Conclusion. In the case of a deep intermuscular phlegmon of the gluteal region, an increase in intra-tissue pressure is observed in 94.8% of cases, and most of them (87.1%) develop tissue hypertension syndrome (compartment syndrome). Therefore, fasciotomy of the concerned gluteal region fascial structures may be considered as the pathogenetically justified method of treatment, against the background of normalization of the tissue pressure index (8–10 mm Hg). The use of ultrasound treatment of a purulent wound and daily irrigation with ozonated solutions at a concentration of at least 20 mcg/l in the postoperative period in patients with deep phlegmon of the gluteal region accelerates the processes of wound cleansing by 1.5–2.5 times. In this case, it becomes possible to close the wounds early with primary delayed sutures.

A comprehensive approach to the treatment of patients with intermuscular phlegmon of the gluteal region allows achieving good results earlier after treatment in 83.3% of patients (55.0% in the control group), while reducing the length of hospital stay to 12.5 ± 2.5 days (19.5 ± 2.5 days in the control group), and in the long term in 92.8% of patients (64.7% in the control group).

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Thermal and shock-wave effects of HIFU - effects on tissue-equivalent phantoms

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Abstract

The nature of changes in the structure of the PAG-3 biophantome under the action of HIFU indicates the significance of shock-wave shifts involved in the formation of the heat pattern and the destruction zone. The thermal effect is accompanied by the accumulation of thermal energy, the limitation of the thermal field, which predetermines the therapeutic efficiency of focused ultrasound exposure, however, it is advisable to take into account the role of mechanical effects in focused ultrasound therapy.

Key words: high-intensity focused ultrasound HIFU, thermal patterns, shock-wave effects, mechanical microflows, biophantom, PAG3, thermal ablation zones.

The propagation of high-intensity focused ultrasonic vibrations (HIFU) in biological tissues forms an acoustic field [1–3] in the form of a set of spatio-temporal thermal and mechanical characteristics of distributions with the formation of interference maxima in local zones due to superpositions of acoustic waves generating shock-wave and thermal effects.

Obviously, the response of biological tissues to such influences should be determined, on the one hand, by the nature of energy distribution and the degree of manifestation of wave

and nonlinear effects in biological structures, and, on the other hand, by the characteristics of a high-intensity focused acoustic field [4-5]. The energy of the ultrasonic wave generates shear stresses and vortex microflows, the velocity gradients of which reach $10^5 - 10^6 \text{ s}^{-1}$, and this is enough to "break" the cell membranes. However, mechanical tissue destruction is considered a side effect of HIFU, and the main therapeutic effect is associated with thermal ablation [1].

But in our opinion, shock-wave shifts caused by the effects of acoustic cavitation, shear microflows and stresses, together with the generation of a local thermal field, are involved in the formation of destruction zones and are capable of initiating sensitization of tumor cells to radiation, cytotoxic therapy. Therefore, it is important to work out the HIFU exposure modes on the simulator, which simulates changes in the mechanical properties of a pathological focus. The aim of this work was to study the distribution of thermal patterns, shock-wave effects on tissue-equivalent phantoms to assess the modes of HIFU exposure.

Of interest was the PAG3 biophant based on polyacrylamide gel, not only because of the simplicity of preparation, but also because of the comparability of acoustic properties with biological tissue. To assess the thermal and mechanical HIFU-associated effects, a modular stand was used, including an ultrasound diagnostic scanner "Angiodin-1" (firm "Bioss", Russian Federation), and an installation consisting of a mobile module "Diater" for HIFU therapy. A flat-concave transducer H-148 S / N 010 (Sonic Concepts, Inc.) with a central oscillation frequency of 2.5 MHz and a focal length of about 7 mm was used as an ultrasonic generator. The possibility of focusing acoustic vibrations created conditions for a local high-energy impact with a radiation intensity of 8.2 kW/cm² and 23.3 kW/cm² in the averaged spot zone up to 0.6 mm. Degassed water was used to ensure the passage of ultrasonic waves.

Preliminarily, 4 thermal sensors were inserted into the PAG3 phantom in sealed PVC tubes of a digital multichannel thermograph (T-8). Heat sensors were placed in the immediate vicinity of the lesion (up to 1 mm), and then installed sequentially at distances of 5-10 mm, 15-25 mm, and 30-45 mm from the focal zone to assess the heat pattern. In total, 22 tissue-equivalent PAG-3 phantoms were used, which were subjected to ultrasound with an intensity of 8.2 kW/cm² and 23.3 kW/cm² in a focal spot with a diameter of up to 0.6 mm with various exposures, and the temperatures were estimated in different spatial zones of HIFU- induced heat pattern (tables 1 and 2).

