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Investigation on calibration coefficients of dose calibrators and their influence on different geometries for beta- and gamma-emitters.

Project summary report

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Abstract

This summary report (abridged from the full report) presents the development and results of the joint project between the Swiss Federal Office of Public Health (FOPH), the Institute of Radiation Physics (IRA) and the Swiss Federal Institute of Metrology (METAS). The project studies the impact of different container geometries and measurement configurations on the validity of calibration coefficients for dose calibrators (also known as activimeters) used in Nuclear Medicine services.

According to the legislation, doses delivered to patients from the use of radiopharmaceuticals must be measured in terms of activity (Bq) using dose calibrators. These instruments make use of calibration coefficients provided by the manufacturer to determine the activity of the radiopharmaceuticals.

The influence of container geometry, filling volume, and positioning system was tested with three radiopharmaceuticals (Y-90, I-123 and Lu-177) known for their uneven response when measured with dose calibrators under different conditions. The results of these measurements are summarized in this report and conclusions and recommendations are drawn for the proper use of these devices.

Broader information about the different work packages, measurement procedures and results of the project are detailed in the full project report.

1 Goals and design of the project

1.1 Overview

The following points are to be investigated in the study:

- Type of containers used, measurement set-ups, holders and handling by users of dose calibrators.
- Dependence of the activity measurement on nuclide settings of the dose calibrators.
- Dependence of the activity measurement on the measuring arrangement (kind, size and material of the container) and practical conditions of the dose calibrators (holder type and position in the well chamber).
- Determination of possible correction coefficients

The three most frequently used radionuclides that have presented discrepancies in their measurement are investigated: Y-90, I-123 and Lu-177.

1.2 Work packages of the project

1.2.1 WP 1: Survey among users

A questionnaire was sent to the users of the selected nuclides asking for information on the containers, geometries, holders and positioning aids used in clinical operation for the types of dose calibrators investigated in this project. The answers provided by the participants were analysed and a summary is given in section 2.

1.2.2 WP 2: Measurements in the field

Measurements were carried out at three different hospitals operating several different types of dose calibrators.

A team from IRA visited the hospitals with a transportable reference ionization chamber, TCIR [1]-[2], to determine the activity of the different sources in a way that is traceable to the SI (International System of Units). Thus, an absolute verification of the measured value determined by the participant could be made for the selected dose calibrators and nuclides.

The discussion of the results will assume that an agreement better than 5% is desirable (10% for Y-90) when comparing the reference (TCIR) activity value and the measured (DUT), since additional sources of uncertainty may contribute to the deviation of the dose applied to the patient.

1.2.3 WP 3: Determination of correction factors

A systematic determination of the effect of different influence factors was performed at METAS using two different dose calibrators. The following parameters were examined:

- different containers
- different filling volumes
- dependence on the positioning of the container
- different holders of the container
- different nuclide settings for each type of dose calibrator.

1.2.4 WP 4: Report and recommendation

The project's report, written jointly by FOPH, IRA and METAS and meant for internal purpose only, as well as the present summary report are the main outcome of the project. Some of the findings will be incorporated into the next revision of the Ordinance of the FDJP on Measuring Instruments for Ionising Radiation and into the updated FOPH guidance on quality assurance for dose calibrators.

2 WP 1: Survey among users

In late summer 2020, a questionnaire was sent to several Swiss Nuclear Medicine services to obtain information on how they measure the activity of complicated radionuclides.

2.1 Overview of responses received

Altogether, 26 Nuclear Medicine services participated in the survey. The following table gives an overview of the main figures characterising the feedback received for all institutions together:

Table 1: Main figures obtained from the survey.

Number of …	
… different dose calibrator types	7
… different dose calibrators used	28
… *Veenstra-Comecer VIK-202* type dose calibrators	22
… *MED-NUVIA ISOMED 2000/2010* type dose calibrators	2
… *Lemer Pax ScintiDOSE*(1) type dose calibrators	3
… *Biodex Atomlab* type dose calibrators	1
… different radionuclide types	6
… I-123 users	26
… Lu-177 users	7
… Y-90 users	16
… other nuclides users(2)	7

(1) This includes ScintiDOSE and ScintiDOSE 2/3 ionisation chambers.
(2) Other problematic nuclides could optionally be mentioned in the survey. The following ones were reported: Er-169, Ra-223 and Re-186.

The *VIK-202* ionisation chamber is the most widely used dose calibrator type in the Nuclear Medicine services that participated in the survey (22 out of 28 in total).

Depending on the radionuclide, the measured activities range over about two orders of magnitude. This shows the importance of checking the linearity of the dose calibrator in order to ensure a reliable measurement of the activity over the whole range used.

Most of the respondents use the calibration coefficients defined by the manufacturer. Only three respondents have self-defined coefficients and two of them are for the aforementioned radionuclides: Y-90 and Lu-177.

Despite I-123 being the most widely used radionuclide, only three services noted the used of the copper dipper for I-123, which allows for a more stable response, regardless of the container's geometry.

3 WP 2: Measurements in the field

At each of the participating hospitals, the IRA-TCIR was placed in the laboratory where the sources were to be prepared, usually a type-C or B work area. For each radionuclide, an aliquot of 1 ml is taken from the stock solution to fill a reference vial which is measured with the TCIR to precisely determine its specific activity (MBq/g). From this reference activity concentration, the reference activities for the additional sources prepared using the same stock solution and mimicking the routine conditions were obtained by gravimetry. The activity values obtained measuring these sources on the dose calibrators were compared to the reference ones after decay correction and background subtraction.

