EFFICIENCY CALIBRATION OF A HPGe DETECTOR FOR [\(^{18}\text{F}\)]FDG ACTIVITY MEASUREMENTS

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ABSTRACT

The radionuclide \(^{18}\text{F}\), in the form of flurodeoxyglucose (FDG), is the most used radiopharmaceutical for Positron Emission Tomography (PET). Due to \(^{18}\text{F}\)FDG increasing demand, it is important to ensure high quality activity measurements in the nuclear medicine practice. Therefore, standardized reference sources are necessary to calibrate \(^{18}\text{F}\) measuring systems. Usually, the activity measurements are performed in re-entrant ionization chambers, also known as radionuclide calibrators. Among the existing alternatives for the standardization of radioactive sources, the method known as gamma spectrometry is widely used for short-lived radionuclides, since it is essential to minimize source preparation time. The purpose of this work was to perform the standardization of the \(^{18}\text{F}\)FDG solution by gamma spectrometry. In addition, the reference sources calibrated by this method can be used to calibrate and test the radionuclide calibrators from the Divisão de Produção de Radiofármacos (DIPRA) of the Centro Regional de Ciências Nucleares do Nordeste (CRCN-NE). Standard sources of \(^{152}\text{Eu}\), \(^{137}\text{Cs}\) and \(^{68}\text{Ge}\) were used for the efficiency calibration of the spectrometer system. As a result, the efficiency curve as a function of energy was determined in wide energy range from 122 to 1408 keV. Reference sources obtained by this method can be used in \(^{18}\text{F}\)FDG activity measurements comparison programs for PET services localized in the Brazilian Northeast region.

1. INTRODUCTION

Short-lived radionuclides are increasingly used in nuclear medicine imaging for a wide range of physiological studies, as they minimize dose exposure to both patient and medical staff [1]. During the past several decades, some new diagnostic imaging tools for nuclear medicine
have emerged. These include the usage of positron emission tomography (PET) which is one of the most important imaging techniques and represents an effective milestone as far as clinical diagnostic is concerned. This diagnostic imaging procedure is based on the detection of very small quantities of biological substances which are labeled with a positron emitting radionuclide. A state of the art PET system consists of multiple, closed packed rings of detectors that enable simultaneous recording of several image planes [2,3].

The radionuclide $^{18}$F, in the form of flurodeoxyglucose (FDG), is widely used in clinical PET applications due to its suitable physical and nuclear properties. $^{18}$F decays to the ground state of $^{18}$O by positron emission (96.86 (19)%) and electron capture (3.14 (19)%) with a short half-life of 1.8288 (3) h. Additionally, the positron has a maximum energy of 633.5 keV and an average energy of 249.3 keV. The 511 keV annihilation photon following the positron emission has an intensity of 193.72 (27)% [4].

The demand for $[^{18}$F]FDG has been increasing very rapidly over the past few years. Therefore, the metrology of this radionuclide is very important. The quality of radioactivity measurements in the nuclear medicine practice, from radionuclide production to patient administration, plays an important role for the success of the diagnostic or the therapy procedures [5].

Usually, the activity measurements are performed in a special type of ionization chambers often referred to as radionuclide calibrators. These equipments consist of a well type ionization chamber coupled to a digital electronic system, which allows direct readings in units of the activity for the radiopharmaceuticals analyzed. Radionuclide calibrators are instruments that require regular checks and adequate operational procedures. For this reason, quality assurance programs for activity measurements in nuclear medicine must be established in clinical routines. As a consequence, nuclear medicine departments require accurate activity standards of $^{18}$F for calibration of measuring systems.

In former works, Capogni et al. [6], Yamada et al. [7], Schrader et al. [8] and Roteta et al. [9] have standardized $^{18}$F activity calibrations by a variety of absolute methods. Short-lived radionuclides such as $^{18}$F may present some problems for the standardization of activities by the conventional counting techniques. Therefore, a simplified procedure for the standardization of this radionuclide has been implemented in order to produce reliable reference sources for calibration purposes.

