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Original Research Paper

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ON THE PROPAGATION OF MEDICINE IN HUMAN BODY TISSUES

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ABSTRACT A numerical study is based on a new generalized hyperbolic model proposed in (Selezov & Kryvonos, 2017) [1]. In this model, the finiteness of the velocity of propagation of disturbances in the medium (tissue) is taken into account, whereas earlier in traditional models based on the parabolic equation this was not taken into account. We consider the initial value (IBV) of the propagation of a concentration from a spherical cavity, in which the concentration is 10 times greater than the concentration in the tissue. Such a problem simulates the evolution of the concentration immediately after injection. Numerical simulation is carried out by the method of finite differences.

KEYWORDS : Medicine, Tissue, Injection, Finite Difference Method

INTRODUCTION

At the present stage of the development of mathematical modeling, problems of modeling the functioning of the human body as a complex biomechanical system are widely used. Such studies allow to predict the reaction of the organism or its individual components both to external impacts and to internal factors.

Actual problems are those associated with modeling injection of injected fluid into body tissues. Such tasks include the tasks of contactless injection of an injection [1], [2], [3]. Consideration of the finiteness of the injection of the injected jet into the medium modeling biotissue was demonstrated in a paper [4], consideration of the finiteness of the injection of the jet into the liquid was considered in the work [5]. The problem of the diffu0sion spread of a medical preparation in tissue after injection was considered in [6]. The vaccine administration system was analyzed in the work [7].

The application of the method of finite differences to the solution of the continuum problems of the space-time processes of geofiltration and mass transfer is presented in the paper [8]. Algorithms of finite-difference schemes are given in the article [9] and work [10].

In this paper, approximate simulation of the injection process is carried out on the basis of a "rigid" model: the internal fixed spherical region is filled with the drug with a high concentration at the initial time, and further the alignment of the concentration to the level in the outer region is investigated. The diffusion coefficient entering into the traditional models described by the parabolic equation depends strongly on the capillary properties of the tissue. With large diffusion coefficients, the concentration of the drug decreases rapidly both in time and in distance. In the case of small diffusion coefficients, hyperbolicity is more evident.

The purpose of this work is to simulate the process of redistribution of the drug after its introduction into the muscle tissue of the organism, taking into account the finiteness of the propagation velocity and the resulting diffusion phenomena.

FORMULATION OF THE PROBLEM

It is assumed that immediately after injection, the injected drug occupies a certain area (here it is approximated by a sphere with a radius) from which it extends to the outer region (tissue) (Fig. 1).

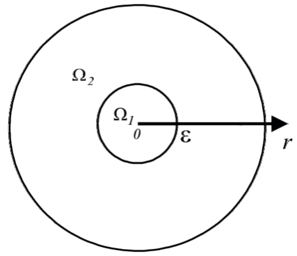

Fig.1. Geometry of the system

The generalized equation has the following form

$$k\nabla^2 C - \eta \frac{\partial^2 C}{\partial t^2} - \frac{\partial C}{\partial t} - k\xi C = 0 \qquad (1)$$

where C wis the concentration of the substance $\left[\frac{kg}{m^3}\right]$, k is the diffusion coefficient $\left[\frac{m^2}{s}\right]$, η the relaxation parameter $[s]$, and ξ the absorption coefficient $\left[\frac{1}{m^2}\right]$. A mathematical problem is formulated for equation (1) in a spherical coordinate system r, θ, φ For the Laplace operator in the case of a spherical scalar perturbation we have the expression:

$$\nabla^2 C = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial}{\partial r}\right) C = \frac{\partial^2 C}{\partial r^2} + \frac{2}{r}\frac{\partial C}{\partial r} \qquad (2)$$

Taking into account the values for equation (1), expression (2), and the initial concentration C_{02} in the region Ω_2, we obtain an equation describing the change in the concentration of the introduced substance during its spread in the soft tissues of the organism

$$\frac{\partial^2 C}{\partial r^2} + \frac{2}{r}\frac{\partial C}{\partial r} - \frac{1}{c^2}\frac{\partial^2 C}{\partial t^2} - \gamma \frac{\partial C}{\partial t} - \xi C = 0 \qquad (3)$$

