Military Institute of Aviation Medicine

Research Protocol

Evaluation of a prototype system for generating conditions of orthostatic hypotension and blood pooling in the lower body

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Project summary

The project aims to construct and evaluate a prototype system that enables military pilots to train under conditions of orthostatic hypotension and ischemic hypoxia. Both of these phenomena are experienced by aircraft crews of mainly highly manoeuvrable aircraft, and their syndromes include loss of colour vision, loss of peripheral vision, blackout and finally G-induced loss of consciousness (G-LOC). A motorised tilt table to generate orthostatic (ORTHO) stress combined with an automatically controlled lower body negative pressure (LBNP) chamber to extort pooling of blood in the lower extremities will be developed in order to obtain new knowledge on counteracting the above-mentioned effects and minimising the risk of their occurrence. This will help optimise the selection procedures of candidates with the best physiological predispositions to work as military pilots. The system will be equipped with modules for monitoring biomedical parameters of a subject, including cerebral oxygenation, which will ensure their safety and provide a source of data for performing advanced analyses. The ORTHO-LBNP system will be subjected to comprehensive laboratory tests. After a successful testing, a research protocol will be developed and a pilot study will be carried out involving pilots and/or cadets of the Polish Air Force Academy. It is anticipated that new indicators will be proposed as a result of the pilot study to enable an objective assessment of the predispositions to pursue a military pilot career. The prototype system developed within the project will also be easily adaptable to the needs of clinical and sports medicine as well as rehabilitation. As an output of the project realisation, the ORTO-LBNP system will be developed at technology readiness level 9 and presented to the scientific community in the form of a series of papers that will report on the results of the system designing phase and the pilot study.

General information

Protocol Title

Evaluation of a prototype system for generating conditions of orthostatic hypotension and blood pooling in the lower body

Short title

Evaluation of the ORTHO-LBNP system

Acronym

ORTHO-LBNP

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Rationale & background information

A number of cardiovascular disorders are observed when human body is subjected to accelerations other than the gravity of Earth. Although the first consideration on the medical aspects of the influence of the variable gravitational field date back to 1818 [1], only the rapid development of human centrifuges, tilt tables and under- or overpressure chambers in the 1960s allowed for controlling the gravitational stimuli quantitatively [2]-[5]. Accelerations directed from head to feet ($+G_z$) and accelerations acting oppositely ($-G_z$) have been of particular interest to space and aviation medicine. In the first case, blood moves toward the lower extremities and its drain from the brain may cause oxygen deficiency leading in sequence to greyout, tunnel vision, blackout, and G-induced loss of consciousness (G-LOC) [6]. The adverse symptoms of $+G_z$ acceleration are additionally intensified if the positive stimulus is preceded by $-G_z$ acceleration, i.e., a push-pull effect occurs [7]. The literature explains this increased regulatory response through the significant contribution of sympathetic activity [8]. A list of states deviating from the Earthly gravity is complemented by weightlessness and microgravity, i.e., zero- and near zero-gravity states, respectively. These aspects are mainly researched in the context of space missions during which, promptly upon entering weightlessness, blood shifts toward the head [9]. The cardiovascular system adapts to the new conditions after a time [10], however blood content in the lower part of the body remains unnaturally low and long-term stay in space impairs vestibulo-cardiovascular reflex [11] and leads to, e.g., a change in heart shape and loss of heart muscle mass [12]. Returns from space missions are also aggressive for the body due to symptoms accompanying them, such as orthostatic intolerance, hypotension, dizziness, and syncope [13]. For the above-mentioned reasons, methods for increasing the body tolerance to $+G_z$ and $-G_z$ accelerations and for counteracting the disadvantageous effects of weightlessness are of fundamental meaning in space and aviation medicine.

In general, three methods for real or simulated changing direction and value of the gravity field vector are used:
- centrifugation,
- head up tilt (HUT) and head down tilt (HDT) tests,
- lower body negative pressure (LBNP) and lower body positive pressure (LBPP) tests.

