Long-term precision was further assessed using five low-spiked samples included in the LOD determination across the same 36 runs. Results indicated that increasing the Sr-90 concentration from 0.030 ng/L (below the method LOD) to 0.300 ng/L led to a marked improvement in analytical performance, with corresponding improvements in both precision and accuracy. Precision improved substantially, as demonstrated by a decrease in relative standard deviations from 21.0% to 5.36%.

Accuracy was evaluated using QC and LOD determination samples prepared by spiking CRM into base urine. The measured concentrations of the three bench QC pools were in strong agreement with the target values, with analytical biases within ± 1% (Table 3). For the LOD determination samples, the observed bias ranged from 34.4% at the lowest concentration to 0.41% at higher concentrations. The LOD 1 sample is below the current LOD, and the LOD 2 sample is 1.4× the LOD, which may impact accuracy at the low concentration range. The larger bias observed at low concentrations also may be attributed to under-correction of the method blank, as an aqueous blank was used instead of a urine blank for all analyses.

Recovery was assessed in accordance with DLS guidelines [19], using two distinct base urine pools spiked with Sr-90 at zero and three reportable concentration levels. Each concentration was spiked in triplicate, resulting in a total of 24 samples. These were analyzed in two analytical runs conducted on separate days, yielding 48 total results. Recovery was calculated as follows:

$$Recovery\ (\%) = \frac{Final\ concentration - Initial\ concentration}{Added\ concentration} \times 100$$

As shown in Table 5, recoveries for Sr-90 spiked at concentrations of 0.100, 0.300, 0.500, 1.500, 2.500, and 7.500 ng/L ranged from 96.8% to 103.8% across both urine pools, demonstrating excellent method accuracy and consistency.

Table 5
Accuracy evaluation of Sr-90 determination based on spike recovery experiments

Sample 1		Sample 2									
		Measured concentration (ng/L)					Measured concentration (ng/L)				
	Replicate	Spike concentration	Day 1	Day 2	Mean ± 2SD	Recovery (%)	Spike concentration	Day 1	Day 2	Mean ± 2SD	Recovery (%)
Sample 1	1	0.000	0.008	0.016	0.014		0.000	0.009	0.025	0.018	
	2		0.011	0.008	± 0.010			0.023	0.019	± 0.013	
	3		0.016	0.021				0.011	0.020		
+ Spike 1	1	0.100	0.103	0.125	0.115	101.7	0.300	0.364	0.309	0.329	103.8
	2		0.113	0.113	± 0.015			0.333	0.334	± 0.050	
	3		0.122	0.115				0.342	0.294		
+ Spike 2	1	0.500	0.496	0.494	0.497	96.8	1.50	1.57	1.60	1.57	103.5
	2		0.491	0.532	± 0.035			1.57	1.54	± 0.05	
	3		0.487	0.484				1.60	1.56		
+ Spike 3	1	2.50	2.54	2.49	2.53	100.6	7.50	7.68	7.66	7.72	102.6
	2		2.57	2.45	± 0.10			7.72	7.61	± 0.23	
	3		2.57	2.55				7.93	7.71		

Stability

Stability testing was conducted to ensure that the levels of Sr-90 in urine were not affected by conditions that samples might encounter during analysis. Three QC pools were utilized to assess the stability of urine samples under various handling and storage conditions. These included bench-top stability, processed sample stability, short-term stability at room temperature, long-term stability under frozen storage conditions (≤ –

60°C), and stability following three freeze–thaw cycles. The mean relative differences between replicate measurements and the initial values ranged from – 4.49% to 2.53% across all QC materials tested (Table 6). These variations were within the ± 15% acceptance criteria established by the DLS at the CDC [19].

Table 6
Sr-90 stability assessment in urine samples (ng/L), based on triplicate measurements (N = 3)

Low QC	Initial measurement	Three freeze-thaw cycles ¹	Bench-top stability ²	Processed sample stability ³	Long-term stability ⁴
Mean ± 2SD	0.625 ± 0.028	0.626 ± 0.044	0.606 ± 0.034	0.607 ± 0.035	0.641 ± 0.045
Acceptable range ⁵	0.595 ± 0.057 (0.538–0.653)				
% difference from initial measurement		0.21	-2.98	-2.93	2.53
Med QC					
Mean ± 2SD	2.05 ± 0.03	1.98 ± 0.08	2.04 ± 0.03	1.96 ± 0.03	2.07 ± 0.05
Acceptable range ⁵	2.01 ± 0.14 (1.87–2.15)				
% difference from initial measurement		-3.43	-0.54	-4.49	1.79
High QC					
Mean ± 2SD	6.13 ± 0.11	5.92 ± 0.32	6.06 ± 0.13	5.88 ± 0.10	6.33 ± 0.20
Acceptable range ⁵	6.01 ± 0.34 (5.67–6.35)				
% difference from initial measurement		-3.41	-1.12	-4.11	1.20
¹ Subjected to three freeze–thaw cycles (frozen at ≤ – 60°C and thawed three times)					
² Original samples (unprepared for instrument analysis) stored at room temperature for 1 day					
³ Processed samples (prepared for instrument analysis) stored at room temperature for more than 1 day					
⁴ Samples frozen for one year, followed by refrigerated storage for an additional year (total of 2 years)					
⁵ Acceptable ranges established as ±2SD from the characterized mean across 36 runs (N = 72)					

