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ZONALITY OF MICROHEMODYNAMICS EXPOSED TO HIGH-INTENSE FOCUSED ULTRASOUND

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ЗОНАЛЬНОСТЬ МИКРОГЕМОДИНАМИКИ ПРИ ВОЗДЕЙСТВИИ ВЫСОКОИНТЕНСИВНЫМ ФОКУСИРОВАННЫМ УЛЬТРАЗВУКОМ

Abstract. High-tech treatment methods are now actively introduced into clinical practice, designed to limit the invasiveness of surgical procedures, among these methods, as one of the promising areas, is focused high-intensity ultrasound (HIFU). HIFU-therapy is based on thermal destruction of tissue, however, the features of the propagation of the heat wave, the state of blood flow in the peripheral zones remain poorly understood. Due to this, the aim of this study was to evaluate the intravital blood flow of the tongue and the swimming membrane of the grass frog in the perifocal zones after HIFU-induced exposure and the nature of the thermal pattern. The obtained data revealed the zoning of blood flow during vital biomicroscopy, which limited the propagation of the heat wave.

Аннотация. В клиническую практику активно внедряются высокотехнологичные методы лечения, призванные ограничить инвазивность хирургических манипуляций, среди которых одним из перспективных направлений является фокусированный высокоинтенсивный ультразвук (HIFU). В основе HIFU-терапии лежит термическая деструкция тканей, однако особенности распределения тепловой волны, состояние кровотока в перифокальных зонах остаются недостаточно изученными. С этой целью проводили исследования прижизненного кровотока языка и плавательной перепонки травяной лягушки в перифокальных зонах после HIFU-индуцированного воздействия и оценивали характер теплового паттерна. Полученные данные позволили выявить зональность кровотока при витальной биомикроскопии, что ограничивало распространение тепловой волны.

Key words: HIFU, high-frequency focused ultrasound, thermal pattern, thermal wave, thermal ablation, microcirculation, blood flow zones

Ключевые слова: высокоинтенсивный фокусированный ультразвук, тепловой паттерн, тепловая волна, термоабляция, микроциркуляция, зоны кровотока.

Introduction. In recent years, high-tech methods of therapy have been widely introduced into clinical practice in order to limit the invasiveness of surgical operations [2]. An example of the introduction of new technologies is the use of high-frequency focused ultrasound (HIFU) in the treatment of neoplasms [1-3]. The HIFU method has several significant advantages (non-invasiveness, repeatability until a clinical effect is achieved, the absence of postoperative changes in healthy tissues) and has minimal surgical risk [6,7].

Over the past 15-20 years, HIFU therapy has become a serious alternative to surgical methods of treatment in oncology and it is actively used in the treatment of benign and malignant neoplasms of the liver, mammary glands, prostate gland, connective tissue, kidneys, brain, thyroid and parathyroid glands [5,6].

The therapeutic effect of focused ultrasound is based on the physical phenomena [9], namely, the generation of heat emitted when biological tissues absorb acoustic energy and mechanical disturbances in a biological environment. The propagation of high-frequency focused vibrations in heterogeneous living tissues forms an acoustic field in the form of complex of spatiotemporal distributions, characteristics of mechanical disturbance. This is accompanied by the formation of an interference maximum in the local zone due to the superposition of acoustic waves generating a thermal field from an external ultrasonic source. Obviously, the response of biological structures to such effects should be determined, on the one hand, by the nature of the energy distribution and the degree of manifestation of wave and nonlinear effects, and on the other, by the characteristics of the high-frequency focused acoustic field [8]. Focused high-intensity acoustic vibrations, forming lengthwise, shear and bending waves in biological tissues, generate a heat wave that causes mechanical, electrical phenomena that affect on the formation of the spatiotemporal continuum of the thermal field in the focus zone. However, a number of questions remain unresolved, one of which is the distribution of the HIFU-induced thermal pattern, which forms spatially inhomogeneous temperature fields, which are able to integrate, thereby increasing the thermal ablation zone, including healthy tissues. Such combination in heterogeneous biological structures with variegated hemodynamics is associated with nonlinear thermal effects that can generate zones with a small temperature difference, which increases the area of thermal damage. In this case, the total and distributed area of temperature patterns depends on the intensity of blood flow in a region, which acts as a heat and mass transfer and limits the propagation of a HIFU-induced heat wave.

