



DOI 10.22363/2313-0245-2022-26-3-243-258

ORIGINAL RESEARCH
ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕLocal hardware hypothermia influence
on the physiological processes

Nidjat A. Guseynov ✉, Marina H. Hammouri , Alexandr A. Muraev , Sergey Y. Ivanov ,
Elena A. Lukianova , Anna S. Klimenko , Mohammad A. Noeerazlighi

Peoples' Friendship University of Russia. Moscow, Russian Federation
✉ nid.gus@mail.ru

Abstract. Relevance. Cold vasodilation is a response to a decrease in local and general temperature. Dose-controlled hypothermia is a therapeutic method for treating various pathological processes. **Materials and Methods.** In our study, we analyzed various indicators of the general condition of the human body under the influence of local controlled hypothermia. The study involved 25 healthy volunteers from the age of 21 to 34, including 14 males and 11 females. The study was carried out at a constant temperature of 25 °C, relative humidity of 30 ± 5%, and an atmospheric pressure of 765mm Hg in silence and moderate illumination. The instruments of these indicators were bio-impedancemetry, angioscanning, as well as general thermometry. We also performed local thermometry of the buccal mucosa to identify temperature correlations between local hypothermia and buccal mucosa temperature. Local controlled hypothermia of the face was carried out by applying an elastic mask to the subject's face. The mask had a system of irrigation tubes connected to the «ViTherm» device, which cooled the liquid and maintained its circulation. Due to the circulation of the cooled liquid in the mask the face was cooled. The mask covered the parotid-chewing, buccal, zygomatic, and infraorbital regions on the right and left. LCG lasted 50 minutes, and the circulating fluid temperature was 18 °C. **Results and Discussion.** The effect of local controlled hypothermia at 18—20 °C did not affect vital signs in healthy adults: active cell mass, electrical reactance, extracellular fluid, oxygen saturation, the duration of systole. pulse. general temperature. At the same time, a decrease in tissue hydration was recorded. The revealed physiological effect of local hypothermia justifies using this temperature regime to reduce postoperative edema. **Conclusion.** Due to the absence of negative effects of local controlled hypothermia on the vital signs of the human body, the development and application of this tool in clinical practice, including the dental surgeon. is relevant.

Keywords: local hypothermia, bio-impedancemetry, angioscanning, thermometry

Funding. The authors received no financial support for the research.

Author contributions. Guseynov N.A.—conducting an experiment, writing the text of an article, searching for literature, analyzing literature; Hammouri M.H.—conducting an experiment; analysis and search of literature; Muraev A.A.—correcting the structure and content of the review text, writing conclusions; Ivanov S.Y.—correction of the structure and content of the

© Guseynov N.A., Hammouri M.H., Muraev A.A., Ivanov S.Y., Lukianova E.A., Klimenko A.S., Noeerazlighi M.A., 2022



This work is licensed under a Creative Commons Attribution 4.0 International License

<https://creativecommons.org/licenses/by-nc/4.0/legalcode>

review text, writing conclusions; Lukianova E.A.—statistical analysis, writing the text of the article; Klimenko A.S.—correction of the structure and content of the review text, writing conclusions; Noeeralzligi M.—Translation and correction of the structure and content of the text. All authors have made significant contributions to the manuscript writing, read and approved final version before publication.

Conflict of interest statement. The authors declare no conflict of interest.

Ethics approval. The experimental clinical study was approved by the local ethics committee of the RUDN University, protocol No. 5 of the meeting of the Ethics Committee of the RUDN Medical Institute, dated February 17, 2022.

Acknowledgements—not applicable.

Consent for publication. All patients provided voluntary informed consent to participate in the study in accordance with the Declaration of Helsinki of the World Medical Association (WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Humans, 2013) and consent to the processing of personal data.

Received 11.08.2022. Accepted 07.09.2022.

For citation: Guseynov NA, Hammouri MH, Muraev AA, Ivanov SY, Lukianova EA, Klimenko AS, Noeeralzligi MA. Local hardware hypothermia influence on the physiological processes. *RUDN Journal of Medicine*. 2022;26(3):243—258. doi: 10.22363/2313-0245-2022-26-3-243-258

Introduction

Cold exposure to the skin has a pronounced physiological effect. At first, there is an increase in peripheral vasomotor tone, which reduces heat loss to the environment to maintain thermal homeostasis. Further prolonged exposure on the contrary disrupts adaptive mechanisms and leads to impaired neuron conductivity, vasodilation, and cold injuries [1—3]. The origin of cold-induced vasodilation (CIVP) is still a matter of discussion [4]. CIVP can be mediated either centrally through the sympathetic nervous system [5, 6] or locally through cold-induced direct peripheral vascular paralysis [7]; authors would like to note the role of arteriovenous anastomoses [8]. The regulation of skin blood flow occurs due to a complex and dynamic interaction of thermal effects emanating from the depths of the body (core) and skin (shell). However, the intensity of vasomotor reactivity to localized thermal stimulation is primarily determined by the thermal state of the whole body [9]. Lewis first claimed that local vasodilation—later known as cold-induced vasodilation (CIVP)—was the cause of increased body temperature [10].

Despite many studies, the mechanisms that cause CIVP are not fully understood [11]. According to some studies, CIVP results from the dilation of arteriovenous

anastomoses (AVA) [12, 13]. However, due to the difficulty in measuring blood flow, the effect of local temperature on AVA vasomotor activity has been little studied. Bergersen et al. [14] found that AVAs below 21 °C maintained AVA closure. The frequency of flashes is related to the overall thermal balance of the body. In situations where there is a need to conserve heat or remove heat, the AVAs remain largely closed or open, resulting in nearly constant low or high blood flow velocities in the afferent arteries. Synchronous closure of the AVA is most likely caused by bursts of efferent sympathetic impulses [15]. The frequency of flashes is related to the overall thermal balance of the body. In situations where there is a need to conserve heat or remove heat, the AVAs remain largely closed or open, resulting in nearly constant low or high blood flow velocities in the afferent arteries.

In a thermoneutral situation the AVA spasms two or three times per minute, causing large and rapid fluctuations in blood flow velocity in the afferent arteries. All cutaneous AVAs have synchronous vasomotion. Fluctuations in blood flow through the AVA also closely correlate with heart rate (HR) and blood pressure variations [16]. Local uncontrolled hypothermia (glove application with ice) is widely used after surgical,

dental interventions, maxillofacial and plastic surgeries. Due to the trigeminal nerve's connection to the vagus autonomic fibers the face is a potent reflexogenic zone [17]. Thus, local uncontrolled cold exposure to facial tissues and close neural connections can lead to local frostbite [18] and have an overall negative effect. The present study assessed the impact of moderate local controlled hypothermia on the human cardiovascular and respiratory systems.

Materials and methods

Experiment design and patients

The study involved 25 healthy volunteers from the age of 21 to 34, including 14 males and 11 females. All subjects were non-smokers, did not have a history of cold injuries or pathologies of the cardiovascular system, and did not take any medications on an ongoing basis. None of the subjects ate food less than 2 hours before the experiment. There was no alcohol consumption in the 24 hours prior to the study. The study was carried out at a constant temperature of 25 °C, relative humidity of $30 \pm 5\%$, and an atmospheric pressure of 765 mm Hg in silence and moderate illumination.

The study was carried out in the functional diagnostics room of the Clinical Diagnostic Center of the Peoples' Friendship University of Russia (Moscow, Russia). All patients provided voluntary informed consent to participate in the study in accordance with the Declaration of Helsinki of the World Medical Association (WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects, 2013) and consent was taken to the processing of personal data. The experimental clinical study was approved by the local ethics committee of the RUDN University, protocol No. 5 of the meeting of the Ethics Committee of the RUDN Medical Institute, dated February 17, 2022.

