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The Absolute Standardization Methods of ^{32}P for Calibrate Nuclear Medicine Instruments in Indonesia

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ABSTRACT

The absolute standardization of ^{32}P radioactive sources employed to calibrate nuclear medicine instruments has been conducted at PTKMR-BATAN. We deemed this activity to be necessary since ^{32}P used in the nuclear medicine fields has a short half-life, and in order to obtain a result of quality measurement, it requires a special treatment. Moreover, in Indonesia, the use of nuclear medicine techniques has developed rapidly. We prepared all the radioactive sources with a gravimetric method by using a *KERN ABT 220-5DM* semi-micro type scale, traceable to the International Unit System. We conducted the ^{32}P standardization by employing a 4πβ(PS)-γ coincidence method with ^{60}Co as a tracer; meanwhile, we conducted the impurity measurement by employing a beta spectrometer system. The result of ^{32}P absolute measurement was 380.05 Bq/mg with a 0.68-percent range uncertainty, with a k=2 coverage factor. This value was used to calibrate a "Capintec CRC-7BT" dose calibrator that was a secondary standard instrument in PTKMR-BATAN. The results showed us that the calibration factor of the "Capintec CRC-7BT" dose calibrator was 1.12 with a 4.7-percent uncertainty.

INTRODUCTION

Nuclear engineering has been applied in the medical fields since late 60s in Indonesia after the first Indonesian atomic reactor has been operated in Bandung. Some Indonesian experts were assisted by foreign experts pioneering the establishment of a nuclear medicine unit at Bandung Atomic Reactor Center (now called Center for Science and Nuclear Technology Application - National Nuclear Energy Agency of Indonesia). In its early days, various obstacles in the development of nuclear medicine in Indonesia occured such as lack of experts, problems in the procurement of radio-pharmaceutical/ radioisotopes, inspection fees deemed to be high, and lack of the nuclear medicine popularity among the public. How nuclear medicine units are required in a country varies greatly depending on the level of its technological advancement, its society's socioeconomic situation, and the level of its priority on the health sector. So far, the health sector has always been deemed to be important in Indonesia and has been made a main priority in the development of the nation.

This study was aimed at describing procedures employed to standardize ^{32}P activities nby using a 4phi beta (plastic scintillation)-gamma coincidence method, with ^{60}Co as a tracer; subsequently, the results of this measurement were used to calibrate PTKMR-BATAN's Secondary Standard Ionization Chamber and nuclear medicine instruments in Indonesia.

A ^{32}P nucleus contains 15 protons and 17 neutrons, one neutron more than that of the most common phosphorus isotope, phosphorus-31 as shown in Fig. 1. ^{32}P has a 14.284-(36)-days half-life, decays with an electron capture model and emits X-ray photon the energy of which is 27 keV (112.5 %), 31 keV (20.9 %), 32 keV (4.5 %). Moreover, it emits

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γ–rays the energy of which is 35.5 keV (6.6 %). Moreover, an Auger electron is found, and there is a conversion of electrons between 22 keV and 35 keV; the average beta spectrum energy is 695 keV and its maximum energy is 1.71 MeV. Furthermore, an average 1.18 keV energy per disintegration is emitted as an internal *bremsstrahlung* [1].

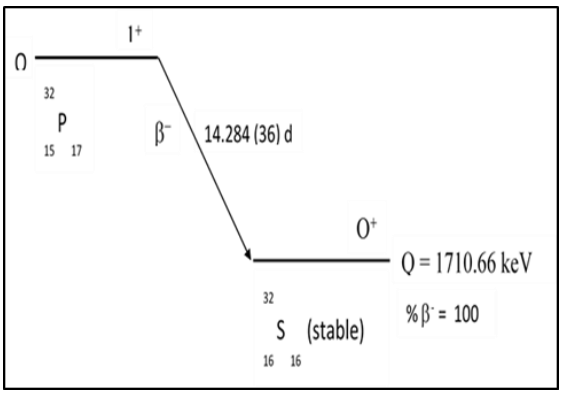


Fig. 1. Decay Schema of ^{32}P [1].

