Utilization of Tandem Systems for the Detection of Impurities in Radiopharmaceuticals

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Abstract. In this work tandem systems were established and characterized using four cylindrical absorbers of materials with different densities for an additional quality control test. The study was performed using two secondary standard systems NPL and a homemade system composed by a well-type ionization chamber made at IPEN and a Keithley electrometer. For the establishment of the tandem systems non sealed sources were utilized. The samples with impurities were measured using combinations with different proportions of radionuclides. The ratio between the measurements with different absorbers presented constant values for each dose calibrator and pure source. The results obtained with the materials with impurities using the absorbers presented constant, but different values, depending on the impurity and its proportion in the mixture. Therefore, the use of tandem systems may be recommended for quality control programs.

1. Introduction

Radiopharmaceuticals are widely used in nuclear medicine departments for diagnostic and therapeutic purposes. The correct administration to a patient of the prescribed activity is an important factor to ensure the confidence in the diagnosis or the therapeutic efficiency, while at the same time keeping the unnecessary worker exposure as low as possible [1]. The staff members are exposed to radiation during withdrawal of radioactive material from the vial, in the preparation and administration of the radiopharmaceuticals.

To assure the adequate quantity of the radiopharmaceuticals, the activity to be delivered to the patient must be checked. This measurement is performed in a dose calibrator with the radionuclide in either the manufacturer's glass vial or, preferably, in the syringe to be used for injection.

The dose calibrator is a combination of a well-type ionization chamber and an electrometer. It is the instrument of choice because it is simple to operate, it measures activities to the necessary levels of accuracy, and it is stable over long periods of time [2].

However, the simple utilization of a dose calibrator, for the activity determination of a material, does not allow the detection of impurities in the radiopharmaceuticals. When impurities are found in radiopharmaceuticals they may produce undesirable consequences, such as increase in the radiation absorbed dose to the patients and to the staff members involved in the procedure.

Tandem methods have been used, since long ago, with thermoluminescent dosemeters [3, 4] and recently with ionization chambers [5, 6]. A tandem system is usually formed by two instruments with different responses for a determined energy range. The tandem curve is obtained by the ratio between the responses of the two independent systems in function of the incident radiation energy.

In this work tandem systems were established and characterized using four absorbers of materials with different densities, as an alternative test for quality control programs in nuclear medicine departments. These tandem systems may allow the indication of the presence of impurities in the radiopharmaceuticals if the ratio between the measurements is different from that obtained at the laboratory in ideal conditions.

2. Materials and Methods

The study was performed using two secondary standard systems of National Physical Laboratory (NPL) and a homemade system. The NPL dose calibrators are constituted by a NPL well ionization chamber and an interface unit Capintec, model NPL-CRC®-15. They belong to the Laboratories of Instruments Calibration (NPL-A) and of Nuclear Metrology (NPL-B) of IPEN, both with traceability to the primary standard laboratory of NPL, England.

The homemade equipment (called IPEN system) was developed at IPEN by Breda et al [7], and it is formed by a well-type ionization chamber, 4π geometry, a Keithley electrometer, model 610C, a stabilized Tectrol power supply, model TC300-02, and a Triel digital multimeter, model MTR 4410.

All three dose calibrators were submitted to the main quality control tests using the standard radiation source set (^{57}Co, ^{133}Ba, ^{137}Cs, ^{60}Co), of Amersham, with traceability to the primary standard laboratory Physikalisch - Technische Bundesanstalt (PTB), Germany, and non-sealed sources of ^{201}Tl and ^{131}I, produced at IPEN, to verify the performance of each system.

For the characterization of the tandem systems, measurements were taken using four cylindrical absorbers (FIG. 1) of brass, PVC, steel and nylon, developed by Dytz and Caldas [8], that were introduced sequentially into the ionization chambers with the sources.

To establish in the quality control program a special procedure to determine the radioactive impurities in radiopharmaceuticals, measurements were taken using the different absorbers with the non sealed sources of ^{131}I and ^{201}Tl (produced at IPEN) in several percentual combinations (from 20 up 80%).
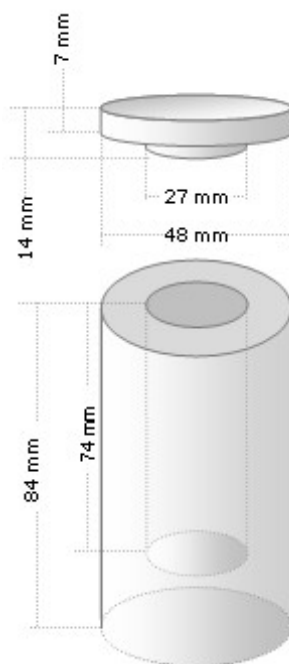

FIG. 1. *Cylindrical absorber for tandem systems*

3. Results

All systems showed a very good stability, with variations always within the recommended limits [9]. The activity values obtained with the NPL-B were used as reference.

