Method Validation of the GammaVision® TCC Calibration Wizard

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Introduction

- Public Health Importance: CDC radionuclide screen provides laboratory support during radiological emergency response

- Gamma Emitters Method: Part of the screen is the High Purity Germanium (HPGe) gamma identification and quantification method (approved for Cs-137, Co-60, Ir-192, Se-75, Tc-99m, I-125, I-131)

- Calibration Method: A single calibration that will give accurate measurements across a wide-range of radionuclides is desirable

- Validation Experiments and Results: Validation of the True Coincidence Correction (TCC) method built-in to GammaVision provides baseline results for overall method accuracy, precision, stability, robustness

PUBLIC HEALTH IMPORTANCE

Radiological Incidents and Emergencies

- Over 100k people may need screening and quantitative assessment for internal contamination from radioactive material
- Accurate measurement of internal contamination is critical for effective medical management and treatment of patients and effective containment of contamination [1]
  - Prioritization of Medical Countermeasures
  - Biomonitoring
  - Epidemiological study
  - Follow-up Care

[1] H. D. Dörr and V. Meineke, Radiation and Environmental Biophysics 45, 237 (2006).

NCRP 161: Clinical Decision Guide (CDG)

- CDG action level equivalent to a 1.3% lifetime (50-y) increased risk of stochastic effects [2]
- Primary tool for communicating risk from an acute exposure following an incident or emergency

Nuclide	LOD (Bq/L)	CDG C/P Day 1 Post Exposure (Bq/L)	CDG C/P Day 5 Post Exposure (Bq/L)
^{60}Co	45.7	11,900	1,000
^{137}Cs	7.2	177,000	29,000
^{131}I	16.8	6,460	2
^{192}Ir	36.6	2,640	190
^{99}Mo	19.2	TBD	TBD
^{75}Se	13.7	TBD	TBD

[2] Management of Persons Contaminated with Radionuclides: Handbook: Recommendations of the NCRP, 2008 (NCRP, Bethesda, Md, 2009).

C/P: Child or Pregnant Woman

HPGE GAMMA EMITTERS IN URINE METHOD

1 of 13 Analytical Methods that comprise the CDC Urine Radionuclide Screen (screening and rapid ID and quantification of 22 priority threat radionuclides)

CDC Urine Radionuclide Screen

Urine "Spot" Sample

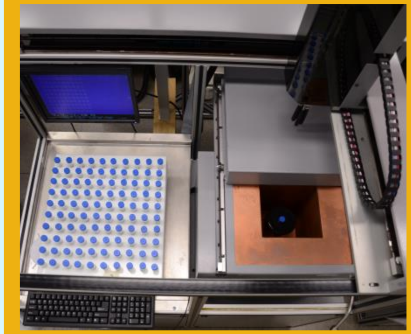
Gamma Radionuclide Screen

Alpha/Beta Radionuclide Screen/Quantification

Alpha (Long Lived) ICP-MS Screen

CDC Photos

Gamma Spectroscopy Quantification



Alpha Spectroscopy Quantification

Mass Spectrometry Quantification

High Resolution Mass Spectrometry Quantification

Six analytical technologies needed to enable the analysis of the priority radionuclides

Gamma Methods

- **Gross Gamma Screen**
  - NaI Well Detectors
  - 5-minute count time
  - Determines if person is contaminated with a gamma emitter(s) above a population background level
  - HPGe method analyzes above-background samples
- **Gamma Spectroscopy Quantification**
  - HPGe Well detectors
  - Count times range 5 – 15 minutes (radionuclide dependent)
  - Report radionuclide activity (Bq/L) to Radiation Studies Section for radiation dose assessment

HPGe Sample – Detector Geometry

- **Well geometry (425 or 450 cc Active Detector)**
  - 15 mL PP centrifuge tube
  - 10 mL sample of patient urine
- **High Efficiency / Low Sample size are desirable for high throughput capacity**
- **Drawbacks**
  - Analysis may require summing correction
  - Larger FWHM energy resolution (compared to traditional coax geometry)