Phosphorus is found in various organic molecules; moreover, ^{32}P is applied in various uses in the medical, biochemical and molecular biology sectors since it can be used to trace a phosphorylated molecule. For instance, it is used to elucidate a metabolism pathway and to radioactively label a DNA. ^{32}P was clinically attempted to be applied in 1930s for the first time [2-5]. Since then, ^{32}P usage has generally been restricted to its colloidal suspension form. ^{32}P form is a component of a complex, insoluble particle [6-9]. ^{32}P is used to detect ophthalmological diseases, tumors, and so on. It can also treat a *polycythemia rubavera* disease, which is the formation of excessive red blood cells. When used, an ^{32}P isotope is injected into the body or tumor, so it will emit beta rays that can inhibit the formation of red blood cells in the spinal cord. In this case, the colloidal suspension prevents the radioisotope from leaving the intended target and disseminating throughout the body.

The Secondary Standard Ionization Chamber belonging to PTKMR-BATAN is a "Capintec CRC-7BT" dose calibrator serving as as a working chamber used to measure the sources of a photon-emitting radionuclide routinely. This dose calibrator is routinely checked up to ensure its relative constancy and accuracy with a standard source obtained from National Metrology Institutes (NMIs) such as the *Physikalisch-Technische Bundesanstalt* (PTB-Germany), *the National Bureau of Standards* (NBS, now the National Institute of Standards and Technology, NIST-USA), the National Measurement Institute of Japan (NMIJ), and PTKMR–BATAN - Indonesia.

This apparatus was calibrated using a standard source standardized with a gamma-ray spectrometry method for ^{137}Cs, ^{60}Co, ^{133}Ba, and ^{99m}Tc *radionuclides*, while ^{131}I and ^{18}F *radionuclides* were standardized absolutely with a 4π β–γ coincidence method; however, ^{125}I is measured with an absolute photon–photon coincidence counting method [10,11].

The standard sources used to calibrate the gamma-ray spectrometer were point sources of ^{152}Eu, ^{137}Cs, ^{60}Co and other point-sources obtained from NMIs and PTKMR-BATAN. The activity concentrations of those radioactive solutions were standardized in the point-source geometry first. Next, that solution standard radioactive solution was prepared in another geometry such in an ampule or vial.

EXPERIMENTAL METHODS

Since ^{32}P radioisotope is a source of pure beta emitters, we cannot directly measure it by using a 4πβ (PS)-γ coincidence system. Accordingly, we use ^{60}Co as a tracer, so we can determine ^{32}P activities absolutely with a higher degree of accuracy. Therefore, when we use it to calibrate a nuclear instrument, it will result in a more precise and accurate measurement value. There were several steps taken in this work. First, we prepared the source of ^{60}Co and measure its activities absolutely. Then, we mixed that ^{60}Co with a ^{32}P radioactive source with a certain ratio and measured the activities of those mixed sources with an absolute method. Next, we determined the activities of the ^{32}P source and made some corrections. Finally, we calibrated the secondary standard equipments that PTKMR-BATAN owned and radioactivity measurement equipments at a nuclear medicine facility in various Indonesian hospitals.

Sources preparation

^{60}Co was obtained from a radioisotope produced at *Amersham*. We prepared it by dripping it on a plastic 98 UPS scintillation. ^{32}P samples (in terms of H_3PO_4 in a HCl solution) was produced by using a thermal neutron irradiation (about 10^{14} neutrons cm^{-2} sec^{-1}) in the Multi-Purpose Siwabessy Research Reactor, Serpong - Indonesia. We relied its production on the ^{32}S (n, p) ^{32}P reaction.

A portion of the ^{32}P solution was mixed with a standardized ^{60}Co solution and partially placed in a 20 ml glass vial in three pieces. The volume of those ^{32}P solutions that were used amounted to about 16 ml since that was the amount of the volume most frequently used in hospitals. The vials that were used

were made by *Wheaton*, USA and were made of *borosilicate* glass, with a 20-ml volume, a 55-mm-tall height, a 30-mm outer diameter and a 1-mm thickness. The mixed solutions of ^{32}P and ^{60}Co were dropped onto a plastic scintillator. Afterwards, those solutions were dried in an infra-red ray. Finally, we covered it with the same plastic. The amounts of ^{60}Co solutions, mixed solutions (^{60}Co and ^{32}P), and ^{32}P solution in the vial glass container were determined with a *gravimetry* method by using a calibrated semi micro scale.

