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Analytical methods for Ir-192 determination and their comparison

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Abstract

The Centers for Disease Control and Prevention (CDC) Radiation Laboratory's primary mission is to provide laboratory support for an effective and efficient response to public health radiological emergencies. The laboratory has developed methods for several radiological threat agents, including Iridium-192 (Ir-192). Ir-192 can be analyzed via its gamma energy through analytical methods such as High Purity Germanium (HPGe) and its beta energy through Liquid Scintillation Counting (LSC). In this work, we present and compare HPGe and LSC rapid response methods for Ir-192 quantification. Both methods show the reasonable results and can be used in emergency situations.

Keywords

Liquid scintillation counting; High purity Germanium; Ir-192 urine bioassay; Tri-Carb®3110; Tri-Carb®5110; Quantulus™ GCT6220

Introduction

The urine radionuclide screen (URS) is a valuable tool designed by the CDC Radiation Laboratory to assist during radiological emergencies. The URS is a panel of methods that can be used to quickly identify samples with elevated levels of radioactivity [1]. The panel employs seven different analytical detection techniques to provide rapid detection screening and radioisotope detection and quantification. The techniques can be divided into two categories: traditional radiometric techniques, such as liquid scintillation counting [1, 2], gamma counting on sodium iodide (NaI) or high purity germanium (HPGe) [3], and alpha spectrometry in passively implanted P-silicon (PIPS) detectors, as well as mass counting techniques utilizing inductively coupled plasma mass spectrometry (ICP-MS) [4–9].

The URS panel of methods is designed to assay 22 radionuclides of interest with Iridium-192 being one of them. Iridium-192 is a manmade isotope with popular applications

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Conflict of interest The authors declare that they have no competing financial interests.

in industry and medicine. It is a strong beta and gamma emitter and one of the four most frequently used radioisotopes worldwide. Ir-192 decays mainly through β- decay into stable platinum (Pt-192). Approximately 5% of decay occurs through electron capture (EC) to stable osmium (Os-192), producing gamma emission peaks of different energies, various characteristic x-rays, and numerous electrons [10]. It emits beta particles at maximum energies of 538 keV and 635 keV and gamma rays at 316 keV and 468 keV, making it useful for non-destructive imaging and medical purposes [10]. This energy range of gamma-ray emissions makes Ir-192 ideal for industrial radiography, which has become a major element of nondestructive testing. One of the most common uses of Ir-192 is for brachytherapy treatment of cancer. The low-energy beta particles and the 74-day half-life are optimal for this treatment. Small “seeds” weighing approximately 5 mg with different Ir-192 activities are inserted into the cancerous tumor and provide constant long-term irradiation of the tumor and surrounding tissue [11–13]. The extensive use of Ir-192 in industry and medicine makes this radionuclide accessible. In its Material Events Database Annual Report for the 2022 fiscal year, for example, the United States Nuclear Regulatory Commission lists several overexposure or near-miss incidents involving Ir-192 in the span of twelve months, as well as six Ir-192 sources lost and not recovered in the past ten years [14]. The combination of extensive use and accessibility may lead to potential exposure of large populations to levels of radiation that could result in a public health emergency, which demonstrates the importance of establishing accurate methods for Ir-192 analysis.

The most important concepts for communicating and assessing the risk from radiation exposure and contamination during radiation emergencies are effective dose and Clinical Decision Guide (CDG) [15]. CDG is a concept for radiation emergency preparedness that establishes a general guideline for medical management and distribution of medical countermeasures. To derive target analyte sensitivities for the methods in the URS, we calculated the urinary excretion activity concentration on the fifth day after a single intake correlated to the CDG dose for a child and pregnant woman (170 Bq/L) or healthy adult (850 Bq/L). The CDC URS has an established method for analyzing Ir-192 using High Purity Germanium (HPGe) [3]. However, strategically surging testing capacity using other available instrumentation during certain situations may be necessary. Liquid Scintillation Counting (LSC) is a viable option for quantifying Ir-192 due to its beta emission [16]. LSC instrumentation is generally more consistent in specification and performance from one laboratory to another, whereas HPGe can come in many different configurations and specifications. Clinical radiobioassay methods on LSC instrumentation are generally more suitable for method transfer and can help expand the national capacity to respond to radiation emergencies. The results of this study demonstrate that quantifying Ir-192 by Liquid Scintillation Counting compares well with the established High Purity Germanium method employed by the URS, confirming capability to expand Ir-192 counting within CDC’s Radiation Laboratory.