Local hypothermia measurement

The study subject was placed in a horizontal position on a medical couch; the sensors of the Bioimpedance device were fixed on the right ankle and the back of the

hand, the portable device angioscan was put on the index finger of the left hand; a mercury thermometer was placed in the right axillary fossa; a local temperature sensor was brought into the oral cavity.

Local Controlled Hypothermia (LCH) of the face was carried out by applying an elastic mask to the subject's face (Figure 1). The mask had a system of irrigation tubes connected to the ViThermo device (Figure 1) (Digital technologies in surgery LLC, Skolkovo, Moscow), which cooled the liquid and maintained its circulation. Due to the circulation of the cooled liquid in the mask, the face was cooled. The mask covered the parotid-chewing, buccal, zygomatic and infraorbital regions on the right and left. LCG lasted 50 minutes and the circulating fluid temperature was 18 °C. We used a portable temperature sensor in the vestibule of the oral cavity to control the amount of cooling of soft tissues.



Fig. 1. Device for controlled hypothermia «ViTherm»

Bio-impedancemetry and angioscanning

Bio-impedancemetry was carried out using the apparatus «Bioimpedance» (AVS-02 «MEDASS», Russia), the principle of which is based on the

assessment of the resistance of biological tissues to direct or alternating electric current. This method is one of the tools for monitoring the dynamics of the remodeling of organs and tissues and changes in the functional state of the whole organism in normal and pathological conditions.

There are several parameters that can be registered by bio-impedancemetry, including: fat and muscle mass, bone mineral mass (kg), body mass index (BMI), active cell mass (kg), extracellular fluid (kg), BMR(kcal/m²/day); phase angle; (active and reactance at a frequency of 50 kHz, extracellular fluid).

Angioscanning was performed with the Angioscan device (Angioscan, AngloCode Electronics, Russia). The principle of operation of the device is to diagnose the arterial wall and the state of endothelial cells using the Parfenov method (Baskova, I., 2014).

Angioscan allows to register the pulse; blood saturation (O₂ saturation); The pulse pressure index (PPI); vascular stiffness (−%); curve type (%); systole duration (%); stress or heart rate variability, calculated according to the Baevsky index (a physiological phenomenon that manifests itself in a change in the interval between the beginnings of two adjacent cardiac cycles), local thermometry carries out with a temperature sensor.

Angioscannig, Bio-impedancemetry and thermometry were performed three times: before LCG

during LCG at the 25th minute of the study and then at the end of LCG at the 50th minute. During the entire study the study subjects lay relaxed and motionless.

Statistical data processing

Using the methods of descriptive (descriptive) statistics to evaluate the studied parameters we calculated the following characteristics: mean, standard deviation (SD), 95 % CI (confidence interval for the mean), median, minimum and maximum values. We used non-parametric tests for statistical analysis: to compare scores before exposure at 25- and 50-minutes paired Wilcoxon test for linked samples.

Results and discussion

Anthropometry

The study involved 25 people: 9 girls and 16 men, Height averaged 173 ± 8.38 cm (166 ± 5.47 cm in girls and 176.5 ± 7.75 cm in men), weight 71.7 ± 15.63 kg (60.7 ± 12.78 kg for girls and 77.9 ± 13.78 kg for men). The average waist circumference is 81.9 ± 10.96 cm (73.2 ± 9.83 and 86.8 ± 8.39 for girls and men respectively) and the hip circumference is 102.6 ± 7.06 cm (100 ± 5.79 cm for girls and 104.1 ± 7.45 cm for men). Table 1 provides a complete description of the characteristics.

Table 1

Characteristics of study participants

	N	Mean	SD	CI (-95 %)	CI (+95 %)	Median	Min	Max
Height (cm)	25	173	8.38	169.54	176.46	170	162	190
m.	16	176.5	7.75	172.37	180.63	177	165	190
w.	9	166.8	5.47	162.57	170.98	165	162	180
Weight (kg)	25	71.7	15.63	65.23	78.13	72	50	104
m.	16	77.9	13.78	70.53	85.22	78	53	104
w.	9	60.7	12.78	50.85	70.49	56	50	85
Waist Circumference	25	81.9	10.96	77.35	86.41	85	63	106
m.	16	86.8	8.39	82.28	91.22	87	73	106
w.	9	73.2	9.83	65.66	80.78	70	63	91
Hip circumference	25	102.6	7.06	99.69	105.51	100	86	118
m.	16	104.1	7.45	100.09	108.03	106	86	118
w.	9	100.0	5.79	95.55	104.45	98	95	112

Bio-impedancemetry

Active cell mass changed insignificantly from 30.5 ± 7.5 to 30.6 ± 7.34 ($p=0.35$) and up to 31 ± 7.21 kg ($p=0.15$). There was a decrease in the indicator «Extracellular fluid» by an average of 0.23 kg after 25 minutes and 0.3 kg after 50 minutes ($p=0.0003$ and $p=0.0002$).

The BMR index changed insignificantly from 861 ± 72.48 (kcal/m²/day) to 863.5 ± 70.03

(kcal/m²/day) ($p=0.38$) and to 863.7 ± 69.44 (kcal/m²/day) ($p=0.4$) after 25 min and respectively at the end of the study.

Table 2 describes bio-impedancemetry in detail. Table 3 presents the results of comparing scores at 25 and 50 minutes using the non-parametric Wilcoxon test for linked samples.

