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РОЗВИТОК ПРИРОДНИЧИХ НАУК ЯК ОСНОВА НОВІТНІХ ДОСЯГНЕНЬ У МЕДИЦИНІ

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Hence, gained data revealed that the early stage of seizure development is characterized by the strengthening of mutually positive links between brain structures with the reduction of negative ones. Generalized seizure cessation observed at the stage of fully developed kindling is characterized by a reduction of positive links between cortical structures while negative links were preserved. The marked involvement of paleocerebellum was observed at the period of ictal discharge formation and their suppression. Gained results are in correspondence with the neurophysiological mechanisms of PTZ-kindled seizure development [1].

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Retention of radiotracers as a Falling-Flow Phenomenon

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Abstract

The proposed a four-compartmental model describes transport kinetics of 99m-technetium radiotracers with considering radiopharmaceutical accumulation, elimination and radioactive decay and retention of radiotracers at lymph nodes.

Key words

Radiotracers, circulatory system, lymphatic system, sentinel lymph node, ^{99m}Tc-radiotracers, transport kinetics of radiotracers, mathematical model.

Introduction

The dynamics of radiotracers in lymph nodes can be studied using various imaging techniques, such as lymphoscintigraphy, positron emission tomography (PET), or single-photon emission computed tomography (SPECT). These techniques allow for the visualization and quantification of radiotracer distribution within the lymphatic system and lymph nodes. When a radiotracer is injected or administered, it enters the lymphatic system and is transported through lymphatic vessels. The radiotracer may encounter several processes and dynamics within the lymph nodes, including lymphatic uptake, lymphatic transport, lymph node filtration, retention and clearance.

By using imaging techniques, the dynamics of radiotracers within lymph nodes can be visualized and quantified. This allows researchers and clinicians to study parameters such as tracer uptake, distribution patterns, retention times, and clearance rates. Such information can be valuable for understanding lymphatic function, evaluating lymph node involvement in diseases, optimizing lymphatic imaging protocols, and developing targeted therapies that utilize lymphatic pathways.

It's important to note that the dynamics of radiotracers in lymph nodes can be influenced by various factors, including the specific radiotracer used, the injection or administration method, the lymphatic system's physiological state, and any underlying diseases affecting lymphatic function.

The tracer-kinetic model

The tracer-kinetic model is based on compartmental assumptions; that means, tracer is assumed to move between discrete "compartments", within each of which tracer is assumed to distribute instantaneously upon arrival. Thus, in a compartmental model, gradients of concentration are assumed to be zero (i.e., their spatial profiles flat) within each compartment at all times. The ideal radiotracer for lymphoscintigraphy would be one that demonstrates rapid uptake into the lymph nodes with prolonged retention.

Size is the major factor determining the behaviour of particulate materials. Particles that are smaller than a few nanometres will mostly penetrate the blood capillary membrane, whereas larger particles (up to about 100 nm) can enter the lymphatic capillaries and be transported to lymph nodes. Larger particles will be trapped in the interstitial space for a long time.

Different authors have different opinions about distribution of radiotracers after an injection. Small-sized molecules (typically of size <5 nm diameter) diffuse rapidly in the interstitium and can permeate to both blood and lymphatic capillaries [3]. Particles smaller than a few nanometers usually leak into blood capillaries whereas larger particles (up to about 100 nm) can enter the lymphatic capillaries and be transported to lymph nodes. However, even large particles were detected in venous blood immediately after subcutaneous injection, probably as a result of direct capillary disruption by the needle [4].

The optimal colloidal size for lymphoscintigraphy is believed to be approximately 50–70 nm. Individual estimates vary from 1 to 70 nm [1], [2]. Larger particles (100 nm) are believed to be trapped in the interstitial compartment for a relatively long period. One study has demonstrated that transport of perfluorocarbon emulsions of 0,08–0,36 μm exhibits an inverse correlation to colloid particle size. Lymph node uptake of colloids of similar size can vary substantially. Differences in surface characteristics of the colloids may account for these observations [2]. Early studies with liposomes have shown that specific surface properties, such as charge, hydrophobicity, and the

presence of targeting ligands, can influence both the rate of particle drainage from a subcutaneous injection site and the distribution within the lymphatic system.

An opposite effect found for lymph node exposure, indicating a retention of the larger-sized molecules at the injection site and thus their reduced transport to the lymph nodes. The exact choice of the tracer size depends on the application. For example, tracers for lymphatic flow imaging should in principle be smaller (5–10 nm) to allow for rapid lymphatic uptake and visualization. On the other hand, the tracers for lymph node imaging should have an intermediate size (10–100 nm) in order to accumulate in this organ and thus provide strong signal. Above 100 nm, the diffusion of the entities in the interstitium and thus entry into the lymphatic system is thought to be limited by the size of the conduits in the extracellular matrix.

