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Review

Radionuclide metrology in the life sciences: Recent advances and future trends

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Abstract

This paper reviews activities in the field of radionuclide metrology applied to the life sciences between the years 2000 and 2005. The requirements for accuracy and consistency in making radioactivity measurements in radiation medicine, coupled with an increased awareness of the role of measurement standards in quality assurance programmes, has prompted a great deal of research in this area. During the past 5 years, particular emphasis has been on: (1) the development of primary standards for radionuclides, (2) development of secondary/transfer standards, (3) development of radionuclide standards for brachytherapy, and (4) inter-laboratory comparisons at the end-user level. Activities carried out by National Metrology Institutions in these areas are reviewed and a look at future trends is presented.

Keywords: Life sciences; Radionuclide metrology; Quality assurance; Review

Contents

1. Introduction

Radionuclide metrology is taking on an increasingly important role in the life sciences. This is due in part to the spread of a culture that recognizes the importance of implementing quality assurance (QA) programmes to ensure the accuracy and consistency of measurements that influence their work. The use of traceable standards for initial instrument calibration and ongoing performance checks are a vital part of such QA programmes. Although QA programmes are implemented in many laboratories in a variety of different disciplines, the field of radiation medicine places particular emphasis on QA because of the

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impact that the results have on human lives. New advances are made every year in the production of potential radionuclides that can be used in both diagnostic and therapeutic applications and new drugs are constantly being developed and tested. All of these aspects involve some kind of measurement of radioactivity content in the sample being investigated, which requires new standards to be developed to meet these needs. It is, therefore, not surprising that much of the recent activity being carried out by the radionuclide metrology community in the past 5–10 years dealing with the life sciences has involved nuclear medicine.

The quality of radioactivity measurements at all levels of nuclear medicine practice, from radionuclide production, to radiopharmaceutical formulation, to patient administration, plays an important role in the quality of care that a patient receives. Because the radiation dose received by the patient is strongly linked to the amount of injected activity, accurate delivery of radiopharmaceuticals requires that the measurements be made on instruments calibrated and maintained through the use of standards.

The importance of standards is also apparent throughout the drug development process. Before a drug can be marketed in most countries, the radiopharmaceutical must undergo a series of clinical trials that demonstrate safety and effectiveness. Such studies usually involve a large number of centres located in different countries. In order to draw the most useful conclusions from the studies, the radioactivity measurements must be performed on instruments that have been calibrated against a common standard. To make this possible, National Metrology Institutes (NMIs), which are given the responsibility of developing and maintaining standards, must establish a degree of equivalence to each other through comparisons.

The purpose of this paper is to review recent advances made in the field of radionuclide metrology of relevance in radiation medicine. Because changes and developments in the field occur at such a rapid pace, the time frame chosen for this review is from the year 2000 until the middle of 2005. Only results reported in the refereed literature are considered.

One can see when reviewing the literature that the main areas of research in radionuclide metrology in radiation medicine reported were:

- development of standards for new radionuclides,
- development of transfer standards,
- development of radioactivity standards for brachytherapy applications, and
- the organisation of national comparisons between NMIs and end-users.

2. Development of standards for radionuclides

2.1. New radionuclides

In attempting to develop the perfect "magic bullet" for the diagnosis and treatment of different diseases, researchers continue to test different types of compounds and radionuclides with which to label them. In order to enable researchers to make accurate assessments of production yields, assay for radionuclidic impurities, and make accurate measurements of the amount of injected radiopharmaceuticals during trials, it is necessary for NMIs to develop standards for new radionuclides under investigation.

During the past five years, NMIs have been very active in developing primary standards in response to the demands of the nuclear medicine community. One of the promising radionuclides being investigated for use in radiotherapy using radiolabeled peptides is ^{177}Lu (Erion et al., 2000a,b; Meredith et al., 1996). Zimmerman et al. (2001) from the National Institute of Standards and Technology (NIST) and Schötzig et al. (2001) from the Physikalisch-Technische Bundesanstalt (PTB) reported on the independent development of primary standards for this radionuclide. For the PTB study, both the $4\pi\beta$–γ coincidence technique and liquid scintillation counting (LSC) using the CIEMAT/NIST efficiency tracing method (Coursey et al., 1986; Zimmerman and Collé, 1997) were used. Both results agreed to within 0.7%, with relative standard uncertainties of 0.22% and 0.4%, respectively. In the NIST study, LSC with the CIEMAT/NIST method was also applied and gave activity results with a relative standard uncertainty of 0.4% that were used to determine a number of calibration figures for Capintec radionuclide activity calibrators.

Another radionuclide that continues to be of interest is ^{188}Re, which is most conveniently obtained from a ^{188}W/^{188}Re generator (Knapp, 1998; Knapp et al., 1997). Although standards for ^{188}Re have existed for some time (Coursey et al., 1990), its half-life is too short (17.00 h) to allow for reference sources to be produced and distributed to end-users on a frequent basis. For this reason, Zimmerman et al. (2002) developed a standard for the ^{188}W and ^{188}Re in equilibrium, which would allow the manufacturers of these generators to calibrate the activity of the generators against a traceable standard. A primary standardisation was carried out using the CIEMAT/NIST efficiency tracing method. In this case, the parent radionuclide ^{188}W, which decays purely by electron capture, accounted for only a very small part of the LSC spectrum, with the majority of the spectrum arising from the β-decay of the ^{188}Re daughter. Therefore, the ^{188}W activity was inferred from the total LSC spectrum and the assumption of secular equilibrium with a relative standard uncertainty of 0.42%. In addition to the primary standardisation, a number of calibration factors for the Capintec radionuclide activity calibrator were determined.

Most radionuclides used in radiotherapy have properties that make them relatively easy to calibrate. This includes undergoing β-decay with relatively long half-lives. Conversely, many radionuclides used in nuclear medicine imaging have short half-lives. This makes it very difficult to produce and calibrate standardised reference sources. Nonetheless, a series of experiments to standardise the