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Australian Primary and Secondary Standard of Activity: Standardisation of F-18

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SUMMARY. The Radiation Standards Project of the Australian Nuclear Science and Technology Organisation (ANSTO) maintains and disseminates the Australian primary and secondary standard for radioactivity measurements. Recently the Activity Standards Laboratories (ASL) participated in an international inter-comparison of the activity of F-18 coordinated by the National Physical Laboratory (NPL) in the UK. At the national level this involved the development of both a primary and secondary standard of activity measurement. The technique employed to standardise this pure beta emitter by the ASL was "$4\pi\beta$–γ Efficiency Tracing Method", using Co-60 as the tracer. A result within 0.1 % of the NPL comparison bench mark was obtained. In this paper details of the technique employed are described.

1. INTRODUCTION

Cyclotron produced fluorine F-18 in the form of the radiolabeled sugar fluorodeoxyglucose (F-18 FDG) is used in a variety of diagnostic modalities. The premier use is in conjunction with positron emission tomography (PET) for the study of neurological function and the detection of neurological abnormalities and malignancies of the cranium.

From the perspective of radiation dosimetry, the quantity of radioactivity administered intravenously to a patient must be known. In nuclear medicine departments radionuclide dose calibrators are used routinely for this purpose. The calibration of such instruments should be traceable to the national primary standard of measurement.

The Radiation Standards Project of the Australian Nuclear Science and Technology Organisation (ANSTO) maintains and disseminates the Australian primary and secondary standard for radioactivity measurements. The maintenance of standards refers in this instance to the establishment of a measurement procedure for determining activity. There is no single technique or apparatus which can be used to determine the activity of all radioactive species. Rather, methods are developed which depend on the decay process of the particular isotope of interest.

In Australian hospitals, activity measurements can be compared indirectly to the primary standard by accepting the value of standardised sources issued by Australian Radioisotopes (ARI) which is a verifying authority. The calibration of the ionisation chambers of the ARI Quality Control laboratories are traceable to the Australian primary standard of measurement for activity for a variety of radionuclides.

Recently, the ANSTO ASL participated in an international inter-comparison of the activity of F-18 coordinated by the National Physical Laboratory (NPL) in the UK. The development and subsequent validation of this standard was used to develop a working (secondary) standard in the form of a calibration of the ionisation chambers. This forms the Australian secondary standard of measurement of F-18 activity. This standard is to be made available to manufactures and users of radiopharmaceuticals in Australia.

2. EXPERIMENTAL

2.1 Decay Scheme of F-18

F-18 decays predominantly by positron emission direct to the ground state of O-18 with an intensity of 96.90 %. The beta particle has a maximum energy of 633.2 keV and an average energy of 249.7 keV NCRP (1). The remaining disintegrations occur via electron capture (*ec*) with an intensity of 3.1 %.

The half-life of F-18 radioactive decay is 1.828 hrs.

No gamma radiation is emitted in the decay. As a result, conventional $4\pi\beta$–γ coincidence counting cannot be used to standardise this radionuclide.

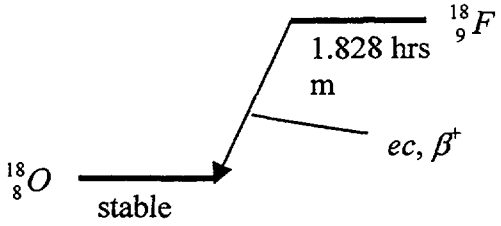

Figure 1. Decay scheme of F-18.

2.2 Primary Standardisation of F-18 by the Efficiency Tracing Technique

The technique employed to standardise this pure beta emitter, "Efficiency Tracing Method" was similar to that used by Smith et al. (2). In this technique the pure beta emitter and a tracer radionuclide are added to the same counting source. The efficiency of the beta detector is than traced back to unity using the tracer radionuclide for which conventional $4\pi\beta$–γ coincidence counting can be used to standardise the absolute beta emission rate. The combined beta count rate at unitary detection efficiency and the known beta emission rate from the tracer radionuclide permits determination of the beta count rate due to the pure beta emitter.

The main requirements of this technique, Campion et al. (3) and Steyn (4), are that;

1) The tracer radionuclide is not a positron emitter. This is due to the inevitable non linearity introduced by an unknown annihilation rate of the positrons within the source, and;
2) The tracers beta end point energy, E_{max}, and average energy, E_{max}, are equal to, or less than, the corresponding energies of the analyte nuclide.

Co-60 was selected as the tracer radionuclide. Co-60 is a β–γ emitter and can be standardised by the conventional $4\pi\beta$–γ coincidence counting technique. The beta particle emission has an intensity of 99.92 %, E_{max} = 317.92 keV and E_{av} = 95.80 keV NCRP (1). Thus the requirements 1) and 2) are satisfied.

Due to the short half-life associated with the decay of F-18, a large number of counting sources cannot be produced and counted for a single solution. To permit adequate statistics to be generated, two solutions were standardised on different days. The inter-comparison of results was made using a Ge-68/Ga-68 check source.

