TECHNISCHE UNIVERSITÄT DRESDEN

Universitätsklinikum Carl Gustav Carus
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Measurement of Hg-197 and Hg-197m by a dose calibrator

R. Freudenberg, M. Vogel, M. Andreeff, J. Kotzerke

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1) I or one of my co-authors hold a position as an employee, consultant, assessor or advisor for a pharmaceutical, device or biotechnology company. **If yes, please specify name/position/company:**

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2) I or one of my co-authors receive support from a pharmaceutical, device or biotechnology company. **If yes, please specify name/position/company/which project and whether support is in kind or monetary:**

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3) I or one of my co-authors hold property rights/patents for (radio)pharmaceuticals, medical devices or medical consulting firms. **If yes, please specify name/position/company:**

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____**No**.____

Motivation

Hg-197 and Hg-197m

- **promising for future application** in nuclear medicine:
  - low energy gamma radiation for imaging
  - Auger and conversion electrons for therapy

- simultaneously **produced by proton irradiation of natural gold** using a cyclotron

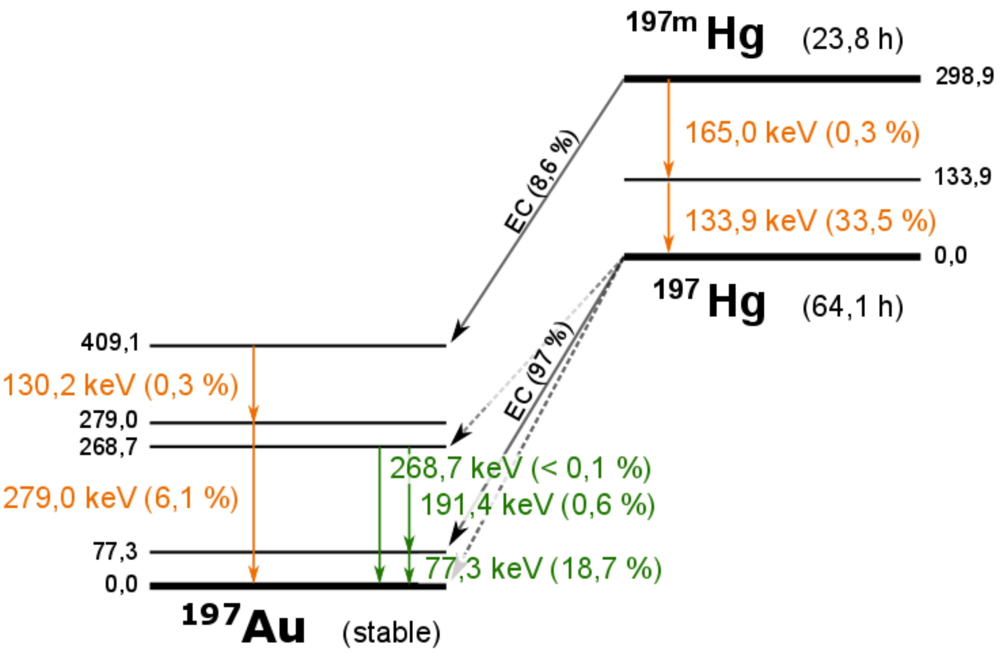

Fig. 1: Decay scheme of Hg-197(m) showing the major photon emissions.
Data from: Nuclear Data Sheets for A = 197 (2004)

Motivation

Hg-197 and Hg-197m

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  - low energy gamma radiation for imaging
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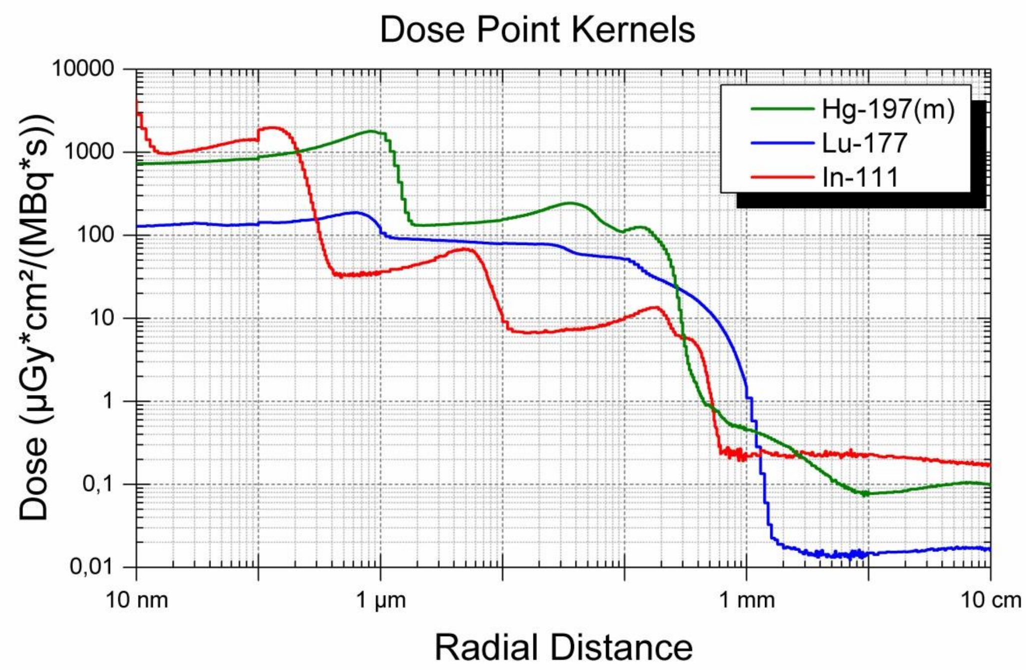


Fig. 2: Dose Point Kernels for different nuclides.

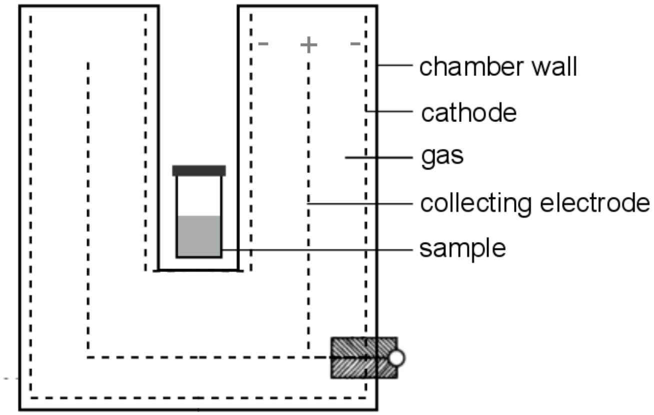
Motivation

Dose calibrator

- **ionization chamber** (*MED Isomed*)
- is used in clinical nuclear medicine laboratory to make measurements of radiopharmaceutical activities

function

- radiation interacts with atoms and molecules, resulting in ion pairs
- electrons move in the applied electrical field
- current produced is proportional to the amount of radioactivity and the energy of the photons
- different **current-activity conversion factors** for different isotopes and geometries



http://www.springer.com/de/book/9783642811876: Nuclear Medicine Part 1A Radiopharmaceuticals Instrumentation Technology Radiation Protection

