Ultrasonic modes to improve the optical clearing of the skin *ex vivo*

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Motivation
Tissue optical clearing

Action of biocompatible osmotic **immersion agent (optical clearing agent)**

→ Refractive indices matching

→ Dehydration

Intact tissue sample

Measurement of optical signal from **the tissue**

Tissue sample after optical clearing

Estimation of diffusion coefficient
diffusion time of agent in tissue
permeability coefficient of tissue for agent
optical clearing efficiency

The goal

The goal of the study is to test ultrasonic modes and to found the most effective for enhancing of skin optical clearing

MATERIALS AND METHODS

Tissue Samples

Ex vivo skin

Optical clearing Agent (OCA)

Aqueous-alcohol-fructose (20%-30%-50%) solution (n=1.4024 at 930 nm)

Experiment Protocol

OCA application → US impact → OCT measurement

MATERIALS AND METHODS

Ultrasound Impact

125 US system
(Dynatronics, USA)

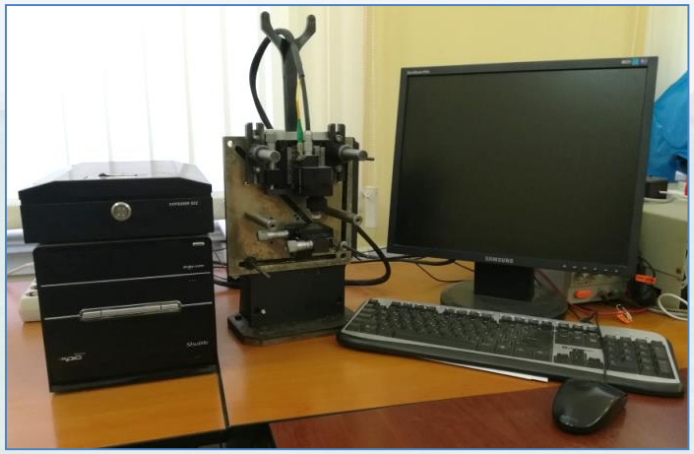
Application of US to the skin sample

Parameters of the continuous modes:

Mode	Frequency, MHz	Power, W	Duration, min
1	1	0.5	1
2	1	1.5	1.5
3	3	1.5	3

MATERIALS AND METHODS

OCT measurements



The Spectral Radar OCT System OCP930SR 022 (Thorlabs Inc., United States) with a wavelength of 930 nm

- B-scan of the intact skin region was recorded by OCT
- The fructose solution was applied topically to the target skin area
- The US was applied to the target area
- Skin OCT scans were recorded every 5-10 min during the exposure of the skin area to the agent. The solution was removed each time before scanning and applied again after scanning
- Scans were used to quantify the change in the optical properties of the skin

MATERIALS AND METHODS

Data Processing

OCT signal was used to calculate kinetics of light attenuation coefficient in the skin from equation:

$$I(z,t) = A_D \cdot \exp[-(\mu_t(t) \cdot z)] + y_0$$

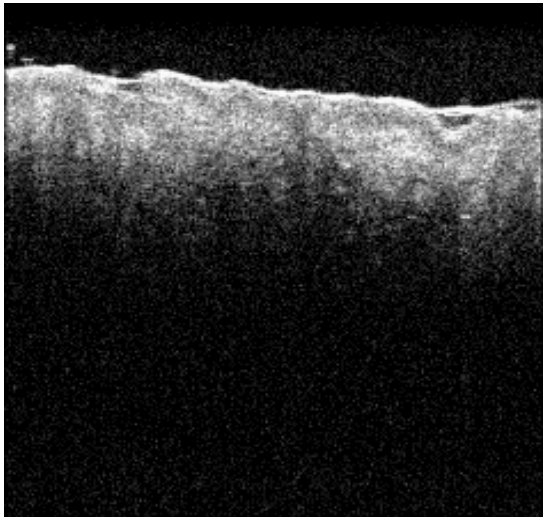
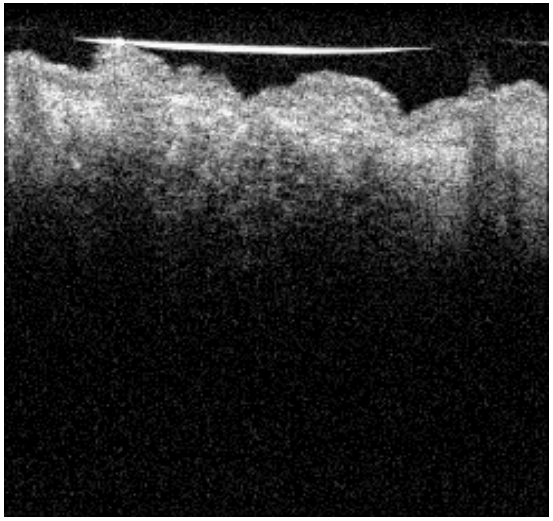
The characteristic time τ and degree of the optical clearing A of skin *in vivo* under action of fructose solution were obtained from the approximation:

$$\mu_{norm}(t) = \frac{\mu(t)}{\mu(t=0)} = A \cdot \exp\left(-\frac{t}{\tau}\right) + y_0 ,$$

where $\mu(t = 0)$ and $\mu(t)$ are the attenuation coefficients measured at $t = 0$ and t, respectively; y_0 is the residual value of that can be achieved.

RESULTS

Typical OCT scans of skin before and after 20 min of agent action start

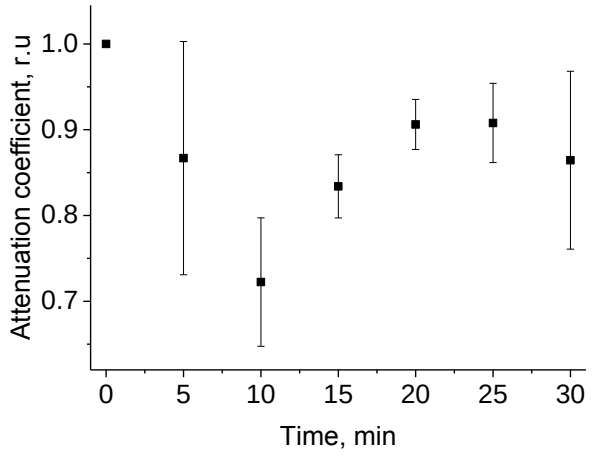
	
Before OC	After 20 min of agent action start

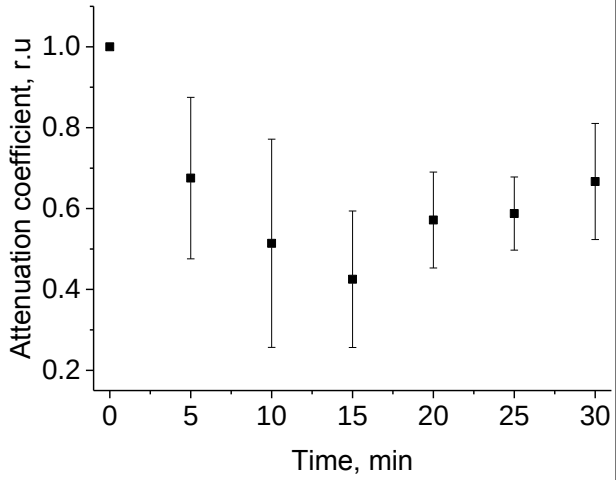
RESULTS

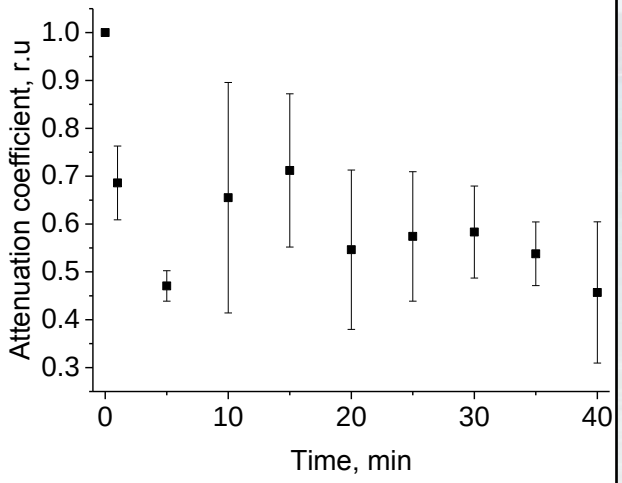
Mode

1	2	3

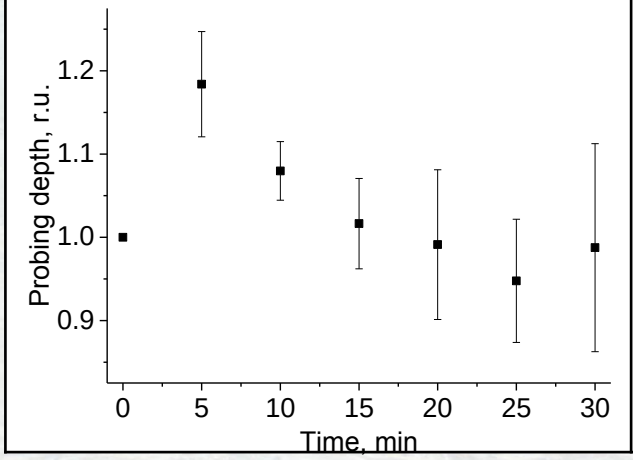
Time-dependences of light attenuation coefficient in the skin

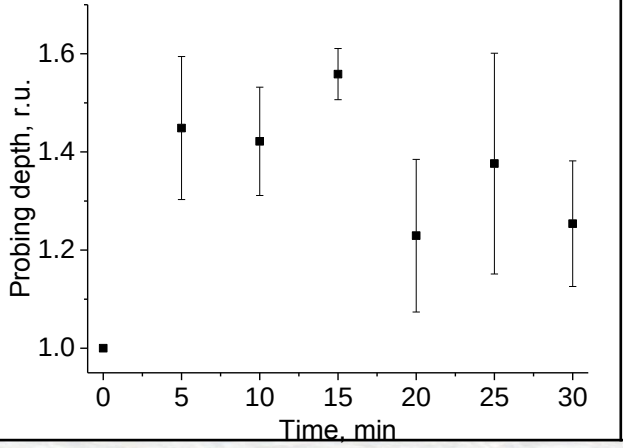


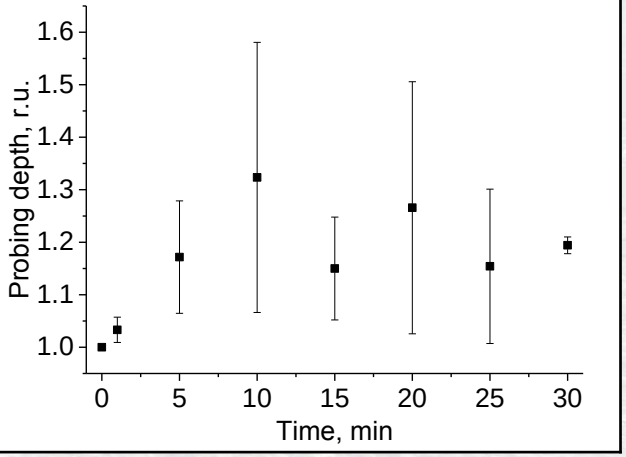




Time-dependences of light penetration depth into the skin







RESULTS

The values of the maximum degree A and characteristic time τ of the optical clearing, the effectiveness OC_{eff} of skin optical clearing, diffusion coefficient D of agent in skin, skin permeability coefficient P for the agent

Mode	**1**	**2**	**3**
A	0.15±0.08	0.45±0.10	0.45±0.05
τ, min	2±1	3±2	2±1
OC_{eff}, %	28±5	47±9	55±2
***D*, cm^2/sec**	1.27×10^{-6}	5.59×10^{-6}	1.06×10^{-5}
***P*, cm/sec**	1.69×10^{-5}	7.45×10^{-5}	1.41×10^{-4}

CONCLUSION

Obtained results shows:

- Decrease of the light attenuation in rat skin *ex vivo* at application of aqueous-ethanol-fructose solution and impact of ultrasound of 3 different modes
- The best efficiency and rate shows the 3rd mode from all used, which has a frequency of 3 MHz and a power of 1.5 W in continuous mode and duration of 3 minutes

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