The standardization methods of radioactive sources ($^{125}\text{I}$, $^{131}\text{I}$, $^{99m}\text{Tc}$, and $^{18}\text{F}$) for calibrating nuclear medicine equipment in Indonesia

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Abstract. The standardization of radioactive sources ($^{125}\text{I}$, $^{131}\text{I}$, $^{99m}\text{Tc}$ and $^{18}\text{F}$) to calibrate the nuclear medicine equipment had been carried out in PTKMR-BATAN. This is necessary because the radioactive sources used in the field of nuclear medicine has a very short half-life in other that to obtain a quality measurement results require special treatment. Besides that, the use of nuclear medicine techniques in Indonesia develop rapidly. All the radioactive sources were prepared by gravimetric methods. Standardization of $^{125}\text{I}$ has been carried out by photon-photon coincidence methods, while the others have been carried out by gamma spectrometry methods. The standar sources are used to calibrate a Capintec CRC-7BT radionuclide calibrator. The results shows that calibration factor for Capintec CRC-7BT dose calibrator is 1.03; 1.02; 1.06; and 1.04 for $^{125}\text{I}$, $^{131}\text{I}$, $^{99m}\text{Tc}$ and $^{18}\text{F}$ respectively, by about 5 to 6 % of the expanded uncertainties.

1. Introduction

The utilization of nuclear technology in all fields has grown rapidly both in the international as well as in Indonesia. In their application, it is required the standard sources that meets the technical requirements so that their products have a sufficient level of quality. Some laboratories use standard to calibrate owned measuring apparatus, as well as the guarantor of quality for their products. One of the requirements that are used to obtain a qualified standard reference material will require an adequate level of homogeneity. Based on the duties and functions as a laboratory of national reference in the field of the measurement of radioactivity, then Center for Technology of Radiation Safety and Metrology (PTKMR-BATAN) must be able of provide a liquid standard source with various types that qualify as standard reference materials so that results of the measurement and testing of samples has a value of accurate, precise and traceable to the International System.

To solve that problems, it is required some procedures to calibrate the radionuclide calibrators that are used by hospitals for routine measurement of activity of $^{125}\text{I}$, $^{131}\text{I}$, $^{99m}\text{Tc}$ and $^{18}\text{F}$ that was administered to patients. Although $^{137}\text{Cs}$ is used to monitor the radionuclide calibrator, standards of $^{125}\text{I}$, $^{131}\text{I}$, $^{99m}\text{Tc}$ and $^{18}\text{F}$ are required to determine the calibration factors for this radionuclide.

Iodine-125 has a half-life of 59.388 (28) days, decay by electron capture and emits X-ray photon at 27 keV (112.5%), 31 keV (20.9%), 32 keV (4.5%), as well as $\gamma$-rays at 35.5 keV (6.6%) and Auger and conversion electrons between 22 and 35 keV (Chiste and Be, 2011). Iodine-131 has a half-life of 8.0233 (19) days, disintegrates through emission to the excited levels of $^{131}\text{Xe}$, the isomeric state $^{131m}\text{Xe}$ included, and $\gamma$-ray at 364.46 keV (82.6%), 636.97 keV (7.12%), and 722.89 keV (1.78 %),
Technicum-99m decays with a half-life of 6.0067(10) hours, mainly by isomeric transition to $^{99}$Tc. The most intense gamma transitions are 2.1726 keV (99.0%) and 140.511 keV (99.0%) (Chiste and Be, 2004). Fluorine-18 disintegrates to the ground state of $^{18}$O by positron emission with an intensity of 96.86(19) % and electron capture with an intensity of 3.14(19)%. The half-life of $^{18}$F is 1.8288 (3) hours. The positron has a maximum energy of 633.5 keV and an average energy of 249.3 keV. The 511 keV annihilation radiation following the positron emission has an intensity of 193.72 %. The decay data are those given by the International Bureau of Weights and Measures, or BIPM (BIPM, 2004).

This paper describes the procedures used to standardize the activity of $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F, and the results of the measurements used to calibrate the nuclear medicine equipments in Indonesia. The volume of $^{18}$F solutions used was about 16 ml because this is the volume most often used in hospitals. Vials that are used are made by Wheaton, USA and are made of borosilicate glass, with a volume of 20 ml, height of 55 mm, outer diameter of 30 mm, and thickness of 1 mm.

