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Determination of volume-specific correction factors and geometry effects of ^{90}Y activity measurement in dose calibrators

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ABSTRACT

Background: Yttrium-90 (^{90}Y) is widely used in nuclear medicine for therapeutic purposes. The radiation dose of radiopharmaceuticals relates to the activity of the radionuclide which is measured in the dose calibrator during radiopharmaceutical preparations.

Objectives: The objectives of this study were to determine volume-specific correction factors and investigate the geometry effects of ^{90}Y activity measurement in dose calibrators.

Materials and methods: Four dose calibrators from two institutes were independently measured. The 3-mL plastic syringe and the 10-mL glass vial were used to investigate the geometry effects using the initial calibration factors for each dose calibrator. The comparison between actual activity and measured activity was expressed as the percentage errors. For volume-specific correction factor, the value for each volume was calculated based on the actual and measured activity at 0.5, 1.0, 1.5, 2.0 and 2.5 mL.

Results: Percentage error showed that ^{90}Y activity measured in the 3-mL plastic syringe and the 10-mL glass vial were inaccurate. The activity measurements in the 3-mL plastic syringe were more accurate than in the 10-mL glass vial at all volumes for both containers in all dose calibrators. Our findings showed that increasing the volume of ^{90}Y could result in underestimate of the measured activity. The maximum volume dependence in the 10-mL glass vial was about 20%. Hence, the volume-specific correction factors were determined for the 3-mL plastic syringe and the 10-mL glass vial for all dose calibrators.

Conclusion: The geometry effect could impact the ^{90}Y activity measurement on the dose calibrators. Using the volume-specific correction factor for each geometry of ^{90}Y to compensate for the geometry effect could improve the accuracy of ^{90}Y activity measurement. However, the volume-specific correction factors are depended on the dose calibrators. Therefore, the institutes need to establish their own volume-specific correction factors for ^{90}Y activity measurement.

Introduction

Yttrium-90 (^{90}Y) is a pure high-energy beta emitting with maximum energy of 2.27 MeV and average energy of 0.9336 MeV that has recently been used in nuclear medicine as a therapeutic radiopharmaceutical in many diseases, for example, hepatocellular carcinoma, non-Hodgkin's lymphoma and rheumatoid arthritis.[1] The radioactivity

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measurement of radiopharmaceuticals administrated to the patients should be considered due to it could influent the efficacy of the treatment. In nuclear medicine practice, the standard instrument used to measure the activity of radiopharmaceuticals is a radionuclide activity calibrator (or also called “a dose calibrator”).

Dose calibrator is a gas-filled detector operated in the ionization chamber region that contains the isotope selector and calibration factor (or “dial setting”) for the activity measurement of each radionuclide. In general, the calibration factor of each dose calibrator is recommended by the manufacturer which is specific to the geometry of the radionuclide. According to international recommendations, the error of administered activity for therapeutic radiopharmaceutical must not exceed 10% of the prescribed dose.[2] For ^{90}Y activity measurement, the containers with different compositions, thicknesses and source geometries can impact the accuracy ^{90}Y activity measurement due to the bremsstrahlung radiation produced from the ^{90}Y radionuclide with container and the dose calibrator chamber wall. Additionally, several studies showed that the calibration factor of ^{90}Y provided by the manufacturer of the dose calibrator might not be suitable for all the conditions of ^{90}Y activity measurement. [2-7]

Therefore, the primary objective of this study was to investigate the accuracy of ^{90}Y activity measurement in dose calibrators by varying the containers and the volumes of ^{90}Y using the initial calibration factor recommended by the manufacturer and routine calibration factor for each dose calibrator. Besides, this study was also aimed to determine the volume-specific correction factors and investigate the geometry effects of ^{90}Y activity measurement in the dose calibrators.