Method comparison

To evaluate the performance of the method described in this study relative to the previously used LSC method [13], both methods were applied to analyze the same set of 10 spiked urine samples, which had been originally prepared for the LSC method. All measured results were decay-corrected to the original preparation date (Table 7). A correlation plot of the results yielded a linear regression slope of 1.026 for Sr-90 (Fig. 5), indicating strong agreement between the two methods with a Pearson correlation coefficient (PCC) of 1.00 and a bias of less than 10% over the concentration range of 0.2–10 ng/L.

Table 7
Method comparison of ICP-MS/MS and LSC for the determination of Sr-90 in urine samples (ng/L)

LSC samples ¹	On ICP-MS/MS (N = 12)			On LSC (N = 20)			Bias to LSC (%)
	Decay corrected results ¹	2SD	CV (%)	Decay corrected results ²	2SD	CV (%)	
LSC PT1	0.180	0.028	7.78	0.165	0.013	3.91	9.19
LSC PT2	0.180	0.024	6.69	0.170	0.013	3.91	5.54
LSC PT3	0.183	0.023	6.36	0.172	0.015	4.40	6.95
LSC PT4	5.18	0.15	1.44	4.97	0.22	2.21	4.23
LSC PT5	5.28	0.23	2.21	5.05	0.23	2.25	4.45
LSC PT6	5.14	0.30	2.91	5.09	0.23	2.27	0.85
LSC PT7	10.7	0.5	2.45	10.3	0.6	3.02	4.31
LSC PT8	10.9	0.4	2.07	10.6	0.5	2.44	2.89
LSC PT9	10.7	0.5	2.32	10.6	0.6	2.82	0.96
LSC quarterly	5.06	0.34	3.36	4.92	0.20	2.01	2.97
¹ Samples were prepared at the CDC on August 14, 2015, and October 1, 2016, by spiking NIST-traceable Sr-90 CRM into pooled, anonymously collected urine.							
² Results were decay-corrected to the original preparation date.							

The precision of the two methods is also compared in Table 7. While the ICP-MS/MS method exhibited slightly greater run-to-run variability at low concentrations, both methods demonstrated comparable precision at higher concentrations.

In terms of sensitivity, the LSC method had a lower LOD of 0.011 ng/L [11], compared to 0.035 ng/L for the ICP-MS/MS method. Although the LOD for ICP-MS/MS is approximately three times higher, it remains well below one-third of C/P CDG value for Sr-90, making it suitable for rapid emergency response applications.

The ICP-MS/MS method offers several operational advantages. It requires only 0.5 mL of urine per sample—compared to 5 mL for LSC—making it more applicable for use across a broad population. Additionally, the simple dilution approach used in this method eliminates the need for the time-consuming column cleanup procedure (e.g., the offline purification system using ESI columns) required by the LSC method.

In contrast, the LSC method involves a more cumbersome workflow. It requires correction for strontium recovery by measurement using ICP-DRC-MS. The overall process spans three different instrumentation platforms—LSC, ICP-MS, and the PrepFAST automated pre-analytical sample preparation system, making it difficult to scale in emergency response scenarios. The streamlined workflow of the ICP-MS/MS method, therefore, provides a significant advantage in terms of scalability, efficiency, and field-readiness.

Proficiency testing (PT) and quarterly check set up

PT is a critical component in evaluating the quality and reliability of a measurement method. Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), PT is typically performed at least twice annually for most analytes to meet regulatory requirements [32]. However, because no external PT programs exist for Sr-90 in urine, we meet the twice yearly assessment requirement using an internal program that mimics the conduct of an externally provided PT challenge.

Nine Sr-90 urine pools were prepared at three concentration levels by spiking certified CRM into a base urine matrix. These pools were designed to span the calibration range of the method, corresponding to 5%, 20%, and 75% of the highest calibration standard (HCS). At each concentration level, three pools were created with target values spaced one standard deviation (SD) apart, calculated using data from the first 22 analytical runs that were originally conducted for establishing QC target values and determining the LOD (see Table 3, Table 8, and Fig. 6).