The PTKMR-BATAN Secondary Standard Ionization Chamber is a Capintec CRC-7BT radionuclide calibrator that is used as a working chamber for the routine dissemination of activity standards for photon emitting radionuclides. The calibrator is checked routinely to ensure constancy and relative accuracy using standard sources from national metrology institutes (NMIs). This apparatus is calibrated using standard sources that are calibrated by the gamma-ray spectrometry method for $^{131}$I, $^{99m}$Tc and $^{18}$F radionuclides, but for $^{125}$I is measured by absolute photon–photon coincidence counting methods. The activity concentrations of radioactive solutions are calibrated in the point source geometry first, and then standard sources are prepared in other geometries by careful gravimetric transfer of the calibrated solution into ampoules or vials.

2. Methodology

2.1. Preparation of sources

Source solutions of $^{125}$I and $^{131}$I in the form of potassium iodide (KI) in H$_2$O was diluted by a factor of 10.25 for $^{125}$I and 6.53 for $^{131}$I. From that solution, point sources were prepared by droping about 10 – 25 mg onto a thin polyethylene plastic backing. After dispensing the droplet of $^{125}$I and $^{131}$I onto the source support, a drop of AgNO$_3$ solution was added immediately to precipitate the volatile iodium anion ($I^-$) as AgI. In addition, the remainder of the original source and the dilution source solution of $^{125}$I were transferred into five PTKMR type glass ampoules. The masses of all samples, about 2 g, were determined gravimetrically using KERN ABT 220-5DM type balance, traceable to SI through the Calibration Laboratory of Indonesia.

$^{99m}$Tc solution is obtained from molydenum generator was prepared in the form of ampoules and thin film layer of mylar. Preparation was carried out by gravimetric method using a calibrated semi-micro balance device because it is more accurate than other methods. 5 pieces of point sources and 3 ampoules were prepared. All of the point sources were dripped on mylar buffer and then dried using infra-red lamp. The dried sources were covered with a mylar layer and coded and ready to be measured.

$^{18}$F is obtained through the reaction $^{18}$O(p, n)$^{18}$F using a cyclotron that is situated in a hospital in Jakarta. The chemical form of $^{18}$F that is used is FDG (Fluoro-deoxyglucose) without carrier solution. Three sets of measurements were made and, for each, between 3 and 5 point sources were prepared together with a single 16 ml liquid source in a vial. The $^{18}$F point source and the solution in the vial originated from the same master solution.

The point sources had a sample diameter of about 4 mm, and the weight varied between 10 and 15 mg. After drying under a heat lamp for about 30 minutes, they were then covered with a film of mylar with a ± 25 µg/cm$^2$ thickness. The samples was measured in the activity range of 10$^3$ Bq to 4.0 10$^5$ Bq. Preparation of the vials is done by gravimetric transfer of a volume of about 16 ml. The density of the solution was measured as 1.033 g/ml.
2.2. Activity measurement

2.2.1. Photon-photon gamma coincidence measurements. All of the $^{125}$I point sources were measured absolutely by a photon-photon coincidence system that was constructed in PTKMR-BATAN. The system using two NaI(Tl) detectors, crystal size of 76 mm diameter x 6 mm thickness with 0.5 mm aluminium window, connected to coincidence unit. The measurements were carried out twice with 25 replicates. Their activity was measured using source to detector distances ranging from 2 to 100 mm, to obtain varying detection efficiencies. Measurements were taken in the energy region between 13 and 100 keV. The duration for individual measurements varied between 100 s at low distance and 500 s at larger distances. Three counting rates were corrected for background, dead time and resolving time for the coincidence count rate. The activity of $^{125}$I was calculated using the equation for photon photon coincidence counting by Schrader and Walz (1987) and Schrader (1990, 2006).

2.2.2. $\gamma$-spectrometry measurements. The activities of all of the point sources were measured by gamma spectrometry. The detector is an HPGe model GC1018 (Canberra, USA), which has a relative efficiency of 10.3% with an energy resolution of 1.69 keV FWHM at 1332.5 keV. The detector is equipped with a model 2002CSL pre-amplifier, and a Canberra model 2020 amplifier and operates at a bias voltage of +4500 V. Signals from the detector are processed by the Canberra gamma spectrum analysis system using GENIE 2000 software (Canberra Industries, USA). The source-to-detector distance was 25 cm. As described above, the gamma-ray spectrometry system was first calibrated using standard sources of $^{152}$Eu, $^{60}$Co and $^{137}$Cs that have traceability to the SI. Three sets of measurements were made with a counting time of 10 minutes in each case. Impurities were also checked using gamma spectrometry.