Materials and Methods

Yttrium chloride ($^{90}YCl_3$)

$^{90}YCl_3$ solution was obtained from the National Centre for Nuclear Research, Radioisotope Centre (Polatom, Otwock-Swierk, Poland) with the activity of 10 mCi or 370 MBq. The product data sheet that indicated the traceable activity concentration, volume, and total activity of the $^{90}YCl_3$ was received. Hydrochloric acid (HCl) was used to adjust the volume of $^{90}YCl_3$ in two containers starting at 0.5 mL. Then, increase the volume of the $^{90}YCl_3$ by adding HCl to 1.0, 1.5, 2.0 and 2.5 mL respectively to investigate the geometry effect on the ^{90}Y activity measurement. The decay correction was applied for the calculation of the actual activity as follow equation:

$$A = A_0 e^{-\lambda t} \qquad (1)$$

Where A is the actual activity of $^{90}YCl_3$ at the time of measurement, A_0 is the initial activity of $^{90}YCl_3$ at the calibration time and $e^{-\lambda t}$ is the decay factor of $^{90}YCl_3$.

Dose calibrators

Four dose calibrators from 2 different centers were used in this work including 2 dose calibrators at the Division of Nuclear Medicine, Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine Ramathibodi Hospital and 2 dose calibrators at the Thailand Institute of Nuclear Technology (TINT).

At Faculty of Medicine Ramathibodi Hospital, the activity of $^{90}YCl_3$ was measured in ATOMLAB 100Plus dose calibrator (Biodex Medical Systems, USA) and CRC®-25 PET dose calibrator (Capintec Inc., USA). According to manufacturer’s recommendation, the calibration factors for ^{90}Y measurement of Atomlab 100Plus and CRC®-25 PET dose calibrator were 375 and 074×10 respectively. At TINT, the activity of $^{90}YCl_3$ was measured in the CRC®-Ultra dose calibrator (Capintec Inc., USA) using the calibration factor of 048×10 and the Victoreen dose calibrator model 34-056 (Victoreen Inc.) using the calibration factor of 112.5×10.

Disposable syringe 3-mL with Combi-Stopper

For syringe measurement, 3 mCi of $^{90}YCl_3$ was aliquot into the 3-mL plastic syringe (Terumo, Japan) before adding HCl to the total volume of 0.5 mL and closed the end of the syringe with the Combi-Stopper (Braun, Melsungen, Germany). To measure the activity, the background radiation was measured and subtracted before measuring at least 3 times to obtain the average of measured activity in dose calibrators. The measurements were repeated by increasing the volume of $^{90}YCl_3$ to 1.0, 1.5, 2.0 and 2.5 mL respectively.

Glass vial 10-mL with rubber stopper

For vial measurement, 3 mCi of $^{90}YCl_3$ was aliquot into the 10-mL glass vial (Farris Laboratories Inc, Tx, USA) before adding HCL to the volume of 0.5 mL and closed the end of the vial with a rubber stopper. To measure the activity of $^{90}YCl_3$, the background radiation was measured and subtracted before measuring at least 3 times to obtain the average of measured activity in dose calibrators. The measurements were repeated by increasing the volume of $^{90}YCl_3$ to 1.0, 1.5, 2.0 and 2.5 mL respectively.

Investigation of the geometry effect

The actual activity and averaged measured activity for each geometry were compared to investigate the geometry effect of $^{90}YCl_3$ activity measurement in the term of percentage error that was calculated as follows:

$$\text{Percentage error (\%)} = \frac{\text{(Averaged measured activity-Actual activity)}}{\text{Actual activity}} \times 100 \qquad (2)$$

Determination of volume-specific correction factors for dose calibrators

Volume-specific correction factor for each geometry of $^{90}YCl_3$ was calculated as follows:

$$\text{Volum specific correction factor} = \frac{\text{Actual activity}}{\text{Average measured activity}} \qquad (3)$$

Results and Discussion

The response of dose calibrators to $^{90}YCl_3$ activity reading in different containers with the initial calibration factor recommended by the manufacturer and the influence of filling volume were explored in this work. The supplier’s traceable activity concentration was used as a reference activity, the decay corrected activity was calculated at the time of measurement.

The percentage errors between the measured activity and the actual activity in different dose calibrators with the initial calibration factors; ATOMLAB 100Plus, CRC®-25 PET, CRC®-Ultra and VICTOREEN model 34-056 are plotted in Figure 1 to Figure 4 respectively.

