The Mechanisms of FDG Transport in the Body during a PET Scan

Yosra Annabi
Free researcher
Tunis, Tunisia

Abstract:- This article mathematically models the migration of radio-active molecules injected into the human body during a medical examination of the Positron emission tomography type. It is a medical examination used (requested) for the detection of cancer in a human body. The article begins with a description of the migration processes of a particle. Then the modeling equations are introduced.

Keywords:- *EDP, Nuclear Imaging, TPE, Convection, Diffusion, Dispersion, Cancer, Wave Equation, Diffusion Convection Equation.*

I. INTRODUCTION

Nature is made up of matter and energy. In this work, we are interested in the transfer of matter and the transfer of energy. There are three modes of material transfer: convection, diffusion and dispersion. Each material has its own properties. Thus, they are not all transferred by these 3 modes simultaneously. On the other hand, each energy has its own mode of transfer. For example, there are three modes of transfer of thermal energy (heat): convection, diffusion and radiation. Electromagnetic energy has other modes of transfer, for example induction or radiation.

II. THE MECHANISMS OF MIGRATION

There are 4 migration mechanisms in nature: convection, diffusion dispersion and radiation. The **convection** is a transport phenomenon which consists in the entrainment of the elements by a fluid in motion. **Diffusion** is an irreversible transport phenomenon that results in the migration of chemical or energetic species in a medium under the effect of molecular agitation. The **dispersion** is a phenomenon linked to the heterogeneity of microscopic velocities. It is linked to parameters relating to the medium and others relating to the transported components. The **radiation** is generated by the molecular agitation of particles or waves.

A. The convection

Convection is a transfer ensured by fluid movements, that is to say gas and liquid. In other words, convection is a mode of transmission of energy or matter by displacement of a fluid. Quite simply, convection means the transport by a fluid. There are several types of convection. We cite natural convection, forced convection, thermal convection, mass convection, thermosolutal convection and thermo-vibrational convection.

Convection is *natural* when it is triggered and continues spontaneously under the effect of differences in densities within the fluid mass. For example in meteorology the ascent of air, generally of thermal origin is accompanied by a downward return current. This circular movement of the air ensures a transfer by natural convection. Convection *thermal* is the transport of heat by moving fluid. The convection *mass* means the entrainment of the elements in solution in the movement of fluid which moves (course of DeMarsily). An example that describes this phenomenon is that of the transfer of salinity between salt water and fresh water. In this example, we are interested in the displacement of minerals in a fluid, namely water. this transfer is carried out thanks to mass convection. Convection *thermosolutal* describes the transport by a fluid in motion with a variation in temperature and concentration. the convection *thermo-vibrational* describes the transport by a fluid in motion with a variation in temperature and vibration of the environment example wall vibration.

- *Natural convection*

Natural convection is the transport by a fluid. Convection is said to be natural as opposed to forced convection. However, it only takes place in the presence of a gravity field, never in a vacuum or space. It is due to a difference in density and perhaps of a thermal or mass or thermosolutal nature, that is to say the transport of heat by the movement of the fluid or mass transport by a fluid or the transport of both at the same time. In the case of thermal convection, the density r(T) varies as a function of the temperature, which, under the action of the gravity field, tends to cause the fluid to rise along a hot wall, and to cause it to descend along a cold wall. The thermosolutal convection, for its part, results from the variation of the density r(T, C) as a function of the temperature and of the mass fraction of the heavy constituent of the fluid mixture. Finally, the mass convection results from the variation of the density r(T) as a function of the mass fraction of the heavy constituent of the mixture.

- *Forced convection*

Forced convection is a special type of transfer in which fluids or energy are forced to move, in order to increase the transfer of particles and energy.

For exemple, several electric or motor-driven machines heat up and may deteriorate. Among these machines we mention computers, refrigerators and televisions. They need cooling systems based on air or oil or cooling pastes in order to regulate the temperature inside these machines and ensure their proper operation. The cooling of these machines is done by forced convection.

