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Internal occupational dosimetry for the occupational worker exposed to [^{18}F] FDG from the Cyclotron-PET/CT Laboratory of the Universidad de Costa Rica

Dosimetría ocupacional interna para el personal trabajador expuesto a [^{18}F] FDG del ciclotrón-PET/CT en el Laboratorio de la Universidad de Costa Rica

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ABSTRACT: The aim of this work is to provide a methodology for evaluating the committed effective dose E(50) due to the incorporation of [^{18}F] FDG in the occupationally exposed worker (OEW) of the Cyclotron-PET/CT Laboratory of the Centro de Investigación en Ciencias Atómicas, Nucleares y Moleculares (CICANUM) at Universidad de Costa Rica using *in vivo* measurements. The measurement system was calibrated to perform *in vivo* measurements and defined as the corresponding bioassay function for the radiopharmaceutical used. The conversion factor was assessed with a known activity of ^{18}F in the geometry and measurement time established. Among the most relevant results, the measurement parameters and the calibration procedure were defined. A value of 1.73 x 10^3 Bq/cps for *in vivo* brain measurements was obtained as a conversion factor. This study provides a methodology, to evaluate the committed effective dose due to the incorporation of ^{18}F-FDG in a radionuclide production and diagnostic center.

KEYWORDS: Committed effective dose, [^{18}F] FDG, Internal dosimetry, in vivo measurements, nuclear medicine.

INTRODUCTION

The Cyclotron-PET/CT Laboratory of the Centro de Investigación en Ciencias Atómicas, Nucleares y Moleculares (CICANUM) of the Universidad de Costa Rica (UCR) is equipped with a 19 MeV Cyclotron (IBA, Kiube, Belgium) for the production of radiopharmaceuticals (principally [^{18}F] Fluorodeoxyglucose), and PET/CT system (Siemens Healthineers, Biograph Vision 450 Edge, USA).

Fluorine-18 (^{18}F) is a radionuclide with a half-life of 109.8 minutes which decays by β+ emission (97% probability) and electron capture (3% probability). The maximum energy of the β+ particles is 0.635 MeV with a maximum range in water of 2.4 mm, producing an annihilation effect when interacting with the electrons in the medium (IAEA, 2021). This results in back-to-back 511 keV annihilation photons (196% probability), making this an attractive isotope for PET/CT imaging (IAEA, 2021).

The synthesis of the radiopharmaceutical in the Cyclotron-PET/CT Laboratory begins with the production of ^{18}F from the Cyclotron through the ^{18}O (p, n) ^{18}F reaction (IAEA, 2021). The product of this reaction is redirected through special lines to hot cells where the synthesis of the [^{18}F] FDG radiopharmaceutical is carried out. Once the process is finished, the dispatch process is performed to send the radiopharmaceutical to the clinical area for use.

Once the radiopharmaceutical is synthesized, an occupationally exposed worker (OEW) must handle it for dispensing it prior to patient injection, during which external and internal exposures may occur. The OEWs are monitored for external

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exposure using personal radiation dosimeters from an accredited laboratory, while the internal exposure requires an *in-situ* quantification technique.

The committed effective dose (E(50) is a quantity that integrates the effective dose of a person given the incorporation of a particular radionuclide and is evaluated in a period of 50 years after the incorporation. This period of 50 years represents the period of possible dose accumulation over a working life (ICRP, 2007). Moreover, the ICRP recommends assigning the committed effective dose to the year the intake occurred for compliance with dose limits (ICRP, 2007).

The aim of this study is to provide a methodology to determine the committed effective dose E(50) due to the incorporation of [18F] FDG in the occupationally exposed worker of the Cyclotron-PET/CT Laboratory of the Universidad de Costa Rica using *in vivo* measurements. The proposed methodology will evaluate the committed effective dose E(50) of the OEWs from two different areas of the same laboratory. One section is related to the monitoring of OEWs that are working in the production of [18F] FDG (the Cyclotron Unit of the Laboratory) in which there are different potential risks of incorporation of the [18F] FDG, especially at the time of synthesis of the radiopharmaceutical.

Moreover, the OEW monitoring procedure must follow our national radiological protection legislation. The second section is the PET/CT Unit of the Laboratory, where the risk of incorporation of [18F] FDG is very low because an intravenous (IV) administration is usually used with the patients. However, it has been noticed that for some patients, it is very difficult to place the IV into the vein due to the course of their treatment. Therefore, in some cases, direct injection into the vein occurs. The OEWs of the PET/CT Unit used all the protection equipment to manipulate the [18F] FDG source, and this study is complementary to the procedure that take place to address the effective dose.

