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Estimation of ultrasound influence on biological tissue

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Abstract

The paper is devoted to problems associated with methods that control BO (biological objects) during physiotherapeutic procedure. Mathematical model of interaction between parameters of ultrasound and BO that can evaluate time of the effective and positive influence of ultrasound on biological tissues is proposed in this article.

1. Introduction

The main goal of the progress for modern physiotherapeutic devices, viz UPA (ultrasound physiotherapeutic apparatuses), is to analyze results of numerous experimental researches and practical use of US (ultrasound) in medicine from the concept of modern biophysical acoustics, furthermore it is optimization of already known device implementations of UPA by the use of the received results.

Central problem for improvement of UPA course immutably remains such question as control of US dosage during physiotherapeutic procedure. There are two essential aspects in this question:

- guaranteed contact between US radiator and biological tissues;
- method for evaluation of influence of ultrasound signal on biological tissues.

Previously, technical decision that guarantees acoustic contact with constant dosage [1] was proposed and was shown that variation of cell membrane permeability is the universal reaction on US influence irrespective of what US factor that acts on cell takes preference [2].

Evaluation of effective influence of US on biological tissues takes central place in order to solve mentioned aims as it gives possibility to control and evaluate process of US interaction with biological structures in real time.

Accordingly, researches and obtainment of adequate mathematical models of biophysical processes US influence and action of US parameters on biological tissues gives ability to:

- receive a method to control effectiveness of US signal influence on biological tissues in real time;
- develop new UPA with controlling system of adaptation;
- increase effectiveness physiotherapeutic procedure;
- improve modern methods and principles of UPA's structures.

Simulation of physico-biological processes of US influence on lipid bilayer cell membrane with the consideration of quantitative method of process evaluation during the procedure [3] will give ability to work out adequate mathematical model that could help study and monitor in real time course of physical processes during US therapy, furthermore could correct US signal's parameters in order to receive fixed rates US dose that was planed.

2. Mathematical evaluation of interaction between ultrasound and cell

We consider biological cell that is effected with US from the point of view of mathematical simulation. For this object of research we formed several specialized models that reflect important peculiarities cell's reaction. The main typical variation of cell's parameters during US therapy is the increase of cell membrane permeability [2].

Membrane permeability P depends on temperature T and membrane's thickness [3]:

$$P = \frac{R \cdot T \cdot u \cdot \gamma}{l} \text{ [cm/s]}, \qquad (1)$$

where R – ideal gas constant (8,31 J/(mol·K)), T – temperature (Kelvin scale), u – substance's activity in surroundings, γ - substance's distribution between water and lipid phase, l - membrane's thickness. Thereafterby, for description of mathematical model interaction between US and the cell peculiarity of membrane's thickness and temperature variation should be considered.

2.1 Peculiarity of membrane's thickness variation in effected with US cell

Membrane potential E has kinetic nature and is defined by the number of transferenced ions through membrane's thickness. In the case of lipid bilayer

membrane, thickness is insomuch small that electroneutrality does not fulfill at all. Thereafterby, potential can be found with the use of assumption about tension constancy of electric field (Goldman's approximation) [5]:

$$E = \frac{R \cdot T}{F} \ln \frac{u_K \cdot c_{Na}(\delta) - u_{Na} \cdot c_K(0)}{u_K \cdot c_K(0) + u_{Na} \cdot c_{Na}(\delta)} \qquad (2)$$

In the simple case of diffusion transference of binary electrolyte comes into being so called diffusion potential (Plank's approximation) [5,7]:

$$E = \frac{R \cdot T}{F} \cdot \frac{u_K - u_{Na}}{u_K + u_{Na}} \ln \frac{c_{K-Na}(\delta)}{c_{K-Na}(0)}, \qquad (3)$$

where Na and K – solution of electrolytes, u_{Na}, u_K - ion's activity in membrane, $c_{K-Na}(\delta)$, $c_{K-Na}(0)$ - electrolyte concentration in membrane (left and right outphased confines accordingly).