Table 8
Observed Sr-90 among-run accuracy and precision for CRM-spiked PT materials and quarterly check samples (ng/L)

Sample ¹	Concentration level	N	Sr-90				
			Mean $\pm$ 3SD ²	CV (%)	T.V.	Calculated SD ³	Bias (%)
Low PT1	5%HCS-SD	10	0.463 $\pm$ 0.030	2.19	0.475		-2.53
Low PT2	5%HCS	10	0.502 $\pm$ 0.073	4.86	0.500	0.025	0.38
Low PT3	5%HCS + SD	10	0.537 $\pm$ 0.058	3.59	0.525		2.30
Med PT1	20%HCS-SD	10	1.90 $\pm$ 0.18	3.09	1.93		-1.36
Med PT2	20%HCS	10	1.98 $\pm$ 0.12	2.08	2.00	0.07	-1.11
Med PT3	20%HCS + SD	10	2.04 $\pm$ 0.12	2.01	2.07		-1.54
High PT1	75%HCS-SD	10	7.12 $\pm$ 0.34	1.57	7.26		-1.91
High PT2	75%HCS	10	7.37 $\pm$ 0.45	2.02	7.50	0.24	-1.69
High PT3	75%HCS + SD	10	7.61 $\pm$ 0.46	2.03	7.74		-1.69
Quarterly check	1/3 of C/P CDG	10	0.658 $\pm$ 0.092	4.66	0.670	-	-1.81
¹ All samples were prepared at the CDC by spiking NIST-traceable Sr-90 CRM into pooled, anonymously collected urine.							
² All results were decay-corrected to the preparation date.							
³ Data are based on the first 22 runs used for QC characterization and limit of LOD determination.							
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Additionally, a urine pool at a concentration of 0.670 ng/L—equivalent to one-third of the C/P CDG level—was prepared and characterized alongside the PT pools. This pool will be used to verify the accuracy and consistency of the method on a quarterly basis moving forward.

The precision observed for these 10 pools across 10 analytical runs over a two-week period ranged from 1.57% to 4.66%. These runs employed two alternating sets of calibrators prepared from different CRM lots. The bias relative to the spiking target values ranged from – 2.53% to 2.30%, indicating high accuracy. This activity was reviewed by CDC, deemed research not involving human subjects, and was conducted consistently with applicable federal law and CDC policy.

For ongoing internal PT, QC officers will randomly select five of the nine PT pools and blind them to analysts. This process ensures the samples are treated and analyzed in the same manner as routine patient specimens, closely mirroring the procedures used in external PT assessments and supporting continued method performance verification.

Sample throughput

In the context of a radiological emergency, where thousands of patient samples may require rapid analysis, sample throughput becomes a critical consideration—alongside analytical accuracy and precision. The method described here is designed with high-throughput capacity in mind. Sample preparation for a batch of 40 patient urine specimens, along with associated calibrators and QC materials, requires approximately 40 minutes. Each sample is analyzed in 4 minutes and 40 seconds, resulting in a total analysis time of about 4 hours per batch. Because sample preparation can proceed concurrently with instrumental analysis, the method supports a daily throughput of approximately 180 samples per instrument within a 24-hour operational cycle.

Conclusions

We have developed and validated a high-throughput method for radiological emergency response using the Agilent 8900 ICP-MS/MS platform to quantify Sr-90 in urine. Utilizing MS/MS with O₂ as the CRC gas effectively eliminated isobaric interference from Zr-90 by more than 99.999%, as well as most polyatomic interferences, except for those originating from Ge and Se. However, the levels of Se- and Ge-derived interferences in urine from the general population were well below the NCRP C/P CDG action level of 2.01 ng/L, ensuring no impact on medical intervention decisions in emergency scenarios.

This method achieves a low LOD of 0.035 ng/L (176 Bq/L) and supports rapid sample throughput through a straightforward dilution protocol. This approach minimizes sample handling and preparation time, enabling rapid scale-up in emergency scenarios. Importantly, the method is

compatible with existing ICP-MS/MS instrumentation used for stable element analyses, allowing laboratories to expand capacity without the need for specialized equipment.

Method validation demonstrated excellent agreement with CRM-spiked urine samples, with biases within $\pm 5\%$ at concentrations above 0.100 ng/L. The slightly higher bias observed at lower concentrations is likely attributable to incomplete correction for the aqueous reagent blank, as deionized water rather than urine was used as the blank for urine samples. The measured baseline signal at m/z 90 in urine was equivalent to 0.010 ng/L Sr-90 (2SD = 0.021 ng/L, $N = 80$), indicating a small background contribution at m/z 90 under the current method and instrument conditions. Although this background contribution is negligible at higher analyte concentrations, it represents a larger proportion of the measured signal at low concentrations, resulting in the slightly higher bias observed near the method LOD.

Compared to the conventional LSC approach, the ICP-MS/MS method offers a simpler, more robust analytical platform with comparable precision and accuracy (within 10%). Furthermore, the ICP-MS/MS method requires only 0.5 mL of urine per sample, significantly less than the 5 mL required for LSC. This reduced sample volume makes the method especially suitable for vulnerable populations such as young children and infants, who typically produce smaller urine volumes.