MATERIALS AND METHODS

Standard source

Due to the short half-life of 18F, a solid standard source of solid 22Na was used to calibrate the *in vivo* detection system. A source (Eckert & Ziegler Group, USA) with an activity of 7.241 MBq (195.70 μCi) ± 3.0% (calibration date: 01 /10/2021). 22Na has a half-life of 2.6 years, with a positron emission decay, resulting in the formation of gamma rays of 511 keV and with an abundance of 179.91% ($I_{\gamma,\ Na22}$ = 1.7991) due to an annihilation process (IAEA, Nuclear Data Services, 2023).

Conversion factor

To calculate the conversion factor of the *in vivo* detection system, the detector efficiency, the decision threshold, the detection limit, and the minimum detectable activity were determined.

The efficiency of the detector from the 22Na source was obtained using the following equation (European Commission, 2018):

$$\varepsilon_f = \frac{N_{net}}{A_{reference} * I_{\gamma,\ reference} * T} \quad (1)$$

where N_{net} corresponds to the difference between the measured counts of the sample (N_G) and the background counts (N_B), $A_{reference}$ is the activity of the reference source (22Na source), $I_{\gamma,\ reference}$ is the emission probability of the reference source, and T is the measurement time, which is the same to be used for OEW measurements.

Next, the conversion factor which relates the detected counts with the activity given by the equation below, was calculated (Castellani *et al.*, 2013):

$$C_{rn} = \frac{1}{\varepsilon_f I_{\gamma,\ F18}} \quad (2)$$

here C_{rn} is the conversion factor, ε_f is the detector efficiency in the established geometry, and $I_{\gamma,F18}$ is the probability emission of 18F.

Since the measurements are affected by the background, the decision threshold (D_T) to avoid false positives with a confidence of 95% was obtained with the following equation (Knoll, 2010):

$$D_T = 2,326\sqrt{N_B} \quad (3)$$

here N_B is the number of background counts.

To make false negatives very unlikely, the detection limit (D_L) for 95% confidence was calculated through the equation (Knoll, 2010):

$$D_L = 4,653\sqrt{N_B} + 2,706 \quad (4)$$

Lastly the minimum detectable activity was obtained using the following equation (Knoll, 2010):

$$MDA = \frac{D_L}{\varepsilon_f I_{\gamma, F18} \cdot T} \quad (5)$$

where MDA is the minimum detectable activity of the detector, ε_f is the detector efficiency in the established geometry, $I_{\gamma,F18}$ is the probability emission of ^{18}F and T is the measurement time established to measure the OEW.

Calibration procedure

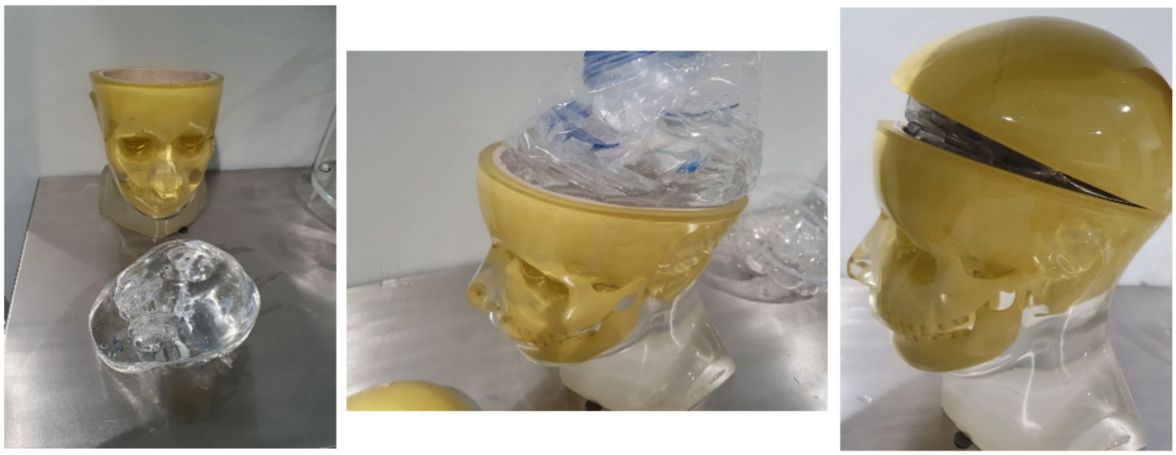
The *in vivo* measurement technique aimed to calculate the retained activity (amount of radionuclide present in brain) was implemented in the Cyclotron-PET/CT Laboratory using a Captus 4000 uptake probe (Capintec Inc, Florham Park, NJ, USA) with a NaI:Tl detector and an anthropomorphic head phantom (Capintec Inc., USA). To perform the measurements on the head phantom, the brain accessory was filled with water (see Figure 1.a). However, the calibration source was too large to fit into the accessory. Therefore, the volume of water inside the head brain insert (1145 ml) was transferred to a plastic bag to place the source in the geometric middle and simulate the brain inside the head phantom (see Figure 1.c).