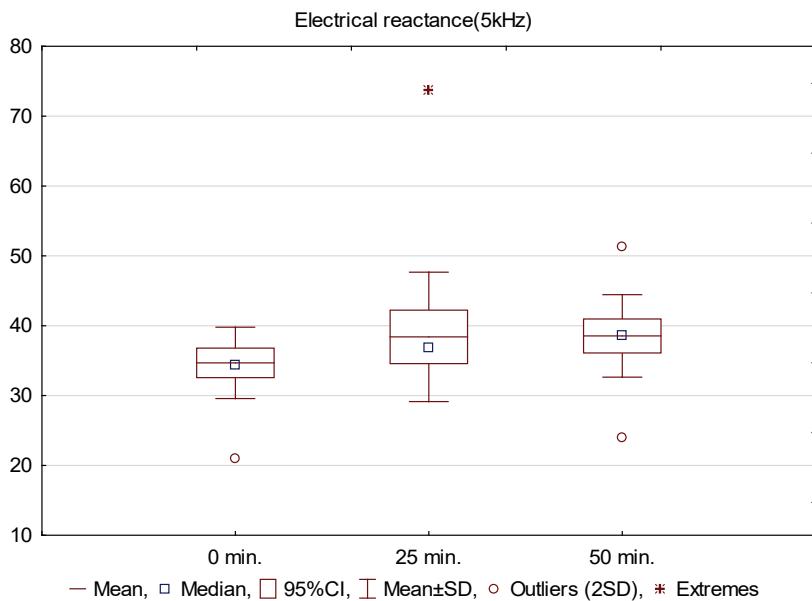
Table 2

Results of bio-impedancemetry

	Mean	SD	CI (-95 %)	CI (+95 %)	Median	Min	Max
Active cell mass (kg)	30.5	7.50	27.38	33.57	32.3	18.8	45.8
25 min	30.6	7.34	27.58	33.65	32.3	18.8	45.3
50 min	31.0	7.21	28.05	34.00	33.2	18.9	45.3
Extracellular fluid (kg)	15.8	2.88	14.57	16.95	15.4	11.6	21.3
25 min	15.5	2.72	14.41	16.65	15.2	11.5	20.9
50 min	15.5	2.77	14.32	16.60	15.2	11.4	20.8
BMR(kcal/m ² /day)	861.0	72.48	831.05	890.89	852.8	698.6	1004.2
25 min	863.5	70.03	834.63	892.44	862.4	699.7	1001.9
50 min	863.7	69.44	835.04	892.36	862.1	703.8	1002.7
Phase angle	6.8	0.81	6.50	7.17	7.0	4.8	8.2
25 min	7.0	0.80	6.66	7.32	7.0	4.9	8.4
50 min	7.1	0.82	6.72	7.39	7.2	4.9	8.5
Active resistance (50khz)	323.5	63.21	297.41	349.59	314.3	227.1	458.9
25 min	332.7	61.75	307.21	358.19	324.1	233.7	469.8
50 min	335.0	62.24	309.31	360.69	324.6	236.3	475.6
Active resistance (5khz)	651.7	97.07	611.66	691.80	640.1	484.8	875.7
25 min	669.6	98.19	629.02	710.08	666.9	497.2	897.2
50 min	677.2	99.34	636.24	718.25	674.6	504.3	911.3
Electrical reactance (50kHz)	38.6	5.44	36.39	40.88	37.8	29.5	50.1
25 min.	40.3	5.63	37.95	42.60	40.4	30.4	52.2
50min.	41.0	5.79	38.56	43.34	41.3	30.7	52.9
Electrical reactance (5kHz)	34.7	5.11	32.57	36.79	34.4	20.9	43.4
25 min	38.4	9.26	34.58	42.23	36.8	22.1	73.7
50 min	38.5	5.90	36.10	40.97	38.5	24.0	51.3

Table 3**Results of the paired Wilcoxon test for linked samples (bio-impedancemetry)**

Compared samples	n	Average Difference (before and after)	SD difference	CI (-95 %)	CI (+95 %)	p
Active cell mass (kg)						
00 min & 25 min.	19	-0.14	0.62	-0.40	0.12	0.35
00 min Vs 50 min.	21	-0.55	2.05	-1.40	0.30	0.15
25 min Vs 50 min.	17	-0.41	2.03	-1.25	0.43	0.37
Extracellular fluid (kg)						
00 min Vs 25 min.	24	0.23	0.28	0.12	0.35	0.0003
00 min Vs 50 min.	25	0.30	0.25	0.19	0.41	0.0002
25 min Vs 50 min.	17	0.07	0.16	0.00	0.13	0.0148
BMR(kcal/m ² /day)						
00 min Vs 25 min.	24	-2.57	11.61	-7.36	2.22	0.38
00 min Vs 50 min.	25	-2.73	10.88	-7.22	1.76	0.40
25 min Vs 50 min.	23	-0.16	3.50	-1.61	1.28	0.78
phase angle						
00 min Vs 25 min.	20	-0.16	0.17	-0.23	-0.09	0.0003
00 min Vs 50 min.	24	-0.22	0.14	-0.28	-0.17	0.0000
25 min Vs 50 min.	18	-0.07	0.08	-0.10	-0.03	0.0074
active resistance (50kHz)						
00 min Vs 25 min.	25	-9.20	9.90	-13.28	-5.11	0.0000
00 min Vs 50 min.	25	-11.50	10.55	-15.85	-7.14	0.0000
25 min Vs 50 min.	25	-2.30	3.12	-3.59	-1.01	0.0025
active resistance (5kHz)						
00 min Vs 25 min.	25	-17.82	7.90	-21.08	-14.56	0.0000
00 min Vs 50 min.	25	-25.51	10.18	-29.71	-21.31	0.0000
25 min Vs 50 min.	25	-7.69	8.41	-11.16	-4.22	0.0002
Electrical reactance (50 kHz)						
00 min Vs 25 min.	24	-1.64	1.05	-2.08	-1.21	0.0000
00 min Vs 50 min.	25	-2.32	1.09	-2.77	-1.87	0.0000
25 min Vs 50 min.	24	-0.68	0.69	-0.96	-0.39	0.0003
Electrical reactance (5 kHz)						
00 min Vs 25 min.	25	-3.72	7.00	-6.61	-0.83	0.0004
00 min Vs 50 min.	25	-3.86	3.02	-5.10	-2.61	0.0001
25 min Vs 50 min.	24	-0.13	6.01	-2.61	2.35	0.0010

**Fig. 2.** Reactance readings (5 kHz)

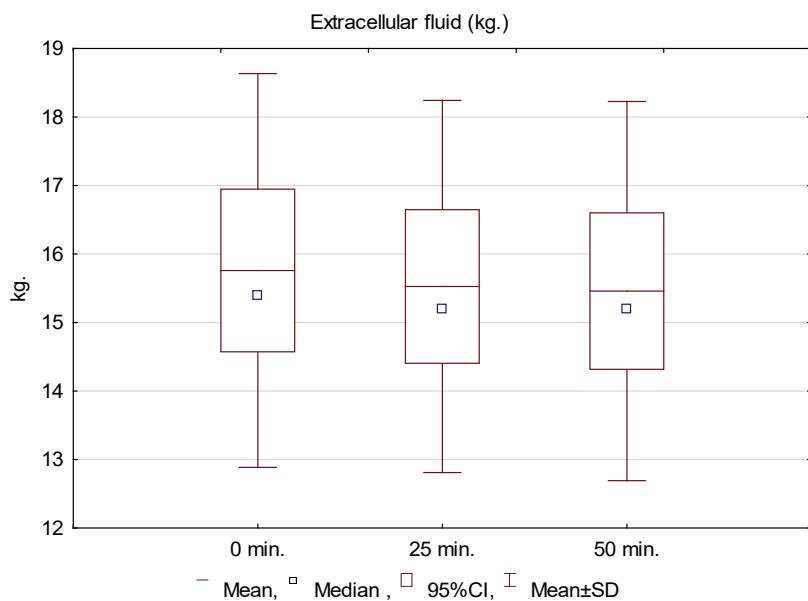


Fig. 3. Mass of extracellular fluid (kg)

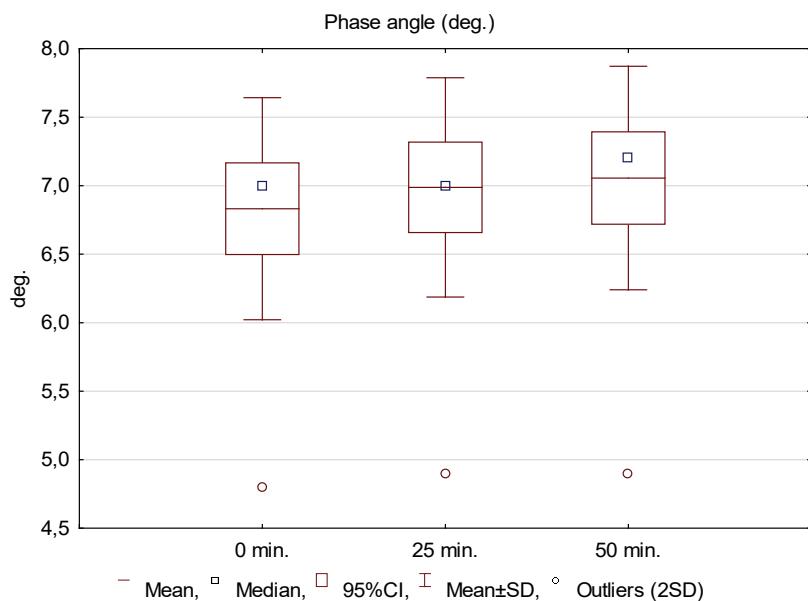


Fig. 4. Phase angle indicators

Angioscanning

The response of the cardiovascular system to LCH of the face was as follows: before the onset of cooling of the face the heart rate averaged 70 ± 14.13 beats/min. During the LCG of the person at 25 minutes the heart

rate decreased and averaged up to 65.5 ± 8.2 bpm; differences compared to the background averaged 4.48 bpm ($p < 0.009$). At the end of the exposure at the 50th minute the heart rate averaged 66.5 ± 9.45 bpm.