Modern human centrifuges enable for mapping acceleration profiles that reflect flight conditions with great accuracy, and the pilot is subjected to real accelerations. Although the centrifuge is recognised as the best flight simulator, high costs of its construction, operation and maintenance have resulted in searching for alternatives. One of them is a tilt table. This device of modest complexity offers a generation of stimuli in the range of -1 g (tilt of -90°, HDT) to 1 g (tilt of +90°, HUT) in the G_z axis. Despite this limitation, even weak stimuli below 1 g in the G_z axis (+1 G_z, in short) trigger a series of reflex reactions whose monitoring allows for assessing the efficiency of the cardiovascular regulatory mechanisms. On the other hand, placing the lower body of the pilot (usually from the waist area down) in an underpressure chamber simulates cardiovascular effects corresponding to stimuli greater than +1 G_z. Some authors report on supine LBNP at -50 mmHg (millimetre of mercury), which induced the hemodynamic response similar to that observed at an acceleration value of +2 G_z [14]. To simulate +2 G_z heart rate (HR) effects in weightlessness, an increase in LBNP to -90 mmHg is required [15]. Other authors attempt to prove that the LBNP test can be a more effective and practical stimulus than centrifugation [16].

The underpressure chamber is often placed on the tilt table in order to strengthen the $+G_z$ stimulus by using LBNP and moving the pilot from supine to vertical position simultaneously. Moreover, this configuration allows for achieving the push-pull effect when the LBNP and/or HUT exposures are preceded by a HDT try. Similarly to the HDT test, the LBPP technique aims to reverse or prevent the effects of orthostatic hypotension. It is however much less commonly used, mainly due to problems met when designing one device purposed for generating positive and negative pressures.

The Military Institute of Aviation Medicine is the only institution in Poland, where candidates for military aviation are verified for their physiological predispositions. They have to meet two main criteria to get the highest health category that predisposes them for training on highly manoeuvrable aircraft. One of them is to obtain the right result of medical and psychological tests, whereas the other criterion is to withstand a linearly increasing acceleration (0.1 G_z/s) up to a value of +5.7 G_z, generated by the human centrifuge available at the institute. In order to verify the possibility of performing selection procedures with a limited outlay, we have developed the ORTHO-LBNP system, i.e., a prototype device consisting of the tilt table to generate orthostatic stress and the underpressure chamber to extort pooling of blood in the lower extremities, as during $+G_z$ accelerations. Although typical values of LBNP do not descent below -100 mmHg, i.e., it would be difficult to achieve of effects corresponding to an acceleration greater than +4 G_z, a properly matched tilt and LBNP profiles can generate physiological disorders at a level sufficient to evaluate the subject's resistance to accelerations or to develop the ability to adapt variable gravitational stimuli.

Study goals and objectives

The objectives of the pilot study can be summarised as follows:

1. Testing the prototype device with participation of humans, where the result measures relate both to feasibility and health outcomes.
2. Checking the system dynamics and verifying how faithfully the system maps the pre-programmed tilt and LBNP profiles.
3. Verifying the signal quality and analysing changes in basic physiological parameters when applying a sequence of the pre-programmed tilt and LBNP profiles.
4. Verifying if new indicators can be proposed for an objectivised assessment of the physiological predispositions of candidates for military aviation.

Study Design

The **pilot study** consists of two research scenarios, in which two different sequences of the interventions taking the form of the pre-programmed tilt and LBNP profiles are to be investigated. The two study scenarios are designed based on the knowledge and experience of the investigators in the fields of examinations of military pilots in real and simulated conditions [17],[18].

Scenario I is designed to initially verify the potential impact of the prototype system on the human body. For this purpose, only basic tilt and LBNP stimuli of relatively slowly increasing intensities will be used, and the group of subjects will include only subjects with flight experience. Up to 20 PAFA cadets shortly before graduation, including women and men, will

be involved in the pilot study (experimental arm 1). The subjects will be healthy, aged between 20 and 30 years old. Scenario I will take almost 24 min.