If a measured value differs by more than 5% from the reference activity, a new calibration coefficient should be determined and used instead of the original one from the manufacturer. For each dose calibrator, it is also possible to group the calibration coefficients for different geometries by calculating an average value. The average calibration coefficients may be used if the differences between the activities measured using individual and average coefficients are not greater than 5%.

3.1 Measurement results for I-123

The results on the measurements performed for I-123 with the different dose calibrators are summarised in table 2.

Table 2: Measurement results for I-123. In the column "Container designation", V stands for vial and S stands for syringe. The default manufacturer sample holder was used for all dose calibrators unless stated otherwise.

Container designation	Nominal volume (ml)	Nominal fill-up quantity (ml)	Original calibration coefficient	Measured activity (MBq)	Reference activity (MBq)	Deviation	New calibration coefficient
Comecer VDC-405 / VIK-202 dose calibrator #1							
V 1	5	2.5	618 x 1 (1)	78.85	68.31	**+14.5%**	668 x 1
V 2	10	2.5		64.92	68.07	**-5.4%**	596 x 1
S 1	1	1		28.35	22.36	**+25.9%**	698 x 1
S 2	3	1		36.84	29.05	**+26.1%**	699 x 1
Comecer VDC-405 / VIK-202 dose calibrator #2							
V 10	5	2.5	540 x 1 (1)	26.31	32.41	**-18.8%**	431 x 1
Comecer VDC-405 / VIK-202 dose calibrator #3							
V 15	10	5	106 x 1 (1)(2)(1)	20.69	21.43	**-3.4%**	918 x 10
S 7	5	2	145 x 1 (1)(2)	12.98	13.50	**-3.9%**	919 x 10

Container designation	Nominal volume (ml)	Nominal fill-up quantity (ml)	Original calibration coefficient	Measured activity (MBq)	Reference activity (MBq)	Deviation	New calibration coefficient
S 8	3	2		7.65	8.063	**-5.1%**	918 x 10
S 9	10	3		13.60	14.24	**-4.5%**	919 x 10
S 10	1	0.5		1.991	2.097	**-5.0%**	918 x 10
MED ISOMED 2000/2010 dose calibrator #4							
V 1	5	2.5	0.094	90.29	68.31	**+30.1%**	0.072
V 2	10	2.5	0.095	77.30	68.07	**+11.6%**	0.085
S 1	1	1	0.066	20.80	22.36	**-8.2%**	0.072
S 2	3	1	0.081	26.91	29.05	**-8.3%**	0.088
Lemer Pax ScintiDOSE dose calibrator #5							
V 1	5	2.5	1.72751954	76.0	68.31	**+11.5%**	1.92529490
V 2	10	2.5		59.6	68.07	**-12.4%**	1.51398370
S 1	1	1	2.27186965	19.3	22.36	**-13.5%**	1.96613328
S 2	3	1		25.8	29.05	**-10.9%**	2.02506543

(1) The *x 1* is a multiplicative factor used by this dose calibrator algorithm, along with the calibration coefficient, to obtain the activity value. This factor can be 1, 10 or 100, as it will be seen in the following tables.

(2) These calibration coefficients are used when a copper dipper is inserted. For the new calibration coefficient measurement and calculation, the users requested to perform a test with and without copper dipper, and it was finally decided to keep using the dipper.

3.2 Measurement results for Lu-177

The results on the measurements performed for Lu-177 with the different dose calibrators are summarised in table 3.

Table 3: Measurement results for Lu-177. In the column "Container designation", V stands for vial and S stands for syringe. The default manufacturer sample holder was used for all dose calibrators.

Container designation	Nominal volume (ml)	Nominal fill-up quantity (ml)	Original calibration coefficient	Measured activity (MBq)	Reference activity (MBq)	Deviation	New calibration coefficient
Comecer VDC-405 / VIK-202 dose calibrator #1							
V 3	20	15	751 x 10	136.40	124.66	**+11.0%**	777 x 10
V 4	20	15		136.00	124.33	**+11.1%**	777 x 10
S 3	3	3		27.32	24.98	**+11.1%**	777 x 10
S 4	20	15		Cannot be measured on the standard sample holder			
Comecer VDC-405 / VIK-202 dose calibrator #3							
V 11	3	0.1	751 x 10	84.76	77.67	**9.4%**	773 x 10
V 12	25	19		143.5	125.4	**14.4%**	784 x 10
V 13	20	12		85.94	76.46	**12.4%**	779 x 10
S 9	10	6		37.11	30.70	**20.9%**	796 x 10
MED ISOMED 2000/2010 dose calibrator #4							
V 3	20	15	0.4 (1)	119.7	124.66	**-2.6%**	0.411
			0.475	142.2		**+15.7%**	0.411
V 4	20	15	0.4 (1)	119.5	124.33	**-2.4%**	0.410
			0.475	141.9		**+15.9%**	0.410

