Applied Radiation and Isotopes 113 (2016) 22–27

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

The concept of minimum detectable activity of radionuclide activity meters and their suitability for routine quality control of radiopharmaceuticals. An experimental study

F. Zagni [a,*], F. Cesarini [a], G. Lucconi [b], G. Cicoria [a], D. Pancaldi [a], A. Infantino [c], S. Vichi [c], M. Marengo [a]

[a] Medical Physics Department, University Hospital, S.Orsola - Malpighi, Bologna, Italy
[b] Postgraduate School in Medical Physics, Physics Department, University of Bologna, Bologna, Italy
[c] Nuclear Engeneering Laboratory of Montecuccolino, University of Bologna, Bologna, Italy

HIGHLIGHTS

- Performance of several activity meters in low-signal conditions was evaluated.
- Minimum Detectable Activity (MDA) was estimated with experimental measurements.
- MDA values are strictly connected to the widely used concept of "Limit of Quantification" or LOQ.
- A generalized procedure for estimating the MDA is presented.
- Feasibility of possible applications (QCs) in the radiopharmacy routine is discussed.

ARTICLE INFO

Article history:
Received 29 July 2015
Received in revised form
4 February 2016
Accepted 8 March 2016
Available online 7 April 2016

Keywords:
Activity meters
Dose calibrators
MDA
Radiopharmacy
Quality Controls

ABSTRACT

Radionuclide activity meters ("dose calibrators") are ionization chambers designed to measure relatively high amount of activities which are normally contained in radiopharmaceuticals. However, in the current radiopharmacy practice, these radiation detectors have been proposed to be used in measurements of samples with lower activity, such as in routine quality control (QC) tests. To check the feasibility of such measurements, in this work we assessed the performance of four different devices in the lower range of detectability, by means of experimental measurements of a radioactive sample. Accuracy and precision of each device was evaluated as a function of the activity contained in the sample in order to estimate a threshold value, or minimum detectable activity (MDA), which, according to our operational definition, may be used to express the concept of Limit of Quantification (LoQ). Moreover, a generalized procedure for the estimation of the MDA was established, which, being device- and radionuclide-independent, it may be adopted by every laboratory.

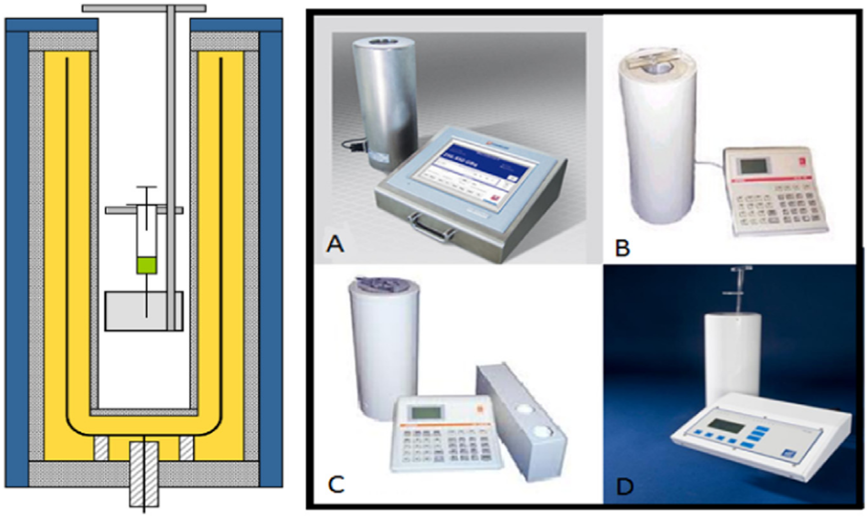
Our results showed a significant variability in the MDA achieved by different activity meters. Hence a single QC test may result feasible with one specific instrument, and not with another one. Moreover, feasibility depends also on the confidence level required for each test. For these reasons, each activity meter should be qualified for its MDA or LoQ by each laboratory according to a procedure such as that described in this paper.

