Artigo Original

Comparison between different methodologies for the determination of minimum detectable activity of the in vivo internal dosimetry system

Comparação entre diferentes metodologias para a determinação da atividade mínima detectável dos sistemas de dosimetria interna in vivo

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Abstract
The minimum detectable activity (MDA) represents the minimum value of activity that can be detected in a counting system. There are several methodologies that can be used to calculate the MDA, however their results can be divergent. In vivo internal dosimetry laboratories should have the MDA for each type of counting geometry, as well as for each type of radionuclide of interest. The objective of this work was to compare three methodologies for MDA calculation with experimentally obtained results. The calculation methodologies used were those suggested by Currie (1968), Health Physics Society N13.30 (1996) and ISO 11929 (2018). The MDA experimental values were obtained by monitoring a physical head simulator with ^{18}F-FDG solution in the corresponding brain region until complete decay. The results for the MDA values using the three different methodologies presented differences according to the activity ranges analyzed. The uncertainties of the calibration coefficient and no-exposed person background were the main parameters that contribute to these dissimilarities. The methodology choice can cause up to 90% differences in the MDA values. Experimental MDA showed a good agreement with MDA values calculated using ISO 11929 and Currie methodologies
Keywords: *Minimum detectable activity; in vivo internal dosimetry; Head phantom.*

Resumo
A atividade mínima detectável (AMD) representa o valor mínimo de atividade que pode ser detectada em um sistema de monitoração. Existem diversas metodologias que podem ser utilizadas para calcular a atividade mínima detectável, no entanto os resultados para cada uma destas podem divergir entre si. Laboratórios de dosimetria interna in vivo devem dispor de parâmetros de cálculo para a atividade mínima detectável para cada tipo de geometria de contagem, bem como, para cada tipo de radionuclídeo de interesse. O objetivo deste trabalho foi comparar três tipos de metodologias de cálculo de AMD com resultados obtidos experimentalmente. As metodologias de cálculo utilizadas foram as sugeridas por Currie (1968), Health Physics Society N13.30 (1996) e ISO 11929 (2018). Os valores experimentais de AMD foram obtidos monitorando de um simulador físico de cabeça contendo na região correspondente ao cérebro com 18F-FDG até o seu completo decaimento. Os resultados obtidos para os valores de atividade mínima detectável utilizando as três diferentes metodologias apresentaram diferenças de acordo com as faixas de atividades analisadas. As incertezas do coeficiente de calibração e das contagens de fundo de pessoas não-expostas foram os principais parâmetros que contribuíram para as variações nos AMD obtidos com as três metodologias de cálculo. Diferenças de até 90% no valor de AMD podem ocorrer dependendo da metodologia de cálculo escolhida. O valor de AMD obtido experimentalmente apresentou boa correlação com os valores calculados usando as metodologias propostas por Currie e na ISO 11929.
Palavras-chave: Atividade mínima detectável; dosimetria interna in vivo; Simulador físico.

1. Introduction

The minimum detectable activity (MDA) is the lowest activity that can be reliably detected in a counting system under specific measurement conditions (1). This concept was developed by Lloyd Currie, 1968 (2) and has appeared frequently in the literature (3) such as the Health Physics Society N13.30 (4), ISO 11929 (5) and others (6,7)Usually, *in vivo* dosimetry laboratories, the MDA is important to be known the different counting systems and, for the main type of radionuclides of interest, aiming at the optimization of the internal monitoring process (8). The Internal Dosimetry Laboratory of the Nuclear Technology Development Center (LDI/CDTN) located in Belo Horizonte - MG, Brazil is contamination of workers of the Research and Production of Radiopharmaceuticals Unit (UPPR/CDTN) involved in the production of ^{18}F-FDG. Studies with phantoms have already been performed for the calibration of the internal contamination monitoring system with ^{18}F-FDG (9–12), these simulators are

used to obtain the calibration coefficient (CC). The CC is one of the most important parameters to calculate the activity present in the sample. It is used to convert the net counts obtained in the counting system while monitoring an individual with suspected internal contamination in the activity of incorporated radionuclide. For the calibration of the counting system, the simulator have to be human-like composition, anatomy, and produced with materials that mimic body composition, as suggested by ICRU 44 (13). The simulator used in this work is an anatomical model of the polyvinyl chloride skull, filled with a colloidal material representing the brain containing ^{18}F-FDG (14). The ^{18}F-FDG accumulates referentially in the brain say, approximately 8% due to high glycolytic metabolism and this radiopharmaceutical is glucose analogous (15).