In addition, the ^{32}P source was prepared in a stainless steel plan-set with a 5-cm diameter. The number of ^{32}P sources that were prepared was 10 sources with weights varying from 8 mg to 110 mg. We took this step in order to determine the self-absorption correction of the ^{32}P sources.

Radioactivity measurement

We measured the ^{32}P radioactivity absolutely by using a 4πβ (PS)-γ coincidence system with ^{60}Co as a tracer. This system consisted of β detectors to detect the β particles and NaI(Tl) detectors to detect photons and some electronics modules to analyze the pulses. The full solid angles of β – detectors consisted of disc-like plastic scintillators combined into one in the Photo-multiplier tube (PMT). A UPS-89 plastic scintillating material was used since it had a highlight output, a fast response to rising time amounting to 0.9 nses and a decay time amounting to 2.4 ns; moreover, it was rather insensitive to photons. Its 418-nm maximum emission wavelength matched the optimum sensitivity of our photo-multiplier well.

The geometry of those β detectors consisted of a 25-mm-high and a 25-mm-diameter cylinder fitted together from two well-polished plastic cylinders. The lower one was 10 mm high and its diameter was 25 mm. The diameter of its disk center was.17 mm with a 2-mm-thick bore on top of it. This mountain could be the locus of a directly-deposited radioactive liquid and could hold the radioactive sources on a piece of VYNS film or Mylar sheet. The top one was 15 mm high and its diameter was 25 mm with with disc-like cavity on the bottom, the height of which was 4 mm and the diameter of which was 17.5 mm designed to accommodate the source stand of the lower scintillator. Figure 2 showed us the sketch. Each of the cylinders was manufactured as a single scintillating piece. Both of the cylinders were kept together through the viscosity of optical grease, instead of through the cement, since the shape of geometry like this was mainly intended to be reusable. This scintillating arrangement was made tight in contact with the PMT window through an acetal resin casing that fitted the PMT housing.

The scintillator could be assembled with and coupled to a selected low-noise *Photonis XP3132* PMT. The commercial voltage divider of this PMT (VD101/A) was modified to be operated in positive polarity (950 Volt) to reduce noise. The typical background count rate was about 1.3 cps. Ratio of the valley peak to a single electron response to this PMT was about 2, so we found no difficulties to set a low-level discrimination in the mid-valley of the single-electron capture.

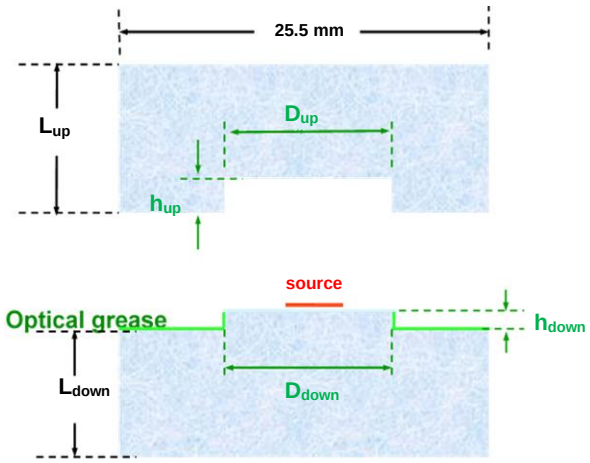


Fig. 2. Geometry of β detector. D = 25 mm, L_{up} = 15 mm and L_{down} = 10 mm. The mounting on the lower cylinder can support radioactive drops or a radioactive source on a VYNS film or Mylar sheet.

This 4πβ detector rested vertically on top of a 5-by-5-inch NaI (Tl) single crystal that was produced by Quartz & Silice (type 127-SPE-127). The source sitting on top of NaI (Tl) interacted with the gamma detector. The photo-multiplier connected to the crystal was an RTC XP2050 type. The crystal and photo-multiplier was housed in the cube shape of 50 cm of side size and 5 cm thick of shielding.