Motivation

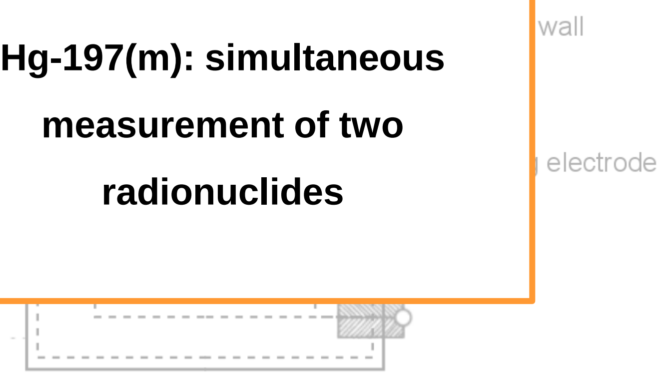
Dose calibrator

- **ionization chamber**
- is used in clinical nuclear medicine laboratory to make measurements of radiopharmaceutical activities

function

- radiation interacts with atoms and molecules, resulting in ion p
- elec d
- curre ou or radic s
- diffe s for different isotopes and geometries

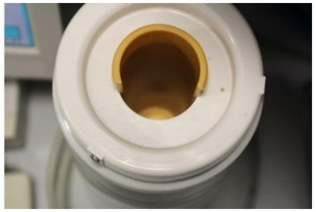
Usually: measurement of one single radionuclide ⟺ **Hg-197(m): simultaneous measurement of two radionuclides**



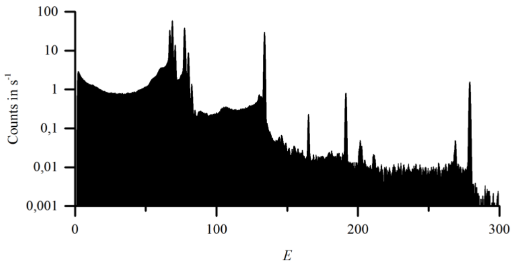
http://www.springer.com/de/book/9783642811876: Nuclear Medicine Part 1A Radiopharmaceuticals Instrumentation Technology Radiation Protection

Method

Aim: measurement of Hg-197m and Hg-197 by a dose calibrator



Determination of radionuclide activity $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$ using gamma spectrometry (HPGe detector)

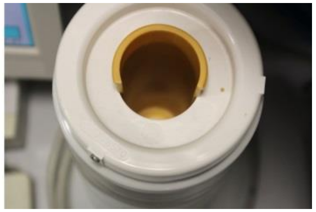


Full-energy peak efficiency calibration of the HPGe detector

http://www.schott.com/pharmaceutical_packaging/german/products/vials/topline-options.html
http://www.canberra.com/products/detectors/germanium-detectors.asp

Method

Aim: measurement of Hg-197m and Hg-197 by a dose calibrator



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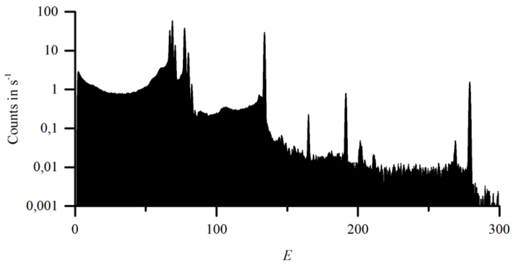

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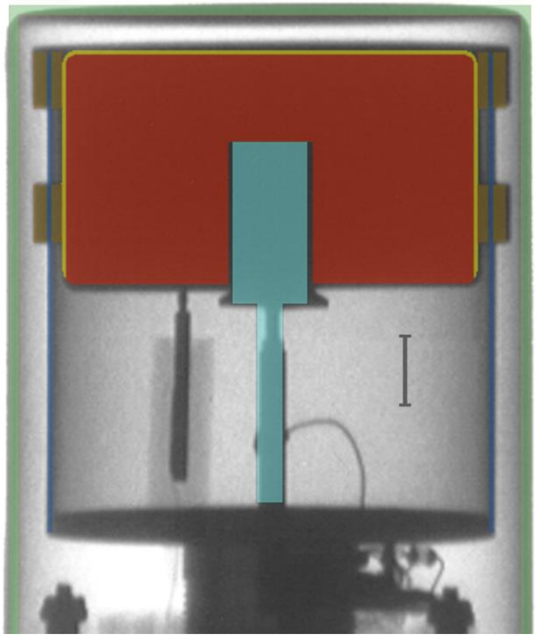
Efficiency calibration of the HPGe detector

Experimental efficiency calibration

- calibration with standard point sources

Characterization with Monte Carlo simulations



- using Geant4
- efficiency values for point source and for vials

Efficiency calibration of the HPGe detector

Results

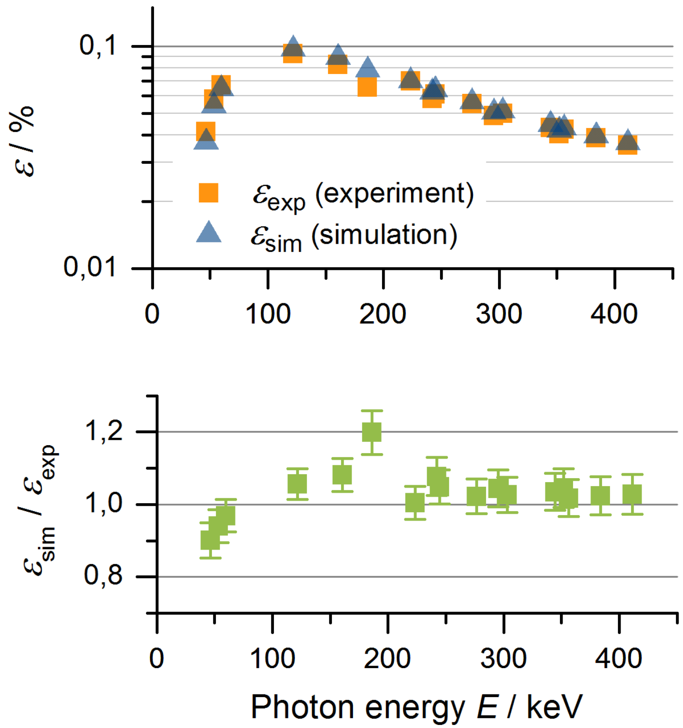


Fig. 3: Comparison between experimental and calculated full-energy peak efficiency *ε* for a source-to-detector distance of 40 cm

