A Computer Simulation of Ultrasound Thermal Bio-effect in Embryonic Models

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Abstract. *At the present time, the usage of ultrasound diagnostic equipment has become an inseparable part of diagnosis for a number of medical investigations. Several scientific studies published in the last years showed that when applying a diagnostic ultrasound system on animals it is possible to create negative changes in tissues. New ultrasound technologies and higher output acoustic powers have brought a possible risk connected to the usage of ultrasound in diagnostics. The knowledge of risk level and exploration of limiting factors is an important point for the assessment of marginal ultrasound exposure values of medical investigation during pregnancy, especially in the first trimester. The contribution presents a MATLAB® application for modeling of tissue heating in human embryos at the developmental age of seven and eight weeks. Recent calculations of US fields, which are generated by several types of various unfocused single transducers (rectangular, circular, and annular), represent maximum temperature elevation of 0.4 °C in embryonic model tissues for the exposure of 1 min. The models of embryonic tissue heating provide comparative studies of possible bio-effect with the purpose to explore limiting factors of ultrasound exposure.*

Keywords

Modeling, ultrasound, bio-effect.

1. Introduction

Safety limits for usage of diagnostic and therapeutic ultrasound (US) devices have been stated by the World Health Organization since 1976. At the present time, experts demand the assessment of other limiting factors within newly developed investigating methods, especially for US medical investigation in pregnancy. Ultrasound is a mechanical oscillation which is a source of energy. When propagating through a medium, the US energy is attenuated and transformed into other forms of energy. Under certain conditions the energy transformation could have a negative impact on living tissues, so called bio-effect. Negative biological effects are divided into mechanical effects (cavitation and acoustic streaming) and thermal effects (heating).

Several scientific works published during last years showed that a tissue heating could occur when diagnostic ultrasound is applied (especially in Doppler mode). The measured heating was over 1.5 °C that represents the temperature elevation over the stated limit needed for undesirable tissue changes. The experiments were realized on pregnant guinea pigs, rats, sheep, and pigs because embryonic and fetal tissues are very sensitive. The most sensitive tissue is neural tissue, [1, 2, 5, 11].

When comparing a human embryo or fetus to examined animal subjects, there are tissue, dimensional, and proportional differences. Moreover, Doppler US methods are used during pregnancy in a limited range. On the other side, the experiments proved the repeated findings of a negative impact on living tissues caused by diagnostic ultrasound. Preliminary results of these experiments have led the World Federation for Ultrasound in Medicine and Biology together with many national US organizations to issue a safety recommendation for usage of US devices during medical investigation. The US equipment should be applied in an appropriate way for diagnostic purposes only with acoustic power as low as possible, [12, 13].

The ultrasound tissue heating is a local event. It affects only very small volumes and the impact depends on the sensitivity of target tissues. The worst case for thermal bio-effect is exposure of bones or ossificated tissues which are not transparent for propagating US waves. Ultrasound is highly absorbed in these tissues and absorption is accompanied by energy transformation. The ossificated or bone tissue becomes a secondary source of thermal energy which could be harmful for enclosed tissues. In case of cranial or spinal tissues, the neighboring tissues are quickly developing and highly sensitive neural tissues, [1].

2. Materials and Methods

A computer modeling or simulation offers possibility to verify the presumptions and results from the animal experiments. The modeling was realized in the software MATLAB®, version 5, which is especially designed for a matrix computation. Moreover, MATLAB® enables easy, quick, and suitable 3D graphical visualization of calculated results.

Embryonic models of US thermal effects are based on a modeling of US fields in homogeneous medium and in a simple biological system, [7, 8]. Absorption of ultrasound waves, and heat transformation are considered in the modeling, too.

The simulation of ultrasound propagation through the embryonic models is mathematically based on equations (1), (2) and (3), [3, 6, 9]. Spatial distribution of acoustic pressure, p, actuated by a transducer's aperture, S, moving by velocity, v, is described by the Rayleigh's Integral:

$$p(\bar{r}_p,t)=\frac{\rho}{2\pi}\int_S \frac{\partial v_n(\bar{r}_t,t-\frac{|\bar{r}_p-\bar{r}_t|}{c})}{\partial t}\frac{}{|\bar{r}_p-\bar{r}_t|}dS\,, \qquad (1)$$

where r_p is the positional vector of the spatial point, r_t is the positional vector of an elementary transducer surface, dS, ρ is the medium density, and c is the US speed. The equation (1) is valid under the condition of zero liquid streaming. For the description of possible US bio-effect it is necessary to know the spatial distribution of US energy, which is expressed by US intensity defined as:

$$I = p \cdot v\,. \qquad (2)$$

When propagating through the medium, the US wave is attenuated according to the equation:

$$I(x) = I_o \cdot e^{-\mu \cdot x}\,, \qquad (3)$$

where μ is the attenuation coefficient, and x is the distance from the ultrasound source. For the modeling the US intensity is defined as ITA value (temporal average). Absorbed US energy is transferred into the heat rate, $\dot{Q}$, resulting in the rate of temperature rise, dT/dt:

$$\dot{Q} = \mu \cdot I = \rho \cdot C \frac{dT}{dt}, \qquad (4)$$

where C is the thermal capacity of target elementary volume of the medium or tissue. The relation (4) is valid under the condition of zero conduction, convection, and radiation. When the heat conduction is considered, the equation (5) can be used. It describes the relation between heat induced by ultrasound and maintained temperature difference, ΔT:

$$\Delta T = \frac{\dot{Q}\cdot R^2}{2k} = \frac{\mu \cdot I}{2k}\cdot R^2\,, \qquad (5)$$

where k is the thermal conductivity and R is the radius of an imaginary sphere, which center is heated by ultrasound due to absorption. On the sphere surface there is a temperature difference, ΔT, related to the temperature of the heated center, [3, 9].

For computation the temporal and spatial discretization is necessary. Integrals are replaced by sums and derivations by differences. The investigative space is divided into a finite number of points – elementary volumes, the transducer's surface into a finite number of points – elementary surfaces. Actuating and propagating signals are sampled.

The temporal and spatial movement of the transducer's surface assesses boundary conditions for the numerical solution because transducer is the only source of mechanical energy within the investigated space. The borders of the space are non-reflective, i.e. standing waves cannot arise.

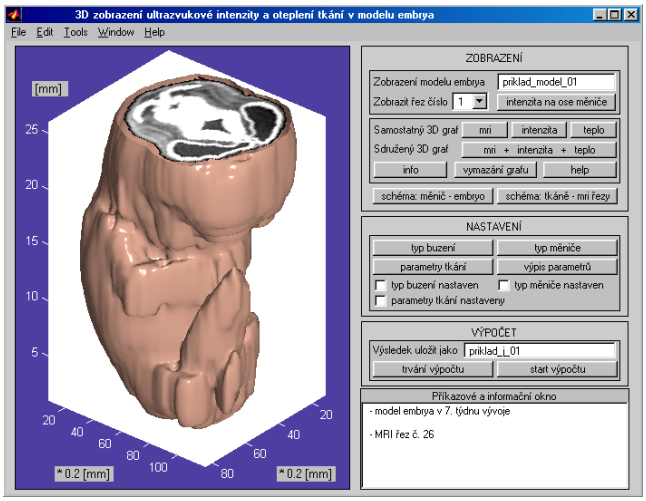

Fig. 1. Main application window with selection buttons for visualization, parameter settings, and starting the simulation

After actuation, transducer's surface elements become elementary sources of US waves which propagate through the investigated space. Between the embryonic model and the transducer there is medium with defined attenuation that simulates mother's tissues (see Fig. 2). When passing the distance between the transducer and the investigated space border, US waves propagate through elementary volumes of the embryonic model. The resulting effect of US waves in a certain spatial point of the investigated space is given according to the Huyghen's Principle by summary of all US waves which were actuated by the transducer and reached this point. The knowledge of US intensity spatial distribution in the embryonic model ensures to evaluate the induced heat or to evaluate the spatial distribution of local temperature increase in tissues.

Two embryonic models of thermal bio-effects represent human embryos at the age of 7 and 8 weeks. These developmental stages are the most dangerous ones from the view of ultrasound exposure, i.e. stages of cranial and spinal ossification and intensive development of organs, especially development of neural system, [1, 4]. The spatial tissue distribution in the models matches with the cross-sections which were taken by a magnetic resonance imaging (MRI). The investigated space of the two embryonic models is divided into elementary volumes characterized by the tissue type. The embryonic model at the develop-

mental age of seven and eight weeks is divided into 40 × 60 × 30 and 44 × 60 × 38 elementary volumes respectively. It means that the elementary volume represents a rectangular parallelepiped with the dimensions of 0.3×0.3×0.9 mm and 0.35 × 0.35 × 0.8 mm respectively. The distance and attenuation between the embryonic model and a transducer are input parameters. The distance and average total attenuation between a probe and an embryo were stated as 50–70 mm and 1.1 – 3 dB/ MHz, [11].

