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RESEARCH

# Microhemodynamic Adjustments and the Type of Autonomic Regulation Under Analog Long-term Isolation Conditions

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## Abstract

This study focused on microhemodynamic and autonomic regulation changes during long-term isolation in a 366-day SIRIUS-23 experiment with 6 healthy volunteers (2 men and 4 women, aged 25–37 years). Heart rate variability analysis and laser Doppler flowmetry were used to assess cardiovascular system responses before, during, and after isolation. Volunteers demonstrated distinct autonomic regulation patterns, dividing into two groups based on vagal tone and vascular center activity. Group 2 showed consistently higher autonomic function throughout the experiment. Microcirculation parameters revealed decreased perfusion in the forehead area for Group 1 and fluctuating dynamics for Group 2. Both groups exhibited endothelial tone reduction and altered blood flow distribution in the toe area with increased shunt flow. Prolonged isolation significantly affects microhemodynamics and autonomic regulation. Individuals with higher vagal tone demonstrated better adaptation. These findings contribute to understanding physiological responses to long-term confinement and have implications for space mission medical support.

**Keywords** Isolation conditions · Cardiovascular system · Autonomic regulation · HRV analysis · Microhemodynamics · Laser doppler flowmetry

## Introduction

Leaving the Earth's surface, members of space crews experience not only the effects of physical factors: microgravity, radiation, noise from the equipment on the orbital station, and others (Shelhamer et al. 2020), but also face isolation, compounded by a limitation in the range of external conditions (Mircea et al. 2024). This isolation is unlike any that can be experienced on Earth. In earthly conditions, almost every one of us can break solitude by expanding our interaction with the surrounding world. Beyond the planet's orbit, even excursions into open space do not expand the confines of isolation.

Yuri Alekseyevich Gagarin, the first human to make an orbital flight, was in such isolation for 108 min. Nowadays space crew members stay in it for about 180 days. For future space travelers, this time will significantly increase and be limited by the duration of the journey into deep space.

Moreover, in the natural conditions of everyday life, each of us experiences the influence of a sufficiently broad spectrum of exogenous ecological conditions that determine adjustments (not so much homeostatic as allostatic) in the

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functioning of a living organism by seeking a constant equilibrium between its internal environment and the external surroundings (Sterling 2012; Goldstein 2019). In a confined orbital object, however, the range of changes in living conditions is limited to quite narrow boundaries.

Social isolation, combined with the extremely limited area of orbital stations and living conditions, provokes a stressful state, while some familiar options for coping with it, such as the ability to take spontaneous walks, are absent among space crews. At the same time, their workload is extremely intense (Jacubowski et al. 2015), and their lifestyle and diet are very monotonous (Axpe et al. 2020).

Prolonged stay of a person in a hermetic environment is accompanied by the effects of factors of a closed living volume, including: an artificial gas environment with relatively elevated levels of carbon dioxide compared to terrestrial conditions, the presence of artificial lighting, a regulated diet, a regime of physical activity, the occurrence of emergency situations, sleep deprivation, etc. Therefore, the study and analysis of the influence of multi-component conditions in an isolated volume on various systems of the human body holds significant scientific and practical importance (Orlov et al. 2023). Staying in a sealed atmosphere under controlled microclimate conditions, dietary conditions, and regulated physical activity has a pronounced effect on all physiological systems. Combined with other factors, such as elevated CO2 levels recorded aboard the International Space Station (ISS) (Fu et al. 2019; Zhang et al. 2021) it can cause specific changes in the bodies of those performing their duties on board orbital stations, intensifying the effects of microgravity and the functional changes it causes (Goswami et al. 2021; Mircea et al. 2024).

In recent years, a project called SIRIUS (Scientific International Research in Unique Terrestrial Station) (http://sirius.imbp.ru/ https://www.nasa.gov/humans-in-space/a-sirius-international-isolation-study/) has been implemented in Russia, consisting of a series of isolation experiments (4, 8, and 12 months) – an analog project for a lunar mission. In the United States, the CHAPEA (Crew Health and Performance Exploration Analog) project serves as an analog for a Mars mission (https://www.nasa.gov/humans-in-space/chapea/).

The global research objectives of these isolation projects are related to studying the constraints experienced during long space flights, including limitations on communication and resources available to the crew, as well as equipment failures and other emergencies, the likelihood of which increases with greater distance from low Earth orbit (LEO) (Belakovskiy et al. 2011; Orlov et al. 2015; Gushchin et al. 2019).

The effectiveness of various resource management strategies such as food systems, waste disposal, and water purification in isolated environments is experimentally evaluated (Baranov et al. 2001; Xu et al. 2024).

In addition, the possibilities of potential conflicts and strategies for effective cooperation are assessed. Researchers are studying the psychological impact of isolation on small groups and the individual included in them, assessing the emotional state, cognitive functions and mechanisms of overcoming psychosocial deprivation (Plomariti et al. 2022; Ushakov et al. 2012).

Undoubtedly, an important aspect of isolation projects is research on how isolation affects physical health, including basic physiological processes and their control mechanisms, as well as the development of crew selection and countermeasures, including medical ones, to help reduce the negative effects of isolation during future real-world space missions (Fedyay et al. 2023).

Hermetic facilities are used for insulation projects, which make it possible to isolate volunteers for various periods of time in controlled environmental conditions: NEK (Ground-based Experimental Complex, IMBP, Russia) and HERA (Human Exploration Research Analog, NASA, USA), Yuegong-1 (Moon Palace, 月宫一号China).

The NEK, where the SIRIUS project was conducted, is located on the territory of the IMBP RAS. It is a complex engineering facility (Fig. 1), consisting of interconnected multifunctional experimental modules:

- small landing module (volume 50 m$^3$)
- medical module (volume 100 m$^3$)
- habitable module: command cabin, private cabins, dining room, wardroom (volume 150 m$^3$)
- warehouse module: storage, greenhouse, gym (volume 250 m$^3$)
- virtual simulator of the planet's surface

The NEK life support system is equipped with autonomous ventilation and air conditioning systems, water supply, sewerage, electricity, and many others. Complex engineering communications form and maintain a habitat with preset parameters, isolating the crew from the environment and simulating the main factors of real space flight, with the exception of weightlessness and radiation exposure (Agaptseva et al. 2024).