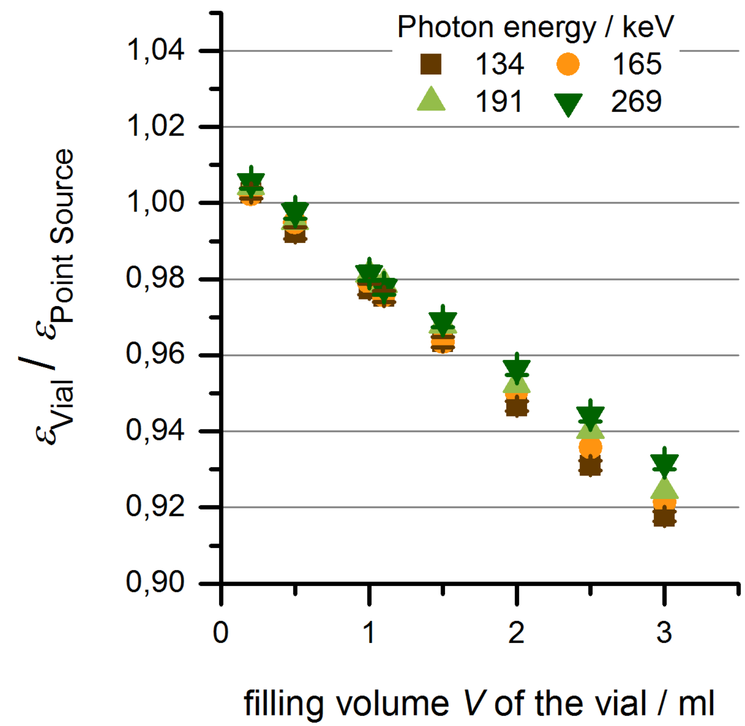
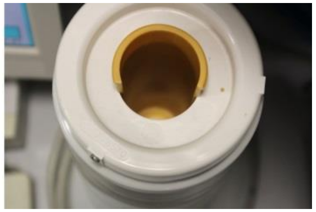
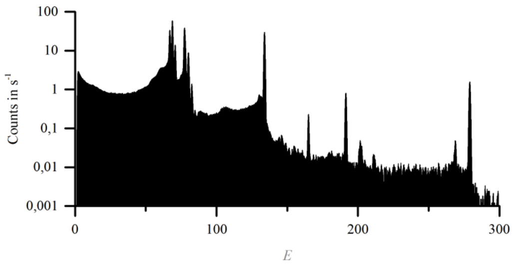


Fig. 4: Comparison between the efficiency for a point source and a vial with different filling volumes

Method



Aim: measurement of Hg-197m and Hg-197 by a dose calibrator



Determination of radionuclide activity $A_{\text{Hg-197m}}$ and $A_{\text{Hg-197}}$ using gamma spectrometry (HPGe detector)

Full-energy peak efficiency calibration of the HPGe detector

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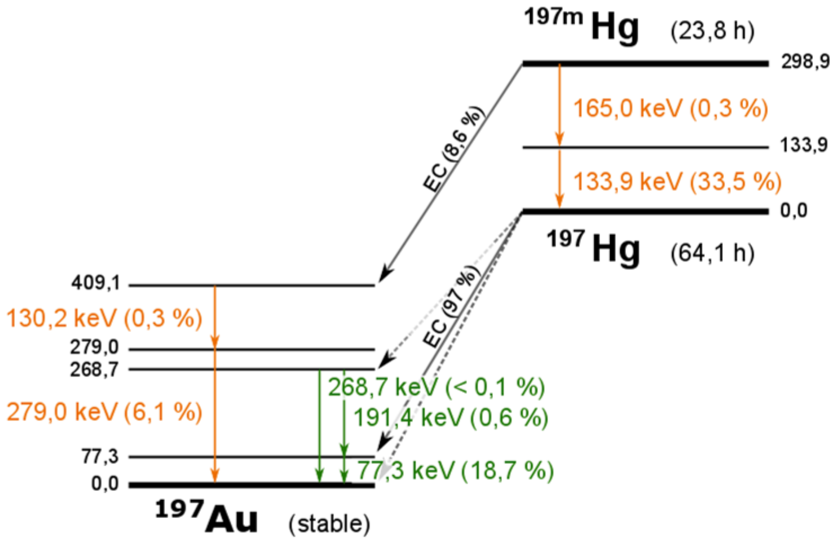
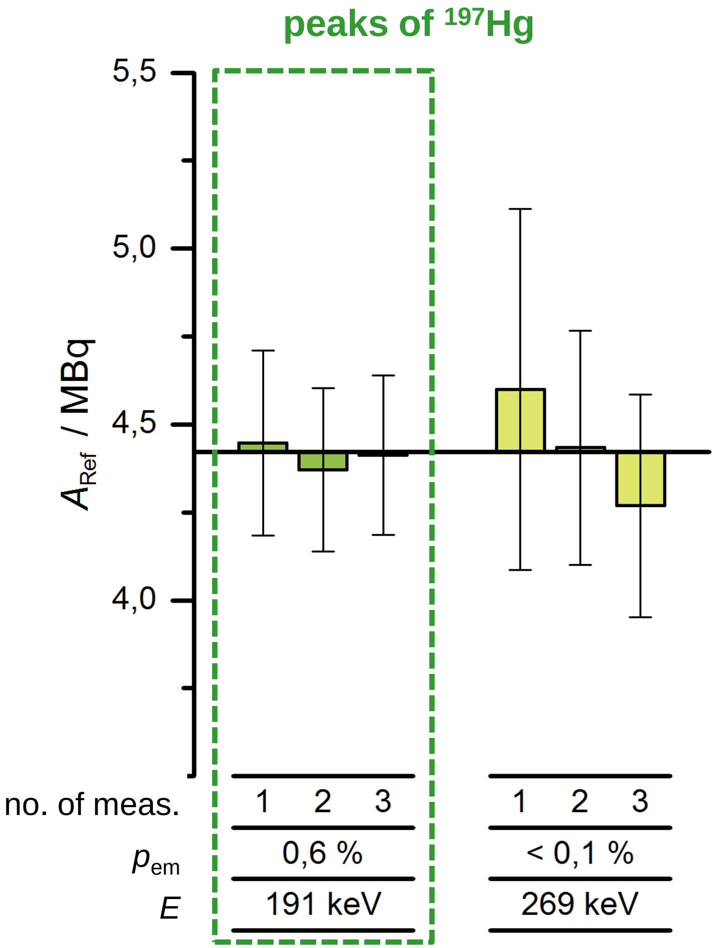
Determination of radionuclide activity $A_{\text{Hg-197m}}$ and $A_{\text{Hg-197}}$