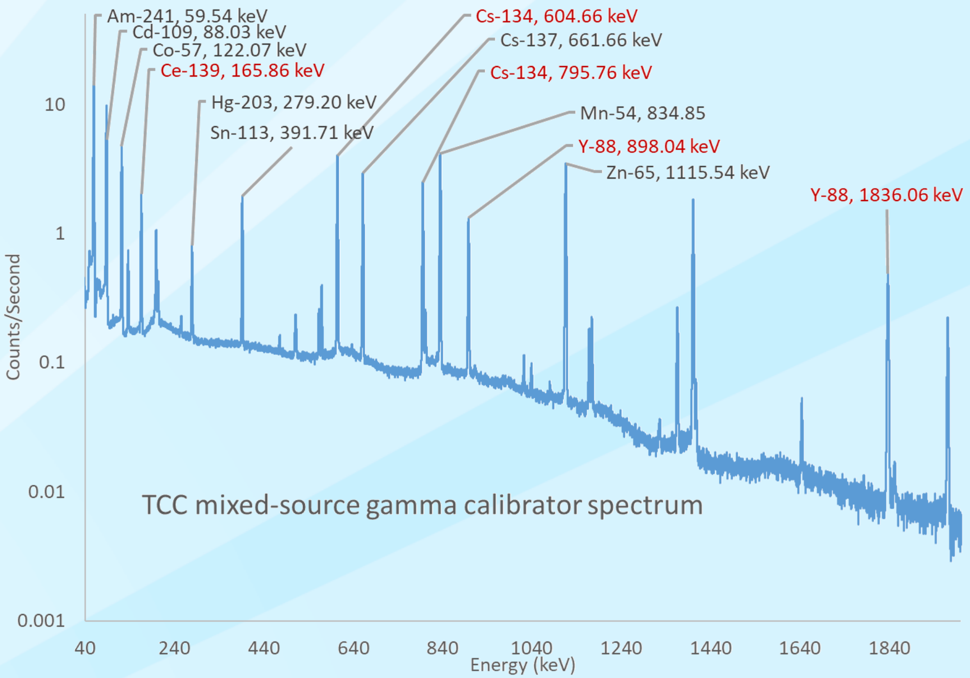
CALIBRATION METHOD

GammaVision Calibration Wizard:

True Coincidence Correction

Calibration Components

- **Obtain one spectrum measurement of the calibrator solution (10 mL fill in 15 mL centrifuge tube)**
- **Wizard creates 5 calibration components [3,4]**
  - Energy
  - FWHM
  - Efficiency (TCC Polynomial)
    - Peak-to-Total Ratio (PTT)
    - Linear-to-Squared Ratio (LS)



Calibrator spectrum with the cascade summing affected peaks in RED

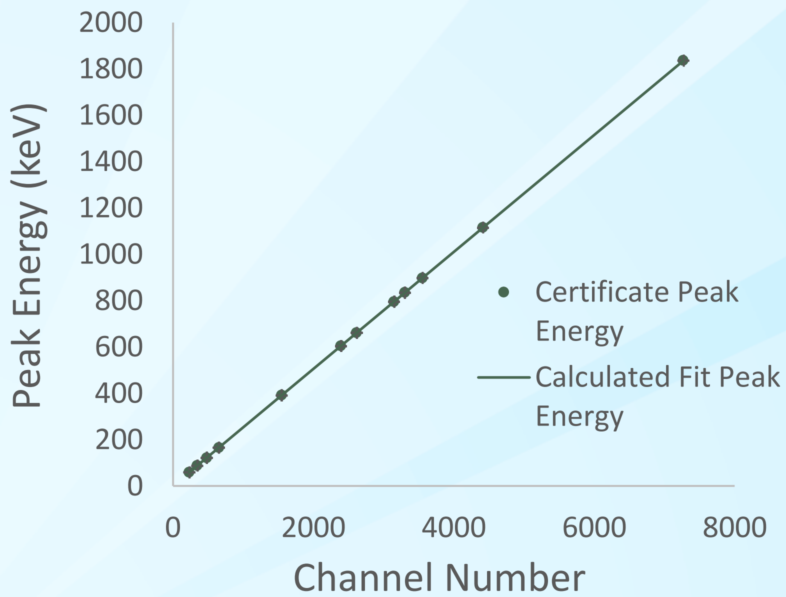
[3]ORTEC. GammaVision (R) Gamma-Ray Spectrum Analysis and MCA Emulator for Microsoft(R) Windows(R) 7, 8.1, and 10 Professional (A66-BW Software User’s Manual Software Version 8.1) Manual Revision L. Advanced Measurement Technology, Inc. 2017.