Our research scope in the SIRIUS project was related to the study of autonomic regulation and the functional state of the microcirculatory bed of the skin in healthy subjects during stay in a hermetic facility according to the scenario of an orbital flight to the Moon.

In any extreme conditions, the body needs stability of the functions of the cardiovascular system (CVS) as one of the most important physiological systems that implements the possibility

**Fig. 1** Ground-based Experimental Complex (NEK). (photos provided by the press service of the IMBP RAS)

of adaptive changes (Goswami et al.2021). And, as has been shown, including in space flights, this is ensured by regulatory mechanisms (Baevsky et al. 2011; Otsuka et al. 2022).

Adaptive changes in the blood flow regulation system affect all structural and functional components of the CVS. The microcirculatory bloodstream (MCB), at the level of which the gas transportation and exchange function is realized, is the final link of these processes.

The human body's CVS performs a number of life-supporting functions, including transporting nutrients and oxygen to cells. In this regard, the MCB of the cardiovascular system, including arterioles, capillaries, arteriovenular anastomoses and venules, is of particular diagnostic interest. MCB directly provides transcapillary diffusion of oxygen and carbon dioxide, the general trophism of peripheral tissue structures of the body, as well as their adaptive stability under changing endogenous or exogenous conditions (Cracowski and Roustit 2020).

A diagnostically significant feature of the MCB is its dynamic nature, as well as temporal and spatial functional heterogeneity. This makes the MCB the first link reflecting disturbances in the system of protective and adaptive reactions aimed at restoring impaired self-regulation both at the level of individual organs and the body as a whole (Corstian et al. 2008; Donati et al. 2013; Gutterman et al. 2016).

At the same time, it is necessary to take into account the regional heterogeneity of the MCB due to the anatomical and topographic features of specific organs and tissues. Such morphological differences directly determine the functional characteristics of microcirculation, which is why different areas of the MCB show different sensitivity to the effects of external and internal pathogenic factors. Thus, the change in MCB reflects the formation of local foci of maladaptation and a violation of homeostasis (Braverman 1997; Segal 2005; Backer et al. 2013; Moore et al. 2015; Dremin et al. 2017; Mizeva et al. 2017; Zherebtsov et al. 2023) having diagnostic potential in extreme physiology (Frolov et al. 2025) and stress physiology (Dunaev et al. 2014).

In the field of space physiology and medicine, the diagnosis of the functional state of the MCB opens up new diagnostic possibilities for assessing the individual body's response to space flight factors, both in their modeling and in real space (Segal 2005; Dunaev et al. 2024).

## Materials and methods

### Research Design

The research was conducted at the NEK in the Scientific Research Center of the Russian Federation – IMBP RAS, which is designed to conduct scientific experiments involving humans in an artificially regulated environment, in the SIRIUS-23 isolation experiment. In isolated conditions of a hermetic facility for 366 days (2023–2024).

There were 6 healthy volunteers (2 men and 4 women). Their age at the time of the start of the background studies ranged from 25 to 37 years. All the subjects received admission from the medical expert commission of the SSC RF - IMBP RAS. The conducted studies were approved by the SSC RF – IMBP RAS Bioethics Commission (Protocol No. 643 dated 07.07.2023).

The measurements procedures (Fig. 2) included sessions on registration of CVS parameters at three stages: 1 session was performed before the start of isolation (the "Background" stage), 5 sessions were held inside the containment facility directly during isolation every 2–3 months, as well as 1 session after the end of isolation (the "After" stage).

The parameter's registration took place directly in the closed facility (Fig. 3) and in laboratory conditions after the end of isolation.

The recording of physiological signals was carried out in a supine position. Before registration, the subjects were lying for 15 min to adapt to the horizontal position and environmental conditions. Next, a 10-minute recording of physiological signals was performed without volitional breathing control, followed by a 3-minute controlled breathing test at a rate of 6 breaths/min (duration of one respiratory cycle of 10 s, slow breathing).