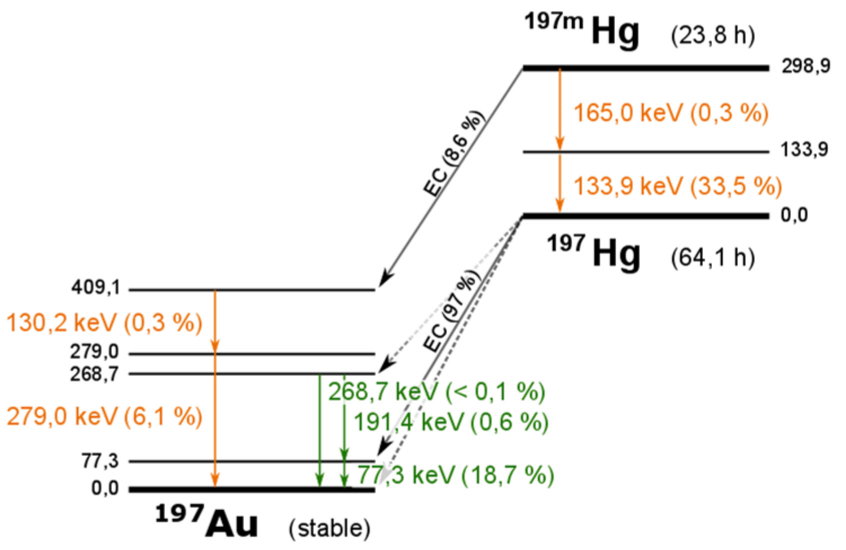


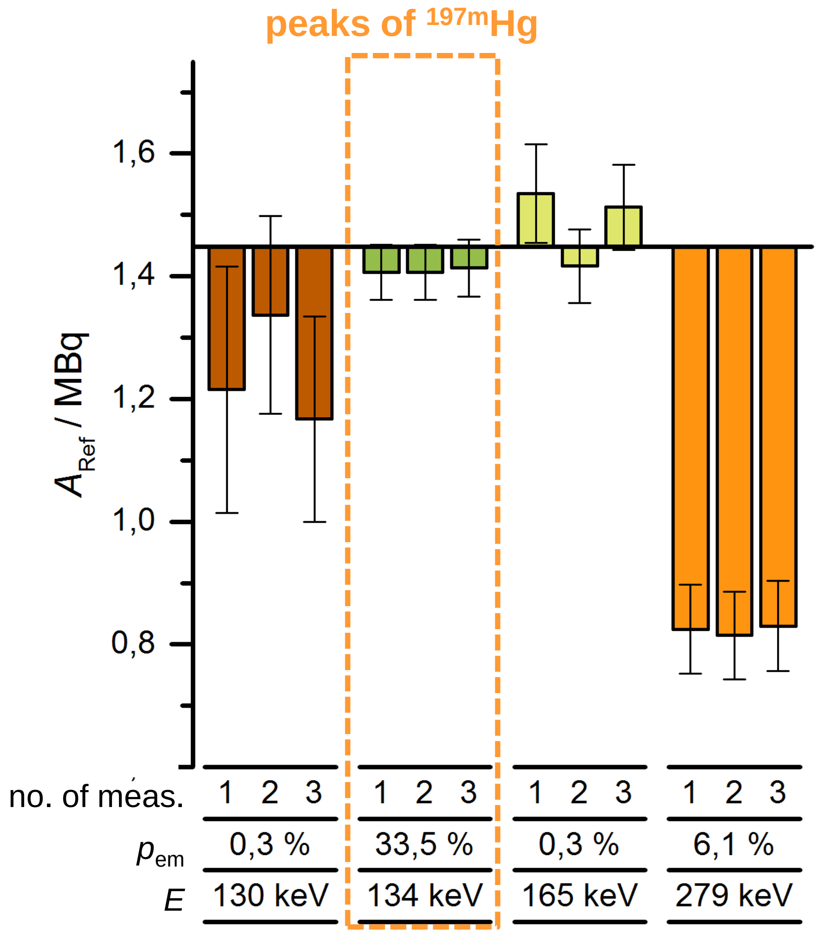


77 keV: low photon energy, close to the "knee" of $\varepsilon(E)$, efficiency is not known precisely

269 keV: low photon emission probability

Determination of radionuclide activity $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$



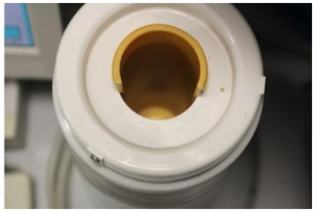


134 keV and 165 keV: good agreement

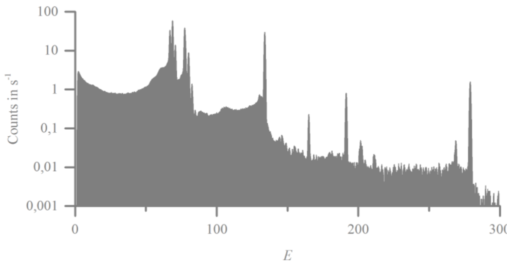
130 keV and 279 keV: indicates a wrong photon emission probability

Method

Aim: measurement of Hg-197m and Hg-197 by a dose calibrator



Determination of radionuclide activity $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$ using gamma spectrometry (HPGe detector) ✓



Full-energy peak efficiency calibration of the HPGe detector ✓

http://www.schott.com/pharmaceutical_packaging/german/products/vials/topline-options.html
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Theoretical background

Response to a single radioisotope:

$$I_s = A \cdot \varepsilon$$

$$\varepsilon = \sum_j p_{\beta j}(E_j) \cdot \varepsilon_{\beta j}(E_j) + \sum_i p_i(E_i) \cdot \varepsilon_i(E_i)$$

Response to a mixture of two radioisotopes

$$I_s = A_1 \cdot \varepsilon_1 + A_2 \cdot \varepsilon_2$$

I_S … detector reading
~ saturation current

A … activity
ε … efficiency
p … emission probability

Measurement of Hg-197m and Hg-197 by a dose calibrator

Theoretical background

Response to a single radioisotope:

$$I_s = A \cdot \varepsilon$$

$$\varepsilon = \sum_j p_{\beta j}(E_j) \cdot \varepsilon_{\beta j}(E_j) + \sum_i p_i(E_i) \cdot \varepsilon_i(E_i)$$

Response to a mixture of two radioisotopes

$$I_s = A_1 \cdot \varepsilon_1 + A_2 \cdot \varepsilon_2$$

I_S … detector reading

~ saturation current

A … activity

ε … efficiency

p … emission probability

Calibration procedure

- ✓ A_1, A_2 are known (HPGe detector)
- ✗ ε_i have to be determined

→ At least two measurements necessary (different activity ratios)

Theoretical background

Response to a single radioisotope:

$$I_s = A \cdot \varepsilon$$

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Response to a mixture of two radioisotopes

$$I_s = A_1 \cdot \varepsilon_1 + A_2 \cdot \varepsilon_2$$

I_S … saturation current ~ detector reading

A … activity

ε … efficiency

p … emission probability

Calibration procedure

- ✓ A_1, A_2 are known (HPGe detector)
- ✗ ε_i have to be determined

→ At least two measurements necessary (different activity ratios)

Routine hospital practice

- ✓ ε_i are known
- ✗ A_1, A_2 have to be determined

→ two measurements necessary

$$I_s = A_1 \cdot \varepsilon_1 + A_2 \cdot \varepsilon_2$$

$$\tilde{I}_s = A_1 \cdot \tilde{\varepsilon}_1 + A_2 \cdot \tilde{\varepsilon}_2$$

(without / with copper shielding)

Measurement of Hg-197m and Hg-197 by a dose calibrator

Theoretical background: Selection of a shielding

without shielding $I_s = A_1 \cdot \varepsilon_1 + A_2 \cdot \varepsilon_2 \rightarrow A_1(A_2) = -\frac{\varepsilon_2}{\varepsilon_1} A_2 + \frac{I_s}{\varepsilon_1}$

with shielding $\tilde{I}_s = A_1 \cdot \tilde{\varepsilon}_1 + A_2 \cdot \tilde{\varepsilon}_2 \rightarrow A_1(A_2) = -\frac{\tilde{\varepsilon}_2}{\tilde{\varepsilon}_1} A_2 + \frac{\tilde{I}_s}{\tilde{\varepsilon}_1}$

- two lines with different slopes
- aim: maximize angle of intersection, i.e. $\frac{\varepsilon_2}{\varepsilon_1} \neq \frac{\tilde{\varepsilon}_2}{\tilde{\varepsilon}_1}$