Container designation	Nominal volume (ml)	Nominal fill-up quantity (ml)	Original calibration coefficient	Measured activity (MBq)	Reference activity (MBq)	Deviation	New calibration coefficient
S 3	3	3	0.4 (1)	24.62	24.98	**+0.1%**	0.399
			0.44	27.08		**+10.1%**	0.400
S 4	20	15	0.4 (1)	119.5	126.61	**-4.2%**	0.417
			0.438	130.8		**+4.9%**	0.418
Lemer Pax ScintiDOSE dose calibrator #5							
V 3	20	15	0.22665117	125.4	124.66	**+2.08%**	0.23137603
V 4	20	15		125.0	124.33	**+2.09%**	0.23139094
S 3	3	3		25.8	24.98	**+4.98%**	0.23793716
S 4	20	15		132.5	126.61	**+6.37%**	0.24109890
Comecer VDC-405 / VIK-202 dose calibrator #6							
V 7	2	0.2	750 x 10	132.6	121.5	**+8.0%**	769 x 10
V 8	5	0.2		132.8	120.4	**+9.1%**	772 x 10
V 9	25	20		670.8	589.9	**+12.5%**	779 x 10
Capintec CRC-55tR #7							
V 7	2	0.2	375 x 10	139.1	121.5	**+13.4%**	426 x 10
V 8	5	0.2		136.5	120.4	**+12.3%**	422 x 10
V 9	25	20		697.0	589.9	**+17.1%**	440 x 10
Capintec CRC-55tR #8							
V 7	2	0.2	395 x 10	133.2	121.5	**+8.5%**	429 x 10
V 8	5	0.2		131.3	120.4	**+7.9%**	427 x 10
V 9	25	20		672	589.9	**+12.8%**	447 x 10
Capintec CRC-55tR #9							
V 7	2	0.2	395 x 10	135.7	121.5	**+10.6%**	438 x 10
V 8	5	0.2		133.9	120.4	**+10.1%**	436 x 10
V 9	25	20		691.0	589.9	**+16.0%**	460 x 10
Comecer VDC-405 / VIK-202 dose calibrator #10							
V 11	3	0.1	751 x 10	80.63	77.67	**3.8%**	760 x 10
V 12	25	19		135.7	125.4	**8.2%**	771 x 10
V 13	20	12		81.6	76.46	**6.3%**	767 x 10
S 9	10	6		35.04	30.70	**14.2%**	783 x 10
Comecer VDC-405 / VIK-202 dose calibrator #11							
V 11	3	0.1	751 x 10	82.73	77.67	**6.5%**	767 x 10
V 12	25	19		138.7	125.4	**6.5%**	776 x 10
V 13	20	12		83.46	76.46	**10.6%**	773 x 10
S 9	10	6		35.93	30.70	**9.2%**	789 x 10

(1) This is a calibration coefficient determined some years before based on a reference Lu-177 source provided by IRA.

3.3 Measurement results for Y-90

The results on the measurements performed for Y-90 with the different dose calibrators are summarised in table 4.

Table 4: Measurement results for Y-90. In the column "Container designation", V stands for vial and S stands for syringe. The default manufacturer sample holder was used for all dose calibrators.

Container designation	Nominal volume (ml)	Nominal fill-up quantity (ml)	Original calibration coefficient	Measured activity (MBq)	Reference activity (MBq)	Deviation	New calibration coefficient
Comecer VDC-405 / VIK-202 dose calibrator #1							
V 5	10	1.3	902 x 100	57.34	48.93	**+21.4%**	921 x 100
V 6	15	1.3		63.28	59.75	**+9.7%**	911 x 100
S 5	1	0.1	890 x 100	4.101	3.546	**+19.5%**	909 x 100
S 5	1	0.4		4.099		**+19.5%**	909 x 100
S 5	1	0.8		3.986		**+16.3%**	907 x 100
S 6	3	1		40.93	36.36	**+16.3%**	907 x 100
S 6	3	2		41.15		**+17.1%**	907 x 100
S 6	3	2.8		40.30		**+14.7%**	905 x 100
Comecer VDC-405 / VIK-202 dose calibrator #3							
V 14	10	2	902 x 100	478.1	476.7	**0.3%**	902 x 100
S 7	5	2	890 x 100	512.5	453.0	**13.1%**	904 x 100
MED ISOMED 2000/2010 dose calibrator #4							
V 5	10	1.3	1.8	56.15	48.93	**+18.8%**	1.515
V 6	15	1.3	1.9	65.64	59.75	**+13.8%**	1.670
S 5	1	0.1	0.56	1.291	3.546	**-62.4%**	1.489
S 5	1	0.4 (1)	0.56	1.275		**-62.8%**	1.507
S 5	1	0.8 (1)	0.49	1.175		**-65.7%**	1.430
S 6	3	1	0.81	23.69	36.36	**-32.7%**	1.204
S 6	3	2 (1)	0.74	22.82		**-35.1%**	1.140
S 6	3	2.8 (1)	0.67	22.59		**-35.7%**	1.042
Comecer VDC-405 / VIK-202 dose calibrator #10							
V 14	10	2	902 x 100	441.4	476.7	**-7.4%**	893 x 100
S 7	5	2	890 x 100	455.9	453.0	**0.6%**	894 x 100
Comecer VDC-405 / VIK-202 dose calibrator #11							
V 14	10	2	902 x 100	416.2	476.7	**17.1%**	886 x 100
S 7	5	2	890 x 100	462.8	453.0	**2.2%**	893 x 100

(1) The different fill-up quantities for the same container are obtained using the same stock solution contents but with additional NaCl fill-up.

3.4 General conclusion

The aim of these measurements was to provide an overview of the situation for these sensible radionuclides when measured on routine in Nuclear Medicine Services. From the deviation values presented, it is clear that the manufacturer calibration coefficients are not adequate to ensure the maximum ±5% deviation from the reference activity value.

In the next section, a detailed and systematic study on the influence of container geometry, filling volume and source positioning is presented to extract conclusions and derive recommendations for an appropriate usage of dose calibrators and their calibration coefficients.

4 WP 3: Determination of correction factors

4.1 Measurement setup and procedure

A systematic determination of the effect of different influence factors was performed at the METAS C-lab for the three radionuclides studied, using the two dose calibrators available, Veenstra VDC-405 / VIK-202 and ISOMED 2000/2010.

The different types of vials and syringes used are listed in table 5, together with the filling volumes obtained by adding saline solution to an initial 1 ml stock radioactive solution.

The influence of a copper cylinder holder for I-123 as an alternative to the standard plastic dipper, was also investigated.