2.2.3. Measurement with ionization chamber. All of the liquid solutions in ampoule or vial glass were measured using the Capintec radionuclide calibrator ionization chamber in two ways, firstly with the predefined calibration factor corresponding to the each ($^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F) button on the activity calibrator and secondly using the dial setting determination method. Preset push-buttons are provided for quick selection of the calibration number of the most often used radioisotopes. Thus, the calibration settings for each radionuclide and geometry should be determined individually.

The determination of the appropriate dial settings in this work was achieved in the manner described by Zimmerman and Cessna (2000). The ratio, R, of the activity measured with the special button on the standard activity, is determined after the gamma spectrometry activity results are known. The ratio R is given by $R = \frac{A_{std}}{A_{cap}}$, where $A_{std}$ is the activity of standard source and $A_{cap}$ is the activity measured by the Capintec radionuclide calibrator. This R value can be used directly as a calibration factor for the $^{18}$F and $^{99m}$Tc when the special button or calibration setting number is used.

3. Results and discussion

The efficiency ($\varepsilon_1$, $\varepsilon_2$) of the detector varied between 0.12 to 0.05. This values is determined by variation of the detector to source distance between 2 mm to 100 mm. The absolute activities of $^{125}$I source could be obtained from a plot of the activity distribution versus $x = f(\varepsilon_1, \varepsilon_2)$, as shown in figure 1. The relative standard deviation (counting statistics) of the measurement result for individual sources varied from 0.4% to 0.5%. The average activity concentration of the $^{125}$I solution derived from photon-photon coincidence measurement results was (441.7 ± 4.0) kBq g$^{-1}$. The relative standard uncertainty components are presented in table 1.

The result of the efficiency calibration for the HPGe detector using $^{152}$Eu, $^{60}$Co and $^{137}$Cs standard sources is shown in figure 2. The energies used to produce the efficiency calibration curve were 244.7, 344.3, 661.6, 778.9, 964.1, 1112.1, 1173.2, 1332.4, 1408.0 keV, resulting in a curve described by the equation efficiency at energy $E = 0.1598 e^{-0.98}$ with a correlation coefficient of 0.9998. The uncertainty of the interpolated efficiency at any point is 1.5 % at $k = 1$. This value was
determined from the residuals between the true efficiencies and the efficiencies obtained from the efficiency curve.

There was no significant impurity detected above 0.05% of the $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F activity. This value was determined when the Capintec radionuclide calibrator was calibrated. The counting time was 10 minutes, and the time difference between the gamma spectrometry and Capintec radionuclide calibrator measurements was about 8 half-lives of $^{131}$I, $^{99m}$Tc and $^{18}$F, respectively. The results of the activity determinations of the $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F solution are shown in table 2. The corrections on standardization of radioactive sources are impurity, dead time, background counts, half-life, and decay on process of counting.

![Figure 1. An example of activity distribution versus $x = f(\varepsilon_1, \varepsilon_2)$](image)

| Component                  | $U_r$(%) | Type |
|----------------------------|---------|------|
| Statistics counting        | 0.54    | A    |
| Counting time              | 0.035   | B    |
| Weighing                   | 0.2     | B    |
| Dead time                  | 0.05    | B    |
| Background                 | 0.35    | B    |
| Resolving time             | 0.1     | B    |
| Decay parameters           | 0.13    | B    |
| Impurity                   | 0       | -    |
| Extrapolation              | 0.5     | B    |
| Combined Uncertainty (k=1) | 0.86    |      |

**Table 1.** Relative uncertainty components of the $^{125}$I activity concentrations (in %).

| Nuclide | Activity (MBq) | Methods     | Dose calibrator (MBq) | Calibration Factor |
|---------|----------------|-------------|------------------------|--------------------|
| $^{125}$I | 7.30           | coincidence | 7.11                   | 1.03               |
| $^{131}$I | 109.23         | spectrometry| 107.22                 | 1.02               |
| $^{99m}$Tc | 214.67         | spectrometry| 201.67                 | 1.06               |
| $^{18}$F  | 744.82         | spectrometry| 715.23                 | 1.04               |