Currently, there are different methods for MDA calculation. Lloyd Currie, 1968 (2) developed one of the first MDA calculation methodologies, which is based on hypothesis testing, which over the years has established itself as the standard method for estimating detection limits, as it is simple and statistically reliable. From concepts based on Currie's work (2), HPS N13.30 standard (4), and ISO 11929 (5) adopted such methodology with some adaptations. However, the methodologies have distinctions in their determinations and consequently variations between the results (7,16).

The objective of this work was to compare three different MDA calculation methodologies suggested by Currie (2), HPS N13.30 (4) and ISO 11929 (5) and to determine an real experimental situation of MDA using a head simulator containing tissue simulator material equivalent to with the ^{18}F-FDG radiopharmaceutical.

2. Materials and methods

Three methodologies were used to calculate AMD. The methodology established by the Health Physics Society (4) is the one with the simplest equation:

$$\text{MDA}_{\text{HPS}} = \frac{3 + 4{,}65\sqrt{\bar{\mu}_B}}{\nu} \qquad (1)$$

where, $\bar{\mu}_B$ is the mean of the counts of unexposed individuals in the region of interest (ROI) of the photopeak; and ν, is the product of the in vivo system calibration coefficient (CC) and the counting time (t), given by the equation:

$$\nu = CC \cdot t \qquad (2)$$

The second methodology was designed by Currie, 1968 (2) considers the uncertainty associated with the mean of the counts of unexposed individuals in the region of interest (ROI) of the photopeak. Currie's MDA equation is:

$$\text{MDA}_{\text{currie}} = \frac{L_D}{\nu} \qquad (3)$$

where, ν is given in equation 2 and L_D, is the detection limit of the in vivo counting system calculated according the equation:

$$L_D \equiv \frac{-b + \sqrt{b^2 - 4ac}}{2a} \qquad (4)$$

For the Currie methodology the terms *a*, *b* and *c* are given according to the following equations:

$$a = 1 \qquad (5)$$

$$b = -(2k_{(1-\alpha)}^2 \sigma_0 + k_{(1-\beta)}^2) \qquad (6)$$

$$c = (k_{(1-\alpha)}^2 - k_{(1-\beta)}^2)\sigma_0^2 \qquad (7)$$

where $k_{(1-\alpha)}$ is equal to 1.645 the significance level α = 0.05; $k_{(1-\beta)}$ is also equal to 1.645 for the power of the test (1-β) = 0.95; and σ_0 is the uncertainty associated with the counts of unexposed individuals in the ROI, and given in the following equation:

$$\sigma_0 = \sqrt[2]{\bar{\mu}_B + \sigma_{\bar{\mu}_B}^2} \qquad (8)$$

The third methodology was presented in ISO 11929 (5). This calculation method take in to account the uncertainty associated with the mean of the counts of unexposed individuals in the region of interest (ROI) of the photopeak and the uncertainty associated to the calibration coefficient. The ISO 11929 formulation works directly in units of activity and the equation is given by:

$$\text{MDA}_{\text{ISO}} = L_D \equiv \frac{-b + \sqrt{b^2 - 4ac}}{2a} \qquad (9)$$

where, L_D has the same equation 4. However, the terms *a*, *b* and *c* are different and given according to the following equations:

$$a = \left(1 - k_{(1-\beta)}^2 \frac{\sigma_\nu^2}{\nu^2}\right) \qquad (10)$$

$$b = -\left(2k_{(1-\alpha)} - k_{(1-\beta)}^2\right)\sigma_0^2/\nu^2 \qquad (11)$$

$$c = \left(k_{(1-\alpha)}^2 - k_{(1-\beta)}^2\right)\sigma_0^2/\nu^2 \qquad (12)$$

where, σ_ν is the uncertainty associated to the product of CC and the counting time (ν).