Declarations

Disclaimer

The findings and conclusions in this study are those of the authors and do not necessarily represent the views of the U.S. Department of Health and Human Services or the Centers for Disease Control and Prevention. Use of trade names and commercial sources is for identification only and does not constitute endorsement by the U.S. Department of Health and Human Services or the Centers for Disease Control and Prevention.

Additional information

Conflict of interest

The authors declare no conflicts of interest.

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Author Contribution

G.X. and J.B. conceived and designed the study. G.X. performed the experiments, developed the methodology, and collected the data, G.X. and J.B. analyzed the data and performed the validation. G.X. wrote the main manuscript text and prepared the figures 1-6 and Tables 1-8. J.B., C.W.M. and L.V.B. supervised the project. All authors (G.X., J.B., C.W.M., and L.V.B.) reviewed and approved the final manuscript.

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Figures

Figure 1a. Optimization of ICP-MS/MS cell gas conditions using O₂

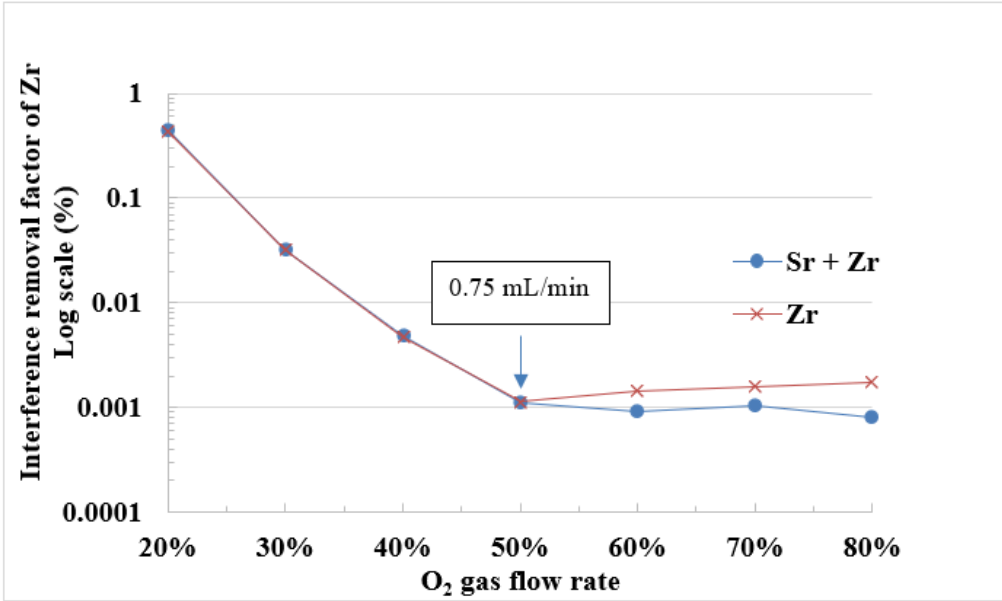


Figure 1b. Percentage of Sr reacting with O₂ to form oxide ions

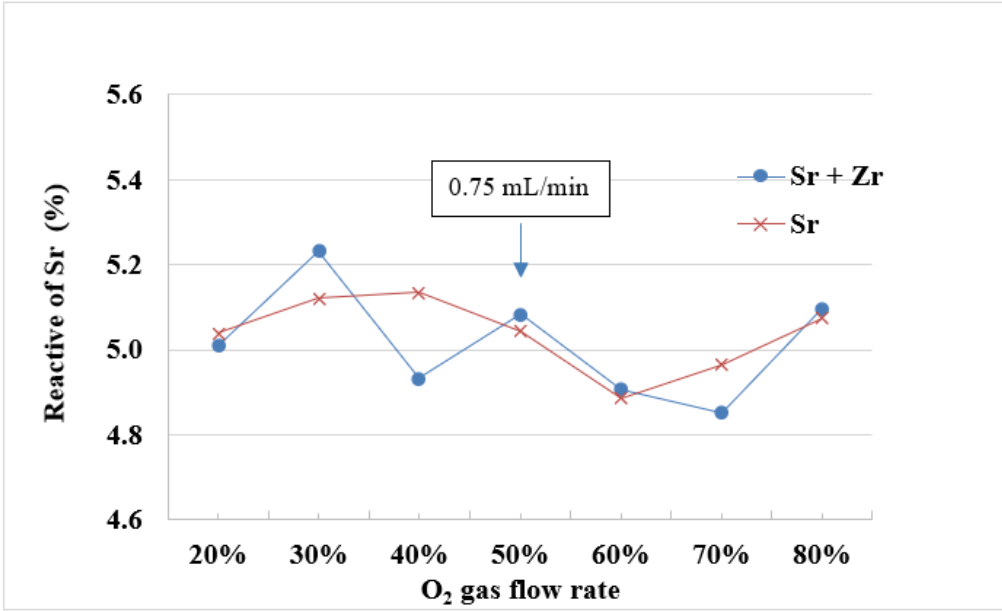


Figure 1

See image above for figure legend.