According to our findings with the initial calibration factors in four dose calibrators, almost all the percentage errors of the 3-mL plastic syringe were less than the 10-mL glass vial from four dose calibrators. Although one notice with volume of 0.5 mL measured on the VICTOREEN dose calibrator, the 10-mL glass vial was more accurate.

For the ATOMLAB 100 Plus dose calibrator with the initial calibration factor of 375, the percentage error of less than 5% were founded in the $^{90}YCl_3$ in the 3-mL plastic syringe in all volumes. Whereas the percentage errors were increased with the volume of $^{90}YCl_3$, the percentage errors were ranged between 17.98 to 24.65% in the 10-mL glass vial. According to manufacturer recommendation, the initial calibration factor of 375 of the ATOMLAB 100Plus dose calibrator was calibrated for the ^{90}Y-Zevalin with a volume of 3-9 mL in the 10-mL plastic syringe. In the 3-mL plastic syringe, our result showed that the percentage error for volume of 1 mL was higher when compared with the volume of 1.5, 2 and 2.5 mL. Hence, this correlated with our findings that the measurements in the plastic syringe were more accurate than the glass vial at all volumes, additionally for the plastic syringe, the higher volumes were resulted more accurate than the small volume.

Similar results were shown in the CRC®-25 PET and the CRC®-Ultra dose calibrators. The accuracy of measurement was better in the 3-mL plastic syringe when compared with the 10-mL glass vial. The differences of activity between the actual activity and the measured

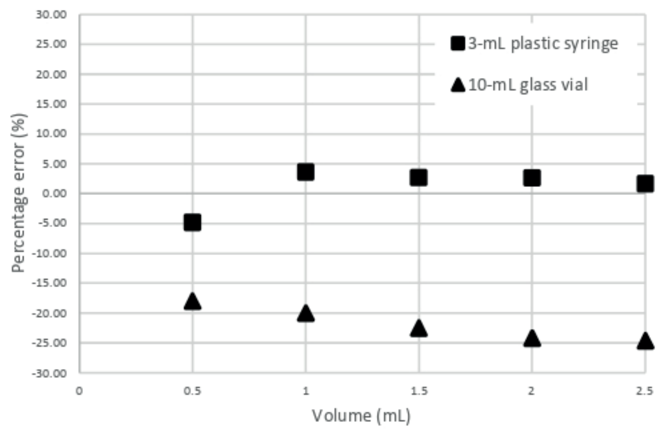

Figure 1 *Percentage errors between the measured activity and the actual activity measured on the ATOMLAB 100Plus dose calibrator with the initial calibration factor of 375.*

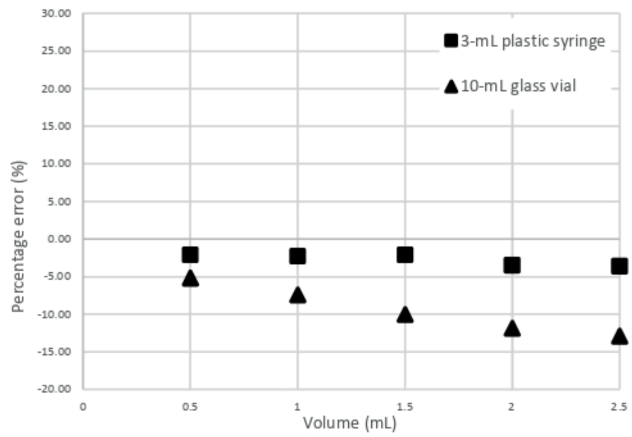

Figure 2 *Percentage errors between the measured activity and the actual activity measured on the CRC®-25 PET dose calibrator with the initial calibration factor of 074×10.*