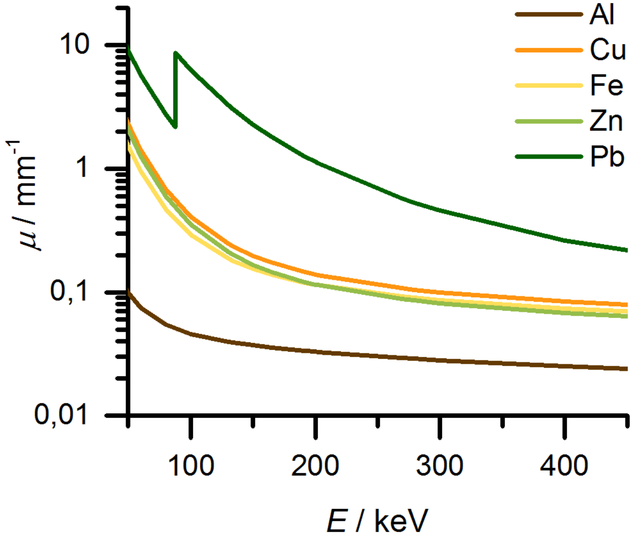


Fig. 5: Linear attenuation coefficient for photons in different materials as a function of photon energy

→ Use copper for shielding

Measurement of Hg-197m and Hg-197 by a dose calibrator

Determination of radionuclide efficiencies ε_i

1. preparation of a **serial dilution** in order to cover a range of activities with different ratios of $A_{Hg\text{-}197m}$ to $A_{Hg\text{-}197}$

2. **determination of $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$** of samples using HPGe detector

3. **multiple measures with dose calibrator** at different times, with and without shielding

4. determination of ε_i by **nonlinear curve fitting of all dose calibrator readings**

Measurement of Hg-197m and Hg-197 by a dose calibrator

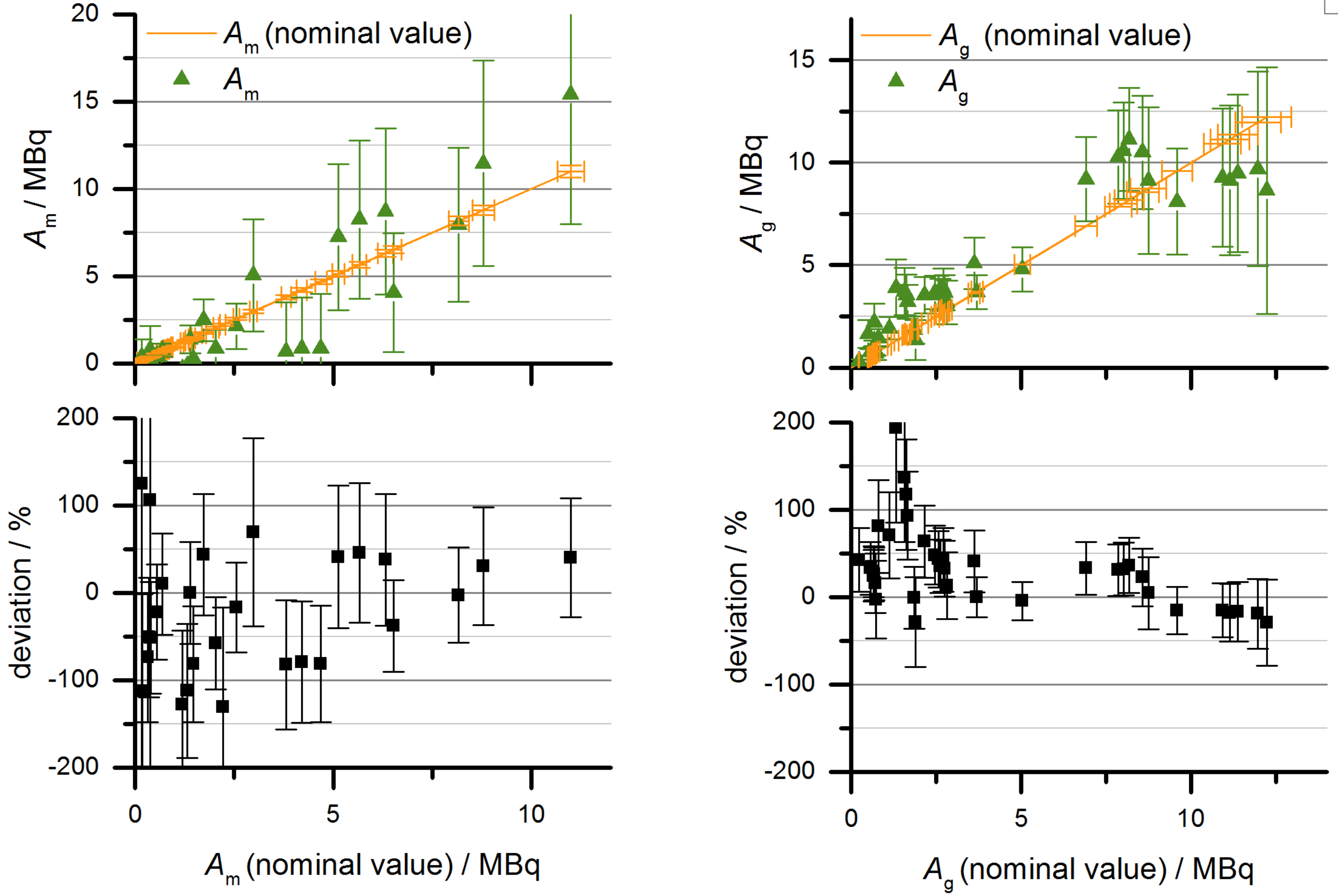
Determination of radionuclide efficiencies ε_i

	ε_m	$\tilde{\varepsilon}_m$		ε_g	$\tilde{\varepsilon}_g$	
shielding	no	1 mm	2 mm	no	1 mm	2 mm
value	9,9 ± 0,9	6,87 ± 0,17	5,3 ± 0,5	14,6 ± 0,5	8,38 ± 0,11	6,36 ± 0,29
relative uncertainty	8,8 %	2,4 %	8,8 %	3,5 %	1,3 %	4,5 %

Measurement of Hg-197m and Hg-197 by a dose calibrator

Calculated activities compared with nominal values

shielding: 1 mm



Measurement of Hg-197m and Hg-197 by a dose calibrator

Consideration of uncertainties

$$\left.\begin{aligned} I &= A_m \cdot \varepsilon_m + A_g \cdot \varepsilon_g \\ \tilde{I} &= A_m \cdot \tilde{\varepsilon}_m + A_g \cdot \tilde{\varepsilon}_g \end{aligned}\right\} \quad A_m = \frac{I}{\varepsilon_m} - \frac{\frac{\varepsilon_g}{\varepsilon_m}\left(\tilde{I} - \frac{\tilde{\varepsilon}_m}{\varepsilon_m} I\right)}{\tilde{\varepsilon}_g - \frac{\tilde{\varepsilon}_m}{\varepsilon_m}\varepsilon_g} \qquad A_g = \frac{\tilde{I} - \frac{\tilde{\varepsilon}_m}{\varepsilon_m} I}{\tilde{\varepsilon}_g - \frac{\tilde{\varepsilon}_m}{\varepsilon_m}\varepsilon_g}$$

elements of uncertainty: $\varepsilon_m, \varepsilon_g, \tilde{\varepsilon}_m, \tilde{\varepsilon}_g, I, \tilde{I}$

Example:

quantity	ε_m	$\tilde{\varepsilon}_m$	ε_g	$\tilde{\varepsilon}_g$	I	$\tilde{I}$	A_m	A_g
relative uncertainty / %	8,8	2,4	3,5	1,3	0,05 … 0,4	0,1 … 1,2	**48 … >100**	**22 … 71**