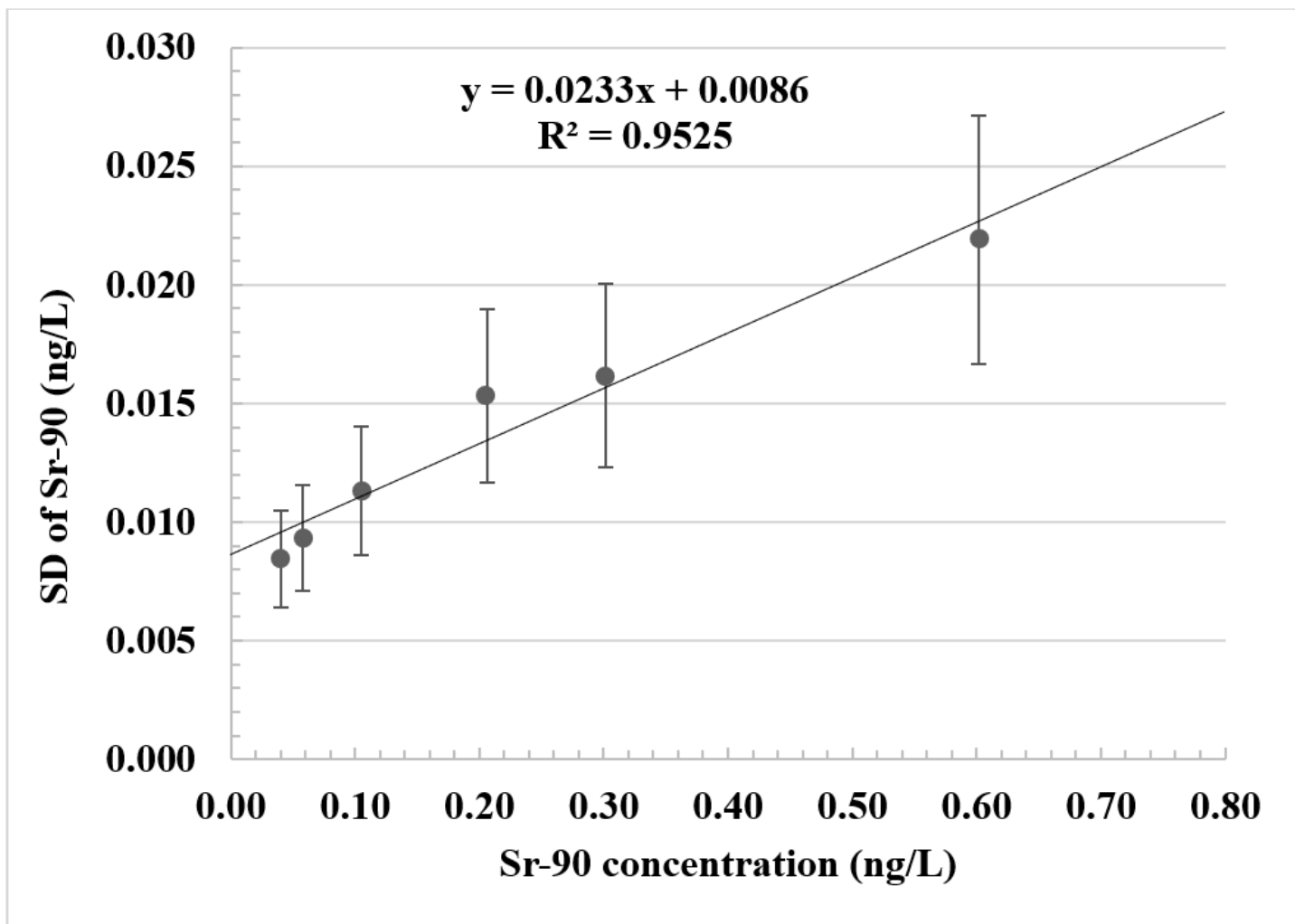


Figure 2

Assessment of the Sr-90 LOD using 36 analytical runs at each concentration level

Figure 3a. Evaluation of potential Sr-88 interference on Sr-90 measurement using spiking experiments