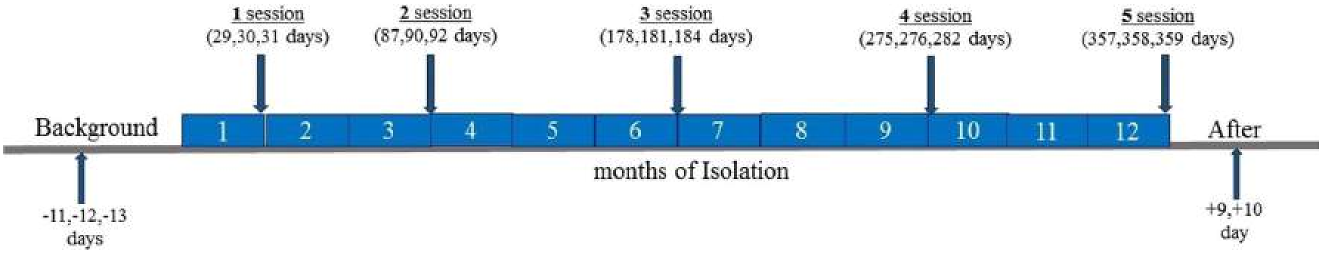


**Fig. 2** The measurements periods during isolation experiment

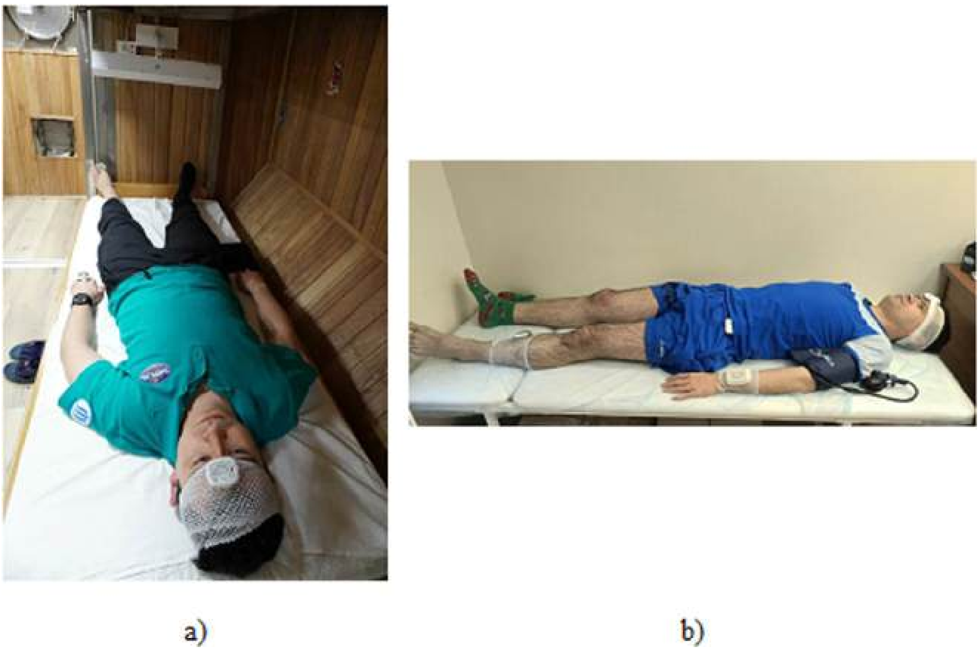


**Fig. 3** Conducting a study in a hermetic facility (**a**) and the "post-flight" period (**b**) (photo by the authors)

## Research Methods

### Analysis of Heart Rate Variability (HRV)

HRV analysis is a classic method of assessing the regulatory autonomous reactions of the body, mainly by balancing sympathetic and parasympathetic control actions, which are mainly controlled by the nervous system. We used standard HRV measurement and analysis protocols in accordance with the recommendations developed by the European Cardiological and North American Electrophysiological Societies and taking into account some methodological aspects of HRV study planning, analysis and presentation of data updated in the following decades after the publication of this document (Laborde et al. 2017).

### Study of Skin Blood Flow

An optical noninvasive diagnostic method, laser Doppler flowmetry (LDF), was used to register peripheral blood flow. The LDF method is based on probing tissues with near-infrared laser radiation and detecting light reflected back from moving red blood cells and stationary tissue structures. The recorded signal is called tissue perfusion or an indicator of blood microcirculation and is directly proportional to the rate and concentration of red blood cells in the diagnostic volume. The advantage of LDF is that it can be used to evaluate the work of local and generalized mechanisms of regulation of microcirculation. Different scientific schools distinguish from 5 to 7 frequency ranges that correspond to the following regulatory mechanisms: endothelial (0.005–0.02 Hz), due to the activity of endothelial cells, including NO-dependent endothelial regulation; neurogenic (0.02–0.046 Hz), due to neurogenic sympathetic adrenergic regulation; sensory peptidergic (0.047–0.069 Hz), reflecting the activity of sensory peptidergic fibers secreting neuropeptides and being the main component of nervous trophic tissues; myogenic or vasomotor (0.07–0.145 Hz), reflecting the oscillatory component of muscle tone of precapillaries regulating blood flow to the nutritional channel; cholinergic parasympathetic (0.16–0.18 Hz), indicating on the work of central trophotropic mechanisms and parasympathetic centers; respiratory (0.2–0.4 Hz) and cardiac (0.8–1.6 Hz) are passive mechanisms reflecting the generalized effect of respiration and heartbeat on the oscillatory activity of the microvessels, respectively (Krupatkin 2018). Changes in blood flow play an important role in hemodynamics. An increase in the oscillation amplitudes in the ranges responsible for vascular tone leads to a decrease in the overall resistance to blood movement. For example, increased sympathetic vasomotor activity causes vasoconstriction and increased resistance, but with a simultaneous increase in the amplitudes of blood flow fluctuations caused by the sympathetic nervous system, the oscillatory contribution to resistance decreases. Probably, such processes serve an adaptive function, smoothing out sudden changes in vascular resistance.

## Equipment and Means of Technical Analysis of Physiological Signals

To register the parameters of the autonomous regulation of the cardiovascular system, the complex for recording electrocardiograms (ECG), processing cardiointervalograms and analyzing heart rate variability "Varikard 2.8" (RAMENA LLC, Ryazan, Russia) was used. Peripheral blood flow parameters were recorded using portable laser blood microcirculation analyzers LAZMA PF (SPE LAZMA Ltd, Moscow, Russia). The devices and the layout of the sensors that register physiological signals are shown in Fig. 4.

ECG signal processing and assessment of neurovegetative regulation with HRV analysis were performed using the ISKIM-6 software (Ramena LLC, Ryazan, Russia). The received signal was edited using visual verification and manual correction of individual RR intervals and classification of QRS complexes. Abnormal complexes not caused by depolarization of the sinoatrial node were excluded from the recording.

Special software LAZMA (SPE LAZMA Ltd, Russia) was used to calculate the parameters of blood microcirculation.

The calculated parameters of HRV indices were computed according to generally accepted standard clinical guidelines (Malik et al. 1996). The endothelial tone (ET) was calculated following (Krupatkin 2018) $ET = \sigma \times P / Ae \times M$ (σ – standard deviation of perfusion, P – mean arterial pressure, Ae – amplitude of endothelial oscillations, M – perfusion level).

