

Application of Digital Anti-Coincidence Counting Method for Primary Activity Determination of ^{59}Fe

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ABSTRACT

As a radiopharmaceutical, the use of ^{59}Fe is classified as a high pharmaceutical risk product. Therefore, a standard reference for activity measurement of ^{59}Fe is necessary to ensure its metrological aspect. This paper describes an alternative method for primary activity determination of ^{59}Fe for establishing a standard reference. The ^{59}Fe solution was prepared using two different cocktails and measured by the $4\pi\beta(\text{LS})-\gamma$ counting system using a digital anti-coincidence counting method with emulated live-time of the extending dead-time. A final activity results at the reference time for the two samples series are (473.32 ± 2.55) kBq/g and (477.14 ± 2.42) kBq/g with quoted uncertainty evaluated at $k = 1$. The final activity was compared to the value obtained from the other two coincidence counting method and found to be in a good agreement within its uncertainty value.

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INTRODUCTION

Ferrous-59 (^{59}Fe) is widely used in the nuclear medicine field as a radiopharmaceutical tracer for studying iron metabolism. As a radiopharmaceutical, ^{59}Fe is classified as high pharmaceutical risk product. Therefore, it must be very carefully characterized in terms of three main parameters: physicochemical, metrological, and biological [1]. The metrological parameter, in particular, precise measurements of activity, is crucial as it directly determines the effective dose given to the patient.

Radionuclide ^{59}Fe decays with a half-life of 44.494(12) days, by several beta minus emissions to the ground state and to four excited states of ^{59}Co , mainly to the 1099 and 1291 keV [2]. A simplified decay scheme of ^{59}Fe is shown in Fig. 1.

The nature of ^{59}Fe makes it possible to conduct an activity standardization with several methods. Most of the primary activity standardization for ^{59}Fe was conducted using the

$4\pi\beta-\gamma$ coincidence counting method, which has been confirmed to give a good result as described in [3-7].

Another method reported by Kossert and Nähle (2014), after a successful activity standardization of ^{59}Fe , is based on liquid scintillation (LS) counters using CIEMAT/ NIST and TDCR method [8]. In this work, we applied a digital anti-coincidence counting method with emulated live-time of the extending dead-time to determine the absolute activity of ^{59}Fe .

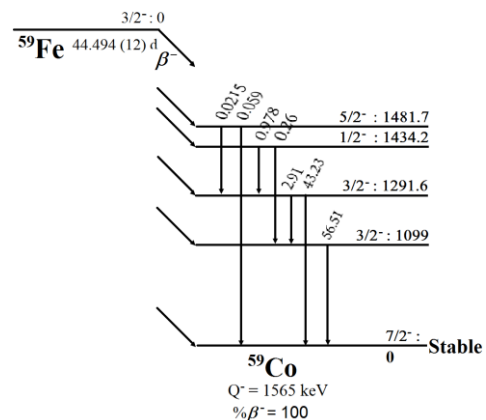


Fig. 1. Simplified decay scheme of ^{59}Fe .

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The anti-coincidence method has been successfully applied to determine the activity of other radionuclides, such as ^{129}I , ^{131}I , ^{18}F , ^{68}Ga , and ^{134}Cs [9-13]. These results were also compared to other methods including the coincidence counting method, and they were found to give equivalent results.

THEORY

The anti-coincidence counting method is a complement of the coincidence counting method with no basic difference between the two methods. Therefore, the count rates of beta-ray (ρ_β), gamma-ray (ρ_γ), and beta-gamma coincidence ($\rho_{\beta\gamma}$) are still necessary to be determined. Unlike the coincidence counting method, in anti-coincidence the $\rho_{\beta\gamma}$ is obtained from the difference between the total gamma-ray count rate ρ_γ and the uncorrelated non-coincident gamma-ray count rate, ρ_α , as described in Eq. (1).

$$P_{\beta\gamma} = \rho_\gamma - \rho_\alpha \quad (1)$$

Taking Eq. (1) into the basic coincidence equation, the source activity value is therefore given by:

$$A = \frac{\rho_\beta \rho_\gamma}{\rho_\gamma - \rho_\alpha} \quad (2)$$

A linear extrapolation of $\rho_\beta \rho_\gamma / \rho_{\beta\gamma}$ as a function of $\rho_\gamma / \rho_{\beta\gamma} - 1$ will yield the source activity A .

