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Applied Radiation and Isotopes 63 (2005) 493–503
Applied Radiation and Isotopes
www.elsevier.com/locate/apradiso

Comparisons of activity measurements with radionuclide calibrators—A tool for quality assessment and improvement in nuclear medicine

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Received 25 March 2005; received in revised form 11 May 2005; accepted 12 May 2005

Abstract

A national program of ongoing comparisons for assaying gamma-emitting radiopharmaceuticals for amount of radioactivity using radionuclide calibrators was begun in 2000. Nuclides of the most wide-spread use in Cuban nuclear medicine, ^{131}I, ^{201}Tl and ^{99m}Tc, as well as two measurement geometries, glass vials and plastic syringes, were employed.

In this paper, the participants' performance is assessed by mean of a statistical analysis of the reported data. Performance tables have been obtained and a χ^2 statistic is calculated from observed and expected frequencies, with the aim of testing the hypothesis about the independence of some characteristics of the comparison results, at a significance level $\alpha = 0.05$. The proportion of satisfactory results in the years 2002–2004 were found to be at the same level, but higher than in 2000. It reveals an improvement of the measurement quality since 2002. The causes of improvement were investigated using the statistical treatment of several data available as supplementary information.

Keywords: Radionuclide calibrator; Activimeter; Comparison; Activity measurements; Nuclear medicine; Statistical analysis; Chi-square test

1. Introduction

The practice of nuclear medicine involves the injection of drugs, labelled with radioactivity, that target specific diseased tissues. The safety and effectiveness of these drugs depend, among other factors, on the ability of the radiopharmacy or clinic to accurately determine the amount of radioactivity, which ultimately determines the dose to the patient, contained in the drug prior to its administration. That is why regulations and limiting values for the uncertainties of activity measurements have been prescribed (European Pharmacopoeia, 2001; Guía, 2002).

The main instrument for activity measurements in the field of nuclear medicine is the radionuclide calibrator, also known as "activimeter". Since the first pilot studies carried out by Garfinkel and Hine (1973) that measured radionuclide sources in US hospitals with different types of radionuclide calibrators, a system of ongoing comparisons using this type of instrument has been reported for a relatively limited number of countries practising nuclear medicine. In the US, a voluntary program of the College of American Pathologists for

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doi:10.1016/j.apradiso.2005.05.051

laboratory intercomparison of radionuclide calibrators (Herrera and Paras, 1983), was operational until the first-half of the 1980s. Since that time, there is no user program in the US directed to the performance evaluation of radionuclide calibrators measurements in clinics and hospitals, although some evaluations of these measurements have been organized using calibrated samples distributed by commercial pharmaceutical laboratories (Paras et al., 1986; Coursey and Calhoun, 1986). On the other hand, since 1975, the National Institute of Standards and Technology has maintained the Measurement Assurance Programme aimed at developing and distributing reference sources and providing calibration services to the radionuclide producers and radiopharmaceutical manufacturers in North America (Golas and Calhoun, 1983; Zimmerman, 2003).

Nowadays, the implementation of ongoing comparison programs for activity measurements of radiopharmaceuticals with the purpose of quality improvement of the end-user service has been reported in the United Kingdom (Woods, 1981, 1987; Woods et al., 1996, 1997a, b; Woods and Baker, 2003; Ciocanel et al., 1999; Baker and Woods, 2000, 2001), Canada (Santry, 1998), Brazil (Iwahara et al., 2001, 2002; dos Santos et al., 2003, 2004), Argentina (Rodríguez Pasqués et al., 1983; Furnari et al., 1992), Hungary (Szörényi and Vágvölgyi, 1983, Szörényi et al., 1998), Germany (Debertin and Schrader, 1992) and the Czech Republic (Olšovcová, 2004; Olšovcová and Dryák, 2003). Results of similar programs in India (Srivastava and Kamboj, 1982; Joseph et al., 2003) and Australia (Smart, 1995) have also been published.

The Radionuclide Metrology Department of the Isotope Center of Cuba (CENTIS-DMR), as the national metrological laboratory for radioactivity, has developed a joint research project with the Centro de Control Estatal de Equipos Médicos, the Cuban regulatory authority concerned with the use of medical equipment in the country. In the frame of this project, there is a national program of ongoing comparisons for assaying gamma-emitting radiopharmaceuticals for amount of radioactivity in radionuclide calibrators that has been operating since 2000. That collaboration has allowed the technical and regulatory capabilities to be linked in such a way that the comparisons can play a more active role as a tool for quality improvement of measurements in nuclear medicine. Results of the 2002 exercises were previously published (Oropesa et al., 2003).

This assessment of measurement capabilities, via a system of ongoing comparisons, requires the use of statistical methods for comparing several characteristics of the reported data, such as accuracy, date, radionuclide and measurement geometry. This would enable problems to be identified and would also facilitate, on the basis of statistical analysis, the evaluation of the efficacy of corrective and preventive actions applied as an outcome of the comparisons. It would also allow any improvement of the measurement quality to be demonstrated. Authors have usually limited themselves only to the exposition of the comparison data including the calculated statistical parameter selected for performance evaluation of the participants and the relative percentage of acceptable or non-acceptable results. Nevertheless, even when an improvement in the participant's performance over time or a better execution for a given nuclide are declared, the comparison of the specific characteristics of the data on the basis of a statistical criteria for supporting such a declaration is rarely shown.

This paper presents and discusses the outcomes of the ongoing comparisons in radionuclide calibrators conducted during 2000–2004. Hypotheses about the independence of several characteristics of the comparison data are evaluated using a χ^2 test. As an outcome of this analysis, no dependence was detected between radionuclide and performance or between measurement geometry and performance. On the other hand, the proportions of satisfactory results in the 2002–2004 years were found to be at the same level, but higher than in 2000. It reveals an improvement of the measurement quality starting from 2002. The causes of improvement are investigated using the statistical treatment of several data available as supplementary information.

2. Comparisons

Comparisons were organized in compliance with the ISO/IEC 43-1 guide (ISO/IEC, 1997), following the known-value scheme. Radioactive samples with a known radionuclide activity were sent to each participant and measured only by that participant. Therefore, it is possible to evaluate the capability of an individual laboratory to measure the activity of the sample and provide numerical results for comparison with the assigned value at CENTIS-DMR. Eleven nuclear medicine departments and the two laboratories of the Isotope Center that are involved in the production of radiopharmaceuticals in the country took part in the comparisons during 2000–2004.

Participants were asked to apply their established routine procedures for measuring the sample activity in the radionuclide calibrator. Supplementary information has been requested about the instrument used and the measurement procedure. Therefore, the exercises checked not only the instruments, but also the procedures used in the routine determinations and the performance of the personnel involved in the measurements.