Physica Medica 49 (2018) 52–57

Contents lists available at ScienceDirect

Physica Medica

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

Technical note

# A Monte Carlo model for the internal dosimetry of choroid plexuses in nuclear medicine procedures

Ernesto Amato[a,b], Francesco Cicone[c], Lucrezia Auditore[b,d,*], Sergio Baldari[a,d], John O. Prior[c], Silvano Gnesin[e]

[a] Section of Radiological Sciences, Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Messina, Italy
[b] Istituto Nazionale di Fisica Nucleare, Sezione di Catania, Italy
[c] Department of Nuclear Medicine and Molecular Imaging, Lausanne University Hospital, Lausanne, Switzerland
[d] Nuclear Medicine Unit, University Hospital "G. Martino", Messina, Italy
[e] Institute of Radiation Physics, Lausanne University Hospital, Lausanne, Switzerland

ARTICLE INFO

*Keywords:*
Choroid plexuses
Monte Carlo
Internal dosimetry
RGD peptides

ABSTRACT

Choroid plexuses are vascular structures located in the brain ventricles, showing specific uptake of some diagnostic and therapeutic radiopharmaceuticals currently under clinical investigation, such as integrin-binding arginine-glycine-aspartic acid (RGD) peptides. No specific geometry for choroid plexuses has been implemented in commercially available software for internal dosimetry.

The aims of the present study were to assess the dependence of absorbed dose to the choroid plexuses on the organ geometry implemented in Monte Carlo simulations, and to propose an analytical model for the internal dosimetry of these structures for $^{18}$F, $^{64}$Cu, $^{67}$Cu, $^{68}$Ga, $^{90}$Y, $^{131}$I and $^{177}$Lu nuclides. A GAMOS Monte Carlo simulation based on direct organ segmentation was taken as the gold standard to validate a second simulation based on a simplified geometrical model of the choroid plexuses. Both simulations were compared with the OLINDA/EXM sphere model.

The gold standard and the simplified geometrical model gave similar dosimetry results (dose difference $<$ 3.5%), indicating that the latter can be considered as a satisfactory approximation of the real geometry. In contrast, the sphere model systematically overestimated the absorbed dose compared to both Monte Carlo models (range: 4–50% dose difference), depending on the isotope energy and organ mass. Therefore, the simplified geometric model was adopted to introduce an analytical approach for choroid plexuses dosimetry in the mass range 2–16 g. The proposed model enables the estimation of the choroid plexuses dose by a simple bi-parametric function, once the organ mass and the residence time of the radiopharmaceutical under investigation are provided.

## 1. Introduction

The number of radiopharmaceuticals and the indications for radionuclide therapies have been expanding over the recent years [1]. There is a growing interest in internal dosimetry procedures [2–4], and refined dosimetry models are currently being developed in order to take into account organ-specific geometrical modelling that enables satisfactory approximations of the reality [5–7]. Additional improvements in quantitative imaging are achievable by applying advanced correction algorithms to SPECT or PET images [8].

Nevertheless, modelling of non-conventional organs is not routinely implemented in available dosimetry software and often requires in-house personalization [9–11]. Among non-conventional organs, choroid plexuses are essential vascular structures localized in the brain ventricles, responsible for the production of cerebrospinal fluid [12,13]. They have a C-shaped morphology that develops mainly along the temporal horns of the lateral ventricles, and follows the interventricular foramina into the third ventricle. Small plexuses are also present in the fourth ventricle. Some authors have reported a choroid plexuses mass of about 2 g [12], however only few studies have attempted accurate *in vivo* volumetric measures [14].