Oxygen saturation averaged 0.97 ± 0.02 ($97\% \pm 2\%$) ($p = 0.144$).

INP during the procedure decreased from 0.025 ± 0.02 to 0.015 ± 0.01 after 50 minutes ($p = 0.015$). Hardness before cooling was on average -0.150 ± 0.15 , after 25 minutes it became -0.206 ± 0.12 ($p = 0.004$) and after 50 minutes it was -0.200 ± 0.1 ($p = 0.029$).

At 25 minutes after the experiment's start the systole duration decreased from 32.3 ± 3.89 to 31.6 ± 3.78 ($p = 0.135$), then remained at the achieved level and slightly changed.

Table 4

Results of angioscanning

Compared samples	N	Average	SD	CI (-95 %)	CI (+95 %)	Mediana	Min	Max
Pulse (bpm)	25	70.0	14.13	64.13	75.79	69	47	120
25 min.	25	65.5	8.20	62.10	68.86	66	45	80
50 min.	25	66.5	9.45	62.58	70.38	64	46	85
O2 (%)	25	0.9709	0.0179	0.9635	0.9783	0.976	0.918	0.998
25 min.	25	0.9711	0.0156	0.9647	0.9775	0.971	0.933	0.999
50 min.	25	0.973	0.0160	0.9667	0.9799	0.979	0.933	0.999
(PPI) (%)	25	0.025	0.0203	0.0165	0.0332	0.020	0.004	0.080
25 min.	25	0.019	0.0172	0.0118	0.0259	0.012	0.002	0.066
50 min.	25	0.015	0.0133	0.0093	0.0203	0.010	0.002	0.052
Age(year)	25	35.0	8.6192	31.4022	38.52	35	20	55
25 min.	25	29.6	8.1142	26.2106	32.91	32	18	45
50 min.	25	28.9	6.9601	26.0070	31.7530	27	18	41
Stiffness(%)	25	-0.150	0.1515	-0.2124	-0.0873	-0.202	-0.384	0.251
25 min.	25	-0.206	0.1234	-0.2574	-0.1555	-0.244	-0.372	0.053
50 min.	25	-0.200	0.0995	-0.2409	-0.1588	-0.226	-0.355	0.022
duration. systoles (%)	25	32.3	3.89	30.67	33.89	34	23	38
25 min.	25	31.6	3.78	30.00	33.12	32	24	36
50 min.	25	31.6	4.09	29.95	33.33	32	23	37

Table 5

Results of the paired Wilcoxon test for related samples (Angioscannig)

Compared samples	n	Average difference (before and after)	SD difference	CI (-95 %)	CI (+95 %)	p
Pulse(bpm)						
00 min. Vs 25 min	23	4.480	10.532	0.133	8.827	0.009
00 min. Vs 50 min	21	3.480	11.875	-1.422	8.382	0.102
25 min. Vs 50 min.	20	-1.000	4.252	-2.755	0.755	0.391
O2(%)						
00 min. Vs 25 min	21	-0.011	0.053	-0.033	0.011	0.728
00 min. Vs 50 min.	21	-0.013	0.054	-0.035	0.009	0.144
25 min. Vs 50 min.	20	-0.002	0.007	-0.005	0.001	0.065
(PPI) (%)						
00 min. Vs 25 min.	25	0.006	0.014	0.000	0.012	0.041
00 min. Vs 50 min.	23	0.010	0.017	0.003	0.017	0.015
25 min. Vs 50 min.	24	0.004	0.008	0.001	0.007	0.015
Age(year)						
00 min. Vs 25 min.	23	5.400	8.196	2.017	8.783	0.001
00 min. Vs 50 min.	25	6.080	8.655	2.507	9.653	0.000
25 min. Vs 50 min.	22	0.680	4.327	-1.106	2.466	0.485
Stiffness (-%)						
00 min. Vs 25 min.	25	0.057	0.136	0.000	0.113	0.004
00 min. Vs 50 min.	24	0.050	0.115	0.002	0.097	0.029
25 min. Vs 50 min.	24	-0.007	0.072	-0.036	0.023	0.054
Duration. systoles (%)						
00 min. Vs 25 min.	20	0.720	4.287	-1.050	2.490	0.135
00 min. Vs 50 min.	21	0.640	4.281	-1.127	2.407	0.434
25 min. Vs 50 min.	17	-0.080	2.914	-1.283	1.123	0.758

End of the table 5

Compared samples	n	Average difference (before and after)	SD difference	CI (-95 %)	CI (+95 %)	p
Stress						
00 min Vs 25 min.	25	3.720	35.511	-10.938	18.378	0.819
00 min Vs 50 min.	23	15.320	44.782	-3.165	33.805	0.121
25 min Vs 50 min.	24	11.600	34.693	-2.720	25.920	0.054