[4]Blaauw, M.; Gelsema, S. J. Cascade Summing in Gamma-Ray Spectrometry in Marinelli-Beaker Geometries: The Third Efficiency Curve. Nucl. Instrum. Methods Phys. Res. Sect. Accel. Spectrometers Detect. Assoc. Equip. 2003, 505 (1–2), 311–315. https://doi.org/10.1016/S0168-9002(03)01075-1.

Energy & FWHM Calibrations

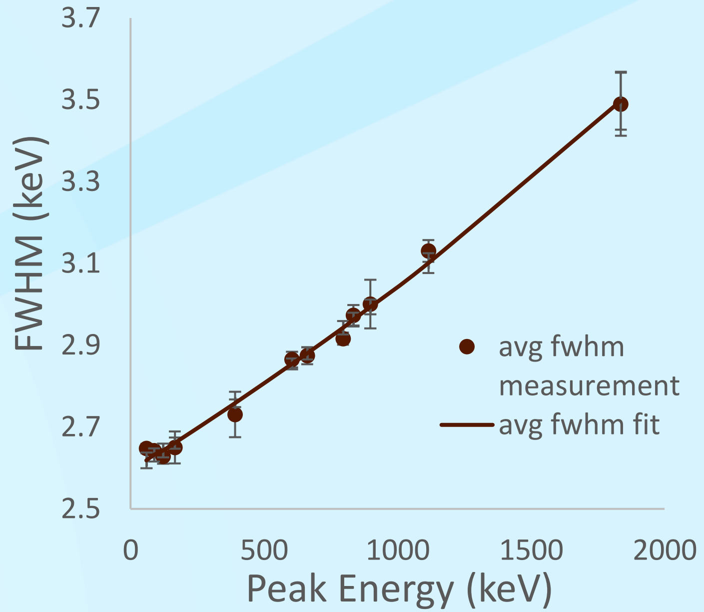
Energy: FEPE has linear relationship to channel (GV uses quadratic[3])

	Average	2σ	C_v
a_0	0.462	0.011	0.024
a_1	2.53E-01	1.11E-05	4.39E-05
a_2	-8.63E-09	1.77E-09	-0.205



FWHM: Quadratic relationship to Energy

	Average	2σ	C_v
b_0	10.27	0.087	0.008
b_1	3.99E-04	7.34E-05	0.18
b_2	1.28E-08	1.24E-08	0.97