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The optimal colloidal size for lymphoscintigraphy is believed to be approximately 50–70 nm [1], but the range 10–100 nm has also been proposed [5]. The results of recent studies correlating the particle profile of 99mTc labelled inorganic colloids with lymph node uptake suggest that colloids with nanometric dimensions are the best suited for a high node uptake [6]. As a general rule, it can be assumed that very small nanoparticles (<10 nm) are best suited for lymphoscintigraphy, whereas large particles (>100 nm) display a longer retention in the first encountered lymph node.

2. Simulation of radiopharmaceutical transport kinetics

Radiotracer kinetic simulation was studied by many authors [9], [10], [11]. In a typical PET study, PET data are sequentially obtained after the radioactive tracer is introduced (usually administrated intravenously) over time. The interpretation of the observed PET data over time is fulfilled in the frame of the “compartments model”, where “compartments” mean physiologically separate pools of a tracer substance. Usually authors consider four/three tissue compartments models. The first compartment is the blood. From the blood, the radiotracers pass into the second compartment, known as the free compartment. The third compartment is the region of specific binding which we are usually interested to observe. The fourth compartment is a nonspecific-binding compartment that exchanges with the free compartment. The transport and binding rates of the tracer are assumed to be linearly related to the concentration differences between two compartments. Data obtained by PET detectors are obtained as the sum of these compartments. The parameters can be estimated by fitting the model to measured PET data with arterial radioactivity concentration as the input

function. However, this method requires the frequent manual sampling of the arterial blood or continuous radioactivity monitoring by external radiation detectors.

In the second case the general elimination rate is higher. After intravenous bolus injection the radiotracer moves from one compartment to the next one. Radiotracer kinetics is described by the system of differential equations. The solution of such system is determination of the effective rate of accumulation/elimination. The next stage is to find all the points and use the approximation method (the smallest square, for example). Standard approach is to apply the functional of the residual function.

Mathematical model of radiotracer transport kinetics

Dynamic of radiotracers is a rather complicated problem. To build a correct mathematical model of radiotracer dynamics we have to take into account a very complicated anatomical structure of an organism and different physiological/ pathologic(al) processes, as well as physical and chemical processes, namely diffusion, accumulation, elimination and radioactive decay of radiotracers. The main problem is to determine the space trajectory of radiotracer movement.

After bolus intravenous administration of the radiotracers the process of transferring the radiotracers by blood vessels is begun and the so-called radiotracer “dilution” process is realized, namely the absorption of radiotracers by other organs and tissues and radiotracers decay. Bolus is a certain amount of medicine, injected into the body intravenously. The injected bolus quite quickly causes a response reaction in the body.

The part of radiopharmaceuticals which is absorbed by cells is immediately metabolized, and metabolic products quickly returned to the general blood circulation. The processes considered in this model are the following ones:

1) radioactive decay of radiotracers; 2) accumulation of radiotracers in the interstitium; 3) accumulation of radiotracers in the lymphatic system; 4) transport of radiotracers from the blood vessels; 5) transport of radiotracers and metabolites from the interstitium in the blood vessels, 6) transport of radiotracers from the lymphatic system to the blood vessels.

The model of transport kinetics of radiotracers is described by a system of differential equations of the 1st order for radiotracer concentration levels in the blood-vascular system, in the interstitium, in the lymphatic system and in the urinary system. The system of equations describes the processes of accumulation/retention of radiotracers in the cells, the radiotracer elimination/washout, and radiotracer radioactive decay. This system is like 4-compartmental models, where the number of radiotracers in each compartment is proportional to the radiotracer concentration:

$$\begin{cases} \dfrac{dx}{dt} = -\lambda x(t) - \beta_{xw} x(t) + \beta_{zx} z(t) \\ \dfrac{dz}{dt} = -\lambda z(t) - (\beta_{zx} + \beta_{zu}) z(t) + \beta_{wz} w(t) \\ \dfrac{dw}{dt} = -\lambda w(t) - \beta_{wz} w(t) + \beta_{xw} x(t) \\ \dfrac{dw_{tr}}{dt} = -\lambda w_{tr}(t) - \beta_{wz} w_{tr}(t) + \beta_{xw} x(t) \\ \dfrac{du}{dt} = -\lambda u(t) + \beta_{zu} z(t) \end{cases} . \quad (1)$$

The next denotations were used in (1): λ is the radioactive decay constant of radiotracers, $x(t)$ is the concentration of radiotracers in the interstitium, $z(t)$ is the concentration of radiotracers in blood vessels, $w(t)$ is the radiotracer concentration in the lymphatic system, $w_{tr}(t)$ is the radiotracer concentration in the lymph nodes, $u(t)$ is the radiotracer concentration in the urinary system, β_{zx} is the rate of radiotracer capture by interstitial cells, β_{wz} is the elimination rate of radiotracers from the lymphatic system in the bloodstream, β_{xw} is the rate of radiotracer movement from the interstitium to the lymphatic system, β_{zu} is the elimination rate of radiotracers from the bloodstream. Thus, the simple system of differential equations (1) has been used to describe the kinetics of radiotracers. The initial conditions are the following ones:

$x(0) = 0, z(0) = 1, w(0) = 0, w_{tr}(0) = 0, u(0) = 0$.