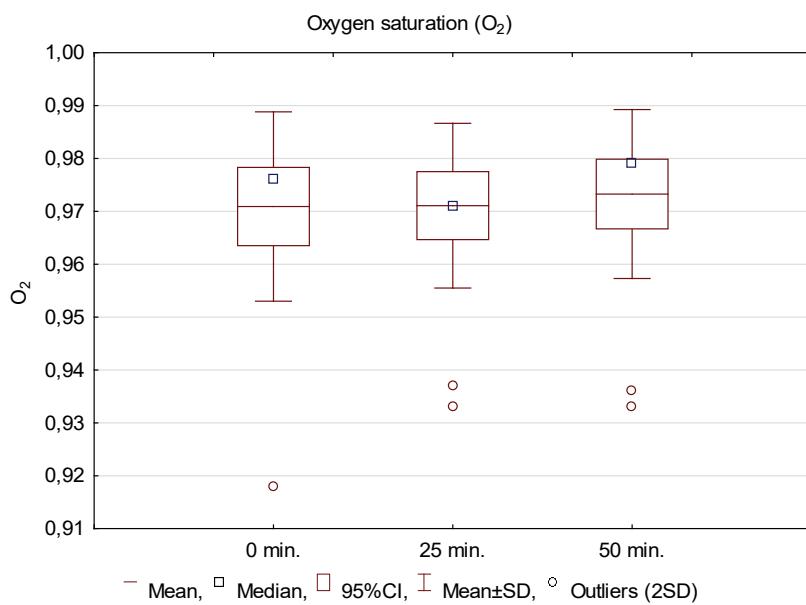


Fig. 5. Oxygen saturation Indicators

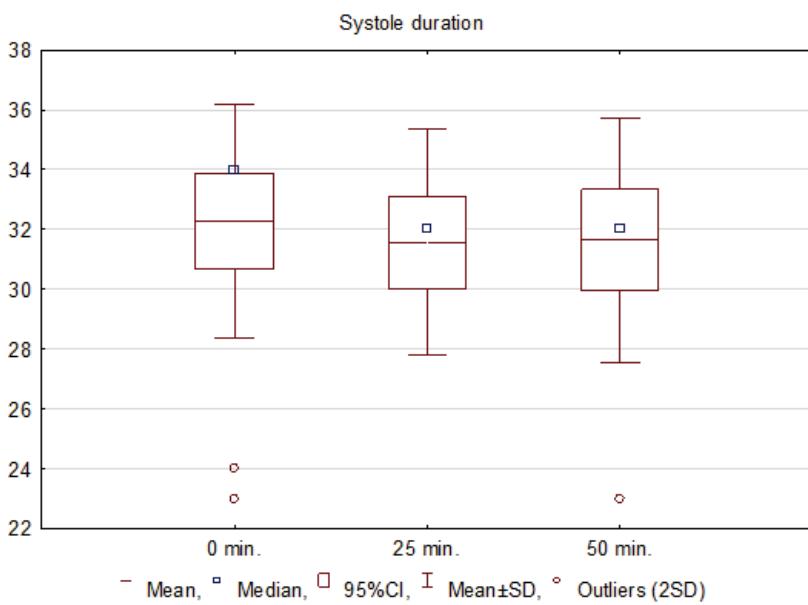


Fig. 6. The duration of systole

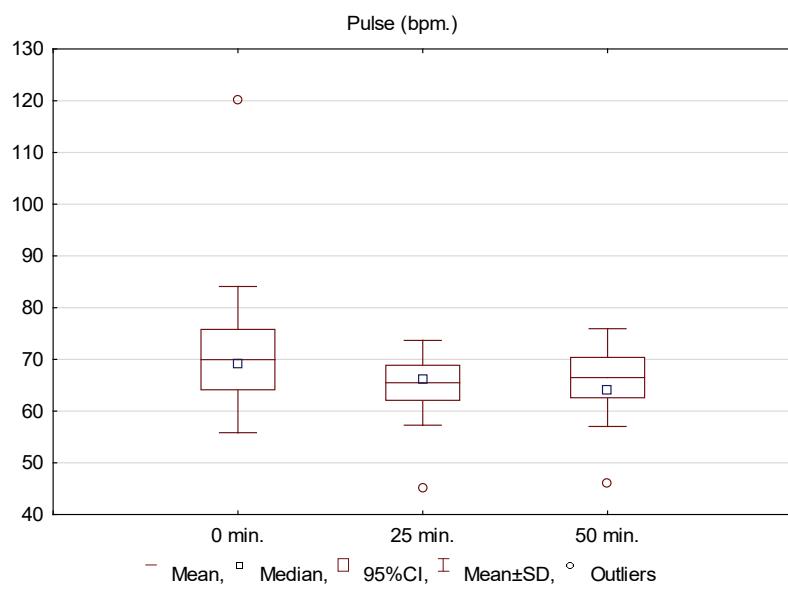


Fig. 7. The pulse rate

Thermometry

In the study group the minimum general temperature at the beginning of the study was $T^o=35.2^\circ$ at 25 minutes $T^{25}=35.3^\circ$ and at 50 minutes 34.9° in the beginning of the study. The maximum general temperature was $T^o=36.8^\circ$ and at 50 minutes $T^{25}=37.0^\circ$ at 50 minutes $T^{50}=36.8^\circ$. The average general initial temperature of the subjects fluctuated within the limits of $T^o=36.2^\circ$ after 25 minutes $T^{25}=36.3^\circ$; at 50 minutes $T^{50}\text{general}=36.2^\circ$. There is a fluctuation in the value of the average total temperature in the amount of $\pm 0.1^\circ$ for 50 minutes (Table 1).

In the study group the minimum local temperature at the beginning of the study was $T^o=35.2^\circ$ at 25 minutes

$T^{25}=35.3^\circ$ at 50 minutes 34.9° . The maximum general temperature at the beginning of the study was $T^o=36.8^\circ$ after 25 minutes $T^{25}=37.0^\circ$ and at 50 minutes $T^{50}=36.8^\circ$. The average general initial temperature of the subjects fluctuated within the limits of $T^o=36.2^\circ$. At the 25th minute $T^{25}=36.3^\circ$; at 50 minutes $T^{50}\text{local}=36.2^\circ$. There is a decrease in the average temperature of the subjects by 0.4° for 50 minutes.

The average local initial temperature of the buccal mucosa in the subjects fluctuated within $T^o=35.3^\circ$ at 25 minutes $T^{25}=35.0^\circ$; at 50 minutes $T^{50}=34.9^\circ$. Over 50 minutes the average temperature decreased by 0.4° .

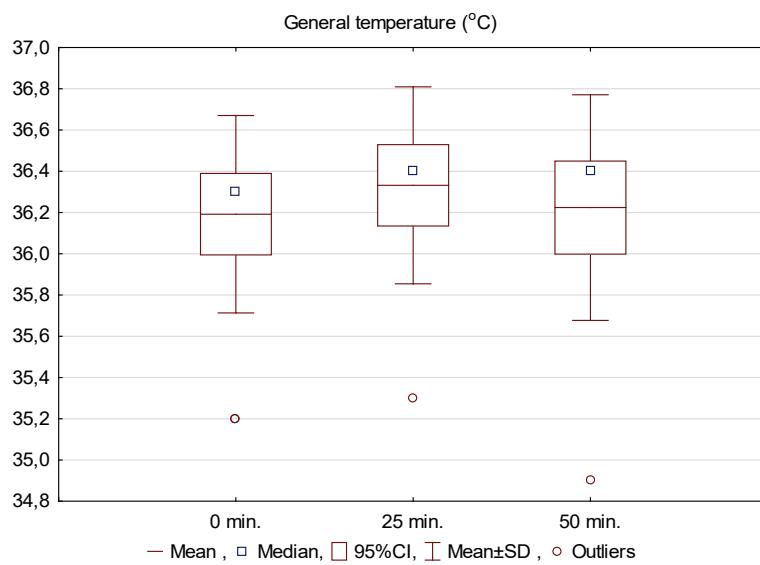
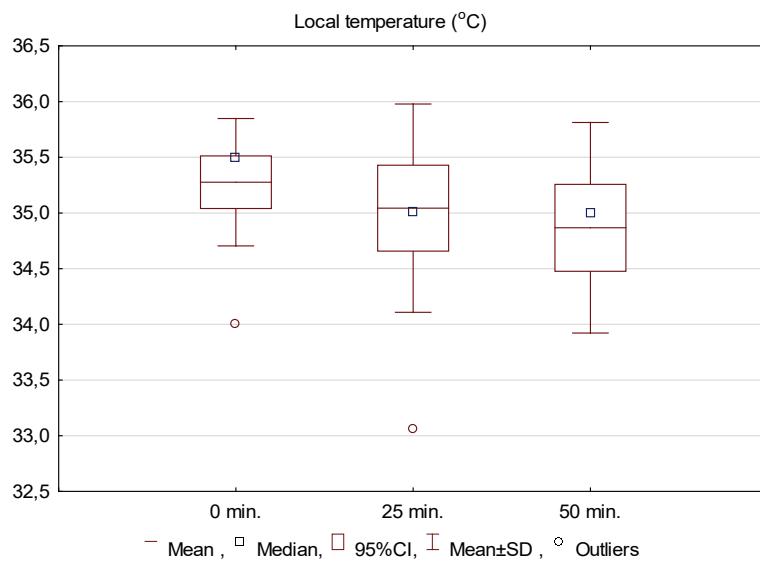
Table 6

Results of thermometry

	N	Mean	SD	CI (-95 %)	CI (+95 %)	Median	Min	Max
T g	25	36.2	0.48	35.99	36.39	36.3	35.2	36.8
25 min.	25	36.3	0.48	36.13	36.53	36.4	35.3	37.0
50min.	25	36.2	0.55	36.00	36.45	36.4	34.9	36.8
T. лок.	25	35.3	0.57	35.04	35.51	35.5	34.0	36.0
25 min.	25	35.0	0.94	34.66	35.43	35.0	33.1	36.5
50min.	25	34.9	0.95	34.48	35.26	35.0	32.9	36.4

Table 7**Results of the paired Wilcoxon test for related samples (Thermometry)**

	n	mean difference	SD	CI -95 %	CI +95 %	p
General temperature						
00 min Vs 25 min.	21	-0.14	0.29	-0.26	-0.02	0.03
00 min Vs 50 min.	17	-0.03	0.32	-0.16	0.10	0.33
25 min Vs 50 min.	18	0.11	0.22	0.02	0.20	0.07
Local temperature						
00 min Vs 25 min.	24	0.23	0.75	-0.08	0.54	0.28
00 min Vs 50 min.	25	0.41	0.82	0.07	0.75	0.06
25 min Vs 50 min.	24	0.18	0.51	-0.03	0.39	0.09

**Fig. 8.** General temperature**Fig. 9.** Local temperature

Discussion

Close neuronal connections between the trigeminal nerve and the vagus, which regulates the vital activity of internal organs, determine the presence of trigeminovagal reflexes (oculo-cardiac, corneal, jaw, lacrimal reflexes). The spinal trigeminal nucleus of the trigeminal nerve receives and processes impulses from temperature receptors. Nevertheless, in the available literature we did not find data for the presence of pathological reflexes associated with temperature exposure to the face.