The accuracy and the precision of the dose calibrators were verified using the standard sources in the same geometry conditions. The results obtained for the accuracy test (1σ, k=1) showed the excellent performance of the measurement systems (2.5 %) considered the limit of acceptance of 10 % [9]. In the case of the precision test, the highest percentual deviation obtained for the activity measures was 2.3 % for the IPEN system, therefore within the recommended limit of 5 % [9].

The reproducibility of each system was checked using all standard reference sources; a good performance was observed for all dose calibrators. The highest percentual deviation between the measured activity and the mean value of the activities was 2.0 % for the IPEN system, therefore within the recommended limit of 5 % [9].

The linearity of the activity response was verified through the radioactive decay of a ^{99m}Tc sample, with initial activity of 1520.70 MBq. The highest deviation obtained was 2.3 % for the NPL-A system; all systems presented results within the recommended limit of $\pm$ 20 % [9].

The correction factors and the calibration coefficients obtained showed variations far below the limit of 10 % [9]. The two NPL dose calibrators showed an excellent agreement for energies above 300 keV, while for ^{57}Co a discrepancy of approximately 3 % was observed. The energy dependence for the IPEN system was smaller than 7 % in the tested energy range.

For the characterization of the tandem systems, measurements were taken using the cylindrical absorbers of brass, PVC, steel and nylon. For the establishment of the tandem systems initially the sources were inserted directly in the dose calibrators and afterwards they were inserted inside of each one of the absorbers, into the dose calibrators. The use of filters modifies the response of the equipments.

The results obtained showed good reproducibility for all systems. Figures 2 and 3 present the tandem curves, i. e., the ratio between the response using the absorbers of steel and PVC, and of brass and nylon, in function of the standard source energy.
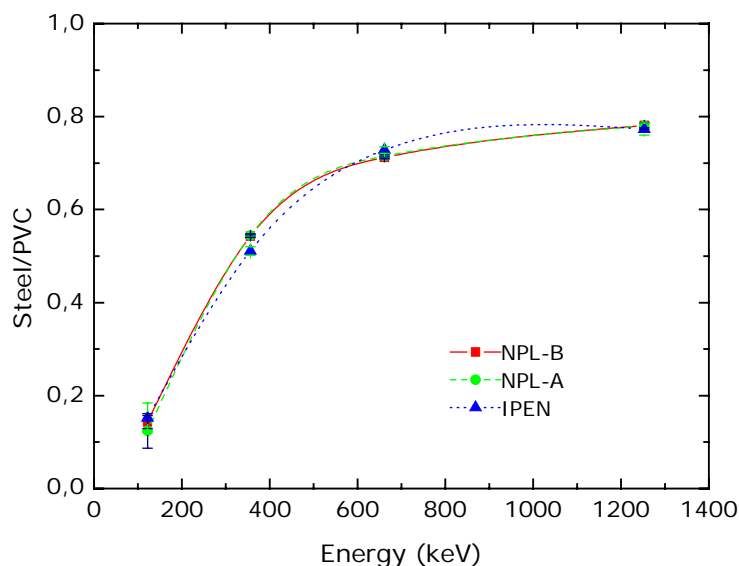

FIG. 2. *Tandem curves of NPL-A, NPL-B and IPEN dose calibrators: ratio between the response using the steel and PVC absorbers in function of the standard source energy*
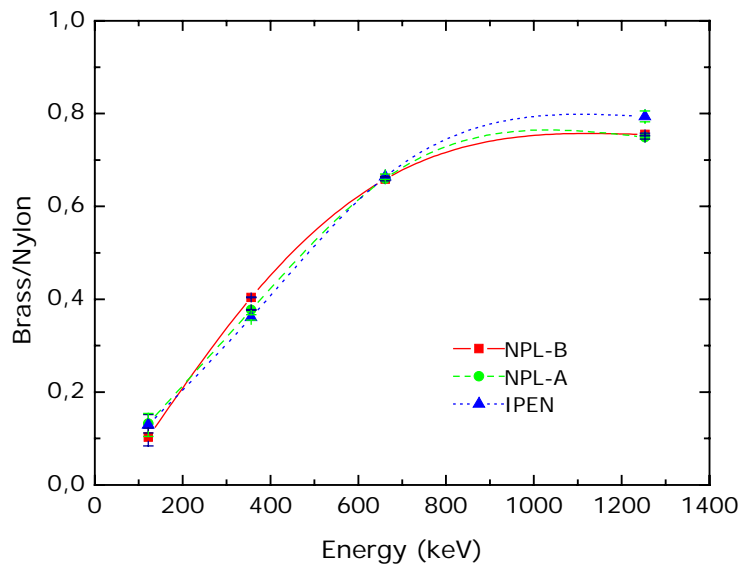
FIG. 3. *Tandem curves of NPL-A, NPL-B and IPEN dose calibrators: ratio between the response using the brass and nylon absorbers in function of the standard source energy*

The ratio between the measurements with different absorbers showed constant values for each dose calibrator and source, allowing the formation of tandem systems that may be recommended for use in quality control programs. The maximum deviation percentual for the response ratios between steel and PVC absorbers was 0.64 % for the NPL-B system, and in the case of brass and nylon absorbers it was 1.6 % for the IPEN system; in both cases the ^{60}Co source was utilized.