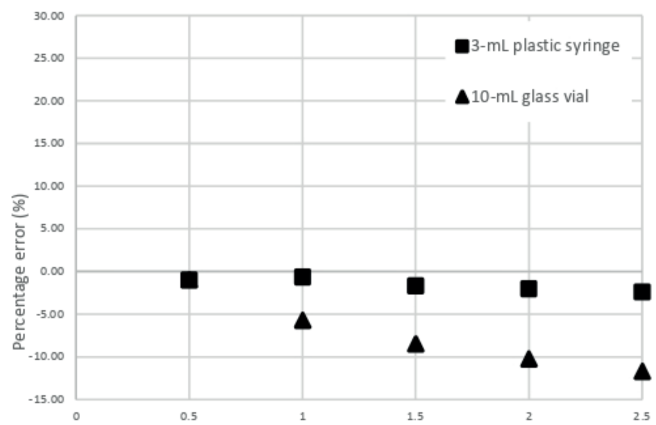

Figure 3 *Percentage errors between the measured activity and the actual activity measured on the CRC®-Ultra dose calibrator with the initial calibration factor of 048×10.*

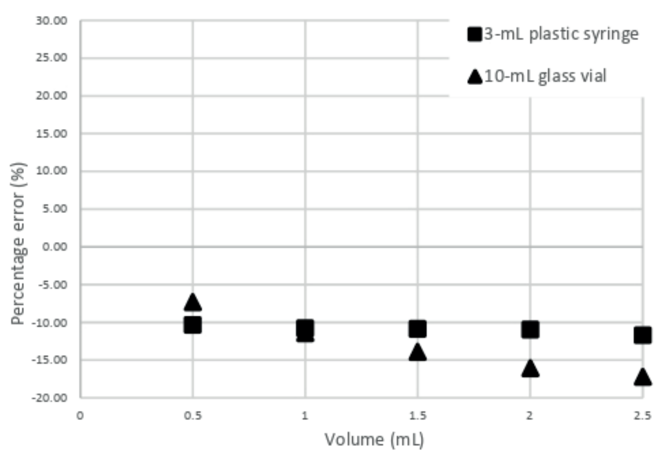

Figure 4 *Percentage errors between the measured activity and the actual activity measured on the VICTOREEN dose calibrator with the initial calibration factor of 112.5×10.*

activity were increased with the volume. Differences of up to 12.91 and 11.72 % for 2.5 mL of $^{90}YCl_3$ in the 10-mL glass vial for the CRC®-25 PET and the CRC®-Ultra dose calibrators respectively. For the CRC®-25 PET dose calibrator, the calibration factor of 074×10 is the routine calibration factor that was calibrated for ^{90}Y-citrate colloid measurement in the plastic syringe by user. As stated by Capintec™ manufacturer, the calibration factor of 48x10 (for the CRC®-Ultra dose calibrator) was calibrated for the 5 mL ^{90}Y solution in the 0.6 mm. glass ampoule.

In case of the VICTOREEN dose calibrator, almost all $^{90}YCl_3$ measurements with the routine calibration factor for ^{90}Y of 112.5x10 were differed from the actual activity more than 5% at all volumes. Differences of up to 11.76 and 17.24% were also found for the 2.5 mL $^{90}YCl_3$ solution in the 3-mL plastic syringe and the 10-mL glass vial respectively. This may occur from two reasons, firstly, the routine calibration factor for ^{90}Y of 112.5x10 is not suitable for the measurement in the 3-mL plastic syringe and the 10-mL glass vial because we don't know that the routine calibration factor for ^{90}Y of 112.5x10 was calibrated in which geometry of ^{90}Y. Secondly, the VICTOREEN dose calibrator was used for long time ago, the leakage of gas that filled in the chamber may cause of the error in the measurement.

The volume-specific correction factors for the plastic syringe and glass vial were also derived for ATOMLAB 100Plus, CRC®-25 PET, CRC®-Ultra and VICTOREEN model 34-056 dose calibrators (as tabulated in Table 1 to Table 4 respectively).

Table 1 Volume-specific correction factors for each volume of $^{90}YCl_3$ in both containers for the ATOMLAB 100Plus dose calibrator.

Volume (mL)	For 3-mL plastic syringe	For 10-mL glass vial
0.5	1.0490	1.2195
1.0	0.9675	1.2521
1.5	0.9737	1.2913
2.0	0.9735	1.3170
2.5	0.9832	1.3303

Table 2 Volume-specific correction factors for each volume of $^{90}YCl_3$ in both containers for the CRC®-25 PET dose calibrator.