B. The diffusion

It is an irreversible transport phenomenon that results in the migration of species in a medium under the effect of molecular agitation. Indeed, the particles of the elements in solution are continuously subjected to molecular agitation. The result of this agitation in all directions produces a transfer of particles only in the presence of a variation. In a homogeneous medium, as many particles are exchanged on average; therefore, no transport phenomenon manifests itself. This is how we define diffusion as the natural tendency of a system to become homogeneous within itself. the diffusion continues both in the mobile and immobile fluid phase. Only the solid slows it down strongly. in 1855, Adolphe Fick proposed phenomenological and empirical laws. It states that the diffusion flux is proportional to the gradient.

There are different types of diffusion. Among which we mention: the diffusion of matter, thermal diffusion also called conduction and the diffusion of particles. Recall that diffusion is a type of passive transport, that is to say carried out without energy. This transport tends to homogenize either the temperature or the concentration of chemical species in a fluid medium. Diffusion is a mode of transfer that takes place on a microscopic scale.

➢ *The diffusion of matter*

The *diffusion* is an irreversible transport phenomenon which results in the migration of chemical species in a medium under the effect of molecular agitation. Indeed, the particles of the elements in solution continuously undergo molecular agitation. The result of this agitation in all directions produces a transfer of particles only in the presence of a variation in the concentration. In a homogeneous medium, two elements exchange, on average, as many particles, therefore, no change in concentration is manifested. This is how we define diffusion as being the natural tendency of a system to make the concentrations of chemical or energetic species homogeneous within itself. The diffusion continues both in the mobile fluid phase and immobile only the solid slows it down strongly. The diffusion is illustrated by examples.

<u>Exemple 1 : *the diffusion of the particles*</u>

Taking the example of two layer of water each having a different concentration of a well-determined component. This component may be of a chemical, radioactive or non-radioactive nature. The phenomenon that tends to homogenize the concentration of this chemical component in the two layers of water is diffusion.

➢ *The thermal conductivity*

Thermal conduction (or thermal diffusion) is a mode of thermal transfer caused by a temperature difference between two regions of the same medium, or between two media in contact, and taking place without global displacement of matter (on a macroscopic scale). It can be interpreted as the transmission of thermal agitation from close to close: an atom (or a molecule) gives up part of its kinetic energy to the neighboring atom. Thermal conduction is a process of internal energy transport linked to molecular agitation and due to a heterogeneity of the medium on a macroscopic scale. It is an irreversible phenomenon analogous to the diffusion phenomenon. In fluids (liquids and gases), this energy transport results at the microscopic level from the anisotropy of the velocity distribution function. In solids, thermal conduction is ensured jointly by the conduction electrons and by the vibrations of the crystal lattice (phonons).

<u>*Exemple 2 : conduction*</u>

We take a food out of the refrigerator and put it on a table. Over time, he loses his coldness. In addition, it balances with the ambient temperature. This temperature change from cold to hot takes place on a microscopic scale, via the contacts between the molecules of the air in the room and the molecule of food.

C. The dispersion

➢ *The kinematic dispersion*

Kinematic dispersion is a phenomenon related to the heterogeneity of microscopic velocities within a porous medium. It is linked to parameters relating to the medium and others relating to the transported solute. The dispersion is the result of a microscopic velocity field different from Darcy's speed, which is a macroscopic speed.

➢ *The dispersion of light*

In wave mechanics, dispersion is the phenomenon affecting a wave propagating in a so-called "dispersive" medium. Dispersion is the optical phenomenon that explains why white light is separated into its constituent colors when it passes through a transparent medium.

D. The radiation

Radiation is the process of emission or propagation of energy and momentum involving a wave or a particle. radiation corresponds to all bodies that emit light and are themselves heated by the light they absorb. There are two types of radiation: thermal radiation and radioactive radiation. Both are characterized by electromagnetic waves.

Thermal radiation is electromagnetic radiation generated by the thermal agitation of particles in matter regardless of its state: solid, liquid or gas. The spectrum of this radiation extends from the microwave domain to the ultraviolet.