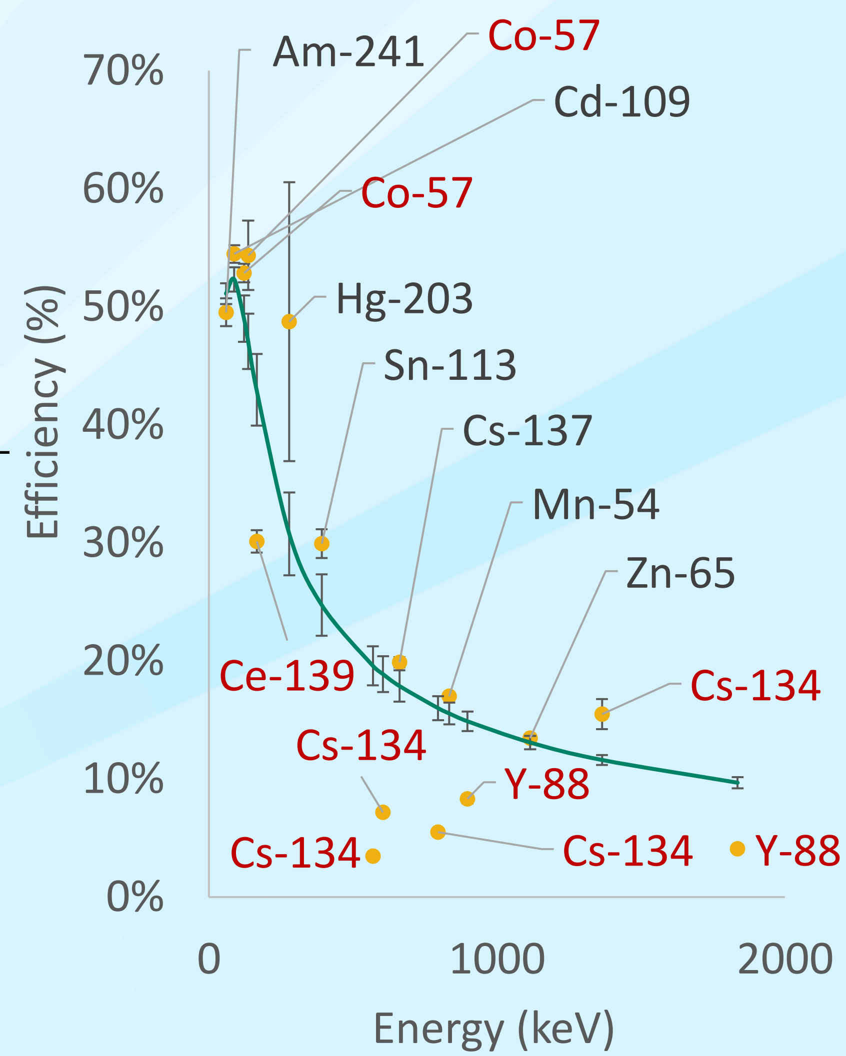
Efficiency Calibration

TCC-polynomial [3,4]: relationship between full-energy peak and full-energy-peak efficiency

$$\ln(\epsilon) = \sum_{i=0}^{5} c_i \ln(E)^i$$

Nuclide	Energy (keV)	Meas. Efficiency (%)		Calc. Efficiency (%)	
		Average	2σ	Average	2σ
Am-241	59.54	63%	1%	62%	4%
Cd-109	88.03	66%	1%	64%	4%
Co-57	122.07	62%	1%	61%	4%
Co-57	136.47	66%	2%	60%	3%
Ce-139	165.86	33%	1%	55%	5%
Hg-203	279.2	62%	16%	41%	6%
Sn-113	391.7	35%	1%	33%	4%
Cs-134	569.33	4%	0%	25%	2%
Cs-134	604.72	9%	0%	24%	2%
Cs-137	661.66	24%	0%	23%	2%
Cs-134	795.86	7%	0%	20%	1%
Mn-54	834.85	20%	0%	20%	1%
Y-88	898.04	9%	0%	19%	1%
Zn-65	1115.54	16%	0%	16%	1%
Cs-134	1365.19	20%	1%	14%	0%
Y-88	1836.06	5%	0%	11%	1%

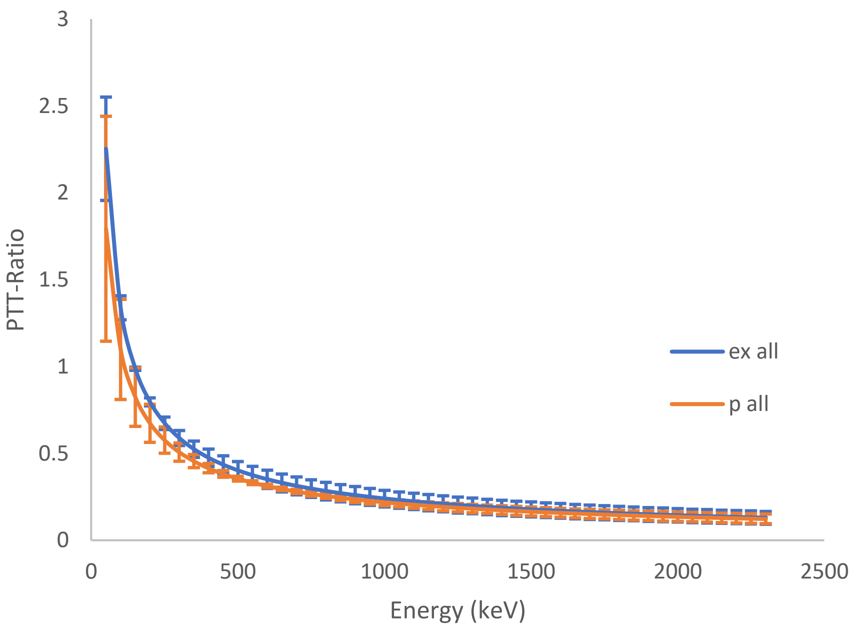
Fit Calculation uncertainty > Measurement uncertainty by ~2x