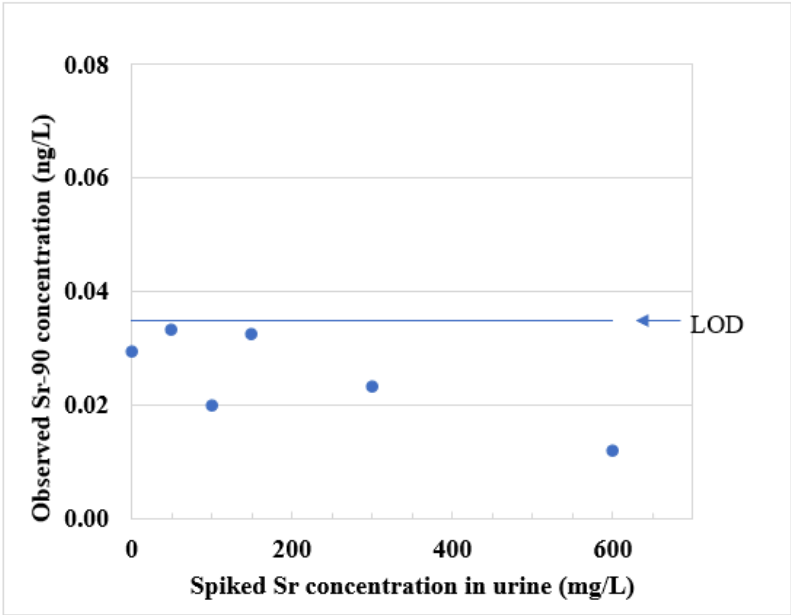


Figure 3b. Investigation of Se-related spectral interference during Sr-90 measurement

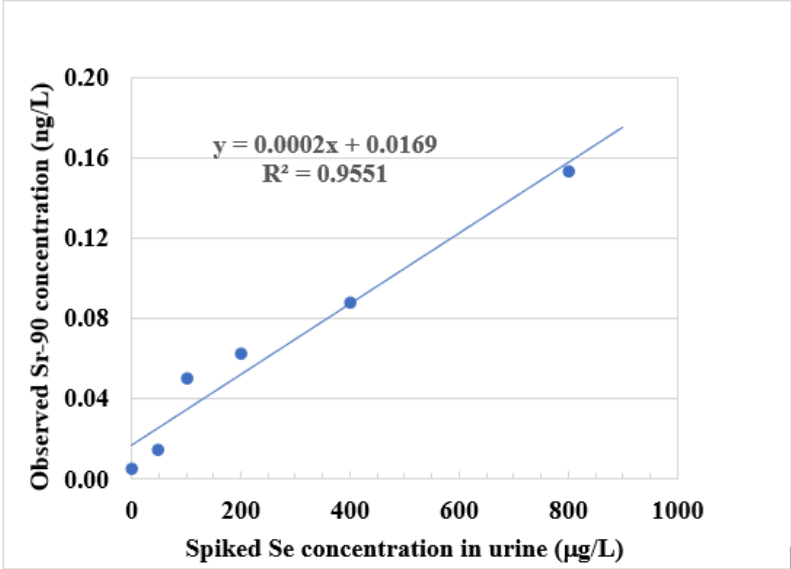


Figure 3

See image above for figure legend.