Conclusions

- **HPGe detector**:
  - $A_{Hg\text{-}197}$ and $A_{Hg\text{-}197m}$ with relative uncertainties between 3,2 and 5,0 % determined

- **Dose calibrator**:
  - Efficiencies for Hg-197 and Hg-197m determined
  - Good agreement between calculated activities and nominal values within the scope of their uncertainties
  - Consideration of the uncertainties is a very important point

Limitations:

- Great uncertainties of calculated activities
- Not applicable in clinical routine at the moment

Conclusions

Alternative method:

- Determination of $A_{Hg\text{-}197}$, $A_{Hg\text{-}197}$ using HPGe detector
- Calculation of $A_{Hg\text{-}197}(t)$, $A_{Hg\text{-}197m}(t)$ using equations for radioactive decay chain

Limitations:

- More time-consuming than measurements with a dose calibrator
- Requires HPGe detector
- Uncertainty of activity ratio, photon emission probability and half life
  - great uncertainties in calculated activities for later times
  - should only be used for short periods of time

Thank you very much for your attention!

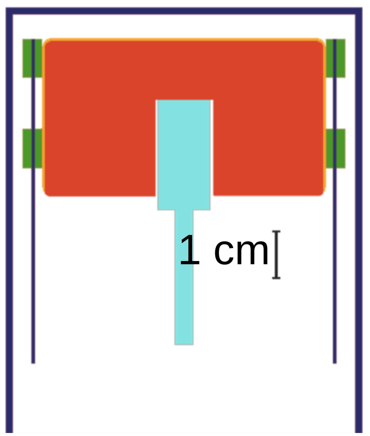
Contact: Robert.Freudenberg@uniklinikum-dresden.de

Maria.Vogel@uniklinikum-dresden.de

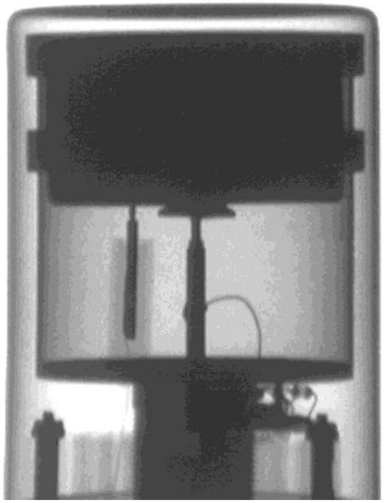
Efficiency calibration of the HPGe detector

Characterization with Monte Carlo simulations

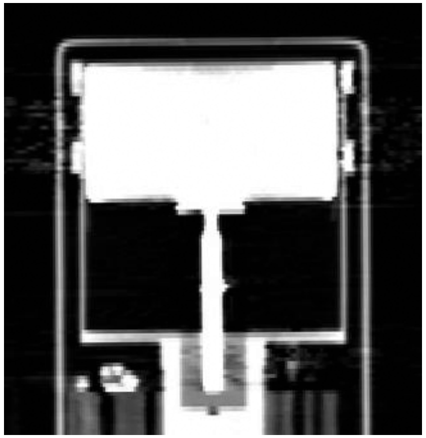
- using the Geant4 toolkit
- geometry was initially modeled using technical dimensions supplied by the manufacturer
- optimization:
  - information from X-ray and CT images
  - comparison between experimental and calculated full-energy peak efficiency for different detector parameter set-ups at the reference geometry (point sources)



Geant4 detector model

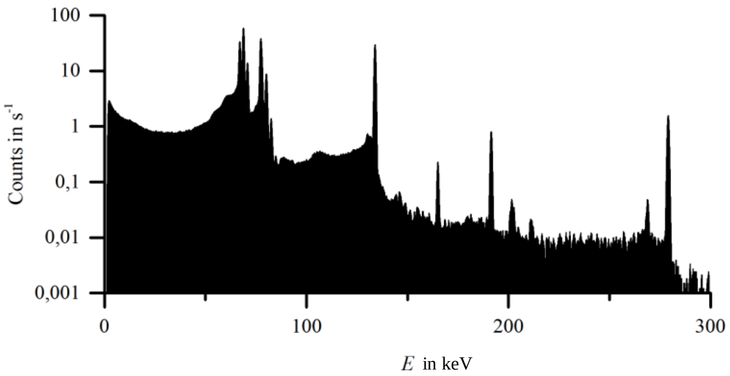


X-ray scan

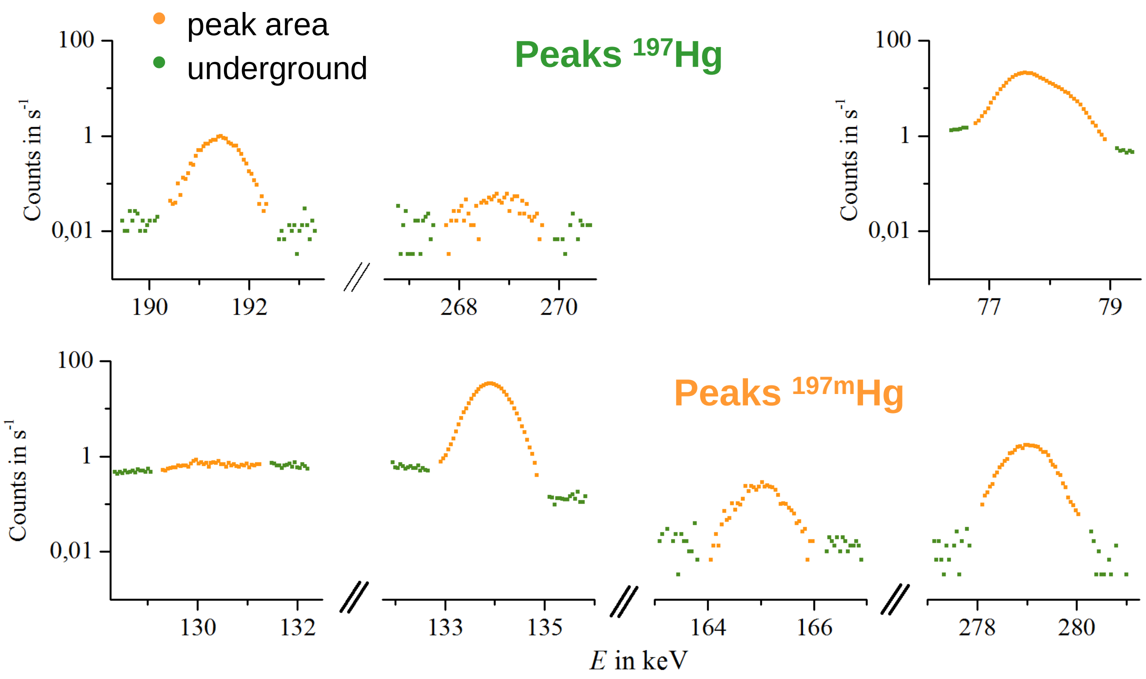


CT scan

Determination of radionuclide activity $A_{\text{Hg-197m}}$ and $A_{\text{Hg-197}}$



detector efficiency ε: $$\varepsilon = \frac{N_{\text{VEP}}}{A_0\, t\, p_{\text{em}}}$$