Cascade Summing Corrections

Peak-to-Total Ratio used to calculate probability of True Coincidence

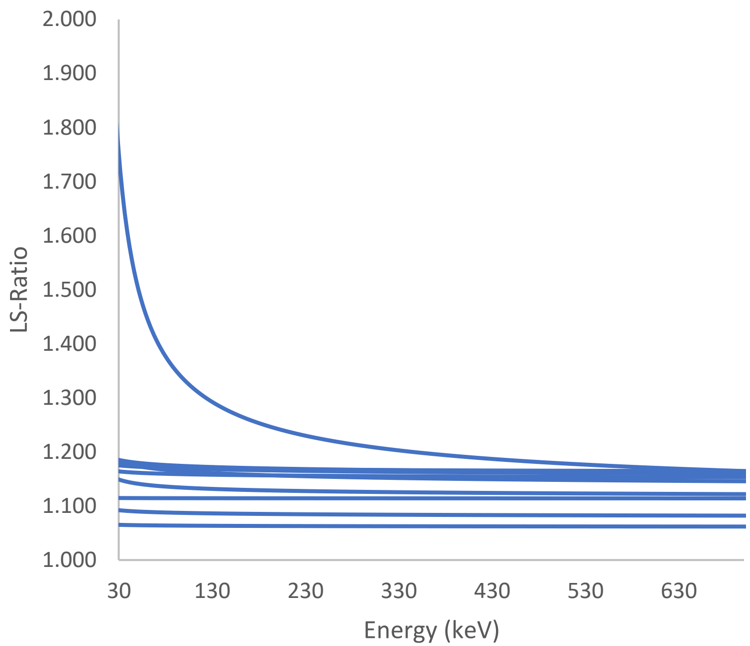
$$\ln r = r_0 + r_1 \ln E$$



	r_0			r_1		
	Average	2σ	C_v	Average	2σ	C_v
ex All	3.74	0.57	0.15	-0.75	0.11	0.15
p All	3.29	1.00	0.30	-0.70	0.16	0.22

Linear-to-Squared Ratio used to average efficiencies over voluminous source (2nd order correction)

$$l(E) = d_0 + d_1 \ln(E)^{-d_2}$$



	Average	2σ	C_v
d_0	1.10	0.05	0.04
d_1	-5.99	11.86	1.98
d_2	0.92	0.93	1.01

CALIBRATION METHOD VALIDATION

Experiments and Results

Calibration Run

- **Consists of multiple measurements of the calibrator spectrum (sets of 5 to 20)**
- **Individual measurement: Live Time ranges from 1 hour to 24 hours**
- **Now have calibrator data over 4 years and 6 detector systems using a different calibrator solution for each year**
  - Eckert & Ziegler SRS#'s (110290, 114539, 118329, 120597C)

Generating Test Calibrations

- **Generate energy, FWHM, and efficiency calibrations for each of the run spectra**
- **Vary geometry setting**
  - Point-source option (L-S ratio parameters are fixed)
  - Extended-source option (L-S ratio parameters are optimized)
- **Vary efficiency and energy tables**
  - May exclude Ce-139 (x-ray summing)
  - May exclude Hg-203 (47-day half-life)
- **Not possible to judge quality of fit –** Must analyze the spectrum with TCC correction on and compare measured and certified activities

Calibration Run with 5 spectrum measurements may yield 5-20 Test Calibrations

Data Processing

- Use test calibrations to analyze spectra from the calibration run
- GammaVision job script (.job) to automate analyses, generate report files (.rpt)
- Excel Macro Worksheet (.xlsm) inspects each .rpt and extracts relevant data
- Access DB (.accdb) aggregates data, generates run statistics

Accuracy

Accuracy aggregated for single calibration run (20 .spc) over test calibrations categorized by nuclide and geometry option (PT or EX) or library (includes or excludes Ce-139 165 keV peak)

Nuclide	PT	EX	w/ Ce-139	w/o Ce-139
Am-241	0.89	0.75	0.95	0.61
Cd-109	0.52	0.72	0.82	0.61
Co-57	0.59	1.09	1.00	0.95
Hg-203	0.73	6.56	3.53	3.56
Sn-113	1.35	7.15	4.02	4.17
Cs-134	3.05	16.21	8.13	10.00
Cs-137	0.77	4.46	2.28	2.64
Mn-54	1.66	4.99	3.02	3.07
Y-88	2.96	6.05	4.74	3.18
Zn-65	0.88	1.99	1.29	1.41
AVERAGE	1.34	5.00	2.98	3.02

Accuracy for single test calibrations (top 5)

Nuclide	clb4 ex b	clb14 pt b	clb2 ex b	clb7 ex b	clb15 pt b
Am-241	0.25	0.49	0.41	0.62	0.56
Cd-109	0.11	0.10	0.27	0.20	0.16
Co-57	0.75	0.72	0.95	0.62	0.86
Hg-203	0.20	0.11	0.43	0.10	0.27
Sn-113	0.47	0.62	0.27	0.59	0.43
Cs-134	0.12	0.88	0.17	0.21	0.39
Cs-137	0.41	0.19	0.70	0.44	0.52
Mn-54	0.66	0.86	0.39	0.55	0.52
Y-88	1.44	0.51	0.81	1.35	1.00
Zn-65	0.61	0.49	0.85	0.79	0.79
AVERAGE	0.50	0.50	0.52	0.55	0.55

Z-score: $\frac{\text{meas.} - \text{expected}}{\text{uncertainty}}$

Accuracy (cont.)