One complicated part of the application of anti-coincidence counting is the correction for dead-time losses as the dead-time loss in beta channel and coincidence channel do not compensate to some extent as in coincidence counting. The live-timed anti-coincidence counting with extendable dead-time circuitry is believed to be able to overcome the problem with dead-time losses.

EXPERIMENTAL METHODS

The master solution of ^{59}Fe in the chemical form of FeCl_3 was obtained from PerkinElmer, Inc. through a key comparison program piloted by the National Metrology Institute of Japan (NMIJ). Two types of samples, i.e. the liquid scintillation (LS) samples and point source samples, were prepared for primary activity standardization and impurity check, respectively. The standardization was conducted using the $4\pi\beta(\text{LS})-\gamma$ anti-coincidence method and the impurities of the solution were analyzed using the gamma-spectrometry method.

Sample preparation

The LS samples were prepared in Ultima Gold™ (UG) and Hionic Fluor (HF) cocktail solutions. Five samples for each cocktail solution were prepared by gravimetrically adding the aliquots of ^{59}Fe solution into 10 mL of cocktail in a 20 mL vial glass. Each sample series is comprised of one sample without an active solution to measure the background counting rate, which was then subtracted. The source masses on both sample series were ranged between 8 and 16 mg. In order to achieve a good homogeneous sample, all samples were shaken and kept in a dark room before they were measured. The point source samples were prepared by dropping the ^{59}Fe solution into a cellulose tape held by a ring holder.

Activity standardization by $4\pi\beta(\text{LS})-\gamma$ anti-coincidence counting

The high-efficiency $4\pi\beta(\text{LS})-\gamma$ counting system developed at Korea Research Institute of Standards and Science (KRISS) in 2010 was used to measure the LS samples of ^{59}Fe . The system consists of two NaI(Tl) detectors for gamma detection and a liquid scintillation detector with two PMTs for beta detection [14]. A schematic diagram of the system is shown in Fig. 2.

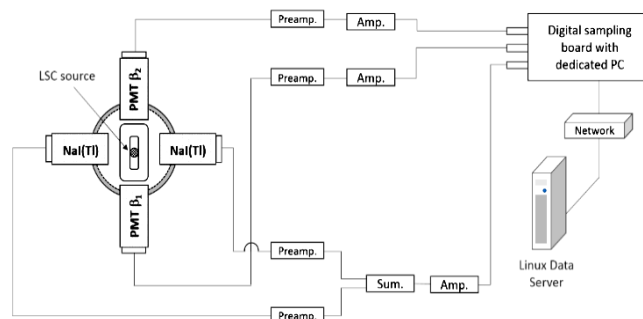


Fig. 2. Diagram of $4\pi\beta(\text{LS})-\gamma$ Coincidence Counting System.

For the current work, we applied a high voltage of 750 V on both gamma channels. The shaping time for both gamma and beta were set at $3\mu\text{s}$ with the threshold level set at 30 and 100 mV for beta and gamma, respectively. A high voltage of 2600 V was applied for the beta anode and 700 V was applied for the beta dynode channel.

A digital anti-coincidence counting method was applied to determine the activity of ^{59}Fe . Data acquisition was performed for 10 minutes for each sample and 10 hours for blank samples using the digital coincidence counting (DCC) technique with emulated live-time of the extending dead-time developed in 2011 [15]. This technique has been widely used with the coincidence counting method

to overcome the difficulty in the standardization of radionuclides with a complex decay scheme. Primary activity standardization of some radionuclide, i.e. ^{134}Cs , ^{137}Cs , ^{113}Sn , ^{131}I , and ^{64}Cu using digital counting technique were reported in a good agreement with other methods [16-19].

The DCC was applied in the data acquisition system to perform the offline analysis as all the information are recorded in RAW data files. RAW data files obtained from measurements were analyzed in Linux data server using programs written in FORTRAN language.