Experimental

Reagent and materials

The Ir-192 source solution (Eckert & Ziegler Analytics, Inc.) was used to prepare five spiked samples in 0.1 M hydrochloric acid in the range of 150 Bq/L to 3600 Bq/L of Ir-192 (see Table 1). This range of activities was intended to represent clinically relevant values using the principles of radiation dose CDG.

For LSC gross alpha/beta analysis, we used Ultima Gold™ AB cocktail (UGAB) (Revvity Health Sciences, Inc. [formerly PerkinElmer]) and 99% nitromethane (ACROS Organics) in the preparation of efficiency (quench) curves plotting Ir-192 counting efficiency versus the transformed spectral index of external standard (tSIE). Deionized (DI) water (≥ 18 MΩ cm) from an Aqua Solutions Ultrapure Water System (Aqua Solutions, Inc.) was used to prepare all solutions. Quality Control (QC) materials at high and low activity (GAB-QC-Low, GAB-QC-High, HPGe-QC-Low, and HPGe-QC-High) were used for all methods at the beginning and end of each run. Urine gross alpha/beta QC materials (GAB-QC-Low and GAB-QC-High) were purchased from Eckert & Ziegler Analytics, Inc. They are spiked into acidified base urine to 1% HNO_3 to yield two quality control pools with Am-241 and Sr-90/Y-90 at high and low levels. QC materials were stored in an ultra-low temperature freezer at approximately − 70 °C.

Four QC sample sets were prepared for the HPGe analysis method. Two sets contained high and low levels of Cs-137, and the others contained high and low levels of Co-60. QC pools were prepared by spiking acidified (0.1 M HCl) deionized lab water with radioactive source solutions of Cs-137 or Co-60 obtained from Eckert & Ziegler Analytics. The certified activities for all radioactive source solutions were traceable to the National Institute for Standards and Technology (NIST) (Gaithersburg, MD, USA).

Instrumentation and labware

Five liquid scintillation counters (Revvity Health Sciences, Inc.) were used for LSC analysis. The instruments will be referred to as Tri-Carb® 3110 #1, Tri-Carb® 3110 #2, Tri-Carb® 5110, Quantulus™ GCT6220 #1, and Quantulus™ GCT 6220 #2. 20 mL LSC plastic vials (Revvity Health Sciences, Inc.); a high-precision analytical balance with an accuracy of 0.0001 g (Mettler-Toledo, LLC); 15 mL and 50 mL conical polypropylene tubes (Becton Dickinson) for solution preparation; a bottle top dispenser with 5 mL to 25 mL capacity (Brinkman Instruments, Inc.); and four electronic pipettes with a total volume range from 5 μL to 5 mL (Eppendorf, Inc) were used for urine spikes and sample preparation.

For gamma analysis performed in this study, five p-type reverse coaxial well-type HPGe detectors (AMETEK) with nominal active volumes of 425 cubic centimeters or 450 cubic centimeters were used as described in our previous work [3]. GammaVision software (Advanced Measurement Technology, Inc AMETEK) was utilized for gamma spectrum acquisition and analysis.

Sample preparation and LSC analysis

LSC instrument optimization was done as described in our previous publications [1, 17]. An optimal Pulse Shape Analysis (PSA) or Pulse Decay Discriminator (PDD) setting was determined for each instrument. Quench curves were prepared at the chosen PSA/PDD setting according to the procedures for gross beta analysis of Sr-90/Y-90. Ir-192 quench curves were also prepared at optimal PSA/PDD settings for Ir-192 analysis. Quench curves were prepared using 20 mL of UGAB and nitromethane as a quenching agent. Parameters, including sample analysis time, external standard analysis time, sample/cocktail volume for 20 mL vial geometry, and the region of interest (ROI), were optimized for each instrument. These parameters are summarized in Table 2 [1, 17]. Samples containing 5 mL of each Ir-192 activity level were fully mixed with 15 mL of UGAB cocktail in a 20-mL LSC plastic vial. The vials were placed in the LSC instrument which performs automated sample analysis.