Scenario II is to compare subjects with and without flight experience using rapid tilt and LBNP stimuli as well as a push-pull stimulus. Up to 30 subjects including up to 15 pilots, i.e., flight school adepts shortly after graduation and/or PAFA cadets shortly before graduation, and up to 15 students of the Aviation High School in Dęblin, Poland, including women and men will be involved in the study (experimental arm 2). The subjects will be healthy, aged between 18 and 30 years old. The students of the Aviation High School will participate in the study as a reference group, without flight experience. Scenario II will take 16 min.

Methodology

Prototype system

The prototype of the ORTHO-LBNP system comprises a tilt table, LBNP chamber and medical monitoring subsystem.

Tilt table

The tilt table is placed on two axes terminated on both sides with guide blocks. One of the axes cooperates with a horizontal rail, whereas the other is associated with a vertical rail. The vertically moved guide blocks are driven by a rotary engine, and the horizontally moved guide blocks support the tilt table. The tilt table and thus the subject move around a variable axis of rotation. As shown in Fig. 1, the subject's body slidingly moves in the head-to-feet axis while changing mainly the level of the upper part of the body, both in HUT and HDT tests. Trajectories of three human body characteristic points, i.e., head, waist and feet, during HUT and HDT tests are illustrated by the red and blue solid lines, respectively. Additionally, displacements of the guide blocks on the horizontal and vertical rails are marked with the white and black dotted lines, respectively. Such a movement of the subject lying on the tilt table can, to some extent, simulate flight conditions at a relatively low technical complexity and average costs. This drive subsystem has been registered in the Patent Office of the Republic of Poland [19]. The tilt table meets the following requirements:

- range of tilt angles: -45° to +80°,
- rate of tilt changes: up to 45°/s.

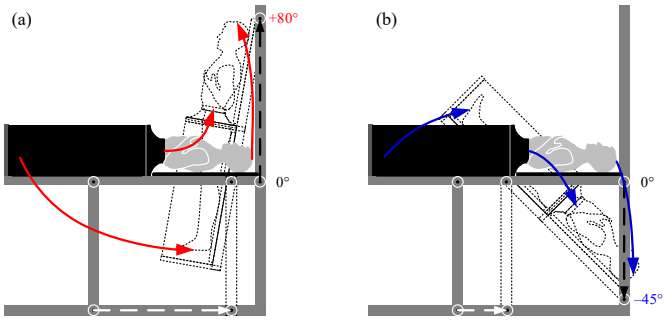

Fig. 1. Trajectories of the body on the tilt table during (a) HUT and (b) HDT tests.

LBNP chamber

Initially, we considered the use of a buffer tank between the underpressure chamber and a compressor or vacuum pump to generate negative pressure, as shown in Fig. 2 (dotted line). This required applying controllable valves between the buffer tank and the underpressure

chamber, and a safety valve to reduce pressure in the tank. The compressor was to achieve a much greater negative pressure in the buffer tank than required in the underpressure chamber. In this way a low–flow compressor could be used to reduce pressure in the chamber at the required change rate. Nevertheless, the constructors decided to use only elements that meet the definition of low–pressure equipment according to Directive 2014/68/EU relating to the making available on the market of pressure equipment. Although this required the use of a high–flow compressor to achieve an appropriate pressure dynamics in the chamber, the subsystem for generating underpressure was simplified by eliminating the buffer tank (Fig. 2, solid line). Additionally, the maximum negative pressure achieved by the compressor can be lower than that in the case of a compressor operating in the configuration with the buffer tank. The LBNP chamber is based on an aluminium frame with thermoformed polycarbonate sheet. As a result of numerical simulations, the maps of equivalent stresses and total displacements for particular segments of the chamber, shown in Fig. 3, were obtained. The LBNP chamber meets the requirements as follows:

- range of generated underpressure: 0 to -100 mmHg,
- rate of underpressure changes: up to 20 mmHg/s.