Finally, impurities of ^{131}I and ^{201}Tl were introduced under controlled laboratory conditions into the radiopharmaceuticals. The results are presented in Fig. 4 and 5.
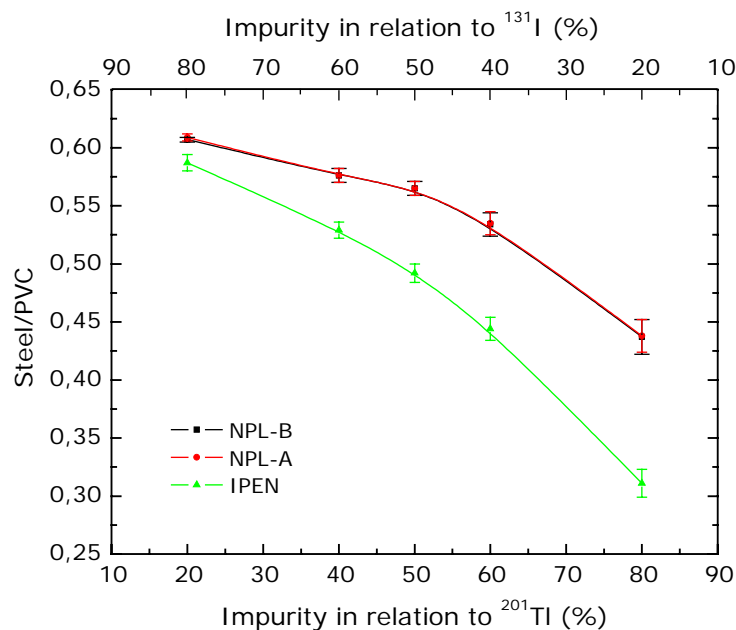

FIG. 4. *Ratio between the response using the steel and PVC absorbers to different impurity percentual of ^{131}I and ^{201}Tl for NPL-A, NPL-B and IPEN dose calibrators*
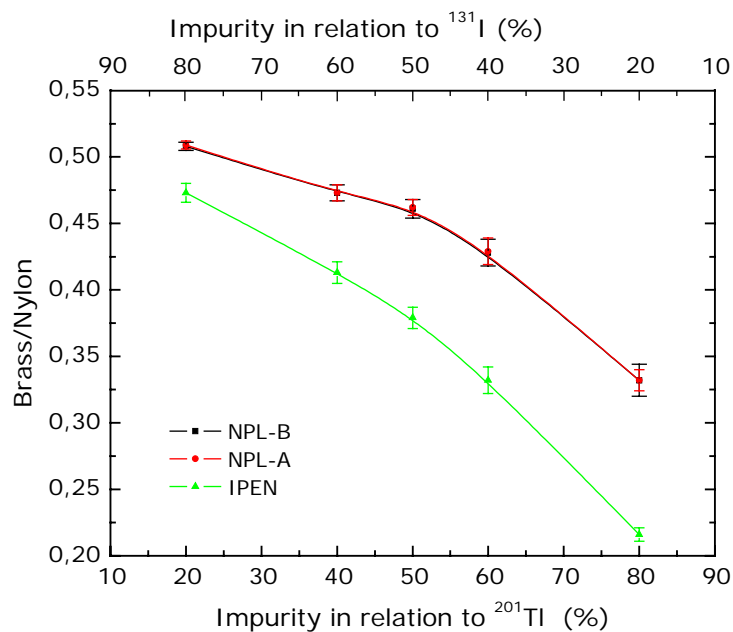
FIG. 5. *Ratio between the response using the brass and nylon absorbers to different impurity percentual of ^{131}I and ^{201}Tl for NPL-A, NPL-B and IPEN dose calibrators*

The reference dose calibrators present the same results, but all three systems show very good performance: the deep decrease in the response ratios demonstrates the applicability of the proposed method. It is very simple to detect the presence of impurities in radiaopharmaceuticals using tandem systems: therefore the method may be applied as an additional quality control test.

4. Conclusion

The dose calibrators showed good results for all tests. The tandem systems showed to be stable and reproducible. The ratio between the measurements was kept constant for all dose calibrators and for each of the radiation sources, confirming the stability of all tandem systems.

The use of tandem systems is specially important and recommended for quality control programs in nuclear medicine departments, because they can indicate the presence of impurities in the radiopharmaceuticals, if the ratio between the measurements is different from that obtained at the laboratory in ideal conditions, avoiding the procedure repetition, and therefore the increase of the patients and to the staff exposure to radiation.

Acknowledgement

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