The activity determination of positron emitters is carried out by the method known as gamma spectrometry, which can be considered as a secondary calibration technique [10,11]. For these measurements, a high-purity germanium (HPGe) detector is widely used due to its excellent energy resolution. An efficiency curve as a function of the gamma-ray energy becomes necessary. This curve is obtained from the acquisition of reference spectra considering the photopeak areas corresponding to the standard activities [12].

The purpose of this work was to perform the standardization of the $[^{18}$F]FDG solution by gamma spectrometry. In addition, the reference sources calibrated by this method can be used in the future to calibrate and test the radionuclide calibrators from DIPRA of the CRCN-NE.
2. EXPERIMENTAL PROCEDURES

2.1. Equipments and materials

A radionuclide calibrator, Capintec, model CRC-15R, was established as the Standard Radionuclide Calibrator (SRC) for the activity measurements comparison program in the Brazilian Northeast region. The main characteristics of the radionuclide calibrator provided by the manufacturer are reported in Table 1. This equipment was submitted to quality control tests (accuracy, precision, reproducibility, linearity and geometry) and the results have been analyzed following the national and international recommendations [13-16].

<table>
<thead>
<tr>
<th>Model</th>
<th>CAPINTEC – CRC 15R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Well-type ionization chamber</td>
</tr>
<tr>
<td>Gas</td>
<td>Argon</td>
</tr>
<tr>
<td>Well Dimensions (cm)</td>
<td>6.1x25.4</td>
</tr>
<tr>
<td>Shielding (mm lead)</td>
<td>3.2</td>
</tr>
<tr>
<td>Maximum Activity (^{99m}\text{Tc})</td>
<td>240 GBq (6.5 Ci)</td>
</tr>
<tr>
<td>Photon energy range</td>
<td>25 keV - 3 MeV</td>
</tr>
<tr>
<td>Resolution</td>
<td>0.001 MBq (0.01 µCi)</td>
</tr>
<tr>
<td>Linearity</td>
<td>Within ±2%</td>
</tr>
<tr>
<td>Manufacturer’s reference calibration geometry</td>
<td>Ampoule with 5 ml of radioactive solution</td>
</tr>
<tr>
<td>Manufacturer’s calibration factors (^{99m}\text{Tc})</td>
<td>080</td>
</tr>
</tbody>
</table>

The secondary reference system for activity measurements was CANBERRA High-Purity Germany (HPGe) coaxial detector, model GC1018, which has a relative efficiency of 10% with an energy resolution of 1.8 keV (FWHM) at 1.33 MeV. In addition, the detector is equipped with a model 2002CSL preamplifier and operates at a bias voltage of (+)4500 V. The experimental spectra were recorded and processed by the Canberra gamma spectrum analysis system using the GENIE 2000 software. In the present experiment, standard sources of \(^{152}\text{Eu}\), \(^{137}\text{Cs}\) and \(^{68}\text{Ge}\) were used for the efficiency calibration of the spectrometer system. Their characteristics are presented in Table 2.

2.2. Measuring Procedures

For the radionuclide metrology, the \(^{18}\text{F}\) sample used to determine the activity was prepared by the pycnometer method using a BIOPRECISA balance [17,18]. In this method, the mass of the solution deposited in the container was obtained by weighing the pycnometer before and after dispensing the drop solution. The master solution had an activity concentration of approximately 42 MBq/g in 0.5 ml and was dispensed in the specific glass vial used at DIPRA/CRCN-NE (Figure 1). Then, the container was filled with distilled water until a 5ml
(reference volume) was completed. Immediately, the container was closed and the diluted solution was adequately mixed by swirling.

Table 2. Standard sources used for the efficiency calibration of the secondary reference system

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life$^a$</th>
<th>Gamma Ray</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>E (keV)$^a$</td>
</tr>
<tr>
<td>Ge-68</td>
<td>270.95±0.16 d</td>
<td>511</td>
</tr>
<tr>
<td>Cs-137</td>
<td>30.05±0.08 a</td>
<td>661.657</td>
</tr>
<tr>
<td></td>
<td></td>
<td>121.7817</td>
</tr>
<tr>
<td></td>
<td></td>
<td>244.6974</td>
</tr>
<tr>
<td></td>
<td></td>
<td>344.2785</td>
</tr>
<tr>
<td>Eu-152</td>
<td>13.522±0.0016 d</td>
<td>411.1165</td>
</tr>
<tr>
<td></td>
<td></td>
<td>778.9045</td>
</tr>
<tr>
<td></td>
<td></td>
<td>867.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1085.837</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1112.076</td>
</tr>
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<td></td>
<td></td>
<td>1408.013</td>
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</tbody>
</table>

$^a$Laboratoire National Henri Becquerel [4]

Figure 1. Preparation of the radioactive solution in the specific glass vial by the pycnometer method.