Volume (mL)	For 3-mL plastic syringe	For 10-mL glass vial
0.5	1.0240	1.0528
1.0	1.0241	1.0833
1.5	1.0208	1.1128
2.0	1.0387	1.1346
2.5	1.0356	1.1451

Table 3 Volume-specific correction factors for each volume of $^{90}YCl_3$ in both containers for the CRC®-Ultra dose calibrator.

Volume (mL)	For 3-mL plastic syringe	For 10-mL glass vial
0.5	1.0102	1.0101
1.0	1.0068	1.0607
1.5	1.0173	1.0929
2.0	1.0210	1.1145
2.5	1.0247	1.1328

Table 4 Volume-specific correction factors for each volume of $^{90}YCl_3$ in both containers for the VICTOREEN model 34-056 dose calibrator.

Volume (mL)	For 3-mL plastic syringe	For 10-mL glass vial
0.5	1.1161	1.0794
1.0	1.1212	1.1293
1.5	1.1226	1.1621
2.0	1.1236	1.1918
2.5	1.1333	1.2083

Based on our study, inaccurate measurement may lead to error in administration of radiopharmaceutical. For clinical nuclear medicine, the administration of radiopharmaceutical should not be differed by more than ±10% of prescribed dose. For our results, the error in ^{90}Y measurement results from the interaction of radionuclide and surrounding materials which can produce bremsstrahlung radiation. The amount of bremsstrahlung radiation is proportional to the atomic number of materials that interact with a beta particle. In our work, the atomic number of the plastic syringe is lower than the glass vial, we assumed that the beta particles can travel through the plastic and interact with the structure of the dose calibrator which can generate more bremsstrahlung radiation so the measured activities of $^{90}YCl_3$ in the 3-mL plastic syringe were higher than in the 10-mL glass vial.[8, 9]

According to the reports from several studies, the uncertainty of the dose calibrator can occur when variations of the radiation sources geometry including type, size, thickness and shape of container and also volume of source.[5, 10-13] D Tyler and MJ Woods revealed the geometry effect of low energy photon activity measurement in the NPL (National Physical Laboratory) of the UK (United Kingdom) Report 56. Their results indicated that variations of the dose calibrator responses were certainly observed when the size of the container and volume of the source were varied especially for a beta emitter radionuclide like ^{90}Y.[5] In addition, Karsten *et al*. also reported the effect of ^{90}Y containers on 21 dose calibrators in 19 hospitals in Germany. Up to 95% of measurement with the P6-type vials were deviated within ±10% from th reference activity. However, the deviation was larger whe remeasured the ^{90}Y activity in their own syringe geometry. [12]

In our work, our resulted indicated that the one calibration factor was not suitable for measurement in al volumes. Consequently, the volume-specific correctio factors could use to improve the accuracy of $^{90}YCl_3$ activity measurement. As seen in our study, the differenc between measured and actual activity can be as much a 30%. This was agreed as the findings by many studies. [11, 13, 14] Hence, the volume-specific correction factors should be determined and applied to compensate the volume effect for ^{90}Y measurement.

Conclusion

This study demonstrated that the accuracy of dose reading of ^{90}Y was very sensitive by the geometry with the differences in containers and the volumes. The initial calibration factor could lead up to 25% error when measuring with the difference container and volume as specified by the dose calibrator's manufacturer. Therefore, it is recommended that the condition of initial calibration factor for each dose calibrator should be checked prior to the dose measurement, especially for ^{90}Y which the dose measurement is primarily affected from bremsstrahlung radiation produced from high energy beta interactions.

Based on our resulted, the effect of changing the volume could impact the accuracy as well even with the correct container. Using the volume-specific correction factor could improve the accuracy of ^{90}Y activity measurement. Hence, the institutes need to establish their own volume-specific correction factors for ^{90}Y activity measurement based on the stated pre-calibrated activity from manufacturer.

Conflict of interest

The authors declare no conflict of interest.

Ethic approval

This research is not involving with human subjects.

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