The γ detector pulses were processed by a chain involving a charge-sensitive *Canberra* pre amplifier Model 2005 and an *Ortec* 460 double delay lines amplifiers. The amplifier's bipolar pulses are put in an *Ortec* 420A timing single channel analyzer (timing SCA). The amplifier's uni-polar pulse was the output to a multichannel analyzer to set, when activated by the logic signals derived from the SCA timing. The low-energy discrimination window or threshold served as the basis of calculation. The β channel signals were processed with an analog processing with the exception that the amplifier used here was a fast *Canberra* 2024 amplifier.

The logic output of the SCAs from both of the channels was put in an in-house module that served to impose a non-extending dead-time range and to tune up the delays in the beta and gamma channels and the width of coincidence windows [12,13]. A 20-μs dead-time was typically employed as a safeguard against the PMT after the pulses or scintillator phosphorescence even though the time spectroscopy of the β-channel with a multi-channel scaler indicated no significant pulses afterwards within 45 μs of the incoming main β–pulses. The measurements were normally taken one day after the plastic scintillation samples were prepared and they were always loaded and changed into a dark room. The delay in the arrival time of spectra between the beta and gamma channel pulses have typical FWHMs ranging from 30 ns to 40 ns, but its 1.1-μs coincidence window was generally used to capture all coincidence pulses.

To obtain various detection efficiencies, we retrieved the measurement data with a beta discriminator variation starting at 0.50 μvolts [14-16]. We determined the absolute activity by using an extrapolation method at a 100-percent detection efficiency. The absolute activity determined with using this method was intended for the ^{60}Co sources and mixed ^{60}Co and ^{32}P sources. The absolute activity of ^{32}P was determined using the equation:

$$Aj_2 = [\{Ajc\ (m_1 + m_2) - (Aj_1 \times m_1)\} / m_2] \quad (1)$$

with:

m_1 = the weight of ^{60}Co in mixed source
m_2 = the weight of ^{32}P in mixed source
Aj_1 = the activity concentration of tracer
Aj_2 = the activity concentration of ^{32}P
Aj_c = the activity concentration of mixed source

After the source activity of ^{32}P could be determined, that activity value was used to calibrate the secondary standard measuring instrument of PTKMR - BATAN as a reference laboratory and also belongs to hospitals in Indonesia. The source used to calibrate was in a 20 ml vial and in the ampules of the PTKMR-BATAN standard.

RESULTS AND DISCUSSION

We had identified that the radionuclide impurity in the ^{32}P solution was ^{33}P. It was unavoidable for it not to be contaminated by ^{33}P (T1/2 = 25.34 days) as a byproduct of ^{33}S (n, P) ^{33}P reaction due to the use of a fast-neutron (65 mb) and thermal neutron (2.3 mb). We checked the impurities by using a beta spectrometer system. We found out that he nuclide impurity was 1 % of ^{33}P in ^{32}P at the initial time. This method was used based on the physical properties of ^{32}P and ^{33}P, where the half-life and maximum beta energy of both of those two sources were significantly different. We made a continuous observation up to several half-life periods. We found out that the amount of impurity contained in the ^{32}P source could be determined. Our estimating the ^{33}P contamination using the calculation gave us approximately 0.7 % at the end of irradiation. This calculation was extended to about 1 % during the measurement time. 1 % of that ^{33}P impurity for that ^{32}P contributed to around 0.7 % due to the thermal power developed by the ^{32}P disintegration accounting for one tenth of ^{32}P.

Figure 3, showed us the correlation curves between the specific disintegration rate and the weights of the samples. We could observe from the curve that the heavier the sample was, the lower the specific disintegration rate would be. This finding showed us that there was a self-absorption factor in the ^{32}P sources that showed us that the heavier the sample was, the higher its absorption factor would be.