An additional study of the dependence of the response with the position of the activity in the chamber's well was performed. The V0 vial with 1 ml stock solution was measured along the chamber in 10 mm steps using a special holder built by METAS for that purpose.

IRA's TCIR was used to obtain the reference activities as described in section 3.

Table 5: Geometries used for the measurements at METAS.

	Container designation	**Nominal volume (ml)**	**Fill-up quantities (ml)**	**Wall thickness (mm)**	**Inner Ø (mm)**	**Make / *Remarks***
Vials	V0	5	1	1.3	17.4	Infochroma, 5 ml Crimp Neck Vial 38 x 20 mm, clear glass, flat bottom; *this is the TCIR reference vial*
	V1	10	1, 2, 4, 8	1.1	17.8	LLG Labware, 10 ml Crimp Neck Vial 54,5 x 20 mm, clear glass, 1st hydrolytic class, flat bottom
	V2	5	1, 2, 4	1.1	17.8	LLG Labware, 5 ml Crimp Neck Vial 38 x 20 mm, clear glass, 1st hydrolytic class, flat bottom
	V3	10	1, 2, 4, 8	~ 1.8 (irregular)	~ 21.5	SGD Pharma, 10 ml Crimp Neck Vial 25.4 x 53.5 mm, clear glass, slightly bulging bottom; *penicillin vial*
	V4	25	1, 4, 8, 18	1.2	27.6	Huayi, 25 ml Crimp Neck Vial 30.0 x 55 mm thick clear glass; *Only used for Lu-177*
Syringes	S1	1	0.5, 1	0.85-0.90	4.7	B. Braun, Omnifix® Luer Solo, PP walls / Polyisoprene rubber seal, 1 ml
	S2	2	1, 2	0.6-0.7	8.8	BD Emerald, PP walls / TPE seal, 2 ml
	S3	3	1, 2, 3	0.6-0.7	9.7	B. Braun, Omnifix® Luer Solo, PP walls / Polyisoprene rubber seal, 3 ml
	S4	5	1, 2, 5	0.6-0.7	12.3	BD Emerald, PP walls / TPE seal, 5 ml
	S5	10	1, 2, 5, 10	0.65-0.75	15.6	BD Emerald, PP walls / TPE seal, 10 ml

4.2 Data analysis and uncertainties

The quantity used for presenting the results in the following sections is the relative difference between the measured and the reference activity. The calibration coefficient used for the measurement will be specified.

The Isomed dose calibrator has a complete matrix of calibration coefficients taking into account the geometry and the fill-up quantity. Hence, the results presented are the activity obtained with the manufacturer's calibration coefficient for each geometry (labelled VF[1]) and the activity obtained with a fixed calibration coefficient, arbitrarily chosen as that for a 10 ml vial filled to 5 ml and labelled FF[2].

Uncertainties on the reference activity values and on the measured values were estimated following the GUM principles [3]. The combined uncertainty for the activity of a container is 2.2% for Lu-177 and Y-90, and 2.5% for I-123. The reading uncertainty of the dose calibrator value is not included, as enough time was taken to wait for stability once the container is positioned and the fluctuation is small compared to the measured value.

4.3 Gamma spectrometry

For each of the three isotopes measured at METAS, a gamma spectrometry measurement was performed at IRA on an HPGe with the reference vial (V0) filled with 1 ml to check radionuclidic purity.

No impurities were found for the Lu-177 sample but three impurities (Te-121, Te-212m, Te-123m) were identified for I-123 and two (Y-88 and Eu-152) were found for Y-90. The activity ratio was lower than 10^{-5} in each case, so their contributions are neglected.

4.4 I-123 measurement results

Each I-123 source measurement in each dose calibrator was performed with the standard sample holder and with the copper dipper. Figure 1 shows the measurement results for vial and syringe geometries respectively. Measurement results are discussed in section 4.8.1.

[1] VF stands for Variable Factor.

[2] FF stands for Fixed Factor.