In this experiment, efficiency was varied by changing the threshold in beta channels. The rates of ρ_β and ρ_γ were obtained by summing up the counts from the output of beta-channel and gamma channel, respectively, and dividing the result by the live-time obtained. We determined the rates of $\rho_{\beta\gamma}$ using Eq. (1), in which the ρ_a was determined from the anti-coincidence output. The ρ_β , ρ_γ , and ρ_a , were then obtained as a function of pulse height of beta discrimination level. Meanwhile, all the information from coincidence beta data file, gamma data file, and efficiency data file were extracted to construct the covariance matrix to be used as the weighting in the least-square fitting. Final data set containing the three count rates with their standard uncertainties and the matrix error for each beta discrimination level were then obtained and saved into a file. A fitting routine was used for extrapolation to the unity of beta detector and the efficiency was performed based on the information saved in the final data file. These procedures of data analysis were performed for both sample and background data. Detail procedures in data acquisition and data analysis were described in [20].

RESULTS AND DISCUSSION

Three RAW data files were obtained from the $4\pi\beta(\text{LS})-\gamma$ counting system, i.e. two data files from the beta channel and one data file from the gamma channel. Using digital coincidence counting technique, it is possible to choose any gamma window without measuring each window setting, separately. Hence, it will reduce the measuring time during the experiment.

Spectrum for each channel was obtained after the files are pre-processed with a typical spectrum as shown in Fig. 3. Based on this spectrum information, gamma window for anti-coincidence measurements was determined. Due to the correlation effect as described by Park, *et al.* (2000), we decided to use the gamma window at 1291.6 keV [21]. The window was set in the program using the value of mean $\pm 2\sigma$ obtained from the Gaussian fit line of each photopeak energy.

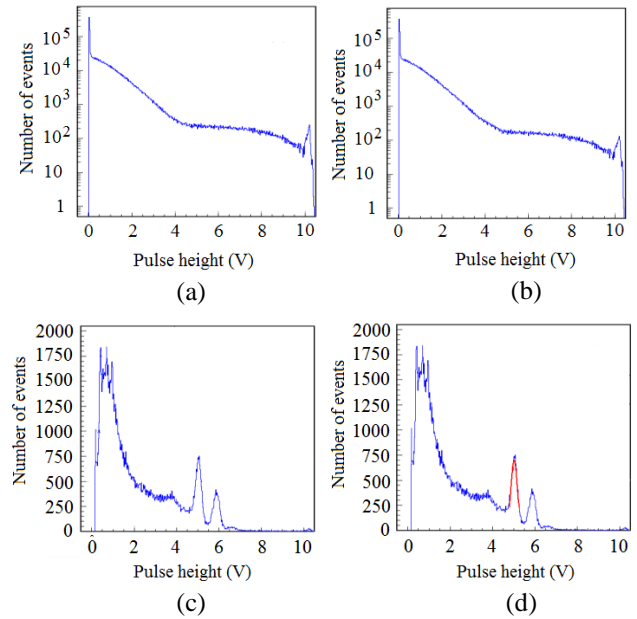


Fig. 3. Spectrum obtained from data acquisition of ^{59}Fe , (a) and (b) spectrum of beta signals obtained from channel beta 1 and beta 2, respectively, (c) gamma spectrum of ^{59}Fe , (d) gamma spectrum of ^{59}Fe with Gaussian fit line on 1291.6 keV photopeak.

The activity of ^{59}Fe was determined by plotting the $\rho_\beta\rho_\gamma/\rho_{\beta\gamma}$ as a function of $(\rho_\gamma/\rho_{\beta\gamma})-1$. Using the fitting routine with the least-squares method, we extrapolate the function into 100 % efficiency of the beta detector to obtain the activity value. An example of the efficiency extrapolation results is shown in Fig. 4.