Table 1

Indicators of temperature sensors at different distances from the thermal ablation zone at an intensity of 8.2 kW/cm² and a single HIFU exposure ($x \pm m$)

Exposure, ms	The internal temperature of the phantom according to the readings of the 1st thermal sensor located at a distance of up to 1 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 2nd thermal sensor located at a distance of 5-10 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 3rd thermal sensor, located at a distance of 15-25 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 4th thermal sensor located at a distance of 30-45 mm from the thermal ablation zone
50	33,4±0,2 C°*	21,1±0,1 C°	20,6±0,08 C°	20,3±0,1 C°
100	40,5±0,3 C°*	23,9±0,08 **	22,1±0,1 C°**	20,5±0,2 C°
150	45,9±0,3 C°*	24,8±0,1*	22,1±0,1**	20,6±0,3
200	49,4±0,5 C°*	25,6±0,1 *	23,6±0,07**	20,6±0,4
250	54,4±0,5 C°*	26,2±0,07*	23,8±0,1*	20,9±0,2
300	60,1±0,3 C°*	26,9±0,08*	23,8±0,06*	21,0±0,1
350	66,7±0,6 C°*	27,5±0,07*	23,9±0,07*	21,1±0,1
400	70,4±0,6 C°*	28,0±0,1*	23,9±0,08*	21,4±0,07

450	74,6±0,2 C°*	28,4±0,08*	23,9±0,05*	21,5±0,08
500	80,6±0,62 C°*	28,8±0,07*	23,9±0,04*	21,7±0,3
1000	>103,3 C°*	30,2±0,09*	24,7±0,06*	22,8±0,4**
5000	>103,3 C°*	31,5±0,1*	24,8±0,06*	22,5±0,08**
8000	>103,3 C°*	33,8±0,1*	25,2±0,05*	22,5±0,04**

Note: * - statistically significant differences ($p < 0.01$) compared to the initial values. ** - statistically significant differences ($p < 0.05$) compared with the initial indicators

With an exposure of 1000 ms and above, it was not possible to clearly measure the temperature in the focal zone due to the limiting upper limit of the digital computer thermograph (T-8).

Table 2

Readings of temperature sensors at different distances from the thermal ablation zone at an intensity of 23.3 kW / cm² and a single HIFU exposure

№	Exposure, ms	Readings of the 1st temperature sensor	Readings of the 2nd temperature sensor	Readings of the 3rd temperature sensor	Readings of the 4th temperature sensor
1	20 ms	31,5±0,2**	22,3±0,2	21,5±0,3	21,4±0,4
2	30 ms	39,1±0,3**	22,9±0,3	21,5±0,5	21,6±0,3
3	50 ms	47,7±0,3**	24,6±0,4*	22,7±0,4*	21,9±0,4
4	80 ms	58,1±0,5**	27,7±0,3*	23,6±0,5**	22,1±0,4
5	100 ms	71,5 ±0,6*	31,2±0,7**	25,5±0,4*	23,1±0,5

Note: ** - the statistically significant results ($p < 0.001$) in comparison with the reference values * - statistically significant results ($p < 0.05$)

These findings indicate a proportional relationship between exposure and temperature in the nearest and perifocal zones. There was no significant increase in temperature at the perifocal zones which indicated that the focus zone was limited.

The temperature rise in the focal zone was evaluated using multiple HIFU exposures to confirm the phenomenon of heat accumulation. The following mode of exposure to local zones of 11 phantoms was used: 5 HIFU "shots", intensity 8.2 kW / cm², exposure 500 ms. The results are shown in Table 3. The phenomenon of heat accumulation in the focal zone can be explained by a change in the magnitude and rate of heat transfer arising from mechanical shifts of the phantom structures and the appearance of the thermal conductivity restrictions in the investigated medium.

Table 3

Temperature increase in the focal zone with 5 HIFU shots with an intensity of 8.2 kW / cm² and an exposure of 500 ms. (n = 11)

№	Shot number	Focal zone temperature
1	1	64,3±0,3*
2	2	83,2±0,4*
3	3	98,8±0,6*
4	4	103,0±1,2*
5	5	>103

Note: * - statistically significant differences ($p < 0.01$).

Thus, a feature of this mode of physical impact on the polyacrylamide hydrogel phantom was a slight temperature gradient in distant zones, which indicates a local increase in temperature in the focus zone. Probably, mechanical microflows form conditions limiting the heat flux, which, on the one hand, forms the phenomenon of local thermal ablation, and, on the other hand, limits heat transfer. This effect is comparable to the features of the formation of a heat pattern in biological tissues.