According to the fact that time of diffusion in membrane is function from membrane's thickness [1]:

$$t = \frac{-\tau \cdot \ln(1 - \frac{c_{K-Na}(\delta)}{c_{K-Na}(0)})}{l}, \qquad (4)$$

where t – time of diffusion in membrane (equivalent to the time of procedure), τ – constant of time for membrane; diffusion potential during time t will look the next way:

$$E = \frac{R \cdot T}{F} \cdot \frac{u_K - u_{Na}}{u_K + u_{Na}} \ln\left(1 - \exp\left[\frac{l \cdot t}{-\tau}\right]\right). \qquad (5)$$

2.2 Peculiarity of temperature spreading in biological cell during US therapy

During interaction between US and biological tissue non homogeneous temperature increase takes place. On account of radiator's duration of action and maximally possible tissue temperature, several types of effect are distinguished: hyperthermia (42°C-50°C), coagulation (near 60°C), evaporation (near 100°C), carbonization (temperature higher than 150°C) and melting (beginning with 300°C). All indicated effects are leading to the cell necrosis or nonreturnable processes of membrane and chemical bonds destruction. Hereby, optimal range of thermal warming for therapeutic procedure should be fixed as temperature from 37°C till 42°C. There are none special changes at this temperatures, scilicet there is no essential cell injury [6].

2.3 Mathematical model of interaction between ultrasound and biological tissue

After we took into consideration main variation in cell that was described by equation (5), mathematical model of cell reaction on US as cellular membrane's thickness variation for binary electrolyte was received:

$$l(\tau) = -\frac{\tau}{t} \cdot \ln(1 - \exp(\frac{-E \cdot F}{R \cdot T(\tau)} \cdot \frac{u_k + u_a}{u_k - u_a})) \qquad (6)$$

Let observe reversed problem that reflects the aim of made research. During the process of US therapy ultrasound waves change physical parameters of biological tissue. In real case during therapy there is no possibility to make dimension through tissue structures. Therefore, there should be set up a transducer for depth dimension of temperature that allows to control tissue reaction. With the help of such transducer fixed absolute temperature $T(\tau)$ in every second of time is numerically compared with fixed temperature T_{kp} that conforms to every interval of time warming. When we know the $T(\tau)$ there is possibility to count out the $l(\tau)$ that reflects membrane thickness in every moment of time. As membrane thickness [illegible] is in the interval [7] $6nm < l_n(\tau) < 10nm$ then meaning of $l(\tau)$ that goes out from this interval should be named as destructive for cell.

If variation of membrane permeability shows [illegible] reaction, there is possibility to monitor the [illegible] therapy with established parameters [illegible] (frequency and intensity of US waves is constant) that is needed for achievement the biggest admissible effect.

3. Experiment

Dimension (Tab.1) were held with the help of next equipment: physiotherapeutic devices УЗТ 1[illegible] МИТ-11 and infra-red camera MoblR® M3.

Tab.1

Temperature dimensions

	Intensity, W/m²				
Work time of US radiator, s	0,05	0,2	0,4	0,7	1
5	29,3	29,6	30,6	30,8	31,[illegible]
10	30	31,2	31,3	32	32,[illegible]
30	30,6	31,2	31,6	30	32,[illegible]
60	31,2	31,5	31,8	32,2	33,[illegible]
90	32,2	32,3	33,3	32,6	32,[illegible]
120	33,1	32,9	32,6	33,3	33,[illegible]
180	33,1	33,8	32,8	33	3[illegible]
240	33,1	33,2	33,8	34	33,[illegible]
270	33,2	33,3	33,4	34,4	3[illegible]
300	33,8	33,9	34,1	34,6	[illegible]

Approximation of data ($f(x) = a \cdot \ln(x+b)$) accordingly to each intensity of US:

$$T_{0.05}(\tau) = 0{,}914 \cdot \ln(x + 4.523) + 27.227$$
$$T_{0.2}(\tau) = 0{,}625 \cdot \ln(x - 2.357) + 29.079$$

$T_{0.4}(\tau)=0{,}853\cdot\ln(x+40.297)+27.619$

$T_{0.7}(\tau)=1.493\cdot\ln(x+107.105)+23.863$

$T_1(\tau)=10.783\cdot\ln(x+2978)-51.544$

Membrane thickness during therapy:

$$l_n(\tau)=-\frac{\tau}{t}\cdot\ln(1-\exp(\frac{-E\cdot F}{R\cdot T_n(\tau)}\cdot\frac{u_k+u_a}{u_k-u_a})),$$

$n=\{0.05;0.2;0.4;0.7;1\}$,

$6nm<l_n(\tau)<10nm$

From the graph (fig.2) can be seen that US breaks integrity of biological membrane. Moreover, the more intensity is higher the faster membrane starts to react on US waves. Increasing membrane thickness provokes next processes in cell:

- variation of membrane permeability for ions of natrium and potassium (concentration of ions in premembrane layers) that leads to water accumulation;
- increase of cell size and as result increase of membrane area.