Sample preparation and HPGe analysis

The energy response, energy resolution, and efficiency of the HPGe detector were calibrated using the protocol described in our previous publication [3]. For nuclide quantification, first- and second-order corrections to the efficiency are applied when the key gamma peaks are affected by cascade summing, such as those used in the Ir-192 analysis.

From each of the five sample pools, 10 mL of Ir-192 solution was aliquoted into separate 15 mL conical polypropylene tubes. Non-destructive gamma analysis was conducted on HPGe instruments using GammaVision software, with a 15-min count time for Ir-192 analysis. The key peaks used for the analysis are the 216.49 keV, 468.06 keV, 308.44 keV, 295.95 keV, 604.40 keV, and 612.45 keV gamma emissions. To determine the activity concentration in Bq/L, an average of the calculated activities is taken, weighted by the peak branching ratios for each peak included in the Ir-192 analysis.

Results and discussion

Ir-192 spikes analysis by LSC using different instruments

The five solutions spiked with Ir-192 were first analyzed by LSC using Sr-90/Y-90 quench curves maintained for the CDC gross alpha and beta in urine method [1]. Measured Ir-192 activities found on Tri-Carb series instruments were all within the uncertainty of the target value, except at the lowest activity concentration level (Ir192-2023-1). The activities found on Quantulus™ GCT 6220 series instruments were almost an order of magnitude lower than target values.

Instrument-specific Ir-192 quench curves were prepared to further investigate the difference in count rates. Analysis performed with Ir-192 quench curves showed counting efficiencies of approximately 12% to 14% on Quantulus ™ GCT6220 instruments, significantly lower than the efficiency of roughly 100% observed on Tri-Carb instruments (Figs. 1, 2). The reduction in counts observed on Quantulus™ GCT instruments results from the Bismuth Germanium Oxide (BGO) detector guard utilized in the GCT 6220 models. This guard reduces the influence of external gamma events on background levels in pure beta samples.

However, many Ir-192 beta counts were mischaracterized as external events and placed into the guard signal column (Table 3). It was theorized that the high-energy gamma events coinciding with beta events in Ir-192 samples interfered with the beta counting efficiency. To confirm this, new Ir-192 quench curves were generated on the Quantulus™ GCT 6220 instruments using transformed data. Within the QuantaSmart™ software, guard signal counts were added to beta signals observed in the beta region of interest (ROI). This data transformation resulted in a detector efficiency of approximately 90% (Fig. 2). Samples analyzed using quench curves with guard counts factored in showed comparable results to those obtained on Tri-Carb series instruments and by gamma analysis via HPGe (Table 4) as well as target values (Table 5).

LSC and HPGe method comparison

The results of gamma analysis using the HPGe method were as expected compared to previously published validation results for Ir-192 [3]. LSC measurements on the Tri-Carb platform (TC) were similar to HPGe. However, LSC precision, given as standard deviation, was 3–6 times better than HPGe (Table 4). This difference in counting precision is not surprising given an LSC detection efficiency of nearly 100%. Additionally, the HPGe detection efficiency for Ir-192 is affected by coincidence summing effects resulting from cascades of gamma emissions. The counting efficiency in the CDC HPGe well detectors is typically between 20% and 25% for the gamma energies of Ir-192. Considering the cascade coincidence summing, the effective counting efficiency for the same energy range is roughly 5%. The enhanced precision of the LSC method is achieved with a 5-min count time compared to the 15-min count time of the HPGe method. Ir-192 bias activity results, presented in Table 6, demonstrate the reasonable correlation between found and target values for both techniques, LSC and HPGe.