The brain is the organ with the greatest retention of [18F] FDG (ICRP, 2015). Therefore, the geometry was established in such a way that the detector was positioned perpendicular to the occipital bone of the skull and at a distance of 25 cm (see Figure 2). The perpendicular position of the detector seeks to minimize photon crosstalk from other organs.

Five successive measurements of 2.5 minutes each were performed with the uptake probe in the established geometry to obtain the detector efficiency. The measurement time used in calibration is the same that will be used for *in vivo* measurements in the occupationally exposed workers of the laboratory. The established time minimized as much as possible the fatigue and stress of the OEW, allowing them to be able to keep their head as long as possible in the same position in which the uptake probe performs the count. Furthermore, the background measurements were considered.

The D_T, D_L, and MDA were calculated using background measurements on the head geometry and with the same measurement time set.

After the calibration, an assessment was made with a known activity of a liquid solution of ^{18}F



a) b) c)

Figure 1. Head phantom assemble for calibration. a) Filling of the brain accessory with water. b) Transfer of the water volume from the brain accessory to a plastic bag and placement of the calibration source. c) Assembly of the head phantom.

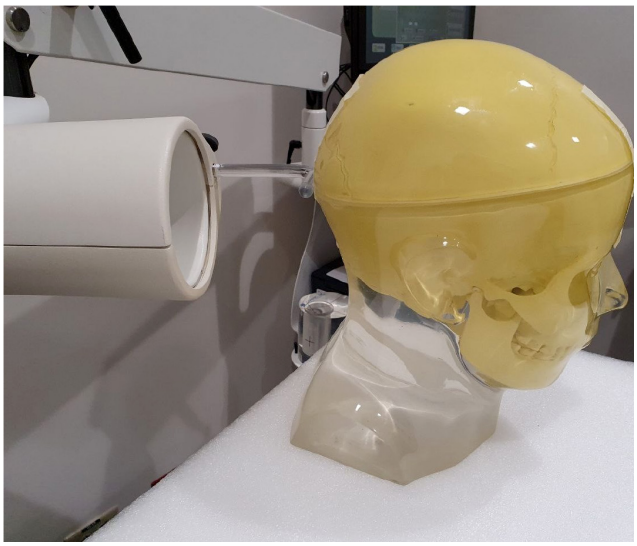


Figure 2. Head geometry for the calibration of ^{18}F-FDG *in vivo* measurements.

well mixed with water in the head phantom with the geometry and measurement time established to test the conversion factor.

Bioassay function m(t)

The Bioassay function describe how a particular radionuclide is retained or excreted at a time *t* after the intake (Castellani *et al.*, 2013). The bioassay function is obtained from the International Commission on Radiological Protection (ICRP) biokinetic models which take into consideration the effective half-life to describe the behavior of a particular radionuclide inside the human body. Therefore, knowing the corresponding bioassay function and the retained activity, it's possible to estimate the incorporation.

Up to now, there are no specific bioassay functions for inhalation, ingestion and injection of [^{18}F] FDG published by the ICRP. Therefore, for the generation of these values, the biokinetic transfer parameters of [^{18}F] FDG after intravenous administration published in the ICRP 128 publication (ICRP, 2015) were used as inputs in AIDE 6.0 (Activity Internal Dose Estimate) software. AIDE has a database of bioassay functions for several radionuclides generated from existing models based on the ICRP 78 publication (Berteli *et al.*, 2008). In addition, it was considered a Type F absorption for inhalation route since ICRP publication 151 recommends this type of absorption for ^{18}F in the absence of specific information (ICRP, 2022).