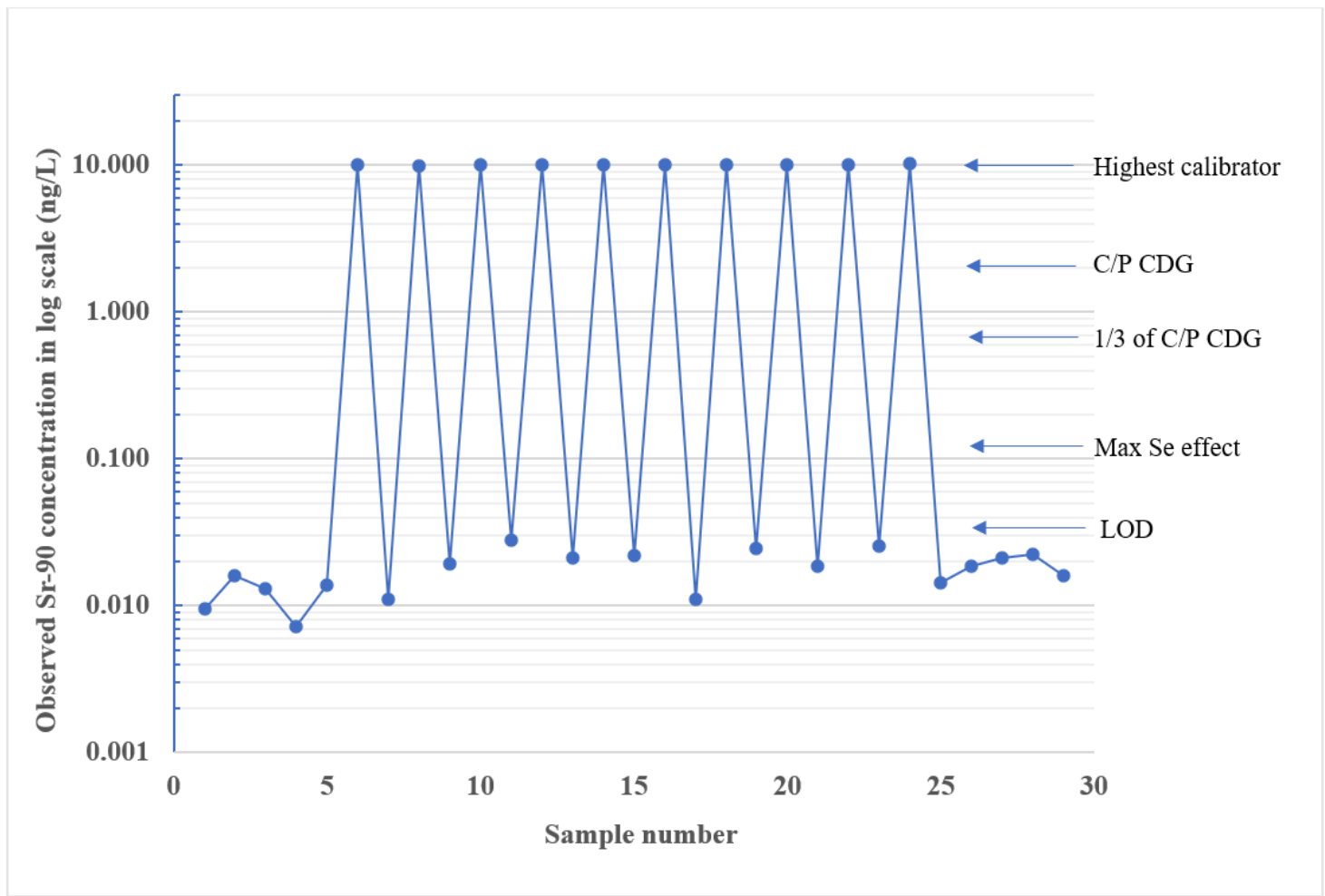


Figure 4

Assessment of sample carryover following analysis of high-concentration Sr-90 samples