Table 3, shows some types of components used to determine the value of the measurement an expanded uncertainty that used the gamma spectrometer equipment, dose calibrator and the coincidence system. Several components have the same uncertainty value, this is because the standard sources used are the same, namely $^{152}$Eu, $^{137}$Cs, and $^{60}$Co. The experimental results showed that if the
specific button is used for about 16 ml solutions, the correction factor, R, would be 1.03, 1.02, 1.06, and 1.04 for $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F, respectively; with an expanded uncertainty of 4.9, 5.7, 5.6, and 5.7 % with 95 % of confidence level at coverage factor, $k=2$. $^{125}$I has an expanded uncertainty smallest because it used absolute methods for standardizing that nuclide.

![Figure 2. Efficiency calibration curve using $^{152}$Eu, $^{60}$Co and $^{137}$Cs standard sources.](image)

**Table 3.** Uncertainty components for the R-value determined by gamma-ray spectrometer and dose calibrator for $^{125}$I, $^{131}$I, $^{99m}$Tc, and $^{18}$F.

| Source of uncertainty                  | $^{125}$I | $^{131}$I | $^{99m}$Tc | $^{18}$F | Type |
|----------------------------------------|-----------|-----------|------------|---------|------|
| **Gamma-ray Spectrometer:**            |           |           |            |         |      |
| Standard Source                        | -         | 0.5       | 0.5        | 0.5     | B    |
| Half-life of standard                  | -         | 0.12      | 0.12       | 0.12    | B    |
| Efficiency                             | -         | 1.5       | 1.5        | 1.5     | B    |
| Intensity of sample                    | -         | 0.6158    | 0.2695     | 0.1962  | B    |
| Half life of sample                    | -         | 0.0237    | 0.0166     | 0.0164  | B    |
| Area of sample                         | -         | 0.56      | 0.56       | 0.67    | A    |
| Dead time                              | -         | 0.05      | 0.05       | 0.05    | B    |
| **Photon-photon coincidence**          | 0.86      | -         | -          | -       | Comb.|
| **Ionization chamber:**                |           |           |            |         |      |
| Half-life of sample                    | 0.0471    | 0.0237    | 0.0166     | 0.0164  | B    |
| Statistics of counting                 | 0.60      | 0.50      | 0.48       | 0.6     | A    |
| Detector response                      | 1.155     | 1.155     | 1.155      | 1.155   | B    |
| Accuracy of reading                    | 1.732     | 1.732     | 1.732      | 1.732   | B    |
| Repeatability                          | 0.577     | 0.577     | 0.577      | 0.577   | B    |
| Non-linearity                          | 0.35      | 0.35      | 0.35       | 0.35    | B    |
| Mass                                   | 0.05      | 0.05      | 0.05       | 0.05    | B    |
| Combined standard uncertainty          | 2.45      | 2.87      | 2.82       | 2.86    |      |
| Expanded Uncertainty (k = 2)           | 4.9       | 5.7       | 5.6        | 5.7     |      |

**4. Conclusion**

Standardization of radioactive sources $^{125}$I, $^{131}$I, $^{99m}$Tc, and $^{18}$F have been successfully carried out in PTKMR – BATAN. The use of standard sources that has been standardized by PTKMR can well be used to calibrate the dose calibrator Capintec CRC 7 BT. Calibration factor values of dose calibrator are 1.03; 1.02; 1.06; 1.04 respectively for the source of $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F, with the value of the expanded uncertainty of a stretch of 4.9, 5.7, 5.6, and 5.7 for a confidence level of 95 % at coverage factor, $k = 2$. PTKMR-BATAN can calibrate the equipment in field of nuclear medicine using a short half-life of $^{125}$I, $^{131}$I, $^{99m}$Tc and $^{18}$F standard source.

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**Acknowledgments**

This activity is funded by DIPA budget of PTKMR-BATAN in 2013-2014 fiscal. The author would like to thank the Government of Indonesia, especially the leaders of all ranks BATAN which has provided the opportunity to successfully complete this study.