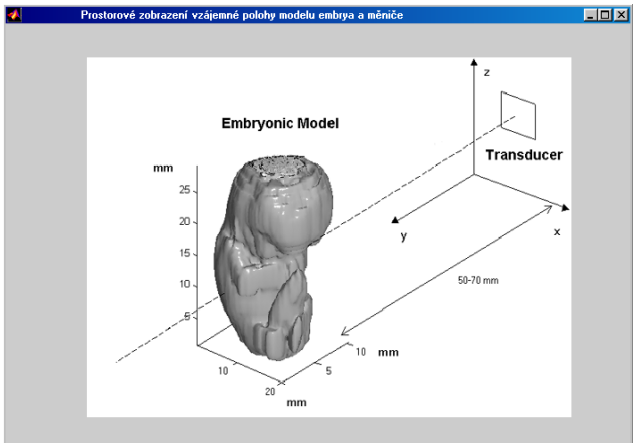

Fig. 2. Spatial location of the embryonic model and the transducer generating a simulated ultrasound field.

For the modeling of US propagation, seven elementary tissues-mediums were chosen: organ tissue, muscle tissue, soft tissue, cartilage tissue, ossificated bone tissue, body humour, and amniotic fluid. Body humours fill embryonic cavities or big vessels. Amniotic fluid surrounds an embryo or fetus. These seven tissue types represent groups of the same or similar embryonic tissues. The tissue types are characterized by input parameters: acoustic impedance, US attenuation, acoustic speed, density, heat capacity, and heat conductivity. Values and their ranges were taken from published scientific works, [3, 9].

The ultrasound field propagation through the embryonic model is simulated for US fields generated by several types of single transducers (circular, rectangular, or annular), several types of actuating impulses (ideal, aperiodic, or damped impulse), and several types of spatial transducer's surface movement (Gaussian, ideal, or exponential spatial movement). Other input parameters are transducer's dimensions, actuating frequency and setting of local tissue perfusion because the thermo-regulation of a biological system can ensure the heat convection up to 50 % of the induced heat, [3].

3. Results and Discussion

The MATLAB® application enables easy and quick handling with input values and imaging of computed results. The main application window is divided into three parts: visualization, settings of input parameters and computation (see Fig. 1).

The imaging part ensures a choice of visualized cross-sections of the model, displaying of table information about all used parameters, creation of single graphs, etc. Parameter settings offer several small windows with editable lines for entering the values. A combination of critical input values together with 3D graphs of computed results provide comparative studies intended for the evaluation of a possible temperature increase.

Examples of computed simulations are shown in Fig. 3 and 4. There are single graphs of cross-sections in the embryonic model at the developmental age of seven weeks displaying scale colors of US intensity and induced heat in tissues respectively. In this case, the US field is generated by a square transducer with the side of 15 mm situated 60 mm far from the model. The actuating impulse has frequency of 3,5 MHz. Resulting US fields are normalized. The values of US intensity and induced heat are related to the maximum permitted value of US intensity I_{SPTA} = 720 mW/cm^2.

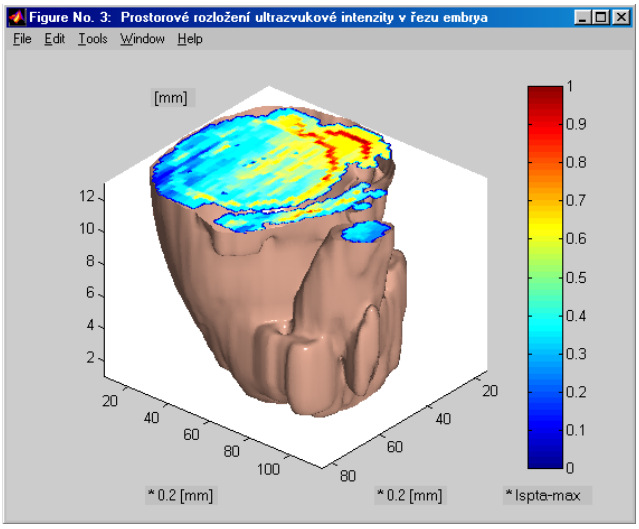

Fig. 3. Single 3D graph of the model cross-section with distribution of US intensity.

For the simulation, it is possible to use published average values of I_{SPTA} for various imaging modes of US diagnostic equipment: B-mode has I_{SPTA} = 0,03 W/cm^2, M-mode I_{SPTA} = 0,1 W/cm^2, Color Doppler Imaging CD-mode I_{SPTA} = 0,3 W/cm^2 and pulse Doppler Imaging PD- mode I_{SPTA} = 1 W/cm^2, [11]. Doppler imaging has a stationary US beam what represents higher possibility of any induced heat occurrence.