Conclusions

Through analysis with different instruments and methods, we found that Ir-192 activity can be quantified with HPGe detectors and liquid scintillation counters. Precision across LSC instruments is optimal when using quench curves prepared for the analyte of interest. Guard signal counts produced on the Quantulus™ GCT 6220 instruments should be considered when analyzing Ir-192 and other gamma-emitting nuclides. Both HPGe and LSC methods can be used to quantify Ir-192 with the activities close to CDG values for child/pregnant woman and adults. Both methods provide comparable results; however, the overlapping decay energies of many beta-emitting nuclides makes utilizing liquid scintillation counting as an identification technique difficult. In emergency response scenarios, where sample throughput must be maximized to quickly assess public health impact, pre-identifying Ir-192 as the analyte of interest before applying liquid scintillation counting methods would lead to the most accurate results. The excellent counting efficiency observed in Ir-192 liquid scintillation analysis paired with the high energy resolution of HPGe detectors has the potential to greatly expand the number of samples analyzed for internal contamination within a given timeframe.

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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. It does not constitute endorsement by the U.S. Department of Health and Human Services or the Centers for Disease Control and Prevention.

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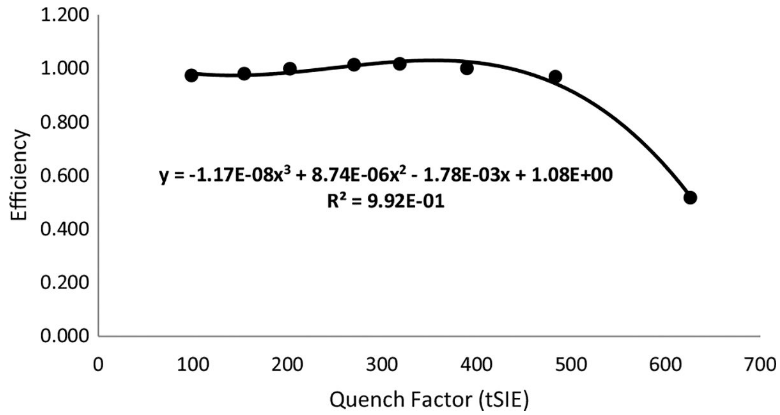

Fig. 1.

Quench indicating parameter measurements in terms of transformed spectral index of external standard (tSIE) effect on efficiency using nitromethane (0 mL to 0.3 mL) as a quench agent in the UGAB cocktail (20 mL) for Ir-192 on Tri-Carb3110 #2

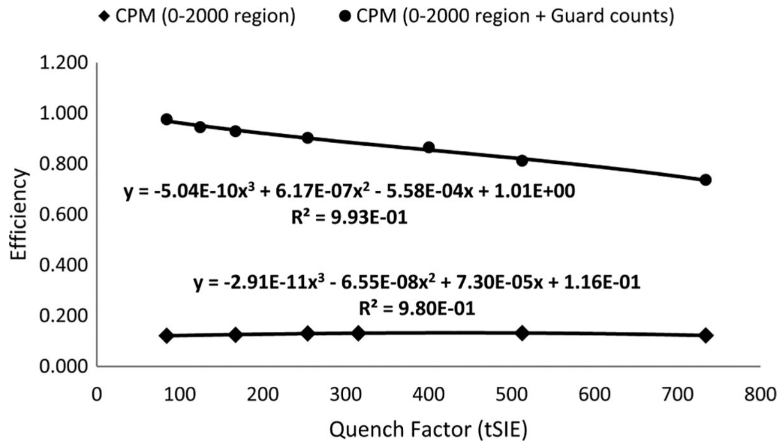

Fig. 2.

Quench indicating parameter measurements in terms of transformed spectral index of external standard (tSIE) effect on efficiency using nitromethane (0 mL to 0.3 mL) as a quench agent in the UGAB cocktail (20 mL) for Ir-192 on Quantulus GCT6220 #1 with (the upper line) and without (the lower line) guard counts

Table 1

Ir-192 spiked samples preparation (gravimetric data)

Sample ID	Specific activity (standard deviation), Bq/L
Ir192-2023-1	157 (20)
Ir192-2023-2	416 (45)
Ir192-2023-3	1180 (100)
Ir192-2023-4	2990 (250)
Ir192-2023-5	3580 (310)

Table 2

LSC method parameters for different LSC instruments [1, 17]