Temperature gradient on multiple HIFU shots, but at different exposures is especially interesting. The dynamics of the change in the temperature gradient was evaluated depending on the number of HIFU shots with an intensity of 8.2 kW / cm² with exposures of 300 ms and 500 ms. The data obtained are presented in tables 4,5.

Table 4

The dynamics of temperature changes in different zones of the phantom with an increase in the number of HIFU shots with an exposure of 300 ms

№	Number of shots	The internal temperature of the phantom according to the readings of the 1st thermal sensor located at a distance of up to 1 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 2nd thermal sensor located at a distance of 5-10 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 3rd thermal sensor, located at a distance of 15-25 mm from the thermal ablation zone	The internal temperature of the phantom according to the readings of the 4th thermal sensor located at a distance of 30-45 mm from the thermal ablation zone
1.	5	73,1±0,3*	33,1±0,1*	23,7±0,1*	21,6±0,12
2	8	78,5±0,4*	34,1±0,08*	23,8±0,2*	21,8±0,1

Note: * - statistically significant differences ($p < 0.01$)

Table 5

The dynamics of temperature changes in different zones of the phantom with an increase in the number of HIFU shots with an exposition of 500 ms

№	Number of shots	The internal temperature of the phantom according to the readings of the 1st thermal sensor located at a distance of up to 1 mm from the thermoablation zone	The internal temperature of the phantom according to the readings of the 2nd thermal sensor located at a distance of 5-10 mm from the thermoablation zone	The internal temperature of the phantom according to the readings of the 3rd thermal sensor, located at a distance of 15-25 mm from the thermoablation zone	The internal temperature of the phantom according to the readings of the 4th thermal sensor located at a distance of 30-45 mm from the thermoablation zone
1.	5	88,5±0,3*	35,4±0,3*	24,0±0,07**	22,7±0,1
2	10	93,5±0,3*	37,6±0,2*	24,1±0,1**	22,8±0,21

Note: * - statistically significant differences ($p < 0.01$); ** - statistically significant differences ($p < 0.05$)

Thus, when using a tissue-equivalent phantom PAG-3, we observed the phenomena of accumulation of thermal energy in the focus area, limited distribution of heat flow, which can be traced with single and multiple HIFU exposure. Such features of the formation of the PAG-3 heat pattern bring it closer in its main characteristics to biological tissue structures. Some differences can be noted in the architectonics of thermoablation zones in polyacrylamide hydrogel at different expositions with visual and ultrasonic (Fig. 6) control.

The nature of changes in the structure of the tissue-equivalent phantom PAG-3 in the focus zone indicates the role of acoustic cavitation and mechanical shock-wave shifts that form a thermal pattern. The latter is characterized by the following phenomena: accumulation of thermal energy, limited heat propagation, which determines the therapeutic effectiveness of HIFU exposure, however, it is advisable to take into account the role of mechanical effects in focused ultrasound therapy.

Thus, the obtained data allow us to suggest the role of shock-wave shifts in the tissue-equivalent phantoms under HIFU exposure, which are involved in the formation of the thermal pattern and in the distribution of temperature regimes in the perifocal zones.

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The incidence of anti-rituximab antibodies in patients with lymphoproliferation

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Introduction.

Monoclonal antibodies have become mandatory for neoplastic targeted therapies as well as chronic inflammatory and autoimmune diseases. Rituximab is a chimeric monoclonal antibody directed against CD20 antigen that is expressed on normal and malignant human B cells [1,2]. It was the first monoclonal antibody to be approved for therapeutic use [2]. Treatment with rituximab at standard weekly dosing is effective in more than 50% of patients with relapsed or refractory CD20-positive follicular non-Hodgkin's lymphoma, but is not curative. It is less effective in other subtypes of CD20-positive lymphoma and for retreatment, even with CD20 still expressed [3]. Thus, binding of rituximab to CD20 is not sufficient to kill many lymphoma cells, indicating that there are mechanisms of resistance.

Many observations show that antibodies to rituximab are generated in some patients during rituximab treatment and may be associated with a less favourable response to treatment. [4-7]. However, antibodies that bind a drug are sometimes found in pre-treatment serum samples, with the amount depending on drug, assay, and patient population. The accurate prediction and assessment of (clinically relevant) immunogenicity remains a challenging endeavor [4].

Purpose of the study - to determine the incidence of anti-rituximab antibodies (ARA) in patients with non-Hodgkin's lymphoma (nHL) treated by rituximab.

Materials and methods.

The study involved 32 patients with nHL (11 newly diagnosed, 21 - resistant / recurrent form), aged from 36 to 70 years (average age 49,5 years), of which 18 women and 14 men and 13 practically healthy individuals, matched by age and sex.