## Statistical Processing

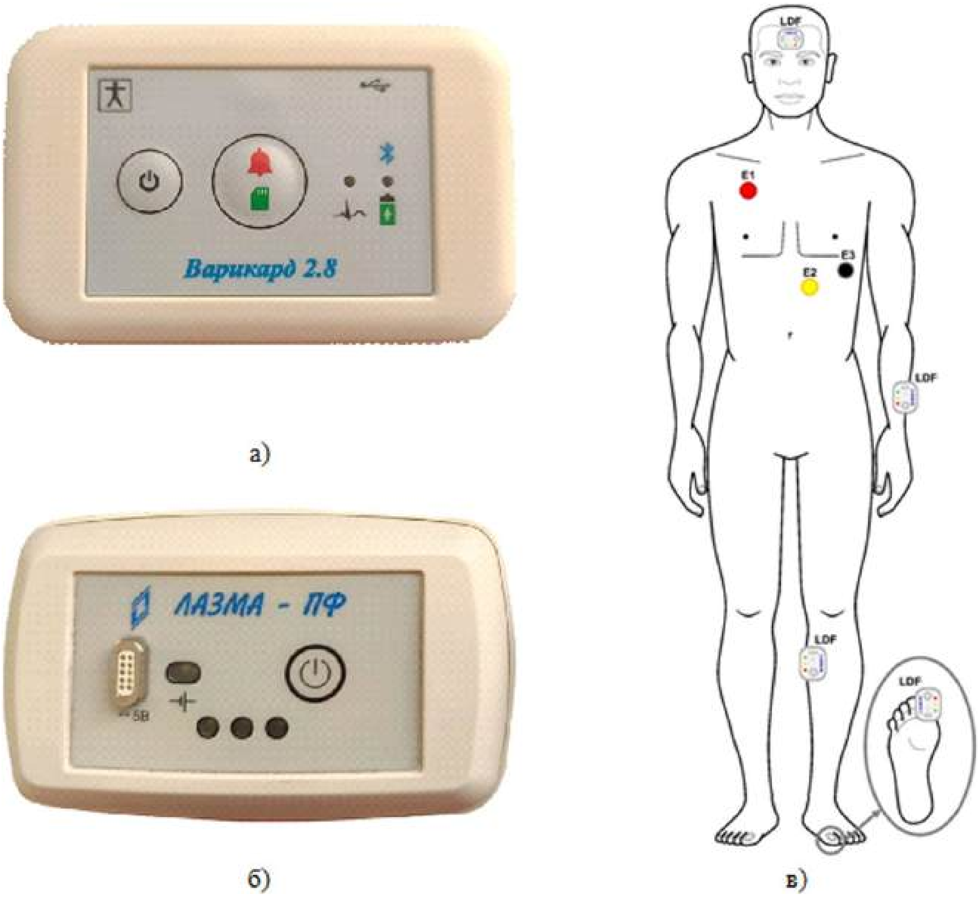
The Ward method was used to divide the test into groups with a fixed breathing rate. The statistical analysis was based on the method of variance analysis (one-way and repeated-measured ANOVA). The graphical interpretation shows the data arithmetic mean standard deviation. Statistical data processing was carried out in the PRISMA 8 program.

## Results

According to the results of the 3-minute (Controlled breath) test based on HRV analysis using cluster analysis (Ward's method), the subjects were divided into groups (Fig. 5): Group 1–2 women and 2 men; Group 2–2 women.

In controlled breathing tests, the activity and sensitivity of the vagus nerve and subcortical vascular centers are studied, including those related to the functional reserves of the autonomic nervous system. At the same time, the so-called slow heart rate waves (LF, ms$^2$) are amplified in the range of 0.15–0.05 Hz (with a period of 7–20 s). HRV spectral analysis makes it possible to assess the sensitivity and functional reserves of the corresponding regulatory links.

**Fig. 4** Devices: Varikard 2.8 (**a**) and portable multimodal LAZMA PF analyzers (**b**) and their placement for recording physiological signals (**c**)



а)

б)

в)

**Fig. 5** Division into groups (Ward's method, division into 2 groups according to CVS reactivity)

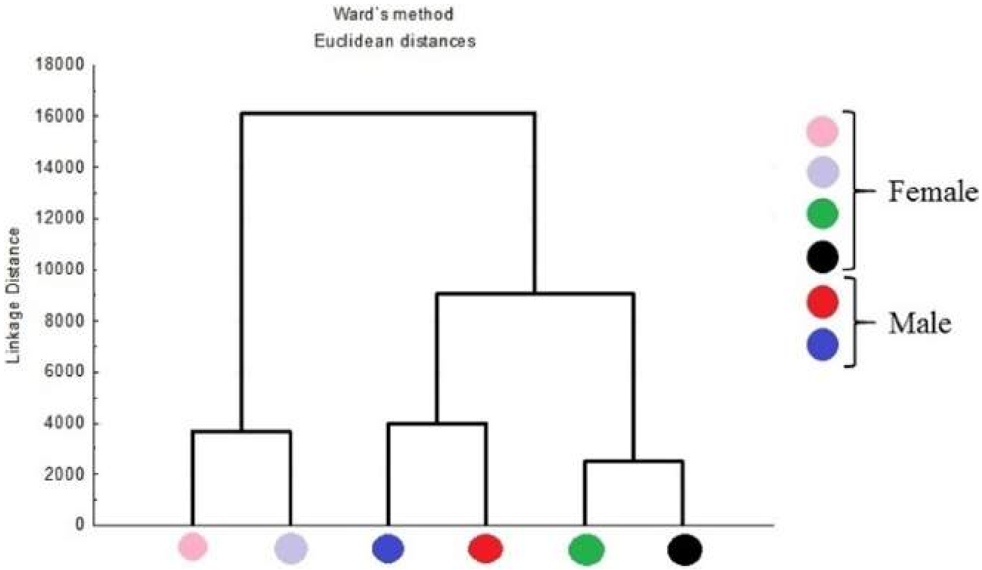
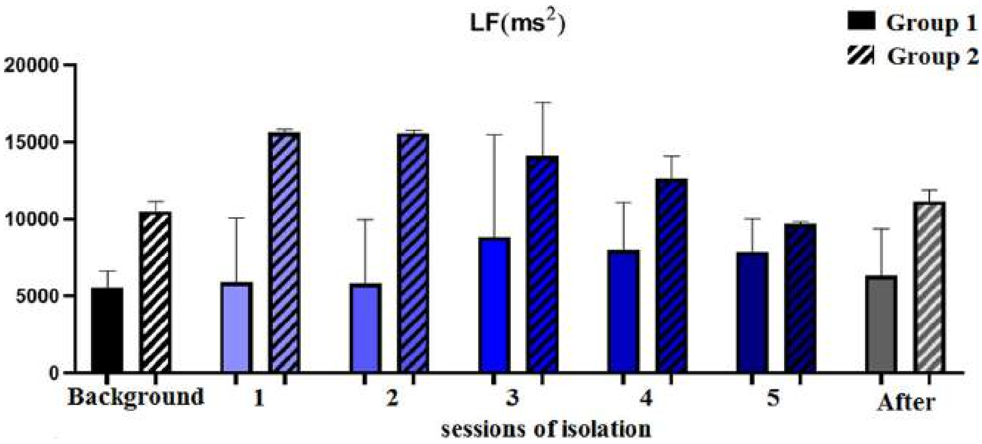