More detail about Currie and ISO 11929 MDA calculation can be found in the work of Kirkpatrick et al., 2013 (7).

The physical head phantom was used to obtain the CC. It consists of a PVC skull filled with a suspension of agar, water, urea and ^{18}F-FDG. The radiopharmaceutical was produced on the GE-PET trace 8 cyclotron on CDTN/CNEN. The CAPINTEC CRC-25R$^{\circledR}$ activimeter was used to aliquot the ^{18}F-FDG activity for preparation of the head phantom. The head phantom

filled with ^{18}F-FDG material was prepared for five experiments. The counting time (*t*) was set to 1000 seconds of live time (i.e. dead time corrected by the software). The counts in F-18 ROI were measured as many times as possible until the total decay of the activity of the phantom. The CC was calculated as the quotient of the counting rate (CPS) and the mean activity in the phantom at the time of the counting (time corrected). The CC unit is (CPS.Bq^{-1}). The results of the mean CC and the standard deviation were calculated from the values obtained for each monitoring procedure in the five different experiments. The obtained CC result was used to calculate the MDA for the three methodologies proposed. The uncertainty associated with CC was used to calculate the MDA of ISO 11929 (5).

Figure 1 - Set-up of monitoring of non-exposed individuals (A) and physical head simulator (B) in counting system with upper part of skull facing NaI(Tl) 75mm x 75mm scintillation.

The value of the CC and its uncertainty can vary considerably depending on the radionuclide activity in the phantom at the time of measurement (17). Thus, three different phantom activity ranges were established to the calculation of the mean CC and it's respective uncertainty: i) activities in the phantom below 300Bq; ii) activities in the phantom above 300 Bq; and iii) full range of activities. The 300 Bq limit was chosen because below this activity the relative error in the counts provided by the acquisition software was higher than 3 %.

To obtain the experimental MDA the head simulator counts were performed until it was no more possible to identify the F-18 photopeak in the spectra. The MDA was calculated based on the last non-zero area in the F-18 photopeak ROI.

Data were analyzed using the Minitab statistical software. Analysis of variance (ANOVA) with Tukey pair wise comparisons was used to compare means between calibration coefficient groups. The significance level (α) adopted was 0.05.

3. Results and discussion

The mean counts of unexposed individuals positioned in the monitoring system, in F-18 ROI, with the counting time of 1000 seconds was 8470 ± 213 CPS.

All the CC calculated in the five experiments are plotted in Figure 2. The dead time, corrected by the software in each measurement, is also shown. The minimum activity in witch CC could be calculated was 27 Bq and the maximum activity used in the CC calculations was 1,5 MBq.
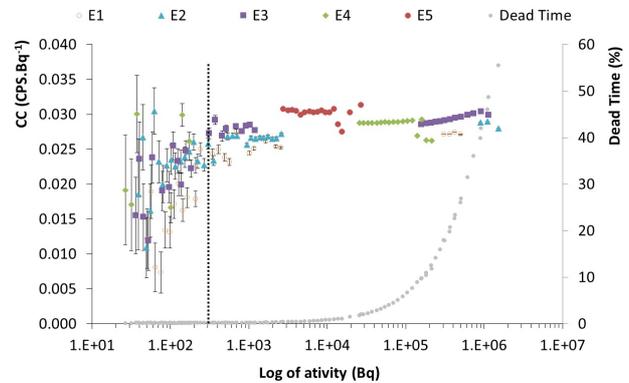

Figure 2 - Calibration coefficients calculated in the five experiments (E1 to E5) and the dead time of the counting system. The dotted line indicate the 300 Bq activity limit.