Functions of activity retention $x(t), z(t), w(t), u(t)$ are presented in the reduced units (normalized on unit of the injected activity). Half-decay period of ^{99m}Tc-radiotracers is equal to $T_{1/2} = 6$ hours.

Results

Radiotracer simulation is one of the main methods of interpretation of radionuclide research results. Quantitative data of radiotracer transport kinetics in the body are presented in the form of “activity-time” or “concentration-time”, which reflect the spatial and temporal processes of change in the concentration of radioactive indicator in the “regions of interest” and characterize the rate of ^{99m}Tc-radiotracers retention and washout in the organ or tissue. The aim of the paper is to describe radiotracer transport in the frame of a four-compartment models: the circulatory system, the lymphatic system, the lymph nodes, the interstitium, and the urinary system. The case of intravenous administration of radiotracers was considered in the paper.

The "time-activity" curves of radiotracer transport kinetic $n(t)$ in the frame of a four-compartmental model can be conditionally divided into four processes $n(t) = z(t) + x(t) + w(t) + w_{tr}(t) + u(t)$.

The simulation results are presented in a form of the "concentration-time" curves in Figure.

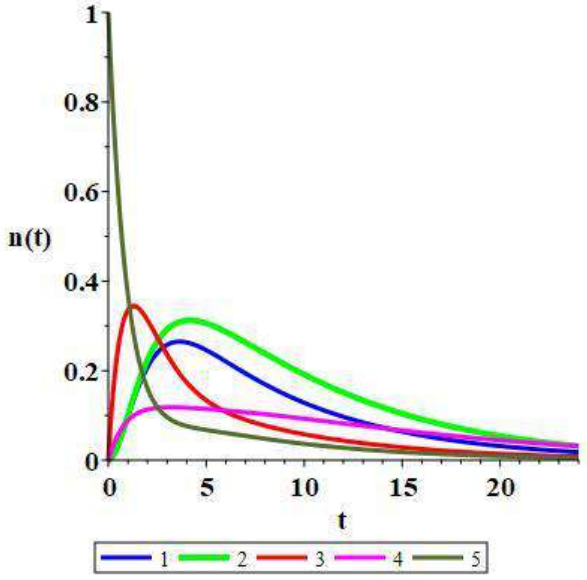

Figure. Concentration-time dependence, $\beta_{wu} = 0{,}15$, $\beta_{zu} = 0{,}15$ $\beta_{zx} = 0{,}75; \beta_{xw} = 0{,}5; \beta_{xw\_tr} = 0{,}5$.

1. The lymphatic system. 2. The lymphatic nodes. 3. The interstitial. 4. The urinary system. 5. The circulatory system.

Discussions

The case of intravenous administration of radiotracers was considered in the model. The aim of the paper is to describe radiotracer transport in the frame of 4th compartment models: the circulatory system, the lymphatic system, the lymph nodes, the interstitium, and the urinary system.

The model can be easily verified by the radioactive tracer concentration data in the circulatory/lymphatic system measured at some time points, and the obtained data can be used to determine of the transport coefficients. Time-activity dependencies were obtained and analyzed for each compartment. The model can be used for individual transport parameter calculation at administration by therapeutic dose loads.

Conclusions

The proposed four-compartment mathematical model describes transport kinetics of 99m-technetium radiotracers at intravenous administration process with taking into account radiotracer accumulation, elimination, retention and radioactive decay.

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КОМП'ЮТЕРНЕ МОДЕЛЮВАННЯ МІЦНІСТІ ФІКСАЦІЇ МЕТАЛЕВОГО ГВИНТА В КОРТИКАЛЬНОМУ ШАРІ ДІАФІЗУ ДОВГИХ ТРУБЧАСТИХ КІСТОК

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Анотація. Проведено комп'ютерне моделювання біомеханічних взаємодій, що виникають при фіксації гвинтів з нержавіючої сталі в діафізарній частині довгих трубчастих кісток для гвинтів АО з діаметром 3,5 мм. Визначалися зміщення та напруження, що виникають в ділянці різьбової частини гвинта та навколишньої кісткової тканині в діапазоні сил від 100N до 1000N, що прикладалися вздовж осі гвинта. При збільшенні зусилля прогресуючи збільшувалися напруження та тиск гвинта на навколишню ділянку кісткової тканини, що при максимальних значеннях може призводити до нестабільності фіксації. При цьому різниця напружень в різних ділянках гвинта коливалася в межах 25-30 %. Дані результати слід враховувати при проведенні оперативних втручань з застосуванням гвинтів та подальших біомеханічних досліджень.

Ключові слова: гвинт, остеосинтез, комп'ютерне моделювання.