**Fig. 6** Dynamics of the LF (ms$^2$) in the controlled breathing test into 2 groups in background, during long-term isolation conditions and after isolation



In group 2, the activity and sensitivity of the vagus nerve and subcortical vascular center (SVC) centers, including those related to the functional reserves of the autonomic nervous system, was higher throughout the isolation experiment, starting from session 1. In group 1, we observed activation of vegetative centers from the middle (3rd session) of the isolation experiment. In this regard, in the future, we will consider the indicators of skin microhemodynamics according to the activity of the SVC (Fig. 6).

As for the indicators of skin microhemodynamics in the assessed regions, the data obtained are shown in Fig. 7. Changes in the in the area of the forehead skin were noted in both groups. In group 1, perfusion ($I_m$, PU) was reduced relative to the background value during 4 study sessions. The results of the group 2 study demonstrate the wave-like nature of the dynamics of the perfusion index with an increase relative to the background study in the 1 st, 2nd, 4th and 5th study sessions and a return to the background values in the 3rd session and after effect.

It was also found that in group 1, endothelial tone (ET, PU) decreased in the isolation experiment, while the reduced value of the relative background value remained in the aftereffect. Unidirectional changes in basal perfusion in both groups were noted in the toe area, however, in group 2, perfusion was higher both in background studies and in isolation. In both groups, the amplitude of endothelial oscillations ($A_e$, PU) decreases in the toe area. In addition, in group 2, the amplitude of neurogenic ($A_n$, PU) and myogenic ($A_m$, PU) oscillations decreases in the isolation experiment, which generally indicates a decrease in regulatory activity. In group 1, changes in these indicators are periodic.

A decrease in the level of nutritional ($I_{mn}$, PU) and shunt ($I_{m\_shunt}$, PU) blood flow in the toe area was observed during isolation. It should be noted that the proportion of nutritional blood flow in the background was higher than that of shunt blood flow, but the picture changed in the isolation experiment. This dynamic indicates that the redistribution of blood flow is more likely to occur through the shunt pathways.

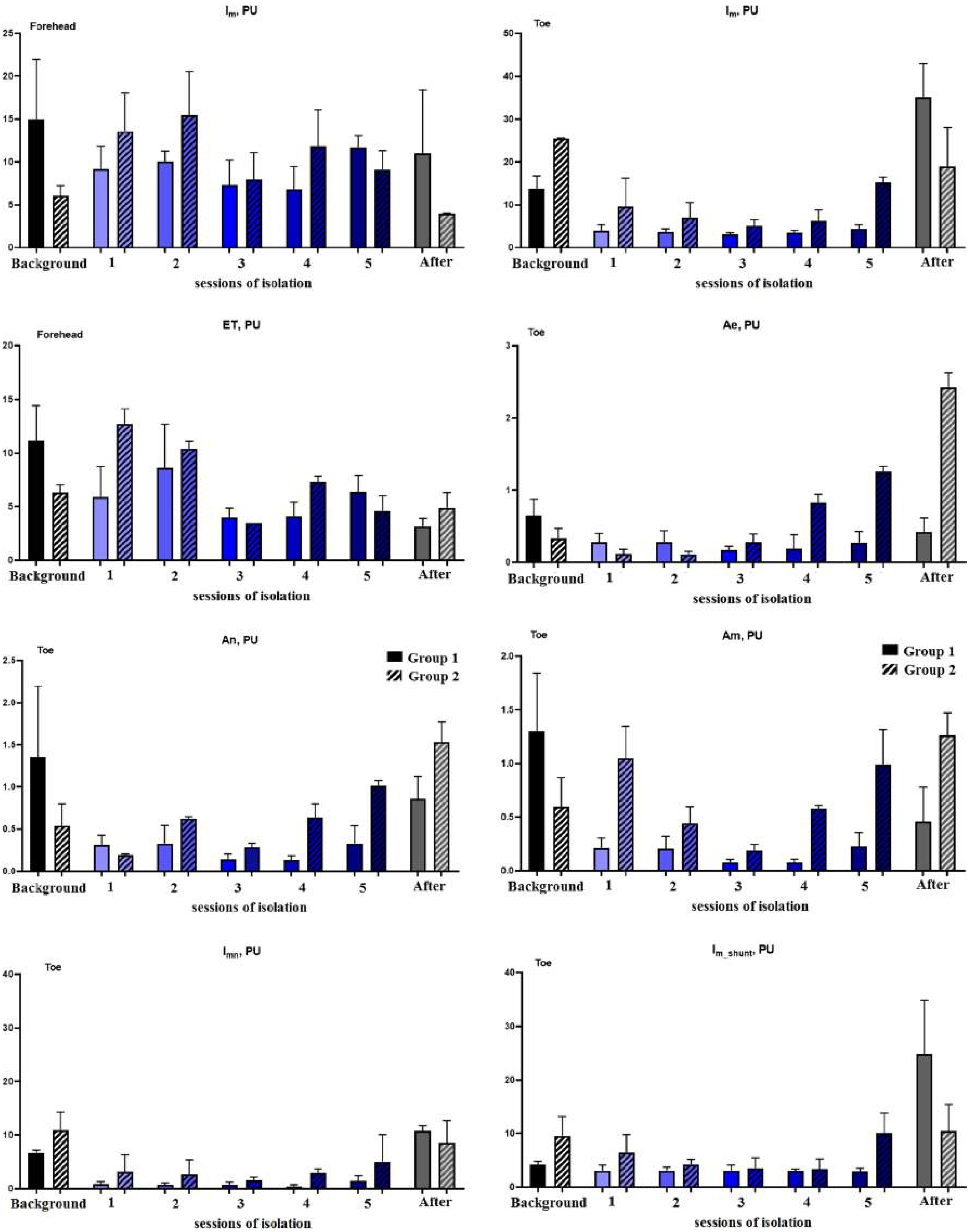


**Fig. 7** Skin blood flow indicators into 2 groups in background, during long-term isolation conditions and after isolation