Run generated 74 test calibrations

- 38 “failing” calibrations: accuracy for at least one nuclide outside 2σ
- 36 “acceptable” calibrations: accuracy for each nuclide within 2σ
- 9 “very good” calibrations, accuracy for each nuclide within 1σ (very good)

Precision

Precision (Relative Standard Deviation) aggregated for single calibration run (20 .spc) over test calibrations categorized by nuclide and geometry option (PT or EX) or library (includes or excludes Ce-139 165 keV peak)

Nuclide	ex	pt	a	b
Am-241	3%	4%	3%	4%
Cd-109	5%	3%	3%	4%
Co-57	7%	4%	5%	3%
Hg-203	22%	3%	18%	22%
Sn-113	21%	3%	17%	22%
Cs-134	39%	10%	32%	42%
Cs-137	15%	4%	11%	15%
Mn-54	12%	4%	9%	12%
Y-88	19%	9%	15%	17%
Zn-65	9%	4%	6%	9%

Precision for single test calibrations (top 5)

- May expect small differences due to FWHM calibration
- Precision virtually identical for all single test calibrations

Nuclide	clb4 ex b	clb14 pt b	clb2 ex b	clb7 ex b	clb15 pt b
Am-241	0.6%	0.6%	0.6%	0.6%	0.6%
Cd-109	0.5%	0.6%	0.6%	0.6%	0.6%
Co-57	0.5%	0.4%	0.4%	0.4%	0.4%
Hg-203	0.4%	0.3%	0.3%	0.5%	0.3%
Sn-113	0.5%	0.4%	0.3%	0.2%	0.4%
Cs-134	0.4%	0.4%	0.4%	0.4%	0.4%
Cs-137	0.4%	0.3%	0.4%	0.5%	0.4%
Mn-54	0.4%	0.3%	0.2%	0.3%	0.2%
Y-88	0.8%	1.1%	0.9%	1.0%	1.0%
Zn-65	0.3%	0.4%	0.4%	0.5%	0.5%
AVERAGE	0.5%	0.5%	0.5%	0.5%	0.5%

Precision: $\frac{\text{St.Dev.}}{\text{Average}}$

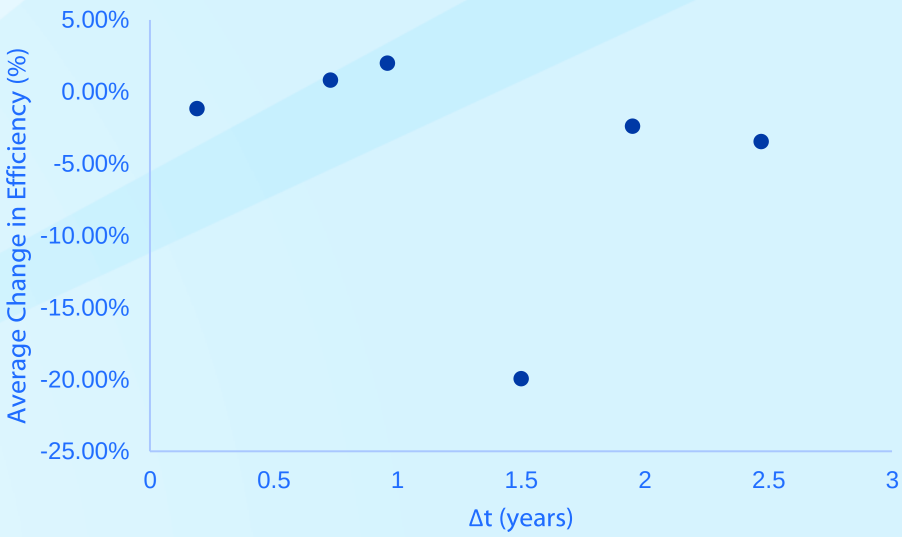
All 74 test calibrations within lab limit (RSD <15%)