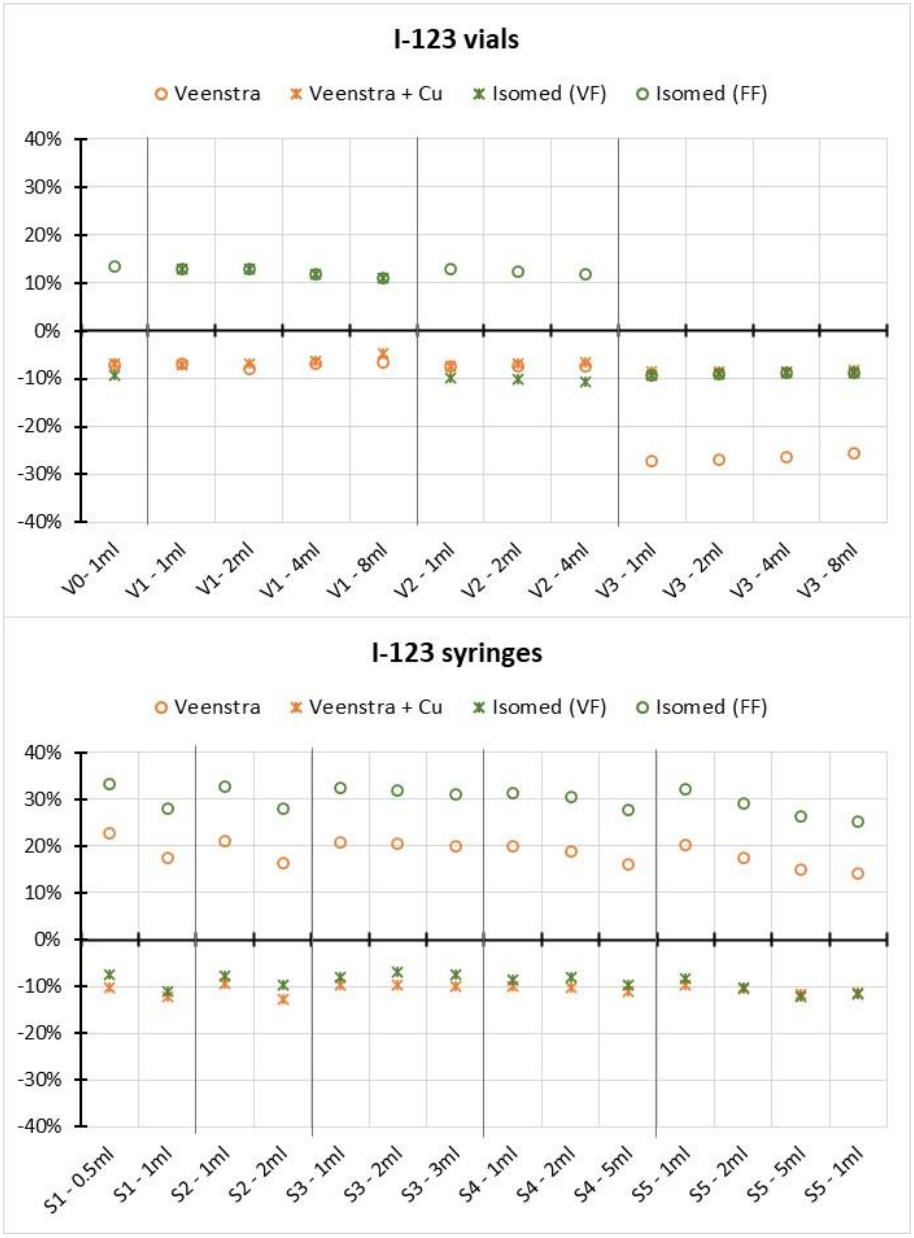

Figure 1: Relative activity differences between the measured and the reference values for I-123 solution in vial and syringe geometries (see table 5 for details) at different fill-up volumes. + Cu indicates the use of the copper dipper.

4.5 Lu-177 measurement results

Each Lu-177 source measurement in each dose calibrator was performed with the standard sample holder in both dose calibrators. Figure 2 shows the measurement results for vial and syringe geometries respectively. A discussion of these measurement results is given in section 4.8.2.

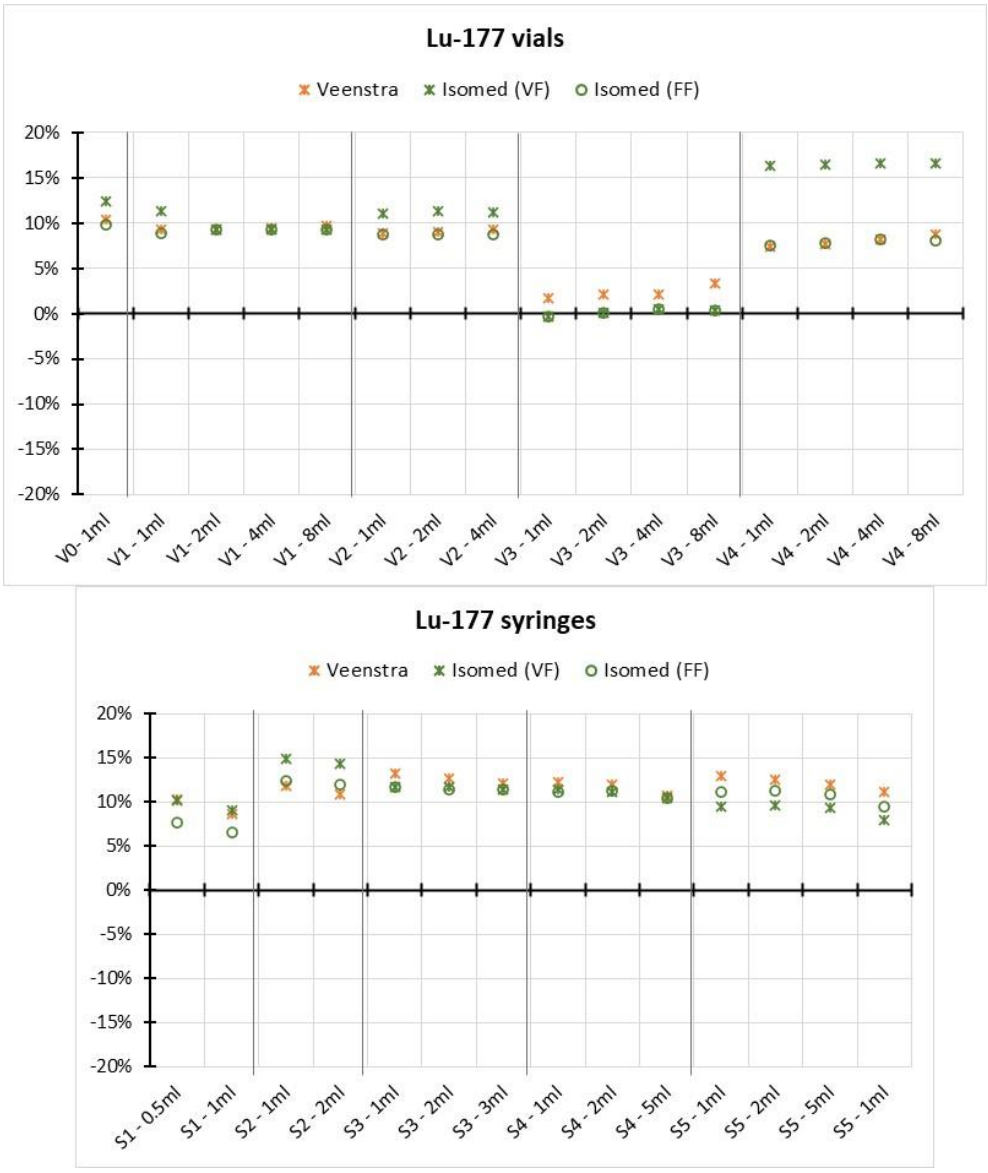

Figure 2: Relative activity differences between the measured and the reference values for the Lu-177 sources in vial and syringe geometries (see table 5 for details) at different fill-up volumes.