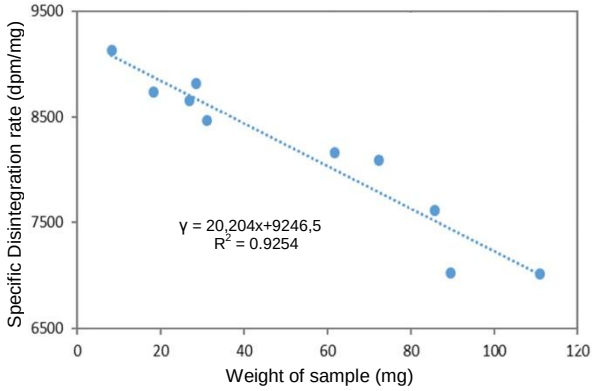
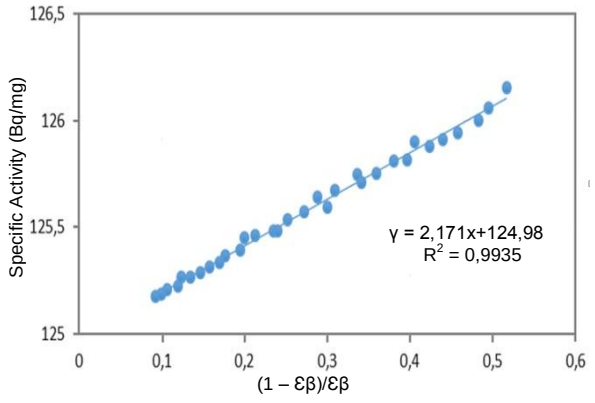


Fig. 3. Self Absorption curve of ^{32}P.

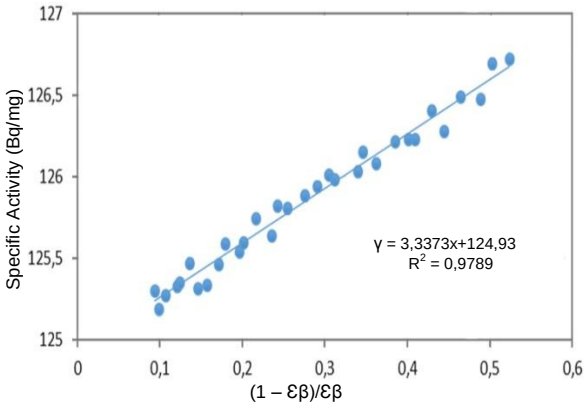
Figures 4(a) and 4(b) showed us the extrapolation curve of the ^{60}Co efficiency using a 4πβ (PS)–γ coincidence system. From the figures, we found out that there were two efficiency curves obtained from the 1173-keV and 1332.5-keV gamma energies. We determined the ^{60}Co activity value by drawing the extrapolation line to a value amounting to ε_β = 100 %.



(a)

Fig. 4(a). Efficiency Curve with superimposed fitting line for 1173 keV gamma energy of ^{60}Co.

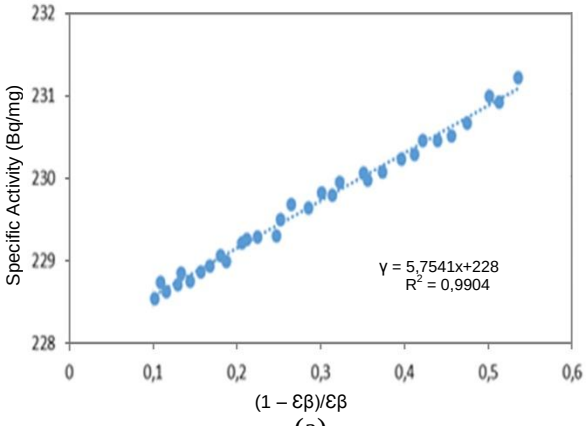
We we found out that the ^{60}Co activity was 124,98 Bq / mg received from the 1173-keV gamma energy gate. Moreover, we found out that the ^{60}Co activity was 124.98 ± 0.4 Bq/mg received from the 1332.5-keV gamma energy gate. The activity result of ^{60}Co was determined by the average value of the second gamma energy.