Evaluation of the committed effective dose E(50)

The E(50) is determined by the following equation (European Commission, 2018):

$$E(50) = Ie(50) \tag{6}$$

where *I* is the estimation of the activity incorporation in a worker in Becquerel (Bq) units and *e*(50) is the committed effective dose coefficient in units of Sv/Bq. The coefficients dose is specified by the ICRP and take into account anatomical, physiological and biokinetic characteristics (ICRP, 2007).

The activity incorporation in a worker can be determined by the following equation (Castellani *et al.*, 2013):

$$I(Bq) = \frac{M(Bq)}{m(t)} \tag{7}$$

where M(Bq) is the retained activity (amount of radionuclide present in the body, in specific body organs, tissues or biological samples) measured with *in vivo* or *in vitro* bioassay measurements, and m(t) is the bioassay function (Castellani *et al.*, 2013).

Since obtaining the committed effective dose is complex due to the great variety of aspects to be taken into consideration, the methodology for evaluating the committed effective dose was implemented using the recommendations of the IDEAS EURADOS Guidelines (Castellani *et al.*, 2013).

RESULTS

Table 1 presents the results of the calibration for *in vivo* measurements of [^{18}F] FDG in head geometry in terms of the conversion factor, the decision threshold, the detection limit, and the minimum detectable activity (MDA) in both Becquerel units and curies.

The most relevant result in Table 1 is the MDA (1043.97 Bq). This value defines the minimum activity that the proposed measurement set-up can reliably measure.

Table 2 presents the results of the assessment to test the conversion factor where the relative error between the reference and measured value was –6.9%.

Table 1. Calibration results for *in vivo* measurements.

Geometry	Conversion factor (Bq/cps)	U_D (counts)	L_D (counts)	MDA (Bq)	MDA (μCi)
Head	$1.73 \times 10^3 \pm 5.19 \times 10^1$	44.01	90.74	1043.97	0.03

Table 2. Results of the assessment to test the conversion factor.

Reference activity (Bq)	Background counts	Counts measures of ^{18}F	Measurement time (s)	Conversion factor (Bq/cps)	Activity M	Relative error %
78074.63	368	6671	150	1.73×10^3	72694.60	–6.9

Table 3 presents the results of the bioassay function generated by the AIDE 6.0 software for inhalation and ingestion of [18F] FDG.

DISCUSSION

When an *in vivo* measurement is done (as this study is proposing), the goal is to calculate the retained activity in a specific organ or tissue at the moment of measure. The biodistribution of [18F] FDG into the human body is well known (Hays *et al.* 2002). For patients or healthy people, the brain is one of the organs with the highest uptake of this radiopharmaceutical, therefore, head geometry is suitable for *in vivo* measurements to calculate the retained activity after an incorporation. This is particularly important to estimate the incorporation of [18F] FDG (see equation (7)) since the bioassay function describe how this radiopharmaceutical is retained in the brain at a time *t* after the intake.

For the assessment of the conversion factor, our goal is to verified that the obtained factor is capable of estimate the retained activity. In our case, the phantom used has a hollow brain made of plastic material. However, this hollow brain has five different compartments, four of them used to simulate the uptake of other radiopharmaceuticals different from [18F] FDG. Therefore, to avoid using these four compartments, a plastic bag was used. It showed to be flexible enough to be accommodated into the head of the phantom. The plastic material of the bag, from our point of view, does not change the attenuation

Table 3. Bioassay function for ^{18}F-FDG, generated by the AIDE 6.0 software for inhalation, ingestion and injection using the biokinetic transfer parameters published in the ICRP 128 publication.

	^{18}F-FDG bioassay function m(t) (Bq Bq^{-1})		
Time (d)	Inhalation (5 μm) Type F	Ingestion	Injection
	Brain	Brain	Brain
0.1	1.46×10^{-2}	2.82×10^{-2}	3.22×10^{-2}
0.2	6.19×10^{-3}	1.27×10^{-2}	1.30×10^{-2}
0.3	2.50×10^{-3}	5.17×10^{-3}	5.22×10^{-3}
0.4	1.01×10^{-3}	2.09×10^{-3}	2.10×10^{-3}
0.5	4.07×10^{-4}	8.40×10^{-4}	8.45×10^{-4}
0.6	1.64×10^{-4}	3.38×10^{-4}	3.40×10^{-4}
0.7	6.60×10^{-5}	1.36×10^{-4}	1.37×10^{-4}
0.8	2.66×10^{-5}	5.49×10^{-5}	5.51×10^{-5}
0.9	1.07×10^{-5}	2.21×10^{-5}	2.22×10^{-5}
1	4.31×10^{-6}	8.93×10^{-6}	8.93×10^{-6}

conditions that the head phantom reproduces (human head). Moreover, the activity used in the bag was well mixed with water to homogenize the source to emulate the retained activity in the human brain.