Excessive cooling of local tissues can lead to decompensation of the inflammatory response after complex extractions of third molars. The critical temperature for changing nerve impulse speed is 27 °C [19]. A decrease in tissue temperature suppresses the metabolic rate of the damaged tissue and enzymatic processes [20].

Zachariassen [21] reported that a 10 °C decrease resulted in a 50 % reduction in enzymatic metabolism. In this study we used a mode with a target temperature of 18 °C, which is more optimal for reducing postoperative edema in the maxillofacial region. The time at which local hardware hypothermia was applied was 50 minutes. In vivo Deal et al. [22] noted in rats that ice application for 20 minutes after surgery reduced vascular permeability and edema.

The edema of post-injury rats was reduced by 30 minutes of immersion in cold water (12.8 to 15.6 °C) [19, 22]. However, for use in the subjects it was decided to perform hypothermia for 50 minutes, which is reasonable.

Several studies have evaluated the effect of cryotherapy on mucosal ridge temperature. Possoff found that cheek thickness varied between 10 and 19 mm among patients, with an average thickness of 15 mm. He noted that after applying ice to the cheek, the temperature of the mucosa was inversely proportional to the thickness of the cheek. When applying an ice bag wrapped in a towel and applied to the cheek for 30 minutes, the temperature of the mucous membrane of the alveolar ridge decreased on average by only 1 °C [23], which is consistent with the results of our preclinical studies, Intraorally. Fouke et al. demonstrated that cold buccal stimulation (a cold cylinder filled with liquid for 12 minutes) decreased oral mucosal temperature by

2.34 °C [24]. According to other researchers, applying cold water or ice [26] has virtually no effect on the mucosal temperature of the alveolar ridge mucosa.

It was of primary interest to obtain data on tissue resistance. An increase in active (at a frequency of 50 kHz) and reactive (at a frequency of 50 kHz) resistance was revealed, which indicates a decrease in the degree of tissue hydration and can be interpreted as an anti-edematous effect of local hypothermia. Reactance is the property of storing variable electrical energy in the form of an electric field. This Reactance is due to the dynamic characteristics of cell membranes, which act as an electrical capacitor [27]. Cell membrane capacity can be used to indicate lean and intracellular body mass associated with extra- and intracellular water balance [28]. This parameter of bio-impedancemetry allows practitioners to consider the volume and reactive density of body tissues to assess the amount of fluid.

Clinically, the most indicative and general parameter of bio-impedancemetry is the phase angle required for diagnosis and clinical prognosis associated with changes in the integrity of cell membranes and changes in fluid balance in the human body [29]. The phase angle expresses changes in the permeability of the cell membrane and the degree of tissue moisture. Therefore, the phase angle depends on the one hand on the capacitive behavior of dependent tissues associated with the cell pool cell size and cell membrane integrity, and on the other hand on its resistance to tissue hydration. Many clinical trials are currently underway, in which the phase angle is proposed as a useful prognostic marker [30, 31, 32]. In this experimental work the phase angle was within the reference values at all time points (0.25–50 minutes), which indicates the absence of negative effects of LCH.

Active cell mass is a measure of body cell mass. This indicator contains information about the mass of metabolically active tissues in the body. Decreased values of the active cell mass may indicate a lack of protein nutrition, as well as low metabolic activity. Active cell mass changed insignificantly from 30.5 ± 7.5 to 30.6 ± 7.34 ($p=0.35$) and up to 31 ± 7.21 kg ($p=0.15$), which indicates the absence of acute pathological factors from the side of LCH at all time intervals.

Edema is the result of an imbalance in the filtration system between the capillary and interstitial spaces. The kidneys play a crucial role in regulating extracellular fluid volume by regulating sodium and water excretion. The main causes of edema are venous obstruction increased capillary permeability and increased plasma volume caused by sodium and water retention [33]. Our results showed a decrease in the extracellular fluid index by an average of 0.23 kg after 25 minutes and 0.3 kg after 50 minutes ($p=0.0003$ and $p=0.0002$). This fact dictates the positive effect of LCH within 50 minutes. In our opinion a gradual decrease in the extracellular fluid index indicates a positive vasoconstrictor, as well as a drainage effect of LCH due to the thermal control of local tissues.

The definition of hypothermia is a drop in body temperature below 35 °C. Cardiac surgeons distinguish four stages of hypothermia: mild, moderate, deep and profound. The organ protection afforded by deep hypothermia ensures safe circulatory arrest as a precondition for cardiac surgery [34].

The brain consumes about 20 % of all oxygen in the body [35]. With a gradual decrease in body temperature, chemical reactions, oxygen consumption and energy requirements decrease. The main protective effect of LCH during circulatory arrest at the cellular level is to reduce the concentration of hydrogen ions. Physical temperature decrease, water dissociation and consequently lower concentration of hydrogen ions significantly slow down biochemical processes, which leads to cell death [36].

This is consistent with studies demonstrating that intracellular acidosis occurs first in the brain, then in the heart and finally in other organs [37]. Mezrow in his study, found that a 10 °C decrease in body temperature reduced brain metabolic activity by a factor of 4 and thus increased ischemia tolerance [38]. For only 5 minutes after which irreversible changes occur in the brain. Our study wants to note a gradual decrease in heart rate to safe values. Initially the average pulse rate for the subjects was 70 ± 14.13 beats/min. After applying LCG at 25 minutes it decreased to the mark and averaged 65.5 ± 8.2 bpm; differences compared to the background averaged 4.48 bpm ($p<0.009$). At the

end of the exposure at the 50th minute the heart rate averaged 66.5 ± 9.45 bpm. A decrease in heart rate is associated with a slowdown in metabolic processes in the body due to various factors: the recumbent position of the subjects, which led to a drowsy state, the use of LCH, and a decrease in cellular metabolism due to controlled angiosperm.

At the same time the INP index decreased from 0.025 ± 0.02 to 0.015 ± 0.01 after 50 minutes ($p=0.015$). Oxygen saturation averaged 0.97 ± 0.02 (97 % ± 2 %) ($p=0.144$). Peripheral vascular stiffness before cooling was on average -0.150 ± 0.15 after 25 minutes it became -0.206 ± 0.12 ($p = 0.004$) and after 50 minutes it was -0.200 ± 0.1 ($p = 0.029$). An increase in vascular stiffness is associated with an increase in the tone of the muscle layer, resulting in a decrease in temperature. The duration of systole 25 minutes after the start (decreased) decreased from 32.3 ± 3.89 to 31.6 ± 3.78 ($p=0.135$), then remained at the achieved level changed slightly. The human brain is subject to self-regulatory mechanisms that link cerebral blood flow to brain oxygen consumption and metabolic activity. As a result, this allows stopping blood circulation safely with normothermia for only 5 minutes, after which irreversible changes occur in the brain tissues.

Conclusion

Our study demonstrated that exposure to local controlled hypothermia of 18—20 °C did not change the principal vital signs in healthy people, while a decrease in tissue hydration was recorded. The revealed physiological effect of local hypothermia justifies using this temperature regime to reduce postoperative edema.