Due to this, the aim of this research is to assess the state of intravital local blood flow, which plays the role of heat and mass transfer in biological structures, restricting the propagation of a heat wave under high-intensity focused ultrasound exposure.

Materials and methods. Grass frogs (Rana Temporaria) supplied by Profsnab LLC were used as the object of the study. The selection of the object was related to:

-the accessibility of the vessels of the tongue and the frog’s membrane for vital microscopy

-the possibility of vital monitoring of blood flow immediately after HIFU-induced exposure

-eventual assessment of thermal patterns and the state of microcirculation in these zones

Prior to experiment, all frogs were anesthetized. A 10% urethane solution in the volume of 0,4 ml/100 g was injected into the spinal lymphatic bag. Animals were placed on a special plate with a «window» for transmitted light, over which the object of the study was neatly straightened and secured.

The experimental work was carried out on a testing unit developed in a laboratory of ultrasonic technologies of Peter the Great St.Petersburg Polytechnic University. It consisted of an emitter H-148 S/N 010 (Sonic Concepts, Inc., USA), generating high-intensity focused ultrasound, with a central oscillation frequency of 2,5 MHz (minimum frequency of 1.4 MHz), an active diameter of 64 mm and a central hole of 20 mm.

An emitter with concave surface focused ultrasound at a distance of about 6.8-7 mm. The possibility of focusing ultrasonic vibrations in a small focal region created conditions for local high-energy exposure with a radiant intensity of up to 8.2 kW / cm^2 in the averaged spot zone up to 0.6 mm without any significant thermal effects on the surrounding structures.

The HIFU is a mobile cone-shaped setup that focuses the acoustic field to the calculated depth.

To ensure the passage of ultrasonic waves, a conducting medium was used, in which degassed water was used. It was poured directly into the cone-shaped circuit, in the upper part of which the N-148 S / N 010 emitter was located, and the lower part of the circuit was covered with a silicone liner to ensure tightness (Fig. 1).

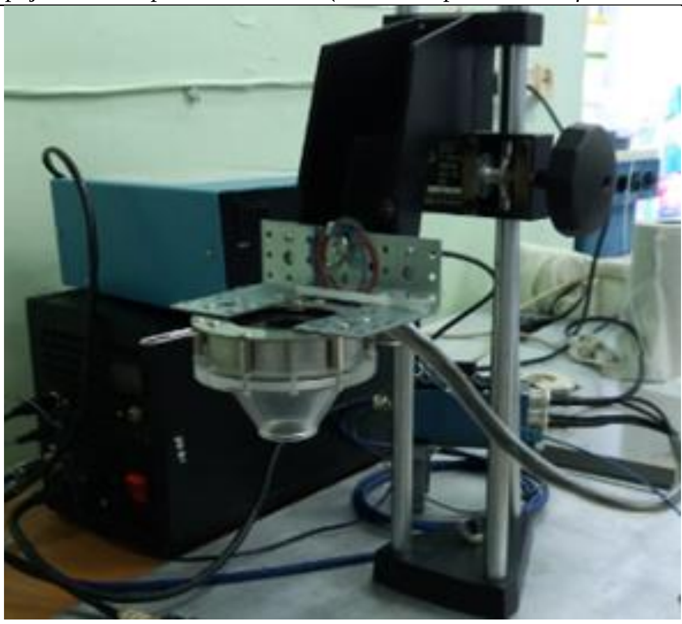

Fig. 1. General view of the conical installation with the emitter H-148 S / N 010

A setup consisting of a binocular microscope (Wild M420, Switzerland) with a lens (63 × magnification), and a digital camera (Basler, Germany) was used for recording visual changes in blood flow in the microvasculature. Observation results were processed using the software "Multimedia Catalog" (Russia).

The structure of the HIFU-induced thermal pattern was evaluated using a Seek Thermal Compact PRO Android mobile camera with micro-USB (Seek Thermal, USA) immediately after exposure to focused ultrasound.