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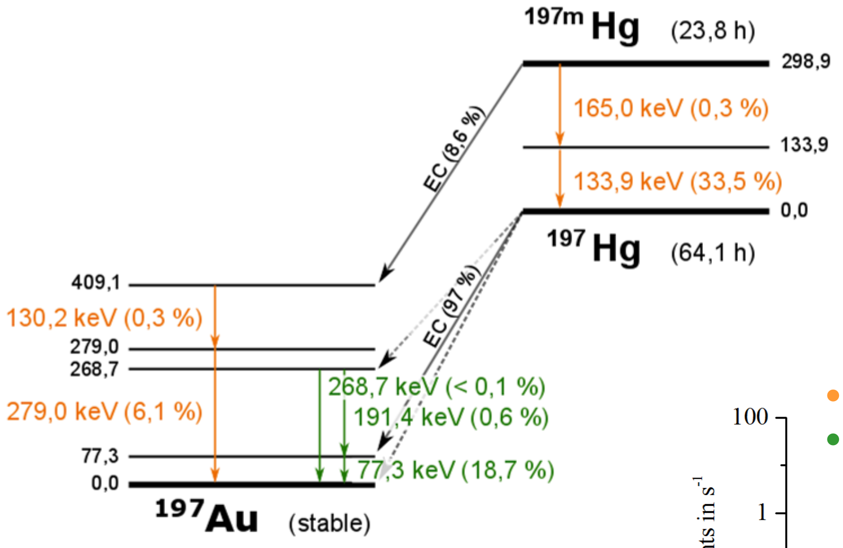
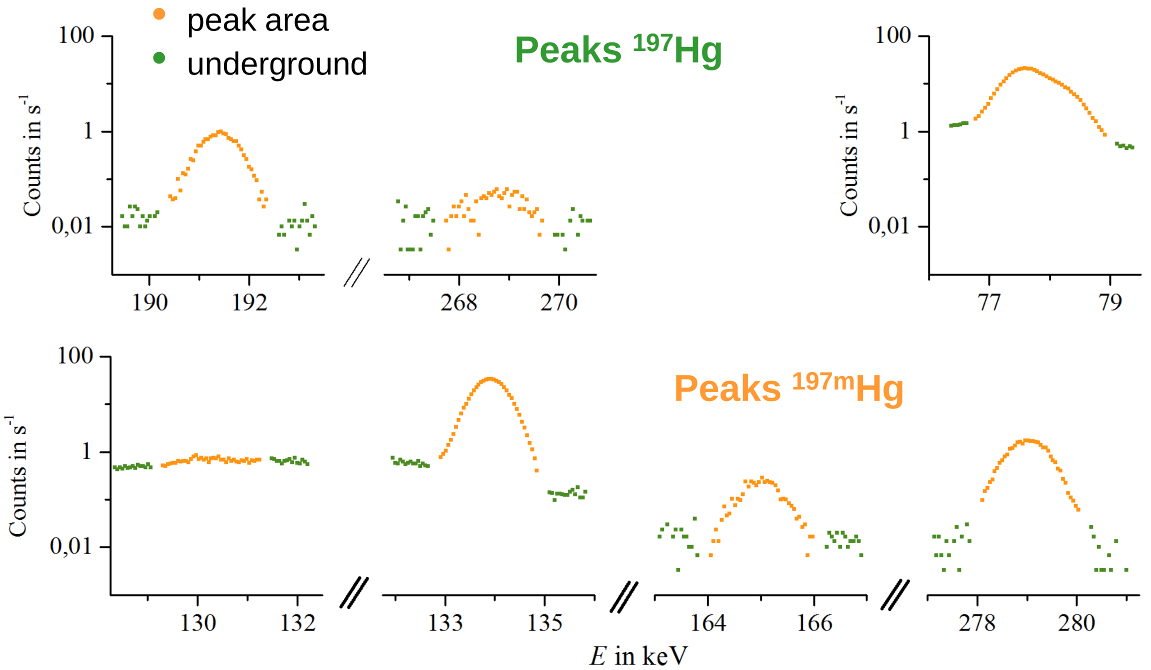
Determination of radionuclide activity $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$



detector efficiency ε: $\varepsilon = \frac{N_{VEP}}{A_0 \, t \, p_{em}}$



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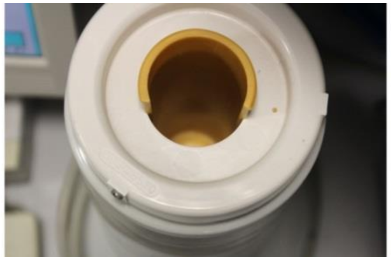
Measurement of Hg-197 and Hg-197m by a dose calibrator

Quality control

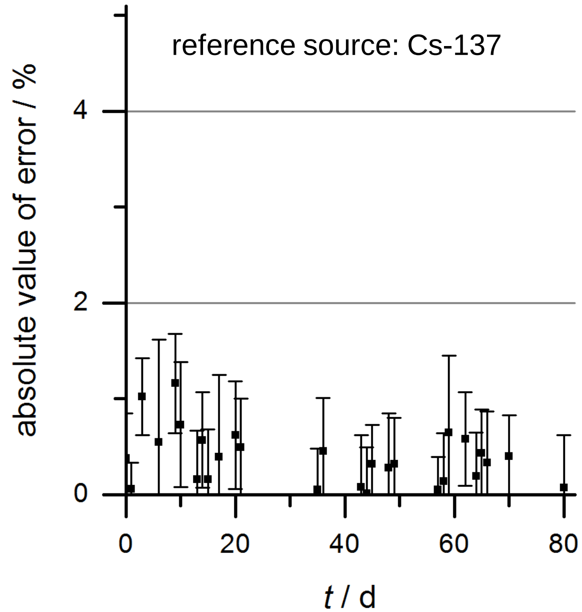
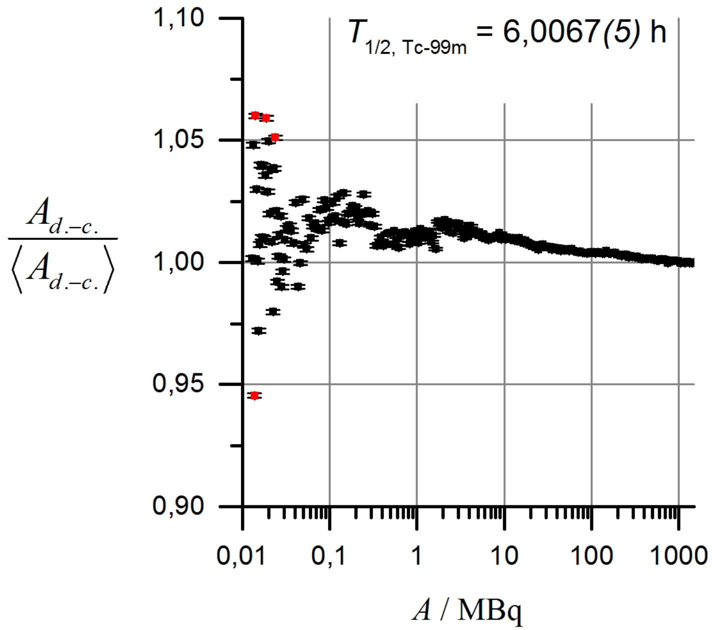
- dose calibrators can remain stable over several years
- they are critical to the work of a nuclear medicine department