The measurement parameters for *in vivo* measurements in brain geometries to evaluate [18F] FDG intakes were established. In the first step, the conversion factor and the MDA were obtained (see Table 1). The obtained relative error (–6.9%) (see Table 2) for the conversion factor shows that it can be used for *in vivo* measurements to evaluate the committed effective dose due to [18F] FDG incorporations. Moreover, our methodology provides an MDA of 1043.97 Bq. This value permits us to detect the most relevant intake incidents in our institution. Values below this limit can be obtained using longer measurement times than 2.5 minutes, with the disadvantage that it could reduce the interest of the OWEs to be measured daily and increase the possibility of movements of the OEWs due to fatigue compromising the measurements.

In addition, Table 3 shows the bioassay function generated by the AIDE 6.0 software for inhalation, ingestion and injection of [18F] FDG. Since there are currently no specific bioassay functions for the inhalation, ingestion and injection of [18F] FDG published by the ICRP, the data generated by the AIDE 6.0 software allows an approximation of the committed effective dose in case of incorporation with this radiopharmaceutical. However, it is recommended to be on standby in case of new publications regarding the biokinetic model of [18F] FDG.

In internal occupational exposures, intakes through ingestion and skin/wounds route can be reduced with the adoption of radiological protection steps and good practices in the workplace, but intakes by the inhalation route are more difficult to control. Therefore, occupational incorporations can occur mainly through the inhalation route. For this reason, in the absence of information, inhalation of an aerosol with an AMAD of 5 μm is assumed by default for occupational exposures (European Commission, 2018). Besides, depending on the results and the type of monitoring, the suppositions may be more complex, and the IDEAS EURADOS Guidelines (Castellani *et al.*, 2013) have recommendations for how to manage different situations.

Considering that the obtained bioassay functions are based on the biokinetic model of ICRP publication 78 (Berteli *et al.*, 2008). The committed effective dose coefficient to be used for evaluating the committed effective dose is the one established in the GSR Part 3 of the IAEA, which follows to the same biokinetic model.

For the evaluation of the committed effective dose, the recommendations of the IDEAS EURADOS Guidelines (Castellani *et al.*, 2013) were used, obtaining as a methodology:

- Measure the retained activity in the brain.
- Estimate the incorporation using the retained activity in the brain and the corresponding bioassay function.
- Estimate the committed effective dose using the incorporation and the corresponding committed effective dose coefficient.

CONCLUSIONS

This study provides a methodology for evaluating the committed effective dose due to the incorporation of [18F] FDG in the occupationally exposed worker of the Cyclotron- PET/CT Laboratory at Universidad de Costa Rica, in accordance with guidelines and recommendations from different international organizations. This will allow determining whether the effective dose from [18F] FDG uptake is below the established limits.

AUTHOR CONTRIBUTIONS

Alexander Bonilla Araya and Erick Mora Ramírez designed the study and developed the methodology. Alexander Bonilla Araya performed the data calculations. All authors analyzed the data and wrote the manuscript.

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Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

RESUMEN: El objetivo de este trabajo es proporcionar una metodología para evaluar la dosis efectiva comprometida E(50) debido a la incorporación de [18F] FDG en el trabajador ocupacionalmente expuesto (TOE) del Laboratorio Ciclotrón-PET/CT del Centro de Investigación en Ciencias Atómicas, Nucleares y Moleculares (CICANUM) de la Universidad de Costa Rica utilizando mediciones *in vivo*. El sistema de medición fue calibrado para realizar mediciones *in vivo* considerando la función de retención correspondiente al radiofármaco utilizado. El factor de conversión fue evaluado con una actividad conocida de 18F en la geometría y tiempo de medición establecidos. Entre los resultados más relevantes, se definieron los parámetros de medición y el procedimiento de calibración. Se obtuvo como factor de conversión un valor de 1,73 x10^3 Bq/cps para mediciones *in vivo* de cerebro. Este estudio proporciona una metodología para evaluar la dosis efectiva comprometida debido a la incorporación de [18F]FDG en un centro de producción y diagnóstico de radionúclidos.

PALABRAS CLAVES: Dosis efectiva comprometida, dosimetría interna, [18F]FDG, mediciones in vivo, medicina nuclear.

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