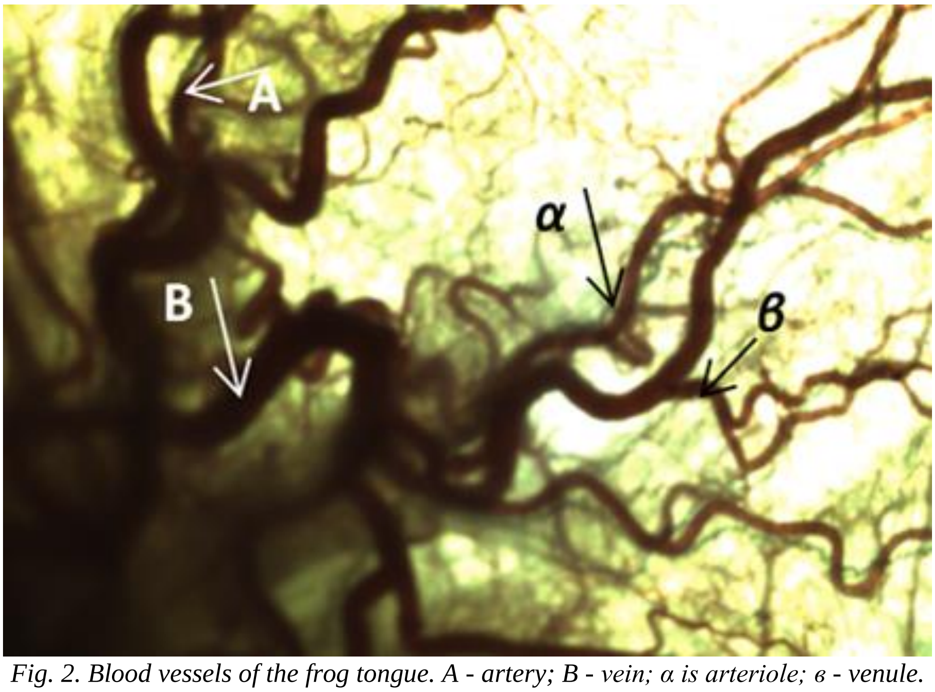

Fig. 2. Blood vessels of the frog tongue. A - artery; B - vein; α is arteriole; в - venule.

After registration of the initial blood flow in the tongue or the frog's swimming membrane (Fig. 2), aqua gel was applied to the surface of the mucosa or skin to ensure tight contact with the cone of the ultrasonic emitter. A single HIFU thermo ablation was carried out with an intensity of 8.2 kW $cm^2$and an exposure of 400 ms. After completion of the acoustic impact, vital vascular microscopy of the tongue and the swimming membrane was performed, on this basis, the state of the blood flow in the focus of exposure and in the peripheral zones was judged.

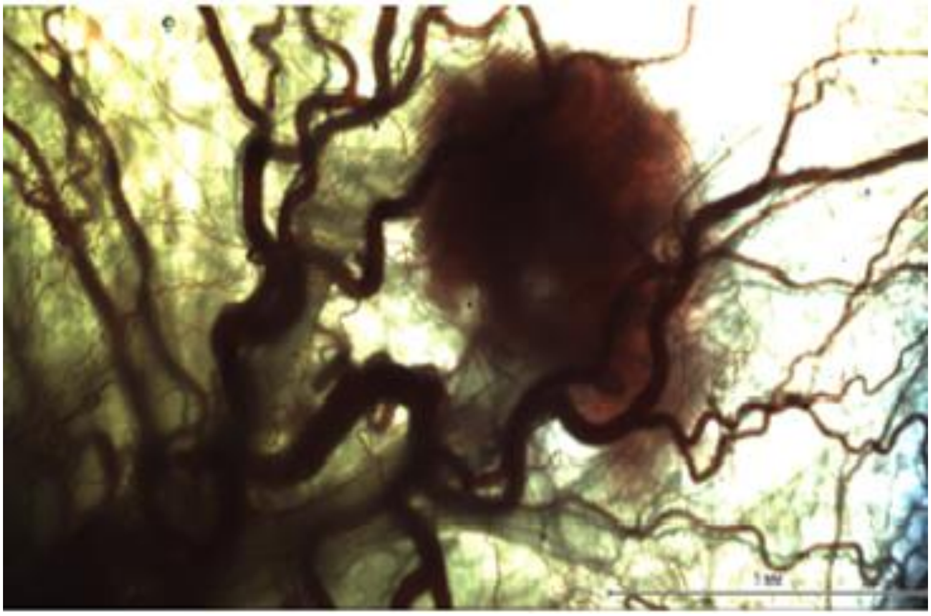

Fig. 3. Thermal ablation pattern after exposure to HIFU.