Radioactive radiation is a magnetic wave or particle that certain unstable atoms, called radioactive atoms, emit by transforming. Indeed, if an atom's nucleus contains too many neutrons and protons, it is said to be unstable. To regain its stability, it ejects neutrons and protons. It then emits particles, that is to say energy, and electromagnetic rays. This is the phenomenon of radioactivity. The radioctive radiations are alpha radiation (α), beta radiation (β), gamma radiation (γ) and X-ray radiation. They are all ionizing.

III. APPLICATION : NUCLEAR MEDICAL IMAGING

Nuclear medicine is an approach consisting in diagnosing or treating a given disease using radioisotopes. Radioisotopes can be administered by intravenous injections, orally or by means of a catheter.

A. The scintigraphy

The tracer attaches to the structures of the organ and then emits signals (gamma rays). These are analyzed thanks to a specific device (gamma-camera), placed in front of the area to be studied. The camera records the concentration of the radioactive product in the different parts of the organ concerned.

B. Positron Emission Tomography (PET)

It is the reference imaging technique in cancer. Positron emission tomography (PET-Scan or PET-Scan in English) is a risk-free and non-painful examination. Positron emission tomography (PET) is an imaging examination in nuclear medicine. During which the use of a form of radioactive sugar to create 3D and color images that allow to see how the cells of the body work. During PET scans, a radiopharmaceutical product is used consisting of a radioisotope attached to a substance in the body, usually a sugar (glucose). It circulates in the body and accumulates in cells that consume a lot of energy, such as cancer cells. Radioactive material emits tiny positively charged particles (positrons). A camera records the positrons and transforms the recordings into images on a computer. This examination is requested by doctors :

- to help diagnose certain cancers;
- to find out how far the cancer has spread (staging);
- to find out if the cancer treatment is effective or as part of the follow-up;
- to check if the cancer has returned after treatment (recurrence) or if it has spread to other parts of the body;
- to help diagnose non-cancerous conditions.

The exam takes place in two stages :

The first step begins with checking the blood glucose level, then setting up a venous route and injecting the tracer. It is a radioactive material injected into a vein in the hand or arm. Most of the time, the most used tracer in PET is the **fluorodeoxyglucose**, abbreviated as $18F - FDG$. It is a radiopharmaceutical molecule analogue of glucose in which the hydroxyl of the carbon 2 of glucose is replaced by fluorine 18.

Fluorine-18 is radioactive, and therefore unstable.. Indeed, when a proton hits the nucleus of an atom, it loses a neutron. This gives a new nucleus, which this time contains 9 neutrons and 9 protons: fluorine-18. One of the protons ends up changing into a neutron by emitting an energetic particle, a positron.

This molecule takes about 1 hour to circulate throughout the body and to be absorbed by the organs. Before settling in for the second stage, the person must urinate. The examination takes place like a CT scan : the patient is motionless in a sitting or lying position on an examination table. The table moves in the device. Detectors inside the device pick up the signal of the radioactive material present in the body. The taking of high definition scanner images with injection of contrast medium, then by the realization of PET images continues for 15 to 20 minutes. All the shots are taken on the same machine. PET scans detect active regions, such as cell growth, in the body. Radioactive material accumulates more in cancer cells than in normal cells, and cancer cells are brighter in the images. Not all cancers appear on PET scans. A computer analyzes the models and creates $3D$ and color images of the examined region.

Conclusion 3 *PET scans detect active regions, such as cell growth, in the body. Radioactive material accumulates more in cancer cells than in normal cells, and cancer cells are brighter in the images. Not all cancers appear on PET scans. The results of the PET scan are often combined with those of other imaging examinations and laboratory analyzes. We often have to do other tests to find out if a region that has absorbed a lot of radioactive material is non-cancerous (benign) or cancerous (malignant). Recent surgery, chemotherapy or radiotherapy as well as certain medications can affect the results of examinations. After the PET scan, the radioactive material is removed from the body through urine or feces (feces). It may take from a few hours to a few days for it to be completely eliminated from the body.*