1. Introduction

Radionuclide activity meters (sometimes improperly called "dose calibrators") are radiation detectors widely used in nuclear medicine and radiopharmacy facilities in the radiopharmaceutical preparation process, such as the measurement of the activity contained in injectable solutions. These devices are re-entrant ionization chambers (Fig. 1a) which are designed to measure, through an electrometer, the charge produced within the internal gas due to the interaction of the ionizing radiation (mostly gamma) emitted from the sample placed inside the well. The reading, in terms of current, must to be corrected by an appropriate calibration factor, in order to convert it to an activity measurement. Several methods have been established to evaluate the calibration

* Corresponding author.

http://dx.doi.org/10.1016/j.apradiso.2016.03.012
0969-8043/



(a) (b)

Fig. 1. Schematic drawing of a cross section of a radionuclide activity meter (a) and the four activity meters tested in this work (b), reported in Table 1.

Table 1
Activity meters tested in this work.

	Manufacturer	Model
A	*MecMurphil s.r.l.*	MP-DC CH8 Standalone
B	*Capintec Inc.*	CRC15-PET
C	*Capintec Inc.*	CRC15-BETA
D	*Veenstra Instruments*	VDC-404

factors, such as the use of a reference source containing a certified amount of activity for each radionuclide of interest, or the use of a cross-calibrated source with similar emission (Zimmerman, 2010). These devices are thus designed to measure relatively large amount of activity and are known to be accurate in the range from few MBq to tenth or hundreds GBq (Zagni et al., 2011).

However, in several circumstances, activity meters are used, or have been proposed to be used, in measurements of activity close to the lower limit of sensibility. For example in routine radiopharmaceutical quality controls, such as the radiochemical or radionuclidic purity checks (Briner and Harris, 1974). In this work we evaluated the performances of several activity meters in the lowest range of measurement, in order to check the feasibility of extending their use, and to determine the limits of usage, in applications concerning the measurement of low activity samples. To this aim, we established an experimental procedure and data analysis in order to estimate the minimum detectable activity (MDA). In fact, while international standards and protocols are available on the standardization of the accuracy and the performances of these devices (IEC,1992, 1994, 2006; ANSI, 2004; IAEA, 2006), no indications are available regarding the MDA estimation for this class of devices.

The determination of the minimum signal for radiation detectors usually involves the statistical analysis of the pulse counts caused by single events, along with background or interfering pulses, in order to evaluate a decision rule for the limit of detection (Currie et al., 1968; Altshuler and Pasternack, 1963). For activity meters this approach cannot be adopted directly since the electronics of these detectors collects the charge in long period of time (typically 2–10 s), compared to the pulses rate on the electrode, so that an average is carried out. Nevertheless, in this work we preserved the same rationale as proposed by Currie, adapting it, as described in the following, to the experimental quantities that are available for measurement with activity meters. Besides, the MDA values we report in this paper may also be referred to the concept of limit of quantification (LoQ) (Currie, 1984, 1999), as the proposed method allows for the evaluation of the detection performance as a function of the amount of activity measured with these devices.

2. Materials and methods

2.1. Activity meters and acquisition setup

Four different activity meters installed at our institution were tested in this work and are reported in Table 1 and Fig. 1b. To evaluate the response at low activity, a vial containing at least 10 MBq of freshly eluted ^{99m}Tc (gamma emitter, half-life 6 h), was assayed with each device at fixed time intervals, until complete decay (i.e. no activity reading). This procedure is very similar to the time-decay method for the routine linearity test which should be performed by each facility within the routine quality assurance program (IAEA, 2006). The background, assessed prior to each measurement series, was automatically subtracted from each activity reading. Since each acquisition sequence took several hours, and in order to record the measurements at precise time intervals, the recording of each measurement was performed in an automated way. For the recent activity meters, such as the MP-DC, the acquisition was performed with the embedded software, which allows for automatic acquisitions at fixed intervals. For the other activity meters, the acquisitions were performed through a webcam, connected to a laptop, suitably programmed to take a picture of the console at predetermined times. Then the pictures were read at once and the data were transferred in digital form for further processing. The timestamps of each picture file were used as acquisition times, since we observed a deviation from the programmed time of some seconds during the whole acquisition, probably due to the webcam lag time.

The procedure was repeated, for each activity meter, using another radionuclide, namely ^{11}C ($\beta+$ emitter, half-life 20.4 min). The acquisition time intervals were chosen as $t_s = T_{1/2}/20$, being $T_{1/2}$ the half life of the radionuclide, in order to obtain equal sampling rates for the acquisitions performed with different radionuclides.

Moreover, the same procedure was repeated several times using the same activity meter, in order to determine the variability