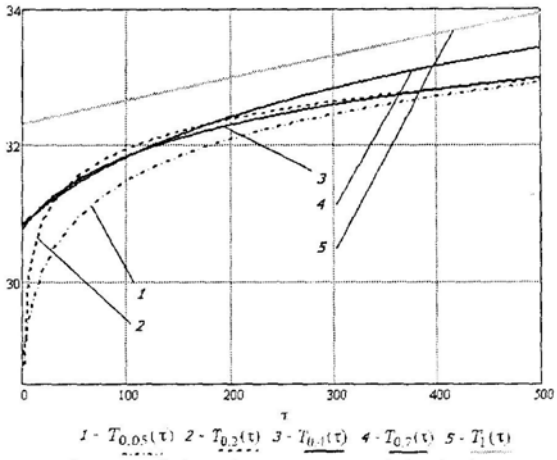

Fig.1. Simulation of temperature variation in time

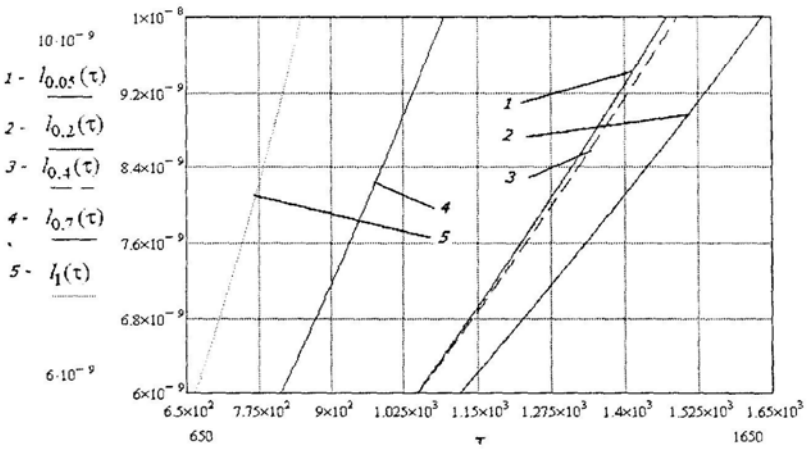

Fig.2. Simulation of membrane thickness in time

This processes lead to changes in fermentative reaction and to growth of substance diffusion across membrane (on account of variation of membrane concentration of substance and increase of membrane area). Acceleration of diffusion on interval τ=650-1150 (s) attests that increase of biological membrane permeability is a factor of positive influence of US on biological object.

Nevertheless, for each curve $l_n(\tau)$ comes a moment of time τ (for $l_1(\tau)$ at time $\tau=84{,}5$ s) when membrane reaches its max dimensions and further effect of US will lead to cell intumescences, cytoskeleton decay, membrane rupture and cell death. In order to avoid the negative effect of US ($f=const$ Hz and $I=const$ W/m²) on biological cell there should be set up an effective time of action.

In the capacity of criteria for positive US action on cell membrane we took its thicken: time τ that fulfils to max size of membrane would be named as the most effective. Depending on what intensity was selected (fig.3) for therapy, $t_{эф.n}$ is the more less the more increase intensity I.

4. Simulation of feedback for UPA devices

Let observe algorithm for feedback work in MCU (Micro Controller Unit). Rudimentary conditions: $f=const$ Hz, $I=1$ W/m². What to determine: permitted effective time for therapy during one procedure.

Step 1. During the first minute of UPA procedure MCU takes a signal from temperature transducer. As a result, we get 10 points (Tab.2) with the help of which after approximation it can be forecasted the moment that is connected with the beginning of thermal damage (fig.3 curve1).

In this case, according to the received function, the beginning of the hyperthermia starts at $\tau=3240$ (s) and the highest possible membrane thickening will at $\tau=810$ (s) (fig.4 curve 1).

Tab.2.

Temperature dimensions

№ of dimension	Work time of US radiator, s	Temperature
1	0	32,31
2	5	32,327
3	10	32,345
4	15	32,362
5	20	32,38
6	25	32,397
7	30	32,415
8	40	32,449
9	50	32,484
10	60	32,519

Step 2. Because of the permanent need of MCU for temperature adaptation, MCU should be programmed to fix meanings from the temperature transducer every 30 s (Tab.3) and to be able to forecast objectionable hyperthermia and also the moment of highest possible membrane thickening (fig.3 and fig.4 curves 2-7 that fulfil 11-16 dimensions).

Tab.3.

Temperature dimensions

№ of dimension	Work time of US radiator, s	Temperature
11	90	32,7
12	120	32,9
13	150	33,1
14	180	33,5
15	210	34
16	240	35

During the analysis of graphs (fig.3) that show temperature variation in time, it can be seen that the longer last the procedure the more rise authenticity to reach negative effect.