4.6 Y-90 measurement results

Each Y-90 source measurement in each dose calibrator was performed with the standard sample holder. Figure 3 shows the measurement results for vial and syringe geometries respectively. A discussion of these measurement results is given in section 4.8.3.

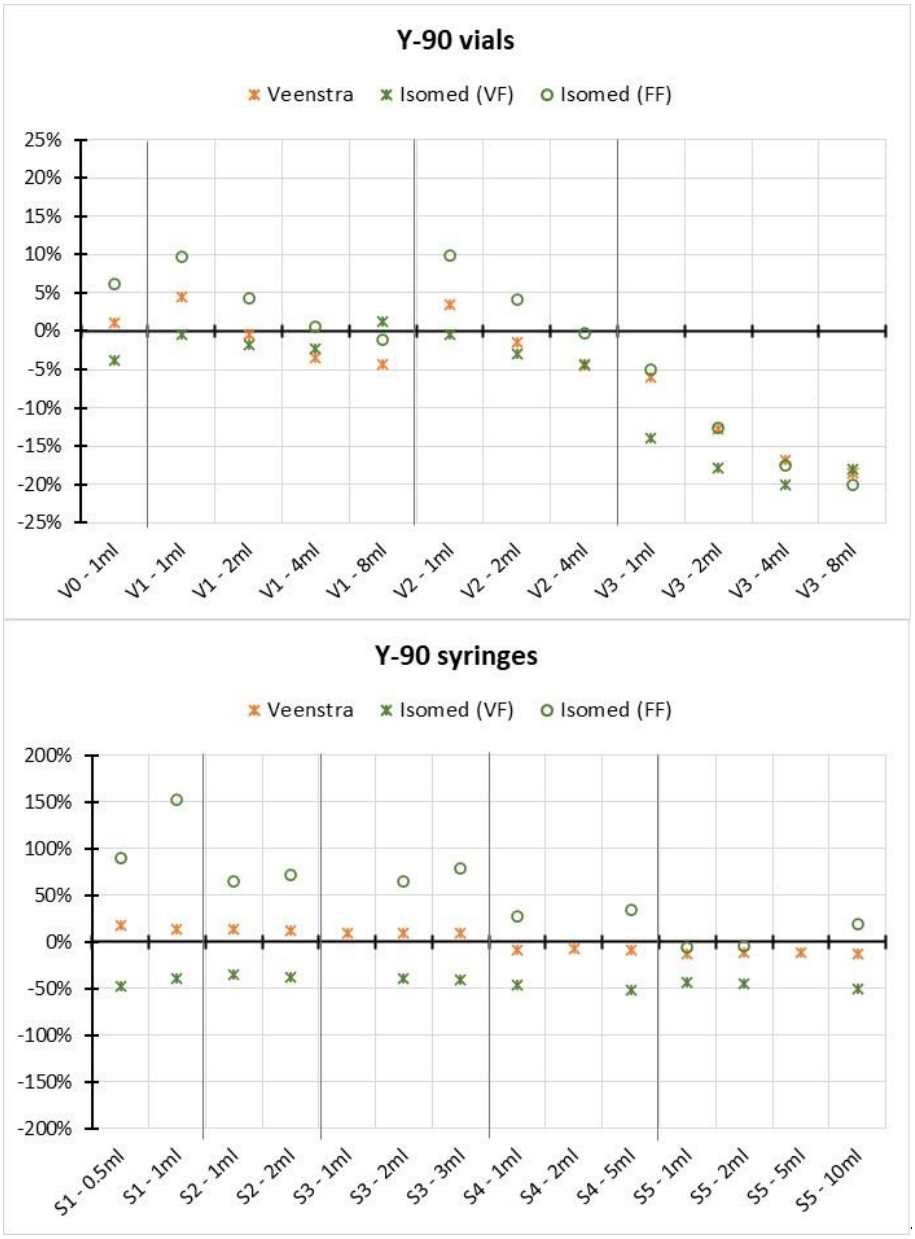

Figure 3: Relative activity differences between the measured and the reference values for the Y-90 sources in vial and syringe geometries at different fill-up volumes.

When purchasing an Isomed dose calibrator there is the possibility to acquire an accessory called Y-90 pSet which is an aluminium alloy dipper to act as the copper dipper in the case of I-123. The idea is that it will homogenise the dose calibrator response for different geometries when measuring Y-90. Measurements were performed using this accessory and the results are shown in the following figure. No special advantage was found on its use for the vials with only a slight improvement for the syringes.