Stability

Small, random fluctuations in efficiency over time

- Possibly related to energy width or electronics parameters
- For in-control detector system, can expect efficiency to be stable (+/-4%)

Years since Initial Measurement	Average Change in Efficiency
0.19	-1.18+/-0.04%
0.73	0.81+/-0.03%
0.96	1.98+/-0.04%
1.5	-19.94+/-0.07%
1.95	-2.39+/-0.05%
2.47	-3.47+/-0.08%



Robustness

- **Demonstrated that the efficiency calculated from fit to measurement data is sensitive**
  - Geometry choice (point-source or extended-source)
  - Choice of peaks in the energy library
  - Choice of peaks in the efficiency certificate
- **Good strategy to test multiple configurations of these options against multiple calibrator spectra to obtain “acceptable” or “good” calibrations**

CALIBRATION METHOD VALIDATION

Impact on HPGe Gamma Emitters in Urine

Method Validation

Accuracy

Very good agreement between average measurement and expectation values over range of nuclides and activities

Measurements accumulated across 4 instruments

Analyte	Approx. CDG Equiv.	Reference Value (Bq/L)	Observed Mean Value (Bq/L)	SD (Bq/L)	Diff. from Ref. (%)	Z-score
^{137}Cs	$\frac{1}{3}$x C/P (5 day)	(8.46±0.16)E+03	(8.66±0.23)E+03	2.21E+02	2.30	0.69
	1x Adult (5 day)	(1.45±0.03)E+05	(1.47±0.05)E+05	4.28E+03	1.40	0.39
	2x Adult (5 day)	(2.90±0.05)E+05	(2.96±0.13)E+05	1.18E+04	2.28	0.49
^{60}Co	1x Adult (5 day)	(4.97±0.06)E+03	(5.04±0.18)E+03	1.31E+02	1.45	0.37
	1x Adult (1 day)	(4.50±0.05)E+04	(4.47±0.16)E+04	1.08E+03	-0.61	-0.18
	8x Adult (1 day)	(5.01±0.05)E+05	(4.98±0.31)E+05	2.91E+04	-0.64	-0.10
^{192}Ir	1x C/P (1 day)	(2.58±0.08)E+03	(2.75±0.14)E+03	1.37E+02	5.69	1.05
	2x Adult (1 day)	(2.60±0.08)E+04	(2.68±0.05)E+04	4.33E+02	1.85	0.85
	4x Adult (1 day)	(5.33±0.16)E+04	(5.33±0.07)E+04	4.99E+02	-0.96	0.00

Precision

Precision as Relative Standard Deviation across 4 instruments is well within the lab limit of 15%

Analyte	Sample No.	Mean Measurement (Bq/L)	Relative Standard Deviation (%)		
			Within Run	Between Run	TOTAL
^{137}Cs	1	2.19E+05	0.13	1.08	1.09
	2	7.34E+04	0.92	1.45	1.71
^{60}Co	1	3.77E+05	1.29	2.51	2.82
	2	1.29E+05	2.09	2.49	3.25
^{192}Ir	1	1.38E+04	1.15	--	1.15
	2	2.67E+03	2.49	1.81	3.07

Instrument Comparisons

- Instrument Variation generally within 3% for Co-60 and Cs-137
- Maintain acceptable Instrument Variation for short half-life analytes (I-131: 8 days and Tc-99m: 6 hours; data taken over 3 days)

		Measurement (Bq/L)						
Nuclide	Level	Instrument 1	Instrument 2	Instrument 3	Instrument 4	BTW Instr. variation	>1 CP?	>1 adult?
I-131	1	1.20E+04	1.10E+04	1.18E+04	1.25E+04	5%	YES	YES
	2	4.37E+03	4.99E+03	4.41E+03	4.78E+03	6%	YES	YES
	3	1.98E+03	1.88E+03	1.75E+03	1.99E+03	6%	YES	NO
	4	6.49E+02	7.39E+02	6.82E+02	7.30E+02	6%	YES	NO
	5	3.15E+02	3.06E+02	2.86E+02	3.10E+02	4%	NO	NO
Tc99m	1	1.06E+06	1.09E+06	1.01E+06	1.05E+06	3%	N/A	
	2	2.52E+05	2.82E+05	2.87E+05	2.55E+05	7%		
	3	6.47E+04	7.31E+04	6.83E+04	7.10E+04	5%		
	4	1.71E+04	1.83E+04	1.76E+04	1.60E+04	6%		
	5	4.03E+03	5.03E+03	4.30E+03	4.39E+03	10%		