A variation of the above technique was developed to permit the incorporation of efficiency tracing data from two sets of experiments without the need for a check source van der Gaast (5). This technique was not used here.

2.3 Counting Source Preparation

Previously it was maintained that in the efficiency tracer technique it was necessary that the tracer and analyte nuclide should be in the same compound Campion et al. (3). It has since been documented, Steyn (4), Bowes et al. (5) and Baerg et al. (7), that it is sufficient that the sources are prepared using a good wetting agent to permit adequately thin and homogeneous sources to be produced from a mixed solution.

A solution of Co-60 was standardised using conventional $4\pi\beta$–γ coincidence counting.

A solution of F-18 in the form of FDG was obtained from the National Medical Cyclotron (NMC) in Sydney. Both solutions were suitably diluted and dispensed to form the mixed counting solution. The mixing ratio was carefully measured.

This solution was then dispensed onto a set of metallised plastic film source mounts. The plastic film; vcar sol vinyl resin (VYNS) was used. The upper surface was coated with an alloy of gold and palladium by evaporation. A spreading agent was used to disperse the solution over a wide area in order to achieve a thin source with minimal self absorption effects. The drop of radioactive solution was dried in an oven at 50°C.

2.4 Counting

The beta emission rate was measured in an atmospheric pressure ionisation chamber with 4π geometry. The chamber was continuously purged with P10 counting gas (10% methane in argon). Gamma radiation emitted in the decays of Co-60 were detected in a NaI(Tl) scintillation detector mounted close to the ionisation chamber. The 1.17 and 1.33 MeV photo peaks were gated to prevent the accumulation of false counts associated with the 511 keV photons due to β^+ annihilation and bremsstrahlung radiation produced in the beta detector.

The source counting efficiency was systematically altered by the addition of metallised VYNS layers, aluminium foil layers and mylar layers to both the upper and lower source surfaces.

It is important to note that following the removal of a source from the counting chamber and its subsequent replacement, the beta chamber was sufficiently flushed with counting gas to maintain a consistent counting environment.

For each counting period the total beta, gamma and coincidence counts were recorded in addition to the counting start time. The gamma and beta channel dead-times, system resolving time and background counting rates were measured.

2.5 Calculations

A summary of the calculations employed is given here. An explanation of the symbols used is given at the end of this section.

The beta count rate was corrected for nonextendable dead-time using equation 1. The dead-time was imposed using a paralysis unit.

$$N_a(\beta) = \frac{N_\beta}{1 - N_\beta T} - B_\beta \quad (1)$$

The beta count rate per unit mass was determined for each source (see equation 2).

$$n_a(\beta) = \frac{N_a(\beta)}{mass} \quad (2)$$

The beta count rate per unit mass due to the Co-60 component was determined from the known activity concentration of the tracer nuclide and the beta detection efficiency, ε_β (see equation 3).

$$[n_a(\beta)]_{Co-60(mixed)} = [a_o]_{Co-60(mixed)} \times \exp[-\lambda_{Co-60}(t_a - t_o)]\varepsilon_\beta \quad (3)$$

The beta efficiency was determined using equation 4.

$$\varepsilon_\beta = \frac{(1 - N_\gamma' T)(N_c' - 2N_\beta N_\gamma \tau_R)}{N_\gamma'(1 - N_\beta' T)(1 - (N_\beta + N_\gamma)\tau_R)} \quad (4)$$

The beta count rate per unit mass at time t_1 was determined using equation 5.

$$n_1(\beta) = [n_1(\beta)]_{Co-60(mixed)} + \{n_a(\beta) - [n_a(\beta)]_{Co-60(mixed)} \times \exp[\lambda_{F-18}(t_a - t_1)] \quad (5)$$

$n_1(\beta)$ was plotted as a function of $(1-\varepsilon_\beta)/\varepsilon_\beta$. A degree 1 polynomial was fitted to the data to allow extrapolation to the y-intercept. This gives the corresponding beta count rate for 100 % counting efficiency (at $\varepsilon_\beta = 1$). Such a plot is shown in figure 2.

The beta count rate per unit mass due to the F-18 contribution is determined using $[n_1(\beta)]_{\varepsilon\beta=1}$ obtained from the y-intercept and equation 6.

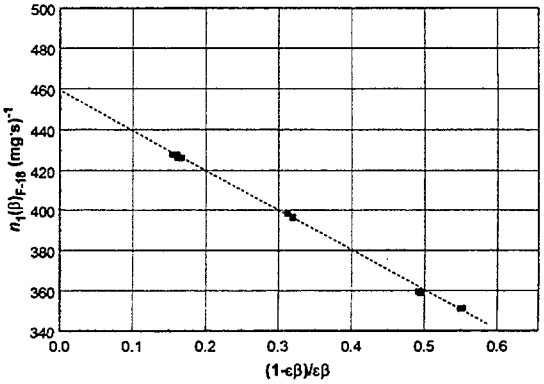

Figure 2. Extrapolation of $n_1(\beta)$ to 100 % beta counting efficiency ($\varepsilon_\beta = 1$).

$$[n_1(\beta)]_{F-18\,(mixed)} = [n_1(\beta)]_{\varepsilon_\beta = 1} - [a_1]_{Co-60(mixed)} \quad (6)$$