It has been recently shown [15,16] that choroid plexuses are a specific target of integrin-binding arginine-glycine-aspartic acid (RGD) peptides, which have been used to study the angiogenetic process both in neoplastic and cardiovascular diseases [17]. In addition, radiolabelled RGD-based peptides have been proposed as potential

* Corresponding author at: University Hospital "G. Martino", Nuclear Medicine Unit, Via Consolare Valeria, 1, 98125 Messina, Italy.
*E-mail address:* lauditore@unime.it (L. Auditore).

https://doi.org/10.1016/j.ejmp.2018.05.005
Received 14 December 2017; Received in revised form 3 May 2018; Accepted 4 May 2018
Available online 10 May 2018
1120-1797/ © 2018 Associazione Italiana di Fisica Medica. Published by Elsevier Ltd. All rights reserved.

therapeutic agents when labelled to $\beta^-$ emitters such as $^{90}$Y, $^{177}$Lu, $^{64}$Cu, $^{67}$Cu or $^{131}$I [18–24]. Besides standard non-target organs, such as kidneys, the liver or the spleen, it might be of clinical interest to estimate the absorbed doses delivered to choroid plexuses, especially in view of the administration of therapeutic radiopharmaceuticals.

There are no specific dose constraints for choroid plexuses in external beam radiotherapy. However, small vessel injury subsequent to cranial irradiation has been previously demonstrated in these structures thanks to susceptibility-weighted magnetic resonance imaging (MRI) [25]. Side effects of this type of radiation-induced damage are essentially related to an increased risk of bleeding [26], but we cannot exclude that additional side effects would develop in case of severe impairment of these structures, given their complex function [27].

The aims of the present study were: i) to assess the dependence of the absorbed dose to the choroid plexuses on the organ geometry implemented in the Monte Carlo simulations, and ii) to propose an analytical model for the internal dosimetry of these structures, scalable with the mass, for a set of clinically relevant diagnostic and therapeutic radionuclides.

## 2. Materials and methods

We defined two Monte Carlo simulation procedures in GAMOS (GEANT4 Application for Medically-Oriented Simulations), which is, with GATE (GEANT4 Application for Tomographic Emission), a user-friendly interface of the GEANT4 code [28]. Both codes (GATE and GAMOS), are devoted to the fields of medical physics and radiation protection [29–32]. The first procedure was taken as the gold standard and consisted in a direct Monte Carlo simulation using a voxelized geometry, obtained from direct organ segmentation. In the second procedure, we introduced a simplified geometrical model of the choroid plexuses, validating its results against those of the former model. Both Monte Carlo simulations were compared with the sphere model of OLINDA/EXM, a software tool commonly employed in internal dosimetry estimations of radiopharmaceuticals and used for diagnostic or therapeutic purposes in nuclear medicine [7].

The following radionuclides were chosen as sources for both models: $^{18}$F, $^{64}$Cu, $^{67}$Cu, $^{68}$Ga, $^{90}$Y, $^{131}$I and $^{177}$Lu (Table 1). All these radioisotopes have been used to label RGD-based peptides for imaging or diagnostic purposes [15–24].

### 2.1. MRI-based Monte Carlo simulations

The choroid plexuses of two patients enrolled in a dosimetric study of $^{68}$Ga-NODAGA-RGDyk at the University Hospital of Lausanne (CH) [16] were manually contoured on gadolinium-enhanced axial T1-weighted images, and used as input for Monte Carlo simulations in GAMOS (Fig. 1a). The contouring was carried out by an experienced operator (FC) with PMOD software version 3.8 (PMOD Technologies, Zurich, Switzerland). The mass of the plexuses obtained were 6.28 g and 5.50 g, for patient #1 and #2, respectively.

In the Monte Carlo calculation, a uniform volume of brain tissue (G4_BRAIN_ICRP, 1.03 g·cm$^{-3}$ density) [33] of 80 × 80 × 80 mm$^3$ was considered, and the central region, in which the choroid plexuses are located, was voxelized according to the MRI data. More specifically, the MRI voxel sizes of the two patients were 0.9766 × 0.9766 × 1.1 mm$^3$ and 0.5134 × 0.5134 × 3.3 mm$^3$, and the corresponding images were composed of 100 × 100 × 31 and 200 × 200 × 10 voxels, respectively.