Conclusions

- TCC calibration using the GammaVision calibration wizard is capable of producing results that are acceptable (if you're in a hurry) or excellent (if you're patient)
- Single calibration approach allows us to speed method development and validation for HPGe gamma emitters
- Excellent calibration results will be even more of a contributor to the success of the method as we reduce count times (15 minutes to 5 minutes for Cs-137 and Co-60 and to 10 minutes for Ir-192

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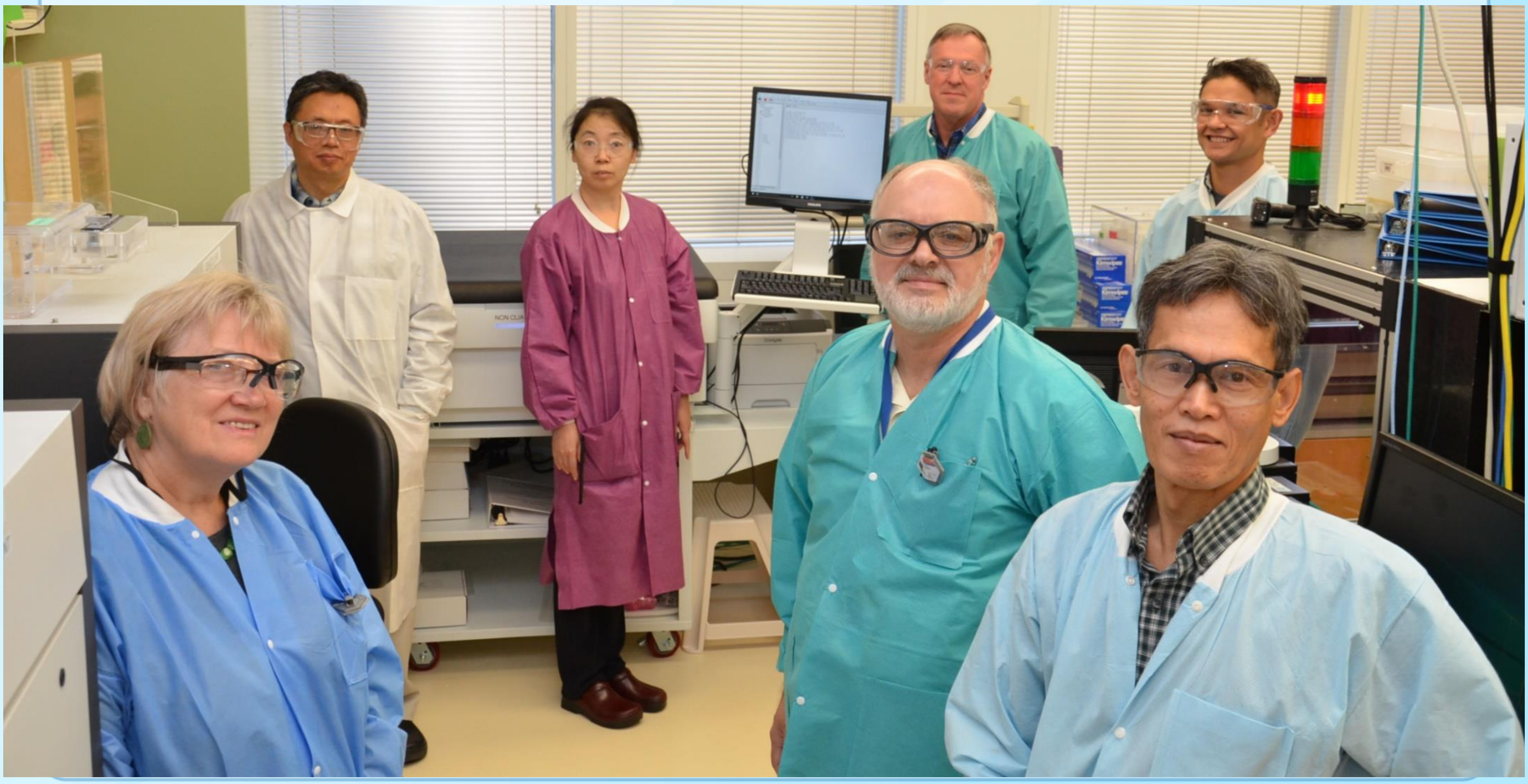

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