Test	Constancy	Activity linearity
Recommended Frequency	Daily	Half-yearly
	Reading of the activity of a long-lived reference source (usually Cs-137)	Measure a short-lived source (Tc-99m) at several time points (from 1 MBq to 1 GBq or more)
	Acceptable error < ± 5 %	

Measurement of Hg-197 and Hg-197m by a dose calibrator

Quality control

Test	Constancy	Activity linearity
	 **Fig. X**: Results of the constancy test.	 **Fig. X**: Results of the activity linearity test using a Tc-99m source and decay-corrected activities $A_{d.\text{-}c.}$

Measurement of Hg-197 and Hg-197m by a dose calibrator

Determination of radionuclide efficiencies ε_i

1. preparation of a **serial dilution** in order to cover a range of activities with different ratios of $A_{Hg\text{-}197m}$ to $A_{Hg\text{-}197}$

2. **determination of $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$** of samples using HPGe detector

3. **multiple measures with dose calibrator** at different times, with and without shielding

4. multiple **controls of $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$** using HPGe detector

Method a)

5. determination of ε_i by **nonlinear curve fitting of all dose calibrator readings**

Measurement of Hg-197 and Hg-197m by a dose calibrator

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3. **multiple measures with dose calibrator** at different times, with and without shielding

4. multiple **controls of $A_{Hg\text{-}197m}$ and $A_{Hg\text{-}197}$** using HPGe detector

Method a)

5. determination of ε_i by **nonlinear curve fitting of all dose calibrator readings**

Method b)

5. **determination of $\varepsilon_{Hg\text{-}197} == \varepsilon_g$** by analysis of dose calibrator readings of decayed samples ($A_{Hg\text{-}197m} \ll A_{Hg\text{-}197}$)

6. **determination of $\varepsilon_{Hg\text{-}197m} == \varepsilon_m$** by analysis of other dose calibrator readings

Measurement of Hg-197 and Hg-197m by a dose calibrator

Determination of radionuclide efficiencies ε_i

Method a)

5. determination of ε_i by **nonlinear curve fitting of all dose calibrator readings**

Method b)

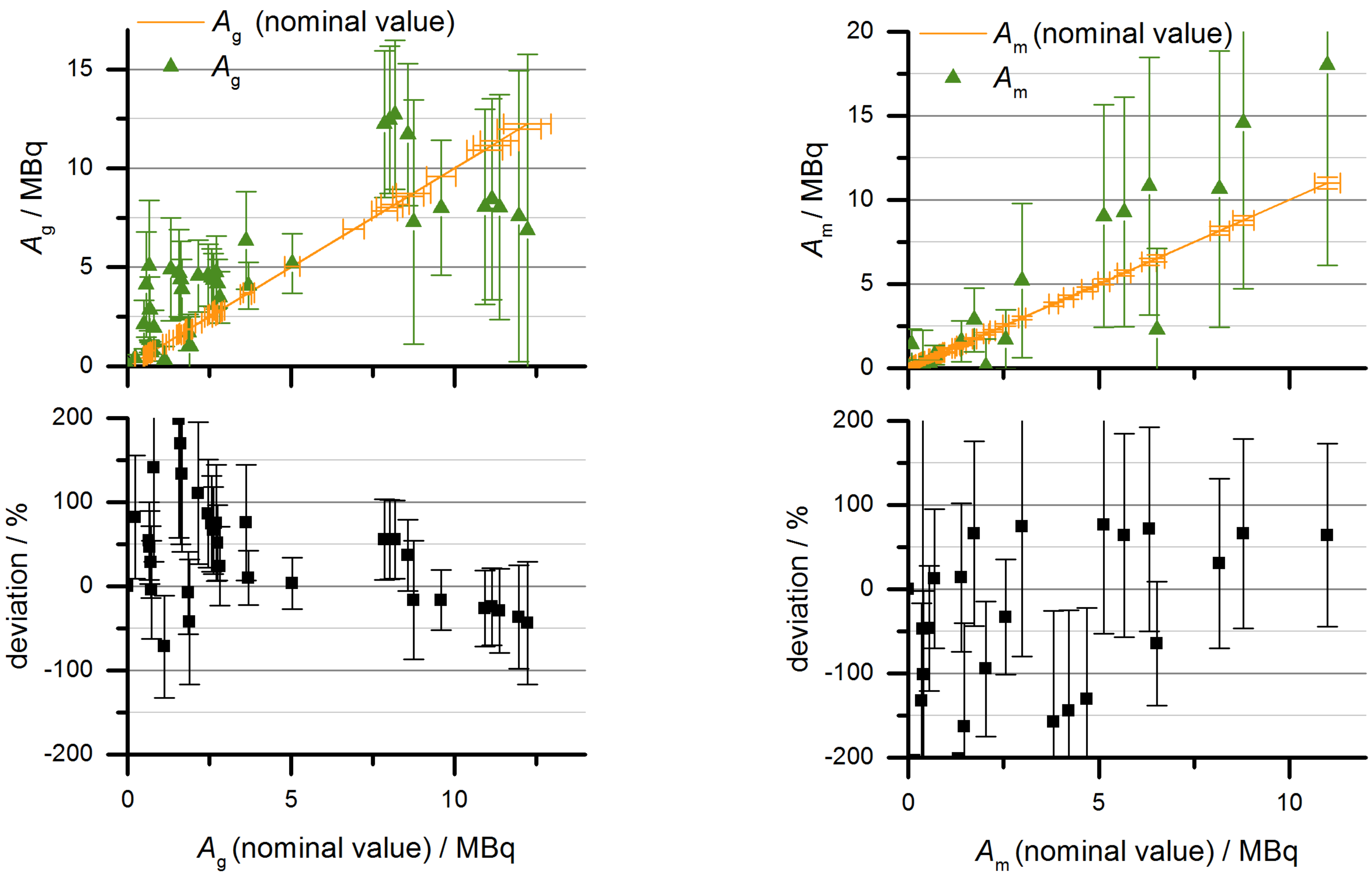
5. **determination of $\varepsilon_{Hg\text{-}197}$ == ε_g** by analysis of dose calibrator readings of decayed samples ($A_{Hg\text{-}197m} \ll A_{Hg\text{-}197}$)
6. **determination of $\varepsilon_{Hg\text{-}197m}$ == ε_m** by analysis of other dose calibrator readings

		ε_m			ε_g		
	shielding	no	1 mm	2 mm	no	1 mm	2 mm
Method a)	value	9,9 ± 0,9	6,87 ± 0,17	5,3 ± 0,5	14,6 ± 0,5	8,38 ± 0,11	6,36 ± 0,29
	rel. unc. / %	*8,8*	*2,4*	*8,8*	*3,5*	*1,3*	*4,5*
Method b)	value	9,1 ± 0,4	6,4 ± 0,3	-	15,28 ± 0,28	8,64 ± 0,22	-
	rel. unc. / %	*4,4*	*4,7*	*-*	*1,8*	*2,5*	*-*

Measurement of Hg-197 and Hg-197m by a dose calibrator

Calculated activities compared with nominal values

Method a), shielding: 2 mm



Measurement of Hg-197 and Hg-197m by a dose calibrator

Calculated activities compared with nominal values

Method b)