## Discussion

The main influencing factors in isolation conditions are psychophysiological stress and physical inactivity, since the artificial gas environment, temperature, humidity, microbiological status, physical activity, daily routine, diet and the level of fluid intake in the hermetic facility are maximally unified (Anisimova et al. 2018).

Previously, during 120-day isolation, the presence of collagens in the urine proteome was detected, which are the basis of the extracellular matrix (Rusanov et al. 2022). The presence of these proteins in the analysis of the proteome may indicate changes in the characteristics of the CVS, since collagen proteins as a components of the extracellular matrix are involved in the modulation of biomechanical characteristics of the CVS (rings of heart valves, heart muscle, interventricular and atrioventricular septa), as well as in the remodeling of the myocardium and blood vessels and the development of autonomic dysfunction of the CVS (Manon-Jensen et al. 2016).

In the course of isolation studies, unique features of changes in the intensity of electrophoretic protein markers were identified, among which special attention was paid to the alpha-chain of fibrinogen and plasminogen, which perform critically important functions in hemostasis (Pastushkova et al. 2025). Fibrinogen is a key component of the blood coagulation system, whereas plasminogen is directly involved in the process of fibrinolysis (Castellino et al. 2005). Special attention should be paid to the fact that both of these processes are under strict control of the vascular endothelium. Endothelial cells produce a range of regulatory factors that coordinate the balance between blood clotting and fibrinolysis. It is noteworthy that the fibrinogen concentration shows significant variability, in particular, under the influence of psychoemotional stress, which is one of the isolation factors (Decamps and Rostet 2005). Therefore, changes in the endothelial characteristics of skin blood flow observed by us during isolation in the scalp and lower extremities may indicate a possible restructuring of vasodilatory function (Ivanov et al. 2020).

In our study, for the first time, the change in MCB parameters depending on the type of autonomic influences in healthy subjects during simulated annual isolation was evaluated. It is shown that a long period of forced isolation and human stay in a hermetic facility leads to significant hemodynamic changes, primarily manifested in the skin of the lower extremities. The decrease in the amplitude of myogenic oscillations in the lower extremities, which we observed in isolation, led to an increase in the tone of precapillary sphincters, which regulate blood flow to the nutrient channel and, as a result, a decrease in the nutritional blood flow (Tikhomirova et al. 2018). In addition, an increase in the proportion of shunt blood flow occurring in isolation conditions leads to a decrease in the volume of capillary blood flow, which can lead to a deterioration in the oxygen supply to this area.

Thus, in the work of Navasiolava et al. (2010), it was shown that forced inactivity in a 7-day experiment with dry immersion led to a decrease in both the overall perfusion level measured in the calf muscle area and the level of maximum achievable endothelium-dependent vasodilation. The decrease in the amplitudes of myogenic oscillations and their contribution to the total power of the spectrum can also be explained by the main influencing factors in isolation conditions on the subjects during the annual isolation experiment.

## Conclusion

Thus, in conditions of isolation, we recorded signs of changes in vasomotor function and changes in the regulatory mechanisms of the CVS. According to the data obtained, two individuals the activity and sensitivity of the vagus nerve and the centers of the sympathetic nervous system (SNS), including those associated with the functional reserves of the autonomic nervous system — exhibited a faster recovery to baseline values. Although the indicators characterizing the cardiovascular system (CVS) remained higher throughout the isolation experiment compared to the dynamics observed in 4 volunteers. It can be inferred that this reflects a greater capacity of the regulatory systems in 2 volunteers with parasympathetic predominance to adapt to the conditions of prolonged isolation.

### Limitations of the Study

It is important to note that the small sample sizes do not allow the obtained results to be generalized to the population level. For the same reason, there is significant variation in individual responses among volunteers.

**Acknowledgements** Acknowledgements to the organizers of the SIRIUS project; all volunteers participated in this study; SIRIUS-23 crew members for conducting techniques in isolation.

**Author Contributions** RVB, DAV, PJA conceived and designed research; PDV and POV collected data; PDV, POV, LYuI, ZhEV analyzed data; PDV, POV, LYuI, ZhEV, RVB, DAV interpreted the results; RVB, PDV, POV, PJA, LYuI, ZhEV, DAV, SVV drafted manuscript. All authors approved the final manuscript.

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**Data Availability** No datasets were generated or analyzed during the current study.

**Code Availability** The underlying code for this study is not publicly available for proprietary reasons.

## Declarations

All studies were carried out in accordance with the principles of biomedical ethics formulated in the 1964 Declaration of Helsinki and its later amendments and were approved by the Commission on Biomedical Ethics of the Institute of Biomedical Problems of the Russian Academy of Sciences (Moscow).

**Consent to Participate** Informed consent was obtained from all individual participants included in the study.

**Consent to Publish** All study participants provided their voluntary written informed consent, which they signed after potential risks and benefits, as well as the nature of the upcoming study, were explained to them.