The F-18 activity per unit mass was then determined in the mixed solution based on the beta count rate attributed to F-18 and the intensity of beta particle emission in F-18 decay (see equation 7).

$$[a_1]_{F-18(mixed)} = \frac{[n_1(\beta)]_{F-18(mixed)}}{I_{\beta(F-18)}} \quad (7)$$

Using the known mixing ratio of F-18 to Co-60, the activity concentration in the F-18 solution was ascertained (see equation 8).

$$[a_1]_{F-18(Master)} = \frac{m_{(mixed)}}{m_{F-18(Master)}} [a_1]_{F-18(mixed)} \quad (8)$$

The activity concentration was corrected for radioactive decay to the reference time t_r using the standard equation (9).

$$[a_R]_{F-18(mixed)} = [a_1]_{F-18(mixed)} \exp\left[\ln(2) \times \left(\frac{t_1 - t_2}{\tau_{1/2(F-18)}}\right)\right] \quad (9)$$

Using this process the activity of a solution of F-18 was determined. The combined uncertainty of the measurement was 1.4 % with 13.5 degrees of freedom.

Symbols used

$N_a(\beta)$ = beta count rate (at time t_a), corrected for dead-time and background beta count rate,
N_β = measured beta count rate (uncorrected for background beta count rate),
T = resolving time,

B_β = beta background count rate,
mass = mass of mixed radioactive solution deposited on source mount,
$[a_o]_{Co\text{-}60(mixed)}$ = activity concentration of Co-60 in mixed solution at time t_o,
$\lambda_{Co\text{-}60}$ = radioactive decay constant for Co-60,
$\lambda_{F\text{-}18}$ = radioactive decay constant for F-18,
N_γ' = gamma count rate corrected for background count rate,
N_c' = coincident count rate corrected for background count rate,
N_β' = beta count rate corrected for background count rate,
N_γ = gamma count rate uncorrected for background count rate,
N_c = coincident count rate uncorrected for background count rate,
τ_R = resolving time,
$[n_a(\beta)]_{Co\text{-}60(mixed)}$ = beta count rate per unit mass due to Co-60 component in mixed solution,
$[n_1(\beta)]_{\varepsilon\beta=1}$ = beta count rate per unit mass at 100% beta detection efficiency,
$I_{\beta(F\text{-}18)}$ = intensity of beta particle emission in the decay of F-18,
$m_{F\text{-}18(Master)}$ = mass of F-18 solution in the mixed solution.
$m_{(mixed)}$ = total mass of F-18/Co-60 mixed solution.

2.6 Secondary Standardisation of F-18

Primary standards of activity measurement are not usually suitable for the routine calibration ofhospital type radionuclide dose calibrators. It is therefore appropriate to use a "working" standard as an immediate step between the primary standard and dissemination of the standard throughout the community. The "working" standard provides a simple measurement of activity by comparison with a calibration factor derived from the primary standard of activity measurement. The working standard is a secondary standard.

The Australian secondary standard of activity measurement is a TPA ionisation chamber of the type described by Sharpe et al. (8). The re-entrant chamber provides almost 4π geometry and is filled with argon to a pressure of ~ 2030 kPa. Such an instrument provides a secondary method which is both precise and rapid.

The primary standardised F-18 solution was dispensed into standard ampoules used in the secondary standard laboratory. Ampoules were filled with 3.6 ml of the standardised F-18 solution. The ampoules were inserted into the secondary standard ion chamber and the ionisation current measured. A calibration factor in the form of $pA \cdot MBq^{-1}$ was ascertained.

2.7 International Inter-comparison of F-18 Activity Measurement

The results of the primary standardisation were used for an international inter-comparison of the activity measurement of F-18.

As a result of the short half-life of F-18 it is not possible that solutions can be disseminated between different national laboratories. Inter-comparison was thus achieved by comparing the measured activity of the F-18 solution to that of a Ge-68/Ga-68 check source solution. The check source was supplied by NPL to laboratories participating in the comparison. Details regarding the Ge-68/Ga-68 activity were not disclosed.

The comparison was done by measuring the response of the F-18 solution and Ge-68/Ga-68 solution in a Vinten ion chamber. Both solutions were contained in standard ampoules supplied by NPL.

Results were reported to NPL in April 2001.

2.8 Verification of results

The F-18 international inter-comparison results were assessed by NPL in mid 2001. A preliminary finding was reported at the Consultative Committee for Ionising Radiation (CCIR) Section II: Measurement of Radionuclides, May 2001. Here it was reported that the results submitted by ANSTO were within 0.1 % of the comparison bench mark Alexiev (9).

3. CONCLUSIONS AND DISCUSSION

A primary standard was developed for the measurement of the activity of F-18. Additionally, a secondary standard was established in the form of a calibration factor for the working standard ionisation chamber. The results were submitted to an international inter-comparison on the activity of F-18 coordinated by the National Physical Laboratory (NPL). Preliminary results of this comparison have indicated the primary standard result to be within 0.1 % of the comparison bench mark.

4. REFERENCES

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