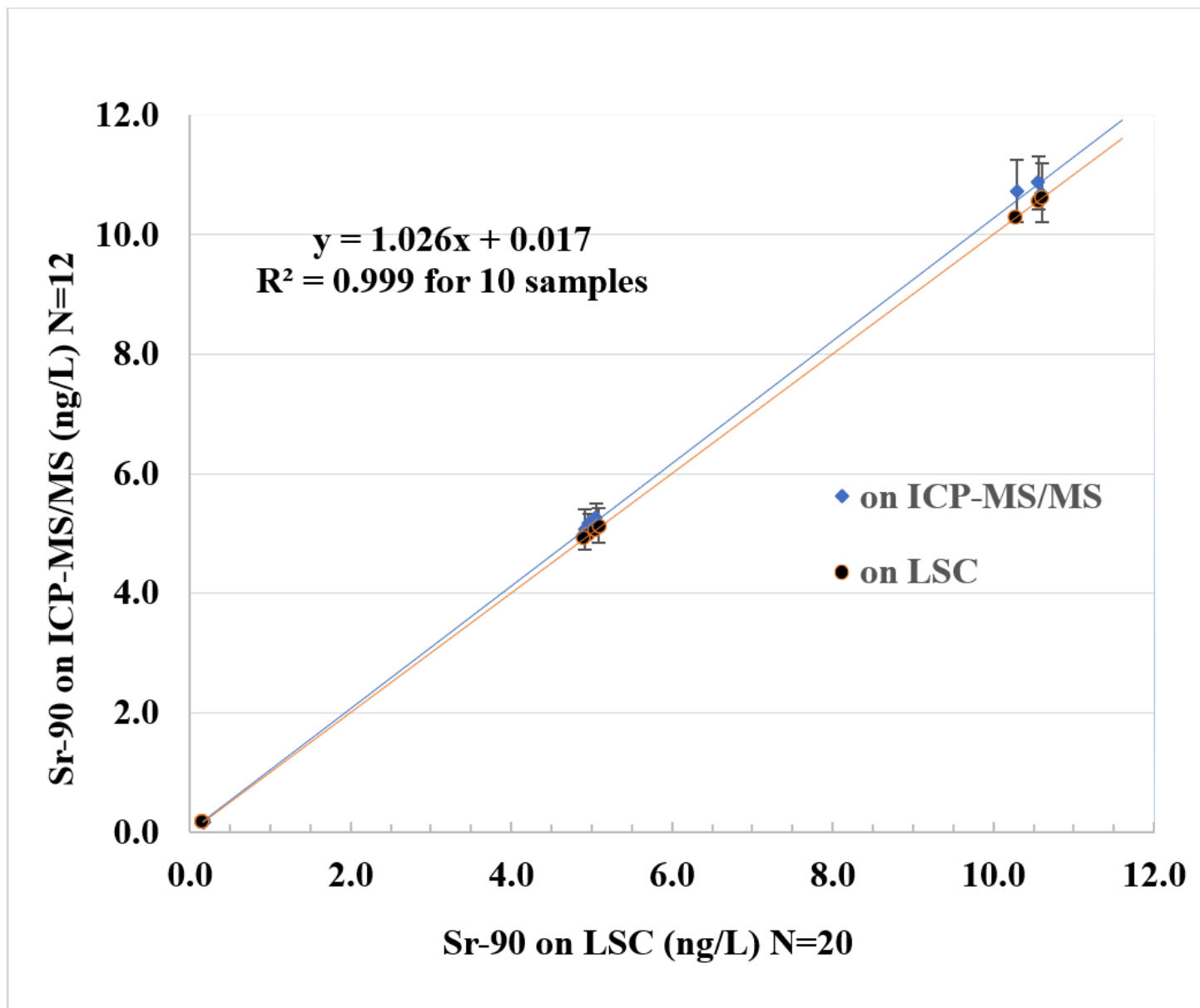


Figure 5

Comparison of Sr-90 measurements obtained by ICP-MS/MS and LSC

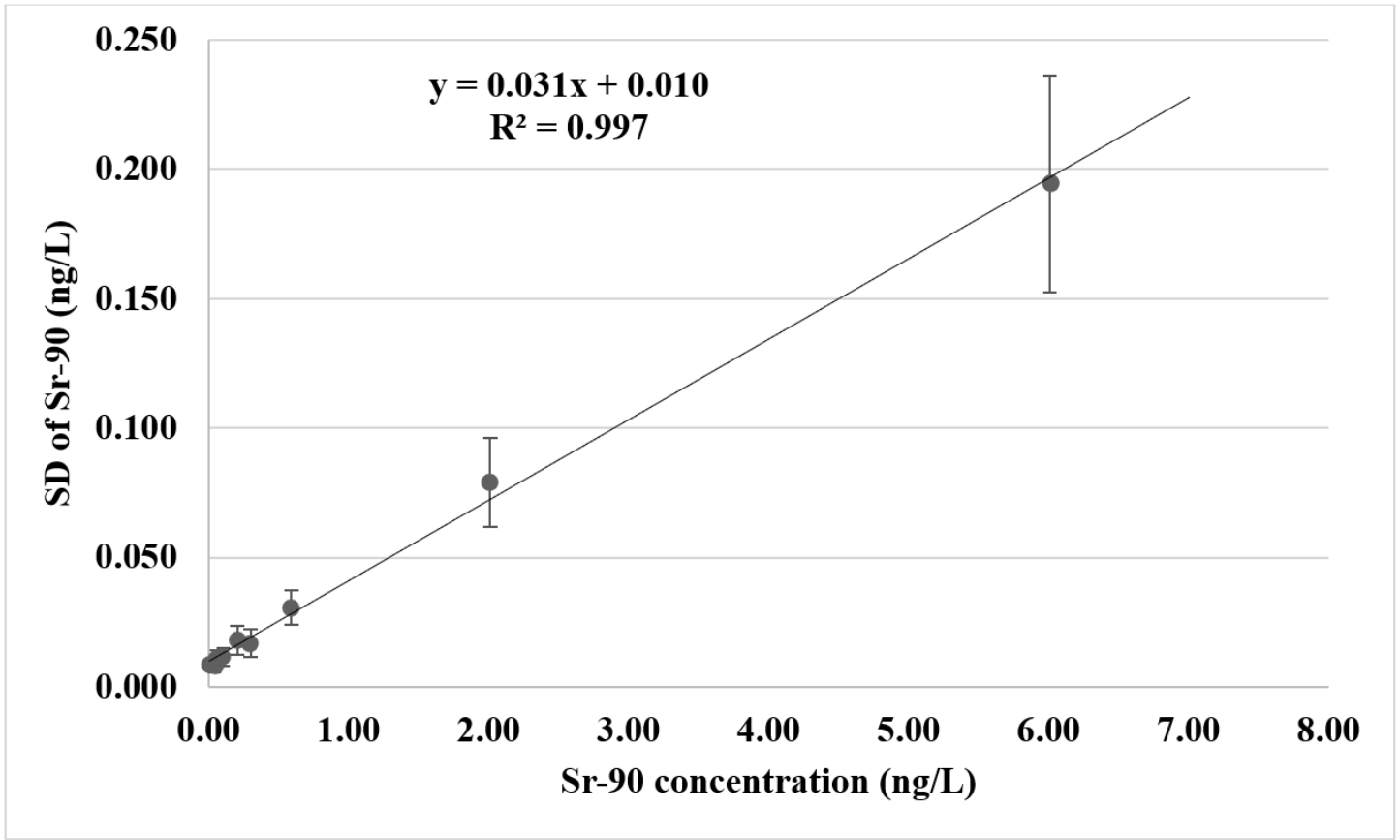


Figure 6

SD estimates for Sr-90 PT urine spikes generated from the first 22 analytical runs during QC characterization and LOD determination