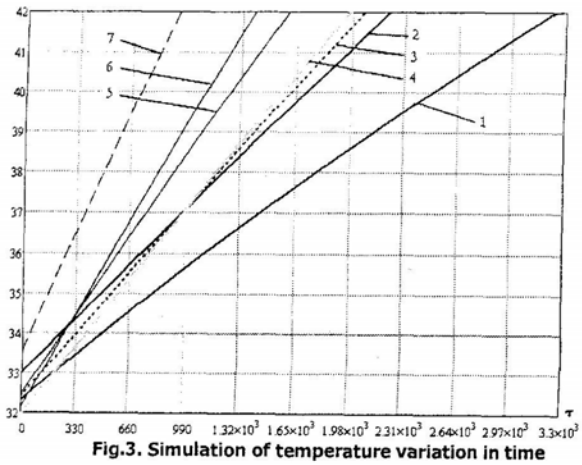

Fig.3. Simulation of temperature variation in time

On this basis, first control parameter τ_{42} should be established. τ_{42} - it is the moment of reaching the 42°C temperature.

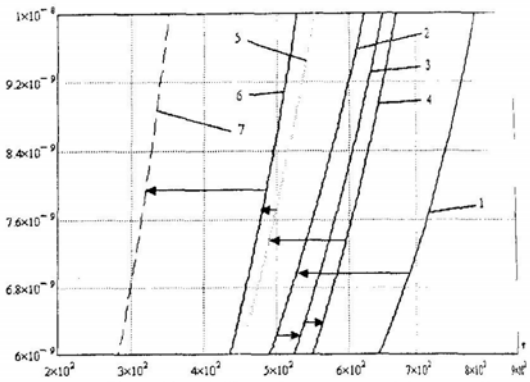

Fig.4. Simulation of membrane thickness in time

As it can be seen from the graphs of membrane thickness variation in time (fig.4), in 11-16 dimensions the moment $l(\tau) \to \max$ reduces, but not evenly. This method of control is sensitive to dramatic increase and to smooth changes in temperature. Let take a view of $\Delta T = \Delta T_n - \Delta T_{n-1}$, where $\Delta T_n = T_n - T_{n-1}$ (Tab.4).

Tab.4.

Temperature dimensions

№ of curve	Work time of US radiator, s	ΔT_n	ΔT
1	60	0,035	
2	90	0,181	0,146
3	120	0,2	0,019
4	150	0,2	0
5	180	0,4	0,2
6	210	0,5	0,1
7	240	1	0,5

Curves 2,5,6,7 (fig.4 pointer to the left) fulfil to time decrease for $l(\tau) \to \max$ concerning to the previous forecast. In this case ΔT exceed the level 0,1: 2 - 0,146; 5 - 0,2; 6 - 0,1; 7 - 0,5; otherwise, when ΔT is less than 0,1 (fig.4 curve 3,4) then the time of highest possible positive effect increases, however the time does not exceed the level of first meaning (fig.4 curve 1).

Step 3. To determinate time for effective procedure the feedback bond should continually compared real time with the time from the forecast.

The continuation of the procedure on each iteration should be available just in case of execute of the next condition: $\begin{cases} \tau < \tau_{42} \\ \tau < \tau_{l_{\max}} \end{cases}$, where τ_{42} - time of hyperthermia's beginning, $\tau_{l_{\max}}$ - time that shows highest possible membrane thickening; otherwise, the procedure should be stopped.

Tab.5.

Membrane thickness dimensions

№ of iteration	Work time of US radiator, s	τ_{42} , s	$\tau_{I_{max}}$, s
1	60	3217	810
2	90	2245	620
3	120	2062	650
4	150	1975	660
5	180	1443	545
6	210	1361	525
7	240	908	350
8	270	406	145

According to the data (Tab.5) received from the iterations, condition was not executed on the 8 iteration. As a result, if the reaction of biological object is in the form of temperature variation, the effective positive time will be 4.5 minutes under the condition that $f = const$ Hz, $I = 1$ W/m^2.

Conclusion

On the base of observed model of interaction between biological tissue and ultrasound practical method for controlling the efficiency of ultrasound influence on biological structures [4] was developed. This method includes functional diagram of automatized device and algorithm of feedback bond work. The proposed realization allows:

- to increase efficiency of treatment; to eliminate absence of therapeutic effect that can be upon condition of non-controlled ultrasound effect or its absence during the physiotherapeutic procedure at all.
- to guarantee effect from the ultrasound therapy by means of action on organs and tissues with the signal that can be corrected and controlled in real time according to the fixed dose of acoustic emanation during the procedure.

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