**Competing interests** The authors declare no competing interests.

**Clinical Trial** Number Not applicable.

## References

Agaptseva, T.N., Kussmaul, A.R., Belakovskiy, M.S., et al.: Analog isolation projects: An opportunity for bench-testing technologies and products designed for long-distance space missions. Journal of Space Safety Engineering **11**, 291–294 (2024). https://doi.org/10.1016/j.jsse.2024.03.005

Anisimova, A.S., Alexandrov, A.I., Makarova, N.E., et al.: Protein synthesis and quality control in aging. Aging **10**, 4269–4288 (2018). https://doi.org/10.18632/aging.101721

Axpe, E., Chan, D., Abegaz, M.F., et al.: A human mission to Mars: Predicting the bone mineral density loss of astronauts. PLoS One **15**(1), e0226434 (2020). https://doi.org/10.1371/journal.pone.0226434

Baevsky, R.M., Chernikova, A.G., Funtova, I.I., et al.: Assessment of individual adaptation to microgravity during long term space flight based on stepwise discriminant analysis of heart rate variability parameters. Acta Astronaut **69**, 1148–1152 (2011). https://doi.org/10.1016/j.actaastro.2011.07.011

Baranov, V.M., Demin, E.P., Gushchin, V.I., et al.: Project SFINCSS-99 simulation of flight of international crew on space station: Experience and lessons learned. In: Model'nyi Eksperiment S Dlitel'noi Izolyatsiei: Problemy I Dosizheniya (Modeling of Prolonged Isolation: Problems and Achievements), pp. 524–530. Ed., Moscow (2001)

Belakovskiy, M.S., Breus, T.K., Voloshin, O.V., et al.: MARS-500: Simulation of a manned flight to the Mars. Moscow: Inst. Biomed. Probl. Russ Acad. Sci. **4**, 1–7 (2011)

Braverman, I.M.: The Cutaneous Microcirculation: Ultrastructure and Microanatomical Organization. Microcirculation **4**, 329–340 (1997). https://doi.org/10.3109/10739689709146797

Castellino, F.J., Ploplis, V.A.: Structure and function of the plasminogen/plasmin system. Thromb Haemost **93**, 647–654 (2005). https://doi.org/10.1160/TH04-12-0842

Cracowski, J.-L., Roustit, M.: Human Skin Microcirculation. Comprehensive Physiology **10**, 1105–1154 (2020). https://doi.org/10.1002/j.2040-4603.2020.tb00131.x

De Backer, D., Orbegozo Cortes, D., Donadello, K., et al.: Pathophysiology of microcirculatory dysfunction and the pathogenesis of septic shock. Virulence **5**, 73–79 (2013). https://doi.org/10.4161/viru.26482

Decamps, G., Rostet, E.A.: Longitudinal Assessment of Psychological Adaptation During a Winter-Over in Antarctica. Environment and Behavior **37**, 418–435 (2005). https://doi.org/10.1177/0013916504272561

den Uil, C.A., Klijn, E., Lagrand, W.K., et al.: The Microcirculation in Health and Critical Disease. Progress in Cardiovascular Diseases **51**, 161–170 (2008). https://doi.org/10.1016/j.pcad.2008.07.002

Donati, A., Domizi, R., Damiani, E., et al.: From macrohemodynamic to the microcirculation. Crit. Care Res. Pract. **2013**(892710), 1–8 (2013). https://doi.org/10.1155/2013/892710

Dremin, V.V., Zherebtsov, E.A., Sidorov, V.V., et al.: Multimodal optical measurement for study of lower limb tissue viability in patients with diabetes mellitus. J Biomed Opt **22**, 1–10 (2017). https://doi.org/10.1117/1.JBO.22.8.085003

Dunaev, A.V., Sidorov, V.V., Krupatkin, A.I., et al.: Investigating tissue respiration and skin microhaemocirculation under adaptive changes and the synchronization of blood flow and oxygen saturation rhythms. Physiol Meas **35**, 607–21 (2014). https://doi.org/10.1088/0967-3334/35/4/607

Dunaev, AV., et al.: Investigation of blood microcirculation in microgravity with the use of portable laser doppler flowmeters. Aerospace and environmental medicine **58**, 47–54 (2024). https://doi.org/10.21687/0233-528X-2024-58-1-47-54

Fedyay, S., Niiazov, A., Ponomarev, S., et al.: Medical support for space missions: The case of the SIRIUS project. Aerospace. **10**, 1–12 (2023). https://doi.org/10.3390/aerospace10060518

Frolov, A., Loktionova, Y., Zharkikh, E., et al.: Effects of Voluntary Changes in Minute Ventilation on Microvascular Skin Blood Flow. J. of SCI. IN SPORT AND EXERCISE **7**, 215–229 (2025). https://doi.org/10.1007/s42978-023-00268-3

Fu, Q., Shibata, S., Hastings, J.L., et al.: Impact of Prolonged Spaceflight on Orthostatic Tolerance During Ambulation and Blood Pressure Profiles in Astronauts. Circulation **140**, 729–738 (2019). https://doi.org/10.1161/CIRCULATIONAHA.119.041050

Goldstein, D.S.: How does homeostasis happen? Integrative physiological, systems biological, and evolutionary perspectives. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology **316**, 301–317 (2019). https://doi.org/10.1152/ajpregu.00396.2018

Goswami, N., White, O., Blaber, A., et al.: Human physiology adaptation to altered gravity environments. Acta Astronaut **189**, 216–221 (2021). https://doi.org/10.1016/j.actaastro.2021.08.023

Gushchin, V.I., Vinokhodova, A.G., Komissarova, D.V., et al.: Experiments with Isolation: Past, Present, and Future. Human Physiology **45**, 730–739 (2019). https://doi.org/10.1134/S0362119719070077

Gutterman, D.D., Chabowski, D.S., Kadlec, A.O., et al.: The human microcirculation: regulation of flow and beyond. Circ Res **118**, 157–172 (2016). https://doi.org/10.1161/CIRCRESAHA.115.305364

Ivanov, A.N., Popyhova, E.B., Tereshkina, N.Y., et al.: Vasomotor function of endothelium. Uspehi Fiziologicheskih nauk. **51**, 82–104 (2020). https://doi.org/10.31857/S0301179820030066

Jacubowski, A., Abeln, V., Vogt, T., et al.: The impact of long-term confinement and exercise on central and peripheral stress markers. Physiology & Behaviour **152**, 106–111 (2015). https://doi.org/10.1016/j.physbeh.2015.09.017