In this case, in the inner region

$$\Omega_1 = \{(r, \theta, \varphi) \mid 0 < r < \varepsilon, \ -\pi < \theta < \pi, \ -\pi < \varphi < \pi\}$$

(the region of direct input of matter), the equation has the form:

$$\frac{\partial^2 C_1}{\partial r^2} + \frac{2}{r}\frac{\partial C_1}{\partial r} - \frac{1}{c_1^2}\frac{\partial^2 C_1}{\partial t^2} - \gamma_1 \frac{\partial C_1}{\partial t} - \xi_1 C_1 = 0 \qquad (4)$$

where $0 < r < \varepsilon, \quad t > 0$

For the outer region

$$\Omega_2 = \{(r, \theta, \varphi) \mid \varepsilon \le r < \infty, \ -\pi < \theta < \pi, \ -\pi < \varphi < \pi\}$$

we obtain

$$\frac{\partial^2 C_2}{\partial r^2}+\frac{2}{r}\frac{\partial C_2}{\partial r}-\frac{1}{c_2^2}\frac{\partial^2 C_2}{\partial t^2}-\gamma_2\frac{\partial C_2}{\partial t}-\xi_2 C_2=0, \qquad (5)$$

Where $\varepsilon < r < \infty, \quad t > 0$

The matching conditions on the boundary $r=\varepsilon$ is defined as follows

$$C_1(r,t)\big|_{r=\varepsilon}=C_2(r,t)\big|_{r=\varepsilon}$$
$$\left.\frac{\partial C_1(r,t)}{\partial r}\right|_{r=\varepsilon}=\left.\frac{\partial C_2(r,t)}{\partial r}\right|_{r=\varepsilon} \qquad (6)$$

The initial conditions for $t=0$ are:

$$C_1(r,t)\big|_{t=0}=C_1^0, \quad C_2(r,t)\big|_{t=0}=C_2^0, \quad C_1^0>C_2^0 \qquad (7)$$

$$\left.\frac{\partial C_1(r,t)}{\partial t}\right|_{t=0}=0, \quad \left.\frac{\partial C_2(r,t)}{\partial t}\right|_{t=0}=0 \qquad (8)$$

Regularity conditions in Ω_1: $C_1\neq\infty$, for $r=0$ (9)

At the initial moment just after the injection of the substance into the tissue, the concentration in the area Ω_1 is greater than in Ω_2. It means that $\frac{C_1}{C_2}>1$ (fig 2)

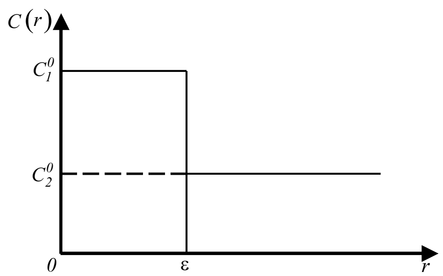

Fig.2 Distribution of concentration C along the radial coordinate at the initial time $t=0$.

Now we introduce dimensionless variables as follows:

$$r^*=r/\varepsilon, \quad t^*=\frac{c_1}{\varepsilon}t, \quad C^*=C/C_{02},$$
$$\gamma^*=\varepsilon c_1\gamma, \quad \xi^*=\varepsilon^2\xi \qquad (10)$$

Equation (3) in dimensionless form with regard to (10) has the form:

$$\frac{\partial^2 C^*}{\partial r^{*2}}+\frac{2}{r^*}\frac{\partial C^*}{\partial r^*}-\frac{\partial^2 C^*}{\partial t^{*2}}-\gamma^*\frac{\partial C^*}{\partial t^*}-\xi^* C^*=0 \qquad (11)$$

For the future equations, considering the dimensionless model, we omit the star sign.

MATERIALS AND METHODS

SOLUTION

Continuous in space and time, the domain of solution of equation (11) is replaced by a discrete one (Fig. 3).