For a certain case of input value settings, it is necessary to consider the type of simulated US imaging when calculating the induced temperature elevation. This means that the result is related to the permitted limiting value I_{SPTA} = 720 mW/cm^2 or to an imaging mode value. Then the computed normalized results are multiplied by the appropriate intensity value. The induced temperature elevation is also affected by the duration of an US exposure which lasts several minutes during a medical investigation.

Recent calculations of the comparative study of US fields, which are generated by several types of various unfocused single transducers (rectangular, circular, and annular), represent the maximum temperature elevation of 0.4 °C in embryonic model tissues for the exposure of 1 min. The maximum is in the beam axis. In the frame of the whole embryonic model, the temperature elevations in simulated tissues differ almost in four orders for one calculation case. Differences depend on the location of transducer and target tissue, on tissue types and settings of input tissue parameters. High amount of input variables creates quantity of combinations. An assessment of critical input parameters and their values and an evaluation of the thermal impact pertain to a medical specialist, for whom the MATLAB application of US thermal bio-effect simulation is developed. Because the current application enables simulations of US fields of unfocused single transducers, the future development of this simulation is concentrated on systems of single transducers which approximate the real US focused probes. A focusing beam results in higher maximum temperature elevations in focused zones of target tissues or neighboring tissues when comparing to unfocused ones.

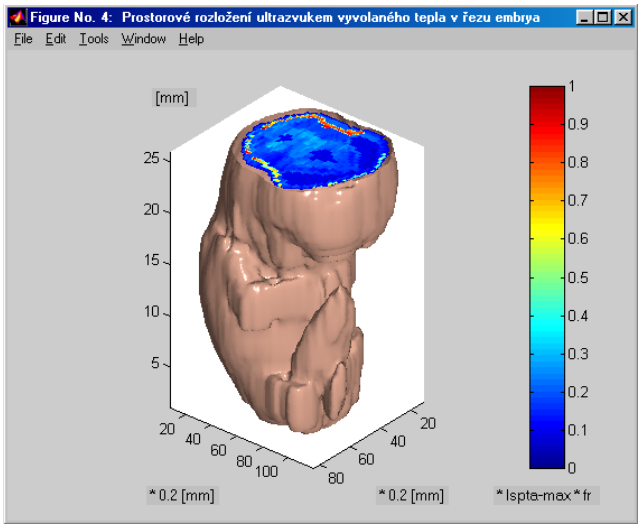

Fig. 4. Single 3D graph of the model cross-section with distribution of heat induced by ultrasound.

In our case, it is necessary to consider that each computer simulation represents a certain simplification when comparing to real events. Used mathematical relations were derived under linear conditions. Basic mathematical equations resulted from an ideal circular-cylindrical symmetry and from ideal plane wave propagation. The embryonic model consists of elementary homogeneous volumes, it means that the whole model is homogeneous in parts. Estimated ranges of the US input values are considered in the modeling because published parameter values were measured on adults` bodies and they might differ from embryonic tissues.

For ultrasound propagation, two special phenomena occur. Non-linearity of the transmission process causes a creation of higher harmonic frequencies in propagating wave signals, however, transmission function of the medium is not ideal and high frequencies are more attenuated. So the both phenomena are equalizing in a certain distance and the shape of propagating ultrasound signals remains nearly the same. The division of transducer's surface into 50 elementary areas solves the problem of spatial impulse response of the transducer.

Combinations of input parameters or their ranges offer comparative studies for an analysis of limiting parameters which can cause a possible negative impact on embryonic tissues. The presented MATLAB® application provides modeling of US fields under special conditions of single transducers.

4. Conclusion

When using an ultrasound device, contemporary medical diagnostics can detect amount of developmental deviations of embryo or fetus. That's the reason why ultrasound diagnostic device is an essential instrument for prenatal care. From the view of an appropriate care, some medical investigations are performed over the frame of diagnostic need because they are required by patients – pregnant women who want to see or record their unborn baby. These cases represent a useless increase of ultrasound exposure of tissues. An operator should consider the possible hazard and benefit together with keeping the recommended limits. The risk level is not still obvious and well known but a caution is important. According to general recommendations, the aim of each ultrasound medical investigation in pregnancy should be an application of the so-called strategy ALARA – as low as reasonably achievable. The presented computer modeling of a possible risk during ultrasound investigations in pregnancy tries to contribute to precising of limiting values for safety diagnostics.

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