Krupatkin, A.I.: Oscillatory Processes in the Diagnosis of the State of Microvascular-Tissue Systems. Hum Physiol **44**, 581–591 (2018). https://doi.org/10.1134/S0362119718050079

Laborde, S., Mosley, E., Thayer, J.F.: Heart rate variability and cardiac vagal tone in Psychophysiological Research – Recommendations for experiment Planning, data Analysis, and data reporting. Front. Psychol. **8** (2017). https://doi.org/10.3389/fpsyg.2017.00213

Malik, M., et al.: Heart rate variability. Standarts of measurement, physiological interpretation, and clinical use. task forse of the European society of cardiology and the North American society of pacing and electrophysiology (Membership of the task force listed in the Appendix): Eur. Heart J. **17**, 334–381 (1996)

Manon-Jensen, T., Kjeld, N.G., Karsdal, M.A.: Collagen-mediated hemostasis. J. Thromb. Haemost. **14**, 438–4482 (2016). https://doi.org/10.1111/jth.13249

Mircea, A.A., Pistritu, D.V., Fortner, A., et al.: Space Travel: The Radiation and Microgravity Effects on the Cardiovascular System. Int. J. Mol. Sci. 25: 11812, 1–19 https://doi.org/10.3390/ijms252111812 (2024)

Mizeva, I., Makovik, I., Dunaev, A., et al.: Analysis of skin blood microflow oscillations in patients with rheumatic diseases. J Biomed Opt **22**, 70501 (2017). https://doi.org/10.1117/1.JBO.22.7.070501

Moore, J.P., Dyson, A., Singer, M., et al.: Microcirculatory dysfunction and resuscitation: why, when, and how. Br J Anaesth **115**, 366–75 (2015). https://doi.org/10.1093/bja/aev163

Navasiolava, N.M., Dignat-George, F., Sabatier, F., et al.: Enforced physical inactivity increases endothelial microparticle levels in healthy volunteers. Am J Physiol Heart Circ Physiol. H248-56 (2010). (2010). 299 https://doi.org/10.1152/ajpheart.00152.2010

Orlov, O.I., Belakovskiy, M.S., Ponomarev, S.A.: A Moon of their own: Luna-2015 female crew experiment. ROOM: Space J. **4** (6), (2015)

Orlov, O.I., Shved, D.M., Gushchin, V.I., et al.: Psychological and physiological aspects of isolation experiments (based on materials from Russian studies). Aerosp. Ecol. Med. **57**, 5–19 (2023). https://doi.org/10.21687/0233-528X-2023-57-5-5-19

Otsuka, K., Cornelissen, G., Furukawa, S., et al.: Unconscious Mind activates central cardiovascular network and promotes adaptation to microgravity possibly anti-aging during 1-year-long spaceflight. Sci. Rep. **12:11862**, 1–13 (2022). https://doi.org/10.1038/s41598-022-14858-8

Pastushkova, L.K., Goncharova, A.G., Kashirina, D.N., et al.: Determination of proteomic markers in dry spots of blood involved in the adaptation of the cardiovascular system in long-term space flights. Part I. Hum. Physiol. **51**, 50–59 (2025). https://doi.org/10.31857/S01311646250106e6

Plomariti, C.E., Frantzidis, C.A., Dimitriadou, C., et al.: Microgravity induced resting state networks and metabolic alterations during sleep onset. Acta Astronaut. **199**, 445–455 (2022). https://doi.org/10.1016/j.actaastro.2022.05.050

Rusanov, V.B., Pastushkova, L.K., Chernikova, A.G., et al.: Relationship of collagen as the component of the extracellular matrix with the mechanisms of autonomic regulation of the cardiovascular system under simulated conditions of long-term isolation. Life Sciences in Space Research **32**, 17–25 (2022). https://doi.org/10.1016/j.lssr.2021.10.002

Segal, S.S.: Regulation of blood flow in the microcirculation. Microcirculation **12**, 33–45 (2005). https://doi.org/10.1080/10739680590895028

Shelhamer, M., Bloomberg, J., LeBlanc, A., et al.: Selected discoveries from human research in space that are relevant to human health on Earth. Npj Microgravity. **6**, 1–5 (2020). https://doi.org/10.1038/s41526-020-0095-y

Sterling, P.: Allostasis: A model of predictive regulation. Physiol. Behav. **106**, 5–15 (2012). https://doi.org/10.1016/j.physbeh.2011.06.004

Tikhomirova, I.A., Baboshina, N.V., Terekhin, S.S.: LDF method capabilities in the estimation of age-related features of the microcirculation system functioning. Regional blood circulation and microcirculation **17**, 80–86 (2018). https://doi.org/10.24884/1682-6655-2018-17-3-80-86

Ushakov, I.B., Gushin, V.I., Larina, I.M., et al.: Content and Structure of Crew's Communicative Behavior and Gonadal Hormone Excretion during LongTerm Chamber Isolation of AllMale International Crew. Human Physiology **38**, 640–648 (2012). https://doi.org/10.1134/S036211971206014X

Xu, Z., Liu, F., Zhang, X., et al.: Development of the Microbial Online Monitoring Module (MOMM) for the Chinese Space Station. Microgravity Sci. Technol. (2024). https://doi.org/10.1007/s12217-024-10125-9

Zhang, S., Lu, W., Wei, Z., Zhang, H.: Air pollution and cardiac arrhythmias: From epidemiological and clinical evidences to cellular electrophysiological mechanisms. Front. Cardiovasc. Med. **8:736151**, 1–19 (2021). https://doi.org/10.3389/fcvm.2021.736151

Zherebtsov, E.A., Zharkikh, E.V., Loktionova, Y.I., et al.: Wireless Dynamic Light Scattering Sensors Detect Microvascular Changes Associated With Ageing and Diabetes. IEEE Trans Biomed Eng **70**, 3073–3081 (2023). https://doi.org/10.1109/TBME.2023.3275654