Results and discussion. The observables structural and functional disorders of microvessels could be the result of both thermal and mechanical effects of HIFU-induced exposure. The following bioeffects were noted in the focal zone: thermal destruction and thermocoagulation of the blood, local ruptures, perivascular hemorrhages in the surrounding tissue, and edema. Disturbance and stoppage of blood flow in microcirculatory bloodstream in the HIFU exposure zone was observed. The latter is reflected in the heat removal rate in the thermal ablation zone. In the perifocal regions, areas with uneven optical density were noted. Perhaps the latter was due to increasing edema against the background of partially preserved blood flow, a decrease in the number of functioning capillaries. In the analyzed area, the diameter of the arterioles decreased by 25-28%, and the venule decreased by 8%.

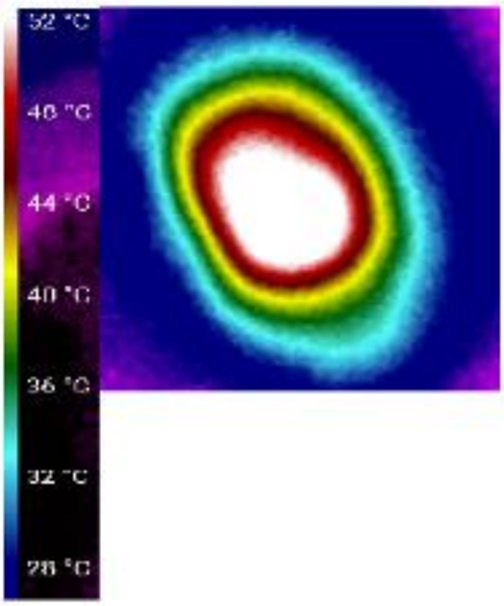

Fig. 4. The zoning of the thermal pattern under HIFU-induced exposure.

As a result of life-time biomicroscopy after HIFU-induced exposure, a clear zoning in the state of blood flow can be distinguished: a destruction zone with a cessation of blood flow is in focus, two zones can be distinguished in the perifocal region - with partially preserved blood flow and preserved blood flow. Thermal imaging also revealed the zoning of HIFU-induced thermal patterns This indicates the formation of temperature zones under acoustic exposure (Fig. 4). The oval shape of the thermal imaging portrait is explained by the transformation of the acoustic wave into mechanical and thermal effects. But shear stresses in a heterogeneous medium give rise to nonlinear dynamic changes in the distribution of the heat wave.

It is conceivable that in areas with partially preserved and preserved blood flow, the necessary heat transfer is provided, which limits the intensity of the temperature wave and reduces the risk of damage to healthy tissues. The zoning of the blood flow allows us to suggest that the geometrical dimensions of thermal patterns can be different, and their size determines the scale of the heterogeneity of the distribution of temperature zones. However, tissue heterogeneity of a biological object induces a complex distribution of the thermal field, which can be represented as the total spectrum of thermal patterns. Additionally, provided that the total area of the thermal pattern approaches to the size of the useful area of irradiation, then the significance of the heterogeneity decreases and vice versa, which requires the introduction of weight coefficients. In addition, the heterogeneity of biological tissues leads to non-linear thermal effects. The latter initiate the process of integration of thermal patterns, which leads to the appearance of zones with a slight temperature gradient. Based on the above, a qualitative model of heat generation in biological tissues was developed with the introduction of the conversion coefficient of the acoustic power of the emitter into thermal power, a general view of which is presented below:

$$\tau = \frac{P}{T} x\ 100\%$$

where τ - coefficient of conversion of the acoustic power of the emitter into thermal power;

P - acoustic power of the emitter;

T - thermal power in focus.

Sample calculation demonstrated that only from 21 to 24% of the acoustic power of the emitter in the focus region is transformed into thermal power, and the other part is converted into mechanoelectric effects, what requires further refinement.

Conclusion. Thus, under the influence of the mechanical and thermal components of the HIFU effect, zoning of the blood flow distribution with various vascular, perivascular changes in the thermal ablation zone and perifocal regions occurs. The latter must be taken into account when calculating the values of heat transfer and heat conduction during therapeutic treatment with high-intensity focused ultrasound.

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