References / Библиографический список

1. Keramidas ME, Kölegård R, Mekjavić IB, Eiken O. Interactions of mild hypothermia and hypoxia on finger vasoreactivity to local cold stress. *Am J Physiol Regul Integr Comp Physiol.* 2019;317(3):R418-R431. doi:10.1152/ajpregu.00103.2019
2. Kounalakis SN, Keramidas ME, Amon M, Eiken O, Mekjavić IB. A 10-day confinement to normobaric hypoxia impairs toe, but not finger temperature response during local cold stress. *J Therm Biol.* 2017;64:109—115. doi:10.1016/j.jtherbio.2017.01.009

3. Keramidas ME, Kølegård R, Eiken O. In Shackleton's trails: Central and local thermoadaptive modifications to cold and hypoxia after a man-hauling expedition on the Antarctic Plateau. *J Therm Biol.* 2018;73:80—90. doi:10.1016/j.jtherbio.2018.02.010
4. Cheung SS, Daanen HA. Dynamic adaptation of the peripheral circulation to cold exposure. *Microcirculation.* 2012;19(1):65—77. doi:10.1111/j.1549—8719.2011.00126.x
5. Flouris AD, Cheung SS. Influence of thermal balance on cold-induced vasodilation. *J Appl Physiol (1985).* 2009;106(4):1264—1271. doi:10.1152/japplphysiol.91426.2008
6. Hodges GJ, Mallette MM, Cheung SS. Cutaneous neural activity and endothelial involvement in cold-induced vasodilatation. *Eur J Appl Physiol.* 2018;118(5):971—978. doi:10.1007/s00421-018—3832-0
7. Keatinge WR. The effect of low temperatures on the responses of arteries to constrictor drugs. *J Physiol.* 1958;142:395—405 doi:10.1113/jphysiol.1958.sp006025
8. Bergersen TK, Hisdal J, Walløe L. Perfusion of the human finger during cold-induced vasodilatation. *Am J Physiol.* 1999;276(3):R 731-R 737. doi:10.1152/ajpregu.1999.276.3.R 731
9. Caldwell JN, Matsuda-Nakamura M, Taylor NA. Interactions of mean body and local skin temperatures in the modulation of human forearm and calf blood flows: a three-dimensional description. *Eur J Appl Physiol.* 2016;116(2):343—352. doi:10.1007/s00421-015-3288-4
10. Lewis T. Observations upon the reactions of the vessels of the human skin to cold. *Heart.* 1930;1915:177—208.
11. Sendowski I, Savourey G, Besnard Y, Bittel J. Cold induced vasodilatation and cardiovascular responses in humans during cold water immersion of various upper limb areas. *Eur J Appl Physiol Occup Physiol.* 1997;75(6):471—477. doi:10.1007/s004210050191
12. Edwards MA. The role of arteriovenous anastomoses in cold-induced vasodilation, rewarming, and reactive hyperemia as determined by ^{24}Na clearance. *Can J Physiol Pharmacol.* 1967;45(1):39—48. doi:10.1139/y67-004
13. Grant RT, Bland EF. Observation on arteriovenous anastomoses in human skin and in the bird's foot with special reference to the reaction to cold. *Heart.* 1931;15:385—411.
14. Bergersen TK, Eriksen M, Walløe L. Local constriction of arteriovenous anastomoses in the cooled finger. *Am J Physiol.* 1997;273(3 Pt 2): R 880-R 886. doi:10.1152/ajpregu.1997.273.3.R 880
15. Bini G, Hagbarth KE, Hynninen P, Wallin BG. Thermoregulatory and rhythm-generating mechanisms governing the sudomotor and vasoconstrictor outflow in human cutaneous nerves. *J Physiol.* 1980;306:537—552. doi:10.1113/jphysiol.1980.sp013413
16. Lossius K, Eriksen M, Walløe L. Thermoregulatory fluctuations in heart rate and blood pressure in humans: effect of cooling and parasympathetic blockade. *J Auton Nerv Syst.* 1994;47(3):245—254. doi:10.1016/0165-1838(94)90185-6
17. Ogino MH, Tadi P. Neuroanatomy, Trigeminal Reflexes. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing. 2022. 326 p.
18. Millet JD, Brown RK, Levi B. Frostbite: Spectrum of Imaging Findings and Guidelines for Management. *Radiographics.* 2016;36(7):2154—2169. doi:10.1148/radiographics.2016160045
19. McLean DA. The use of cold and superficial heat in the treatment of soft tissue injuries. *Br J Sports Med.* 1989;23(1):53—54. doi:10.1136/bjsm.23.1.5320.
20. Hubbard TJ, Denegar CR. Does Cryotherapy Improve Outcomes With Soft Tissue Injury? *J Athl Train.* 2004;39(3):278—279.
21. Zachariassen KE. Hypothermia and cellular physiology. *Arctic Med Res.* 1991;50(Suppl 6):13—17.
22. Deal DN, Tipton J, Rosencrance E, Curl WW, Smith TL. Ice reduces edema. A study of microvascular permeability in rats. *J Bone Joint Surg Am.* 2002;84(9):1573—1578.
23. Possoff A. External thermal applications in postextraction therapy. *J Am Dent Assoc.* 1955;50(2):147—156. doi:10.14219/jada.archive.1955.0040
24. Fouke JM, Wolin AD, Bowman HF, McFadden ER Jr. Effect of facial cooling on mucosal blood flow in the mouth in humans. *Clin Sci (Lond).* 1990;79(4):307—313. doi:10.1042/cs0790307
25. Bierman W. The History of Fever Therapy in the Treatment of Disease. *Bull N Y Acad Med.* 1942;18(1):65—75.26.
26. Van der Westhuijzen AJ, Becker PJ, Morkel J, Roelse JA. A randomized observer blind comparison of bilateral facial ice pack therapy with no ice therapy following third molar surgery. *Int J Oral Maxillofac Surg.* 2005;34(3):281—286. doi:10.1016/j.ijom.2004.05.006
27. Swantek PM, Crenshaw JD, Marchello MJ, Lukaski HC. Bioelectrical impedance: a nondestructive method to determine fat-free mass of live market swine and pork carcasses. *J Anim Sci.* 1992;70(1):169—177. doi:10.2527/1992.701169x
28. Altmann M, Pliquett U, Suess R, von Borell E. Prediction of lamb carcass composition by impedance spectroscopy. *J Anim Sci.* 2004;82(3):816—825. doi:10.2527/2004.823816x
29. Barbosa-Silva MCG, Barros AJD, Wang J, Heymsfield SB, Pierson RN Jr. Bioelectrical impedance analysis: population reference values for phase angle by age and sex. *Am J Clin Nutr.* 2005;82:49—52.
30. Nescolarde L, Piccoli A, Román A et al. Bioelectrical impedance vector analysis in haemodialysis patients: relation between oedema and mortality. *Physiol Meas.* 2004;25(5):1271—1280. doi:10.1088/0967-3334/25/5/016
31. Maggiore Q, Nigrelli S, Ciccarelli C, Grimaldi C, Rossi GA, Michelassi C. Nutritional and prognostic correlates of bioimpedance indexes in hemodialysis patients. *Kidney Int.* 1996;50(6):2103—2108. doi:10.1038/ki.1996.535
32. Pupim LB, Kent P, Ikizler TA. Bioelectrical impedance analysis in dialysis patients. *Miner Electrolyte Metab.* 1999;25(4—6):400—406. doi:10.1159/000057482
33. O'Brien JG, Chennubhotla SA, Chennubhotla RV. Treatment of edema. *Am Fam Physician.* 2005;71(11):2111—2117.
34. Gocoł R, Hudziak D, Bis J, Mendrala K, Morkisz Ł, Podsiadło P, Kosiński S, Piątek J, Darocha T. The Role of Deep Hypothermia in Cardiac Surgery. *Int J Environ Res Public Health.* 2021;18(13):7061. doi: 10.3390/ijerph18137061. PMID: 34280995; PMCID: PMC 8297075.
35. Jain V, Langham MC, Wehrli FW. MRI estimation of global brain oxygen consumption rate [published correction appears in *J Cereb Blood Flow Metab.* 2010 Dec;30(12):1987] [published correction appears in *J Cereb Blood Flow Metab.* 2011 May;31(5):1336]. *J Cereb Blood Flow Metab.* 2010;30(9):1598—1607. doi:10.1038/jcbfm.2010.49
36. Norwood WI, Norwood CR. Influence of hypothermia on intracellular pH during anoxia. *Am J Physiol.* 1982;243(1):62—65. doi:10.1152/ajpcell.1982.243.1.C62
37. Jonas RA, Bellinger DC, Rappaport LA, Wernovsky G, Hickey PR, Farrell DM, Newburger JW. Relation of PH Strategy