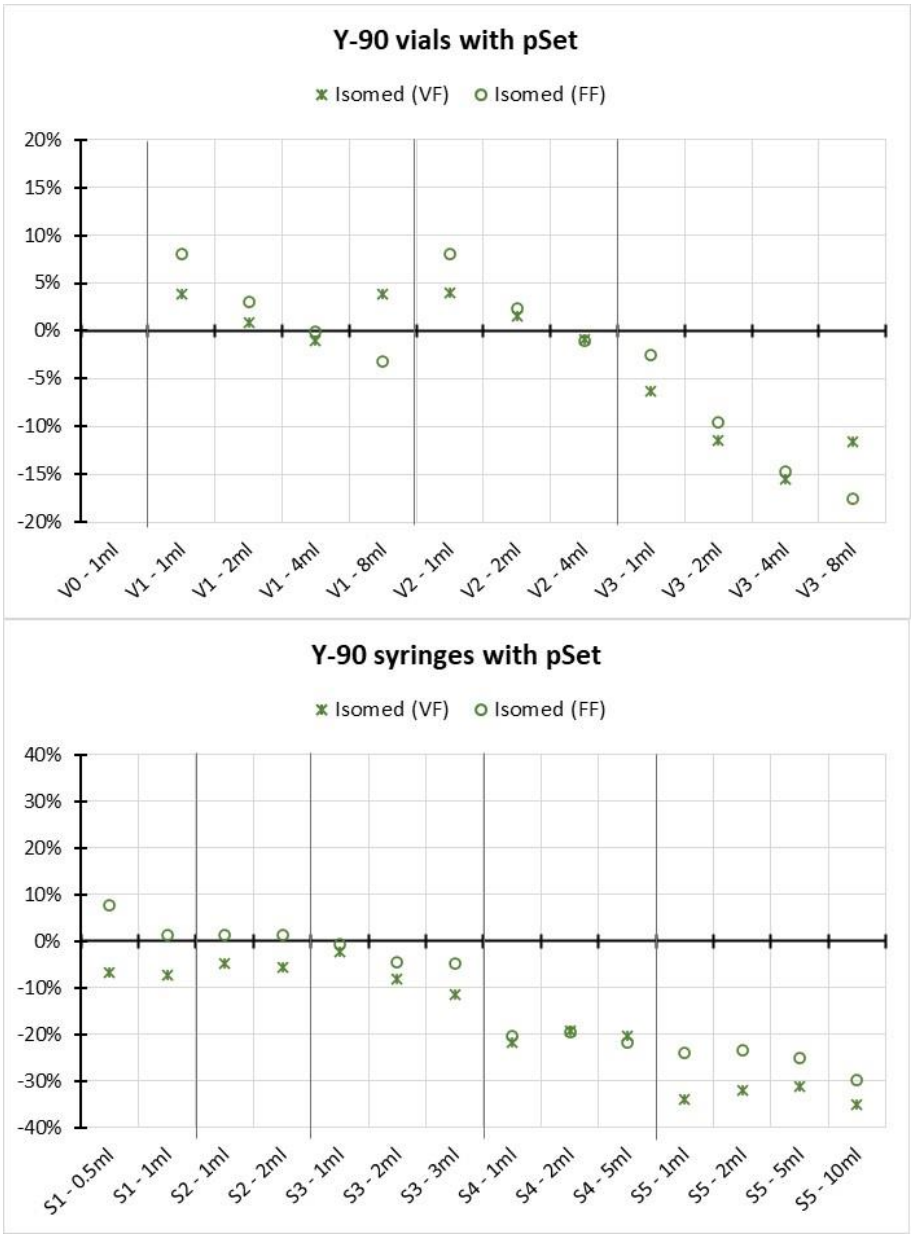

Figure 4: Plots showing the Isomed dose calibrator response when using the pSet with different source geometries for vials and for syringes.

4.7 Position dependence

The variation, within geometries, of the relative activity differences observed in the previous plots, are mainly due to the changes in the following parameters:

- position of the source in the ionisation chamber,
- container wall (material and thickness of the vials and syringes),
- geometry of the source itself (self-absorption).

A systematic investigation of the first of these parameters was performed using the special holder. The V0 reference vial of the 3 different radionuclides above (I-123, Lu-177 and Y-90) was used for that purpose. The measurements were taken in 10 mm steps from the lowest

point to within a few centimetres of the top of the well. When several different calibration coefficients are available, the best suited for a 5 ml vial filled with 1 ml was used.

Figure 5 shows the results for the I-123 measurements. Similar behaviour is observed with the two other isotopes.

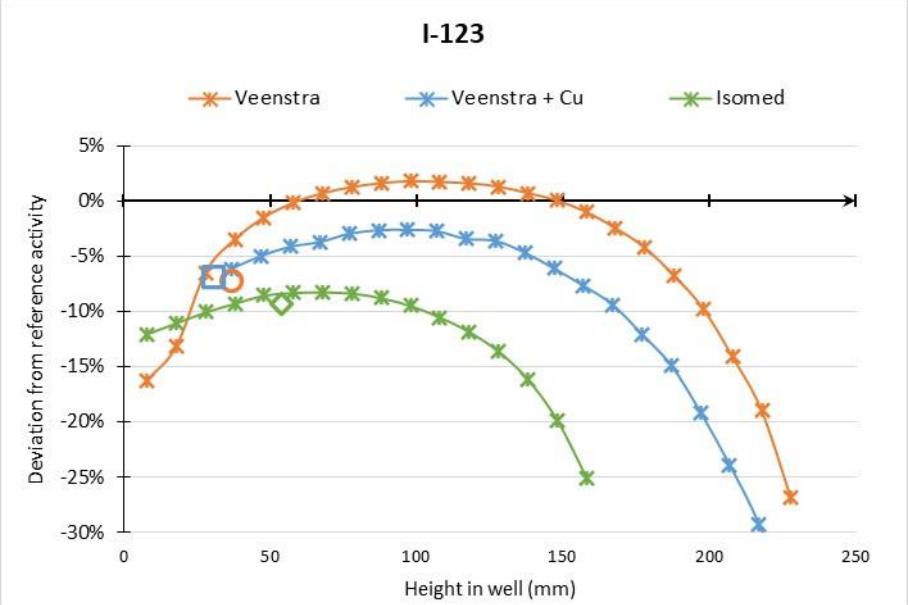

Figure 5: Height-dependence of the relative difference of activity for V0 vial filled with 1ml I-123 solution. The Veenstra results are also shown for the copper dipper in addition to the default configuration. The empty single symbols (square, circle and diamond) show the result when using the manufacturer's default holder in each dose calibrator.