(b)

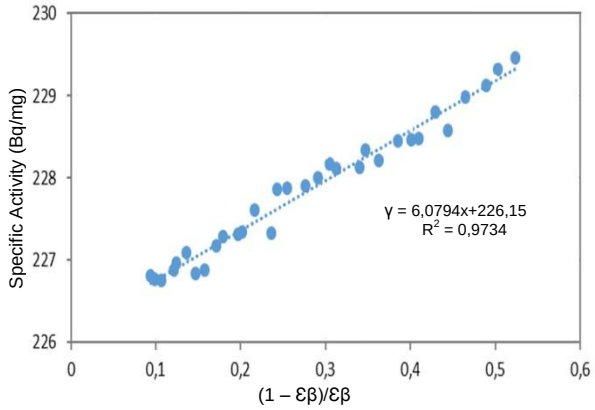
Fig. 4(b). Efficiency Curve with superimposed fitting line for 1332.5 keV gamma energy of ^{60}Co.

Figures 5(a) and 5(b) showed us the extrapolation curve of the mixed sources efficiency of ^{32}P and ^{60}Co using a 4πβ-γ coincidence system. From the figures, we found out that there were two curves of efficiency obtained from the 1173-keV and 1332.5-keV gamma energies. The activity value of the mix sources was determined by drawing the extrapolation line to a value with ε_β = 100 %. We found out that the activity of the mixed sources was 228.00 ± 0.4 Bq/mg from the 1173-keV gamma energy gate and that the activity of the mixed sources was 226.15 ± 0.4 Bq/mg from the 1332.5-keV gamma energy gate. The specific activity of the mixed sources was determined with the average value of the second gamma energy result. We found out that the absolute specific activity of the mixed sources was 227.07 ± 0.4 Bq/mg.



(a)

Fig. 5(a). Efficiency Curve with superimposed fitting line for ^{32}P & ^{60}Co mixed sources for 1173 keV gamma energy of ^{60}Co.



(b)

Fig. 5(b). Efficiency Curve with superimposed fitting line for ^{32}P & ^{60}Co mixed sources for 1332.5 keV gamma energy of ^{60}Co.

We obtained the extrapolation curves by measuring the 1173-keV and 1332.5-keV gamma energies. The efficiency ranging from 92 % to 65 % showed a very linear trend, and it was used to extrapolate up to the 100-percent β-counting efficiency. Table 1 showed us the value of the uncertainty budgets for a 4πβ (PS)-γ coincidence counting system, while Table 2 showed us the uncertainty values of the calibration of the Capintec dose calibrator.

Table 1. Uncertainty budget for standardization of ^{32}P.

Parameter	Standard Uncertainty (%)
SD of counting	0.36
Weighing of ^{60}Co (tracer)	0.05
Weighing of ^{32}P	0.05
Half-life of ^{60}Co (tracer)	0.02
Half-life of ^{32}P	0.16
Efficiency extrapolation	0.54
β-β resolving time	0.30
Combined standard uncertainty	0.68
Expanded uncertainty	1.36

Table 2. Uncertainty components for the R-value determined dose calibrator for ^{32}P.

Source of uncertainty	Stand. uncert. components (%)	
	^{32}P	Type
Standard source	0.68	B
Half-life of sample	0.16	B
Statistics of counting	0.40	A
Detector response	1.155	B
Accuracy of reading	1.732	B
Repeatability	0.577	B
Non-linearity	0.35	B
Weighing	0.05	B
Comb. standard uncertainty	2.31	B
Exp. uncertainty (k = 2)	4.62	B

The final activity of the ^{32}P results was (380.05 ± 0.68) Bq/mg by the time the source was obtained. The results served as a reference to determine the calibration factor of Radioisotope Calibrator "Capintec CRC-7BT", which was the secondary standard instrument at PTKMR - BATAN. We obtained a value of 1.12 with 4.62 % expanded uncertainty at the coverage factor, k=2 as the calibration factor of Capintec CRC-7BT used to measure ^{32}P.

CONCLUSION

We standardized the radionuclide of ^{32}P by using a 4πβ(PS)-γ coincidence counting method with ^{60}Co as a tracer. The result served as primary standard to calibrate the secondary standard instruments at PTKMR-BATAN; moreover, we found out that the calibration factor of "Capintec CRC-7BT" dose calibrator was 1.12 with a 4.7-percent expanded uncertainty. PTKMR-BATAN could calibrate the equipment in the nuclear medicine field by employing a short half-life of ^{32}P standard source, so the application this nuclear technology in the health sectors can be done securely and safely for workers, the society and the environment.

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