- and Developmental Outcome after Hypothermic Circulatory Arrest. *J. Thorac. Cardiovasc. Surg.* 1993;106:362—368.
38. Mezrow CK, Midulla PS, Sadeghi AM, Gandsas A Wang W, Dapunt OE, Zappulla R, Griep RB. Evaluation of Cerebral Metabolism and Quantitative Electroencephalography after Hypothermic Circulatory Arrest and Low-Flow Cardiopulmonary Bypass at Different Temperatures. *J. Thorac. Cardiovasc. Surg.* 1994;107:1006—1019.

Влияние локальной аппаратной гипотермии на физиологические процессы организма

Н.А. Гусейнов ✉, М.Х. Хаммори , А.А. Мураев , С.Ю. Иванов ,
Е.А. Лукьянова , А.С. Клименко , М.А. Ноиразлиги 

Российский университет дружбы народов, г. Москва, Российская Федерация
✉ nid.gus@mail.ru

Аннотация. Актуальность. Холодовая вазодилатация является ответной реакцией на снижение температуры как локальной, так и общей. Дозированная контролируемая гипотермия является терапевтическим методом лечения различных патологических процессов. **Материалы и методы.** В нашем исследовании мы проанализировали различные показатели общего состояния организма человека под воздействием локальной контролируемой гипотермии. В исследовании участвовали здоровые добровольцы в количестве 25 человек, мужского (14) и женского (11) пола в возрасте от 21 до 34 лет. Исследование проводили в кабинете при постоянной температуре 25 °C, относительной влажности $30 \pm 5\%$, атмосферном давлении 765 мм рт. ст., в тишине и умеренной освещенности. Инструментами оценки являлись биоимпедансиметрия, ангиосканирование, а также общая термометрия. Также была проведена локальная термометрия слизистой оболочки щеки для выявления температурных корреляций между локальной гипотермией и температурой слизистой щеки. Локальная контролируемая гипотермия лица проводилась наложением упруго-эластичной маски на лицо испытуемого, охлаждающему жидкость и поддерживающему ее циркуляцию аппаратом ViTherm. За счет циркуляции охлажденной жидкости в маске, происходило охлаждение лица. Мaska перекрывала околоушно-жевательную, щечную, склеровую и подглазничные области справа и слева. Локальная контролируемая гипотермия длилась 50 минут, температура циркулирующей жидкости составляла 18 °C. **Результаты и обсуждение.** Нами было выявлено, что воздействие локальной контролируемой гипотермии 18—20 °C не изменяло основных показателей жизнедеятельности у здоровых людей: активная клеточная масса, реактивное сопротивление, внеклеточная жидкость, насыщенность кислородом, длительность систолы, пульс, общая температура. При этом было зарегистрировано снижение гидратации тканей. Выявленное физиологическое влияние локальной гипотермии обосновывает использование данного температурного режима для снижения послеоперационных отеков. **Выводы.** В силу отсутствия отрицательных эффектов локальной контролируемой гипотермии на показатели жизнедеятельности организма человека, актуальна разработка и применения данного инструмента в клинической практике, в том числе хирурга стоматолога.

Ключевые слова: локальная гипотермия, биоимпедансиметрия, ангиосканирование, термометрия

Вклад авторов: Гусейнов Н.А.—проведение эксперимента, написание текста статьи, поиск литературы, анализ литературы; Хаммори М.Х.—проведение эксперимента; анализ и поиск литературы; Мураев А.А.—коррекция структуры и содержания текста обзора, написание выводов; Иванов С.Ю.—коррекция структуры и содержания текста обзора, написание выводов; Лукьянова Е.А.—статистический анализ, написание текста статьи; Клименко А.С.—коррекция структуры и содержания текста обзора, написание выводов; Ноиразлиги М.—перевод и коррекция структуры и содержания текста статьи. Все авторы внесли существенный вклад в подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Информация о конфликте интересов. Авторы заявляют об отсутствии конфликта интересов.

Информированное согласие на публикацию. Все пациенты предоставили добровольное информированное согласие на участие в исследовании в соответствии с Хельсинкской декларацией Всемирной медицинской ассоциации (Хельсинкская декларация WMA—Этические принципы проведения медицинских исследований с участием человека, 2013 г.) и согласие на обработку персональных данных.

Этическое утверждение. Экспериментально-клиническое исследование одобрено локальным комитетом по этике РУДН, протокол № 5 заседания Комитета по этике Медицинского института РУДН от 17 февраля 2022 г.

Благодарности—неприменимо.

Поступила 11.08.2022. Принята 07.09.2022.

Для цитирования: Guseynov N.A., Hammouri M.H., Muraev A.A., Ivanov S.Y., Lukianova E.A., Klimenko A.S., Noeerazlighi M.A. Local hardware hypothermia influence on the physiological processes // Вестник Российского университета дружбы народов. Серия: Медицина. 2022. Т. 26. № 3. С. 243—258. doi: 10.22363/2313-0245-2022-26-3-243-258

Corresponding author: Guseynov Nijat Aydin oglu—PhD student of the Department of Oral and Maxillofacial Surgery and Surgical Dentistry, Peoples' Friendship University of Russia, 117198, ul. Miklukho-Maklaya, 10, Moscow, Russian Federation. E-mail: nid.gus@mail

Guseynov N.A. ORCID 0000-0001-7160-2023

Hammouri M.H. ORCID 0000-0002-0886-9160

Muraev A.A. ORCID 0000-0003-3982-5512

Ivanov S.Y. ORCID 0000-0001-5458-0192

Lukianova E.A. ORCID 0000-0002-6440-6662

Klimenko A.S. ORCID 0000-0001-8591-3746

Noeerazlighi M.A. ORCID 0000-0002-3636-9091

Ответственный за переписку: Гусейнов Ниджат Айдын оглы—аспирант кафедры челюстно-лицевой хирургии и хирургической стоматологии, Российский университет дружбы народов, Российская Федерация, 117198, Москва, ул. Миклухо-Маклая 10. E-mail: nid.gus@mail.ru

Гусейнов Н.А. SPIN-код 9417-7948; ORCID 0000-0001-7160-2023

Хаммори М.Х. SPIN-код 5987-3291; ORCID 0000-0002-0886-9160

Мураев А.А. SPIN-код 1431-5936; ORCID 0000-0003-3982-5512

Иванов С.Ю. SPIN-код 2607-2679; ORCID 0000-0001-5458-0192

Лукьянова Е.А. SPIN-код 9522-7490; ORCID 0000-0002-6440-6662

Клименко А.С. SPIN-код 1804-8548; ORCID 0000-0001-8591-3746

Ноиразлиги М.А. ORCID 0000-0002-3636-9091