Parameters	TC3110 #1	TC3110 #2	TC5110	GCT6220 #1	GCT6220 #2
PSA/PDD (keV)	125	165	135	160	160
Sample volume (mL)	5	5	5	5	5
Cocktail volume (mL)	15	15	15	15	15
Sample analysis time (min)	5	5	5	5	5
External Std analysis time	2 Ω (15 s)	2 Ω (15 s)	2 Ω (10 s)	60 s	60 s
High energy beta ROI (keV)	0 – 2000	0 – 2000	0 – 2000	0–2000	0 – 2000
LOD for high energy gross beta, Bq/L	44.6	44.6	44.6	40.3	40.3

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Table 3

Results table for Ir-192 quench curve on Quantulus™ GCT6220 #1 (from QuantaSmart™ software) showing counts removed from gross beta region by detector guard

Sample ID	Quench factor (tSIE)	CPM Gross beta counts (0 – 2000 keV region)	CPM Guard counts (0 – 2000 keV region)	CPM Gross beta counts + guard counts (0 – 2000 keV region)
BKG	792.63	2.3	141	143
Ir192-Std1	734.03	94	609	703
Ir192-Std2	512.65	103	667	770
Ir192-Std3	400.33	107	697	804
Ir192-Std4	315.2	100	730	830
Ir192-Std5	254.28	100	728	828
Ir192-Std6	167.23	96	754	850
Ir192-Std7	124.71	98	762	860
Ir192-Std8	84.27	94	791	885

Table 4

Measured Ir-192 activities on different instruments

Sample ID	Instrument							
	Target Activity (SD) Bq/L	TC3110#1	TC3110#2	TC5110	GCT#1	GCT#2	AVG LSC measurement	HPGe
GAB-QC-low	1760 (42)	1800	1770	1780	1720	1740	1762 (32)	–
GAB-QC-high	105,000 (1835)	105,000	105,000	106,000	104,000	105,000	105,000 (707)	–
Ir192-2023-1	157(20)	167	152	172	189	146	165 (17)	171 (44)
Ir192-2023-2	416 (45)	413	444	420	470	450	439 (23)	419 (75)
Ir192-2023-3	1180 (103)	1110	1130	1130	1170	1130	1134 (22)	1150 (133)
Ir192-2023-4	2990 (250)	2910	2840	2830	2640	2850	2814 (102)	2920 (331)
Ir192-2023-5	3580 (305)	3480	3420	3440	3640	3490	3494 (86)	3510 (358)
GAB-QC-low	1760 (42)	1740	1810	1840	1770	1700	1772 (55)	–
GAB-QC-high	105,000 (1835)	104,000	105,000	106,000	104,000	104,000	105,000 (894)	–

LSC data was processed using Ir-192 quench curves with guard counts factored in. Target values for gross alpha beta (GAB) quality control (QC) samples were calculated from the average of 50 measurements. Target values for Ir-192 samples are based on gravimetric data. Standard deviation of HPGe measurements is based on the average of 12 measurements

Table 5

Bias of activities measured on different LSC instruments compared to target values

Sample ID	Bias (%)				
	TC3110#1	**TC3110#2**	**TC5110**	**GCT#1**	**GCT#2**
GAB-QC-low	2.3	0.1	1.1	− 2.4	− 1.2
GAB-QC-high	0.2	− 0.2	0.6	− 0.5	− 0.3
Ir192-2023-1	6.4	− 3.2	9.6	20.4	− 7.0
Ir192-2023-2	− 0.7	6.7	1.0	13.0	8.2
Ir192-2023-3	− 5.9	− 4.2	− 4.6	− 0.9	− 4.1
Ir192-2023-4	− 2.7	− 5.2	− 5.2	− 11.6	− 4.8
Ir192-2023-5	− 2.8	− 4.4	− 4.0	1.8	− 2.7
GAB-QC-low	− 1.1	2.7	4.3	0.5	− 3.6
GAB-QC-high	− 0.4	− 0.4	0.7	− 0.5	− 0.7

Table 6

Bias of measured activities compared to target values for LSC and HPGe (average of all measurements)

Sample ID	Bias (%)	
	LSC	HPGe
Ir192-2023-1	5.2	8.9
Ir192-2023-2	5.6	7.0
Ir192-2023-3	− 3.9	− 2.5
Ir192-2023-4	− 5.9	− 2.3
Ir192-2023-5	− 2.4	− 2.0