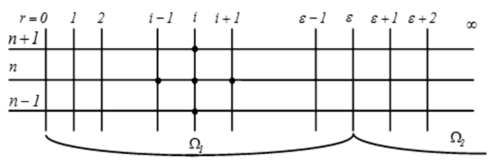

Fig.3 System sampling template

The differential equation and boundary conditions are replaced by discrete analogs by the method of finite differences. The construction of solutions of an algebraic system is carried out using explicit numerical methods by means of the time-recursive formulas. Predictor-corrector method was used here. In the first step we determine the concentration (13), and on the second one we use the refined concentration value at the given point to determine the concentration at the next time-step (14):

$$C_i^*=A+\Delta t^2\left(B+C-D-\xi C_i^n\right) \qquad (13)$$

$$C_i^{n+1}=A+\Delta t^2\left(B+C-E-\xi C_i^n\right) \qquad (14)$$

where:

$$A=2C_i^n-C_i^{n-1};$$
$$B=\frac{C_{i+1}^n-2C_i^n+C_{i-1}^n}{\Delta r^2};$$
$$C=\frac{2}{r_i}\frac{C_i^n-C_{i-1}^n}{\Delta r};$$
$$D=\eta\frac{C_i^n-C_i^{n-1}}{\Delta t};$$
$$E=\eta\frac{C_i^*-C_i^{n-1}}{\Delta t}..$$

The boundary conditions are:

$$C_{11}^{n+1}=C_{12}^{n+1}, \quad C_{2k}^{n+1}=C_{2k-1}^{n+1},$$

$$C_{1\varepsilon}^{n+1}=C_{2\varepsilon}^{n+1}=\frac{C_{1\varepsilon-1}^{n+1}+C_{2\varepsilon+1}^{n+1}}{2}. \qquad (15)$$

In this case, the subscripts determine the position of the point along the radial variable, and the upper ones determine the time.

To perform sampling, one must specify the step n space and the time step. Let the link between above steps is governed by Courant-Friedrichs-Levy condition given as follows:

$$\Delta t=\frac{c_{kfl}\Delta x}{c+u}, \qquad (16)$$

Where c_{kfl} – the safety factor, C – the local speed, u – the velocity of the medium, while if Δt_1, Δt_2 are the time-steps for the each areas.Then the time-step for the entire system is defined as $\Delta t=\max(\Delta t_1;\Delta t_2)$

NUMERICAL SIMULATION AND ANALYSIS OF THE RESULTS

At the initial moment of time, a substance (liquid) is introduced into the muscle tissue, which occupies a certain spherical volume where the relative concentration of substance is $C_1^0/C_2^0=10$. After the introduction of substance the relaxation process begins, at which the concentrations in the inner and outer regions under consideration are equalized. This process depends on the coefficients f η and ξ for the external and internal areas Ω_1 and Ω_2 which in general, can be different. When matter is redistributed in the above regions, wave phenomena arise,i.e. in the outer region a pressure wave, and in the inner region rarefaction wave propagate.

At each point of the region under consideration, the concentration changes with time (Fig. 4), and there is a redistribution of the introduced volume of matter into the region Ω_2, which leads to an equalization of the concentration of the substance throughout the volume under consideration.

CONCLUSION

A finite-difference algorithm for computing on the basis of a generalized hyperbolic model is presented. The results of calculations in the initial time interval show the propagation of waves in the process of equalizing the concentrations of the inner and outer regions, the dependence of the relaxation time and the residual concentration.

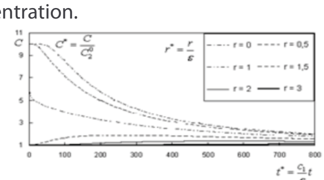

Fig.4. The time change of concentration at different points in the system.

One of the main characteristics of the process under investigation is the time during which the substance is redistributed in the tissues of the body. This time is obtained from the solution of equations (4), (5) and depends on the parameters γ and ξ (Fig. 5.)

With this increase in the parameters, the relaxation time increases.

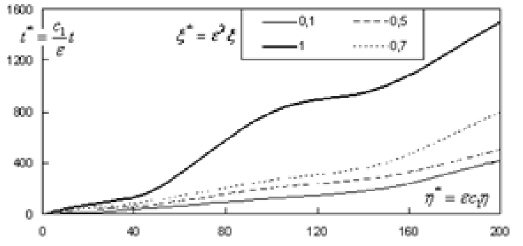

Fig.5. Dependence of the relative relaxation time on the parameter for different values of the parameter .

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