C. Modeling

As the exam takes place in two phases, we will consider the mathematical models for each phase. In the phase of injection of the radio-active product into the veins. The radioactive sugar migrates in the human body thanks to the three macroscopic and microscopic transport mechanisms : convection, diffusion and kinematic dispersion. In the article [1], we presented a mathematical model of the transfer red blood cells in the blood. As it is a question of the migratory phenomenon, we will remind them. This article does not detail the laws of physics or mathematical theorems. This is a description of the flow phenomena related to blood movements. The blood circulatory system is a closed system. It continues its self-rotation to infinity thanks to driving forces such as cardiac electrical impulses; the mechanical force due to pulmonary ventilation and the related return forces to the movements of the valves of the large veins. Thus, macrocirculation is carried out by forced convection. On the other hand, the microcirculation, that which takes place in microscopic capillaries is satisfied thanks to the diffusion, deformation of red blood cells and the elasticity of the capillary walls. Cell exchange is carried out by different forms of diffusion, for example, natual diffusion or facilitated diffusion. There are also other passive mechanisms such as filtration or osmosis. The second type of transport of intracellular nutrients is that of active transport. For more details the reader can refer to [5].

- *Modeling of transport in organs*
  The migration of the radio-active molecule in the organ is related to a transfer in a porous medium. The mathematical modeling equation is therefore :

$$\omega \frac{\partial C}{\partial t} + div(-D\nabla C + C) = f \text{ dans } \Omega_T \qquad (1)$$

with C the concentration of radioactive sugar in the veins and D the matrix of diffusion and kinematic dispersion. Indeed, in a fluid at rest, the transport equation under the effect of diffusion is

$$\omega \frac{\partial C}{\partial t} = div(d\ \nabla C) \qquad (2)$$

In the mobile fraction of the fluid, the convection phenomenon appears and the transport equation becomes :

$$w_c \frac{\partial C}{\partial t} + (w - w_c)\frac{\partial \tilde{C}}{\partial t} = div(w D\, grad C - C\vec{U}) \qquad (3)$$

with
wc **:** the kinematic porosity,
w-wc **:** the porosity of the motionless fraction,
C **:** the concentration of radioactive sugar in solution of the mobile fraction,
$U^{\rightarrow}$ **:** Darcy's velocity,
D **:** the matrix of diffusion,

The dispersive flux is defined by

$$\Phi = -D\, grad C \qquad (4)$$

When the dispersion and the diffusion coexist, we fnd the equation 1.

- *Modeling of transport in veins*
  The modeling of the migration of the FBG molecule in the veins is done thanks to Poiseuille's law. By moving from a model in an organ (porous medium) to a model in a vein (pipeline), the physical laws taken into consideration change. Darcy's law is no longer applicable. It is replaced by Poiseuille's law. Indeed, the properties of the medium influence several phenomena, in particular the speed. Some scientists explain Darcy's law by an application of Poiseuille's law to the pore scale.
  $Q = (\pi r4)/(8\mu).(\Delta P/L)$ (5)

Q denotes the flow velocity of the liquid, r the internal radius of the pipe, ΔP the pressure difference between the two ends of the pipe, L the length of the pipe and μ the viscosity of the liquid.

- *Modeling of the transport of a radioactive wave*
  In the second phase of the examination, the radio-active components emit gamma rays thanks to fluorine. This is the phenomenon of radiation. Radiation is magnetic waves. Their migration is modeled by the wave equation, also called the d'Alembert equation :

$$\frac{\partial^2 u}{\partial t^2} = c^2 \Delta u \qquad (6)$$

where u is a function defined on Rn ×R, the first n coordinates being the space coordinates and the last the time. The constant c is the speed of propagation of the wave or a celerity. A solution of the wave equation in 3 dimension is explained in the following article :

Theorem 4 *Let be the parallelogram R =*]0,*a*[×]0,*b*[×]0,*c*[*and let the following problem be :*

$$\begin{cases} \frac{\partial^2 u}{\partial t^2} &= \frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} & ,t > 0 \text{ et } (x,y,z) \in R \\ u(x,y,z,0) &= f(x,y,z) & (x,y,z) \in R \\ \frac{\partial u}{\partial t}(x,y,z,0) &= g(x,y,z) & (x,y,z) \in R \\ u &= 0 & \text{on the faces of } R \end{cases} \qquad (7)$$