These results suggest that some of the variations in the differences between different geometries from the reference activities observed in the measurements in the previous sections are due to measurement height differences. The results also stress the importance of always measuring the radioactive sources under the exact same conditions to ensure the validity of the result. In particular, the manufacturer's calibration coefficients are valid when used with the provided holder in its default location.

4.8 Discussion

4.8.1 I-123 measurements results

The results of the I-123 measurements (see Figure 1) show that the manufacturer’s default calibration coefficient cannot guarantee a 5% accuracy with respect to the reference value for any geometries.

In the Veenstra chamber, using a copper dipper to hold the sources reduces the difference between the responses with respect to the reference value. It allows the use of one mean calibration coefficient for vials and another for syringes. Without copper dipper, specific calibration coefficients must be used for each container type. Different filling volumes do not require specific coefficients.

4.8.2 Lu-177 measurements results

Lu-177 presents a varied response for different vials, and a more homogeneous one for the syringes (see figure 2). This means that a specific calibration coefficient should be used for each type of vial and a mean coefficient can be used for all syringes.

4.8.3 Y-90 measurements results

Y-90 shows a highly variable response depending on the measurement configuration that ranges between 5% and 20% deviation from the reference activity (see figure 3). In this case, dedicated calibration coefficients must be used for each measurement configuration meaning type of container and filling volume.

It is worth to mention that, in this study, Y-90 was measured in the form of a colloidal solution. It can also be frequently found in the form of glass or resin microspheres, in which case, the difference of the source geometry implies the use of specific calibration coefficients. This particular case is not investigated here, but it will be reviewed in a follow-up project.

5 WP 4: Report and recommendation - Conclusion

The results of the measurements carried out in this project show the importance of having calibration coefficients adapted to the measurement geometry used. Indeed, the difference between the measured and the reference activity may be as large as several tens of percent.

Using the default calibration coefficients provided by the dose calibrator manufacturer may not be advisable for all geometries for some radionuclides, and a specific calibration of the instrument may be needed. In Switzerland, both IRA and METAS can perform these specific calibrations providing traceability to international standards of activity. A strategy tailored to the needs of the user should be adopted for the calibration of the dose calibrator.

We can state the following rule of thumb: when there is a difference of more than ± 5% between the reference activity and the activity measured with the dose calibrator, it is recommended to recalculate the calibration coefficient. In order to simplify the use of different calibration coefficients among measurement geometries for the same radiopharmaceutical, an average calibration coefficient may be used when the absolute difference between the activity measured with individual and average coefficients is not greater than 5%.

For the radionuclides studied in this project, we can make the following recommendations:

Recommendation for I-123:

- A specific calibration coefficient for each geometry may be required and must be calculated on each dose calibrator. No dependence on the fill-up level is required.
- Using a copper dipper (Veenstra dose calibrator) would allow to define a single calibration coefficient for all vials and another one for all syringes. No dependence on the fill-up level is required.

Recommendation for Lu-177:

- The manufacturer’s default calibration coefficients allow the measurement within 5% with respect to the reference value for some glass vial types only (usually the one used by the provider to determine the calibration coefficient).

- For the other vial types and for syringes, a specific calibration coefficient is required.
- A single calibration coefficient can be used for all syringe types.
- For vials, calibration coefficients can be averaged for vials with similar size and thickness.
- No dependence on the fill-up level is required.

Recommendation for Y-90:

- The manufacturer's default calibration coefficients allow the measurement within 10% with respect to the reference value for some glass vial types or syringe types only.
- For the other vial and syringe types, as the measured deviations are large, a specific calibration coefficient is necessary, in particular for syringes.
- Different fill-up levels may require different calibration coefficients.

Other general recommendations:

- As the chamber response depends on the positioning of the source, whenever the holder of the dose calibrator is modified (as it is often the case in hot cell environments), it must be verified that the positioning of the sources to be measured is the same as in standard conditions.

The current legal provisions in Switzerland [4] do not address these issues and do not provide a specific procedure for these specially demanding radionuclides. The revision of the ordinance currently underway will provide an opportunity to make special provisions for the determination of calibration coefficients for the radionuclides particularly concerned by this problem.

Whenever new coefficients should be calculated, they must be obtained with sources of traceable activity, and the changes should be documented in a calibration certificate (of a reference source or of the dose calibrator itself) to be presented at the time of the instrument verification in order to allow for their metrological traceability.

The ageing of the instrument is one additional parameter that should be taken into account when tailoring the calibration strategy of a dose calibrator. The current legal provisions foresee a verification of the instrument, and it is required that the measured activity for these sources is within ±10% of their reference values (±20% for Sr-90/Y-90). This implies that a dose calibrator having drifted by nearly -10% (pressure loss is a common phenomenon which lowers the measured value after several years) would still be acceptable, but the calibration coefficients determined as it was newly installed would be unchanged and thus yield measurement results that have drifted by roughly the same amount. Therefore, a strategy to correct for this phenomenon is needed if an accuracy of ±5% is expected. Stability control using the dedicated source, required by the dose calibrator's quality control programme and OFSP's directive [5], is essential for monitoring this particular situation.

Visits to Nuclear Medicine services have shown that some users are not aware of these issues and that these requirements are not always applied consistently. A communication effort on the correct use of dose calibrators will be issued by the FOPH.

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