For the gamma measurements, the secondary reference system was calibrated using standard sources of $^{152}$Eu, $^{137}$Cs and $^{68}$Ge that have traceability to the SI. In this study, all samples were individually placed 15 cm above the surface of HPGe detector. In order to obtain
accurate results, the [$^{18}$F]FDG sample was counted at the reference geometry used to calibrate the measurement system. No significant impurity was observed in the acquired spectra.

From the analysis of the recorded spectra, experimental efficiencies were calculated and the calibration curve was obtained by fitting. The energies used to create this curve are reported in Table 2. According to Deberting and Helmer [19], there is a great variety of analytical functions and semi-empirical expressions used to describe the efficiency dependence on the energy. Polynomial functions are among the simplest analytical functions that fairly accurately fit the measured efficiency values [20]. In this study, a third degree polynomial equation was utilized as the best approach for determining the efficiency curve.

The activity of the radionuclide $^{18}$F in the sample measured by gamma-spectrometry was calculated using the following relation:

$$A = \frac{N}{I \times \varepsilon \times T}$$  \hspace{1cm} (1)

where A is activity, N is the net counts under the peak obtained for each photopeak, I is the photon emission intensity, $\varepsilon$ is the counting system efficiency and T is the spectrum acquisition time. Equation (1) also allows the efficiency evaluation at the energy of each gamma transition for each standard calibrated radioactive source.

Thereafter, the [$^{18}$F]FDG solution was measured using the SRC. Because of the short half-life, the gamma spectrometry and radionuclide calibrator measurements were made simultaneously. The schematic diagram of the experimental procedures involved in accurate activity measurements and distribution of the reference sources is illustrated in the Figure 1.

3. RESULTS

The result of the efficiency calibration for the HPGe using $^{152}$Eu, $^{137}$Cs and $^{68}$Ge standard sources is shown in Figure 2. In relation to the [$^{18}$F]FDG solution, its spectrum can be found in Figure 3. Once a sufficient number of data were acquired experimentally in the energy region of interest (from 122 to 1408 keV), the analytical expression of the efficiency curve was determined. The experimental results obtained in this study are presented in Table 3. The reference source characterized by this method was used for testing and calibration of SCR. Activity determination using the gamma spectrometry and SCR produced consistency between the results, reaching a percentage error of 3.7%.
Figure 1. Schematic diagram of the experimental procedures involved in activity measurement of the reference sources.

Figure 2. Experimental efficiency curve using $^{152}\text{Eu}$, $^{137}\text{Cs}$ and $^{68}\text{Ge}$ standard sources.
Figure 3. $^{18}$F spectrum obtained in the secondary calibration system.

Table 3. Results of the activity measurements of $[^{18}F]$FDG solution by gamma spectrometry and SRC/ionization chamber.

<table>
<thead>
<tr>
<th>Activity (Bq) - HPGe</th>
<th>Activity (Bq) - SRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>17778 ± 3.8</td>
<td>17116 ± 1.6</td>
</tr>
</tbody>
</table>

4. CONCLUSION

A method for obtaining reference sources for testing and calibration of $^{18}$F measuring systems has been established. The efficiency curve has been determined experimentally using $^{152}$Eu, $^{137}$Cs and $^{68}$Ge standard sources. Standardizations were carried out on a solution of $[^{18}F]$FDG using gamma spectrometry and the result was used to calibrate the Standard Radionuclide Calibrator. According to the obtained results, this method will serve as a secondary reference system for the standardization of $[^{18}F]$FDG solutions for quality assurance in activity measurements of radiopharmaceuticals. In addition, these reference sources will also be used in the regional comparisons of $[^{18}F]$FDG activity measurements.
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REFERENCES