The average CC and coefficient of variation (CV) calculated in the head simulator experiments for different ^{18}F-FDG activity ranges in the phantom were presented in Table 1. Results show higher uncertainties for CC values calculated for activities < 300 Bq than the CC values for activities > 300 Bq. This fact was expected due to poor counting statistics at low activity. However, data in table 1 also show that CC obtained for activities < 300 Bq were significantly lower than CC calculated when the phantom has activities higher than 300 Bq. Since the software made automatic corrections for the dead time, the increasing efficiency of the counting system at lower activities were not expected. Nevertheless, it occur. Future analysis of the automatic correction algorithm of the software should be made.

Table 1 – Calibration Coefficient, CV and Tukey pairwise grouping calculated for different phantom activities range.

Phantom Activity Range	CC (CPS.Bq^{-1})	CV (%)	Tukey Pairwise Grouping
< 300 Bq	0.021	15.3	B
> 300 Bq	0.028	6.3	A
Full range	0.026	12.9	A

Results of MDAs calculated using the three methodologies are shown in Table 2. The MDAs obtained using the CC of the activity range below 300 Bq presented high values in relation to the other ranges for all calculation methodologies. This range of activity highlights the increase in uncertainties due to the low counting rate, which explains the high variation between the results. It is noteworthy that the majority of contaminations in the routine of radiological practices occurs in the low activity range (9).

Table 2 – MDAs (Bq) obtained by the three calculation methodologies, for different activity ranges present in the simulator.

Methodology	MDA (Bq) according the phantom activity range		
	< 300 Bq	> 300 Bq	Full range
HPS, 1996	20 ± 3	15 ± 1	17 ± 2
Currie, 1968	36 ± 5	27 ± 2	30 ± 4
ISO 11929	38 ± 6	28 ± 2	31 ± 4

Differences of 80% and 90% can be observed between HPS (4) MDA values compared to Currie (2) and ISO 11929 (5) respectively (p<0.05) for activity range < 300 Bq .There was no significant difference between Currie (2) MDA and ISO 11929 (5). The same pattern was repeated for the activity range > 300 Bq and for the full range.

The main differences between the methodologies analyzed are in the approach to the system CC and BG uncertainties. The methodology proposed in ISO 11929 (5) takes into account in its calculation the uncertainties associated with CC and $\bar{\mu}_B$. The approach proposed by Currie considers only the uncertainties associated with the $\bar{\mu}_B$ of the system. The methodology suggested by HPS N13.30 considers $\sqrt{\bar{\mu}_B}$ as uncertainty associated with counts of unexposed individuals in the region of interest (ROI). Only to illustrate, the $\bar{\mu}_B$ measured in this paper was 8470 ± 213. The square root of BG is about 92, which is much lower than the uncertainty measured for the system under analysis. This fact explains why the HPS N13.30 MDA were always lower among all MDA evaluated at all activity ranges. In this work Currie and ISO 11929 methodology resulted in similar MDA values. Differences between these two methodologies may arise if uncertainties associated to $\bar{\mu}_B$ are lower or CC uncertainties were higher than 15%.

It is also noteworthy that the MDA value of the system in question, calculated by Oliveira and collaborators (18), using the methodology suggested by HPS

N13.30 was 16 Bq. It is very close to the values obtained for the activity range > 300 Bq (MDA = 15 Bq) and for full activity range (MDA = 17 Bq) using the same methodology.

Mean MDA experimentally obtained based on the last non-zero area in the F-18 photopeak ROI was 37 ± 8. This mean value was compatible to ISO 11929 and Currie calculated MDA for the < 300 Bq activity range. In this activity range, system operates closer to the detection limit. This fact may explain the best correlation of calculated and experimental MDAs.

5. Conclusions

In this work it was observed that the use of different methodologies for MDA calculations can result in differences up to 90%.

ISO 11929 (5) MDAs showed higher values in all activity ranges, in contrast HPS N13.30 (4) MDAs were always lower in all activity ranges evaluated with statistically significant differences between the other methodologies, especially due to the uncertainty approach.

Experimental MDA showed a good agreement with MDA values calculated using ISO 11929 and Currie methodologies.

Considering the three calculation methodologies used in this work and the experimental tests (2,4,5) the monitoring system MDA is between 15 and 38 Bq.

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