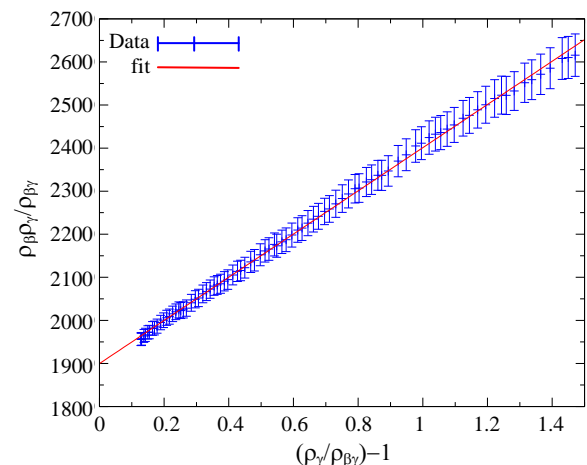


Fig. 4. Fitted efficiency extrapolation curve for ^{59}Fe .

The results of UG samples provide a maximum of 93 % of beta efficiency while the HF provides a maximum of 90 % of beta efficiency. The difference of the efficiency range between the two cocktails was caused by the nature of the cocktails themselves, which affect the efficiency of beta detection inside the cocktail solution as explained in [22]. However, since the efficiency

curves obtained from both sample series were extrapolated to 100 % efficiency, the differences in maximum efficiency values between the two cocktails can be neglected.

The results of activity determination for both UG and HF sample series as the reference time are given in Table 1. Uncertainties were evaluated using combined standard uncertainties, which correspond to uncertainties with $k=1$.

Table 1. Results of activity standardization of ^{59}Fe .

Sample ID	Eff. Range (%)	Specific Activity (kBq/g)
$^{59}\text{Fe}_{\text{anticoin_UG}}$	17 – 93	473.32 ± 2.55
$^{59}\text{Fe}_{\text{anticoin_HF}}$	5 – 90	477.14 ± 2.42

In Table 1, we can see that there is a 0.80 % difference between UG and HF samples, which might come from the instability of UG cocktails as explained by Fitzgerald *et al.* (2014) [23]. However, this level of difference is still acceptable and in a good agreement with the results when we expand the uncertainty coverage factor to $k = 2$. The uncertainty budgets for activity determination of ^{59}Fe is given in Table 2.

Table 2. Relative standard uncertainty budget for the activity standardization of ^{59}Fe .

Parameter	Type	Relative standard uncertainty (%)	
		UG	HF
SD of counting	A	0.18	0.15
Weighing	B	0.14	0.14
Half-life of ^{59}Fe	B	0.02	0.02
Impurities of ^{59}Fe	B	0.02	0.02
Eff. Extrapolation	B	0.35	0.35
β - β resolving time	B	0.30	0.30
Combined standard uncertainty		0.51	0.51
Expanded uncertainty		1.02	1.02

The highest contributor to uncertainty in this experiment was from the efficiency extrapolation with a value of 0.35 %. This is because the systematic uncertainty coming from the data acquisition system creates scatter in the data sets. In addition, it is also affected by the estimated uncertainty due to the variation of the source masses, which enter the efficiency extrapolation as explained in [24]. Impurities of the master solution of ^{59}Fe were also taken into account in the uncertainty evaluation. The value was obtained from gamma-ray spectrometry analysis on point source samples, which show an impurity of ^{60}Co in the solution with an activity of (91 ± 7) Bq/g. The activity ratio of ^{60}Co to ^{59}Fe at the reference date is approximately 0.02 %.

The final activity results were compared and found to be in a good agreement with the result from $4\pi\beta(\text{LS})-\gamma$ and $4\pi\beta(\text{PC})-\gamma$ coincidence counting method, which respectively reported the final activity of ^{59}Fe as (472.06 ± 3.00) kBq/g and (471.80 ± 3.45) kBq/g, with quoted uncertainty evaluated at $k = 1$.

CONCLUSION

The primary activity of ^{59}Fe has been successfully determined using the digital anti-coincidence counting method with emulated live-time of the extending dead-time applied to the $4\pi\beta(\text{LS})-\gamma$ counting system. The final activity found by this method is in good agreement with an uncertainty level measured by the coincidence counting method. This result shows that the digital anti-coincidence counting method can be used as an alternative method for primary activity determination of ^{59}Fe .

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