The difference in voxel size is due to the retrospective nature of the present analysis, which used MRI scans that were not initially dedicated to the study of the choroid plexuses. Although radioactivity was not uniformly distributed within the choroid's volume (Fig. 1b), we considered a homogeneous radionuclide source within the organ volumes. This choice was made in order to compare our dose estimations with those of the OLINDA/EXM sphere model, which assumes a uniform activity distribution within the sphere.

Radiation emissions were simulated according to the `RadioactiveDecay` module of GEANT4 [34], whose models are based on the Evaluated Nuclear Structure Data File (ENSDF) [35,36].

Concerning the physics interaction models, we adopted the parameterizations of the electromagnetic interactions optimized for low energies, as implemented in the `GmEMExtendedPhysics` package [34].

In order to obtain an appropriate spatial sampling and a satisfactory statistical accuracy, we set a range cut of 50 μm and $10^8$ events per simulation. This number of events was chosen in order to obtain data with statistical errors lower than 5%. No variance reduction methods were used in our Monte Carlo simulations.

Fig. 1c and d show the choroid volumes obtained for patient #1 and the tracks generated by 1.5-MeV electrons which originated within the organ volume of the same patient.

Average radiation absorbed doses and dose-volume histograms were obtained from the Monte Carlo-generated three dimensional dose maps.

### 2.2. Monte Carlo simulations in a simplified geometrical model

A simplified geometrical model of the choroid plexuses was implemented in a second set of Monte Carlo simulations. The geometry of each plexus was modelled by a cylinder, representing the atrial and temporal parts, and a parallelepiped, representing the body part, and forming a 45° angle between each other, as shown in Fig. 2. The dimensions of these parts were adapted according to the MRI data, in order to reproduce the plexuses' masses of the patients. In Table 2, the dimensions assumed for the two patients are listed.

For these simulations the number of events was set to $10^6$, enough to obtain dose values with statistical errors less than 5%.

The relative percent error ε was assessed between absorbed doses obtained from Monte Carlo simulations based on the simplified geometry, and those obtained from MRI-based Monte Carlo simulations, which were taken as gold standard. Furthermore, ε was assessed between both Monte Carlo-based dose calculations and dose evaluations using spheres of same masses in OLINDA/EXM [7].

### 2.3. Analytical model for the dosimetry of choroid plexuses

The aforementioned simplified geometrical model was adopted to study the dependence of the absorbed dose on the choroid plexuses' mass.

The cylindrical and parallelepiped components of the simplified geometry were scaled to cover a total organ volume ranging from 2 to 16 ml (i.e. 2, 4, 8, 12 and 16 ml). This volume range was chosen based on previously published imaging data, which used an angio-CT volume rendering technique [14]. Maximum and minimum volumes were calculated taking into account the mean dimensions ± 2 standard deviations on both the right and the left of the choroid plexuses. Choroid plexuses of the third and fourth ventricles, which are smaller and more difficult to evaluate, were not considered in the calculation.

In the formalism introduced by the Medical Internal Radiation Dose

**Table 1**
Average electron and positron energies and branching ratios of the considered nuclides.

| Nuclide | $< E > \beta^-$ | $< E > \beta^+$ |
|---|---|---|
| $^{177}$Lu | 133 keV (100%) | – |
| $^{67}$Cu | 141 keV (100%) | – |
| $^{131}$I | 181 keV (99%) | – |
| $^{64}$Cu | 190 keV (39%) | 278 keV (17.4%) |
| $^{18}$F | – | 250 keV (96.7%) |
| $^{68}$Ga | – | 740 keV (89%) |
| $^{90}$Y | 934 keV (100%) | – |

Download English Version:

https://daneshyari.com/en/article/8248672

Download Persian Version:

https://daneshyari.com/article/8248672

Daneshyari.com