It is assumed that the functions f and g are zero on the faces of R. A solution of the system 7 is :

$$u(x,y,z,t) = \sum_{l,m,n \in \mathbb{N}^*} \left(K_{l,m,n} cos(\delta t) + L_{l,m,n} sin(\delta t)\right) sin\left(\tfrac{l\pi}{a}x\right) sin\left(\tfrac{m\pi}{b}y\right) sin\left(\tfrac{n\pi}{c}z\right) \qquad (8)$$

with the Fourier coefficients :

$$\begin{cases} K_{l,m,n} = \frac{8}{abc}\int_0^a\int_0^b\int_0^c f(x,y,z,)\ sin\left(\tfrac{l\pi}{a}x\right)\ sin\left(\tfrac{m\pi}{b}y\right)\ sin\left(\tfrac{n\pi}{c}z\right) dxdydz \\ L_{l,m,n} = \frac{8}{abc\delta}\int_0^a\int_0^b\int_0^c g(x,y,z,)\ sin\left(\tfrac{l\pi}{a}x\right)\ sin\left(\tfrac{m\pi}{b}y\right)\ sin\left(\tfrac{n\pi}{c}z\right) dxdydz \end{cases} \qquad (9)$$

with $\delta = \pi\sqrt{\frac{l^2}{a^2} + \frac{m^2}{b^2} + \frac{n^2}{c^2}}$.

IV. CONCLUSION

This article presents three equations to model the transport mechanisms present in a TPE exam. Thus, the radio-active particles injected into the veins, migrate in the body by means of Poiseuille's law. Arriving at organs such as the brain or the heart, the modeling of particles is done thanks to the laws of porous media. Finally, the radioactive rays emitted by the particles Fluorine-18, during the imaging phase, are modeled mathematically by the wave equation. A solution of this equation in 3D is presented.

REFERENCES

[1]. Annabi, Y. (2022). *Hemodynamics : Macroscopic and Microscopic Modeling*, International Journal of Innovation in Science and Mathematics, Volume 10, Issue 4. http://ijism.org/administrator/components/com_jresearch/files/publications/IJISM_976_FINAL.pdf

[2]. Gires P.Y. (2017). *Poiseuille and the flow of liquids in the capillary*.URL : journals. openedition.org/bibnum/1091

[3]. Annabi, Y. (2012). *Introduction to Applied Mathematics*, European University Editionss, ISBN : 978-3-8417-8154-3.
[4]. Annabi, Y. (2022). *Introduction to multi-scale modeling*, European University Editionss, ISBN : 978-613-9-50445-9.
[5]. Annabi, Y. (2022). *Introduction to hemodynamic*, European University Editionss, ISBN : 978-620-3-43779-9.
[6]. LeDoux, J. (2021). *La circulation, PCEM1*, course manual,Faculty of Medicine of Tunis. URL :www. fmt.rnu.tn,
[7]. MbayaT E., M. I. Doris, M. L. and Paulin, B. B.(2016). *Physical and mathematical modeling of blood flow in the abdominal aortic aneurysm*, International Journal of Innovation and Scientific Reasearch, Volume 26, No. 1
[8]. Vafai K. (2005) *Handbook of porious Media*, Taylor & Francis Group.
[9]. Md Tofiz Uddin, Yanling Bai, Yu Lijuan (2019) *Study on Motion Management of HelicalTomotherapy*. Cancer Therapy and Oncology International Journal. URL : https://juniperpublishers.com/ctoij/PDF/CTOIJ.MS.ID.555864.pdf University Editionss, ISBN : 978-620-3-43779-9.
[10]. E. Bombardieri, M. Maccauro, E. de Deckere, G. Savelli and A. Chiti (2001) *Nuclear medicine imaging of neuroendocrine tumours*; Annals of Oncology 12 (Suppl. 2) : *S*51-*S*61. Kluwer Academic Publishers. Printed in the Netherlands.
[11]. S. Kauhanen, M. Seppänen, H. Minn and P. Nuutila (2010) *Clinical PET Imaging of Insulinoma and Beta-Cell Hyperplasia*; Current Pharmaceutical Design, 16.