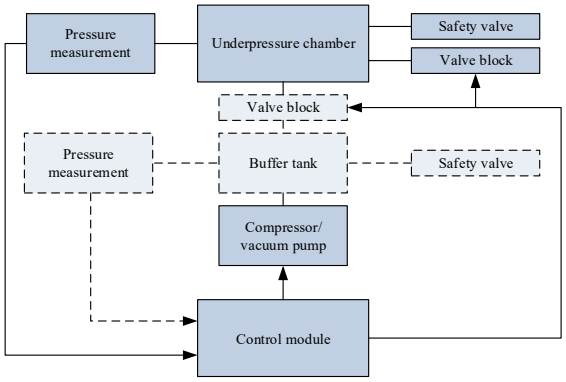

Fig. 2. Pneumatic subsystem for generating underpressure in the LBNP chamber.

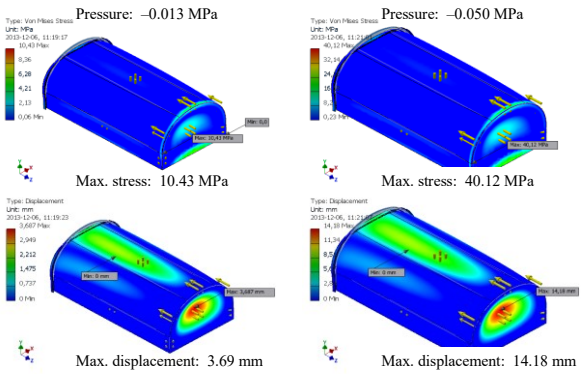

Fig. 3. Strength analysis of the LBNP chamber.

The tilt table and LBNP chamber underwent tests for compatibility with the harmonised standards in regards to machinery Directive 2006/42/EC, and hence these two mechanical subsystems have been CE marked. Moreover, the safety of the prototype system has been confirmed by the positive results of laboratory tests carried out with respect to Directive 93/42/EEC concerning medical devices.

Physiological monitoring

A subsystem for monitoring physiological parameters in subjects undergoing tilt and underpressure tests is necessary to carry out examinations safely and to classify subjects

reliably. The constructors decided to build their own measurement subsystem where all the medical recorders in the form of modules were integrated in electromagnetically (EM) shielded enclosures to which the wires from the electrodes and sensors located on the subject's body were connected as in modern operating tables. Fig. 4 (a) shows the general configuration of the subsystem that consists of modules for the following types of diagnostics: ECG, pulse oximetry (POx), electromyography (EMG), skin conductance level (SCL), NIBP, body temperature (TEMP), impedance reography (REO), electroencefalography (EEG), capnography (CAPNO), near infrared spectroscopy (NIRS), and continuous non-invasive arterial pressure (CNAP). The modules for measuring ECG, EMG, SCL, TEMP, REO, and EEG were developed entirely by the engineering team, whereas the POx (WW3711 by Smith Medical), NIBP (Advantage Mini by SunTech Medical), CAPNO (miniMediCO2 by Oridion Medical), CNAP (CNAP by CNSystems Medizintechnik AG), and NIRS (7610 OEM by Nonin) modules were built on the basis of commercially available certified OEM solutions. In addition to the commercial off-the-shelf 2-channel NIRS device, we used an in-house-designed 6-channel module to record oxygenation changes in the left and right frontal lobe, motor cortex, and visual cortex. All the modules were connected to the operator's station and the control module via the data hub. The module set and data hub were closed in a propacPRO series EM shielded enclosure by Schroff (Fig. 4 (b)), but the in-house-designed NIRS module was enclosed separately in another propacPRO housing due to its size (Fig. 4 (c)). The medical monitoring subsystem has been certified with a CE marking indicating conformity with the standards harmonised with Directive 93/42/EEC.

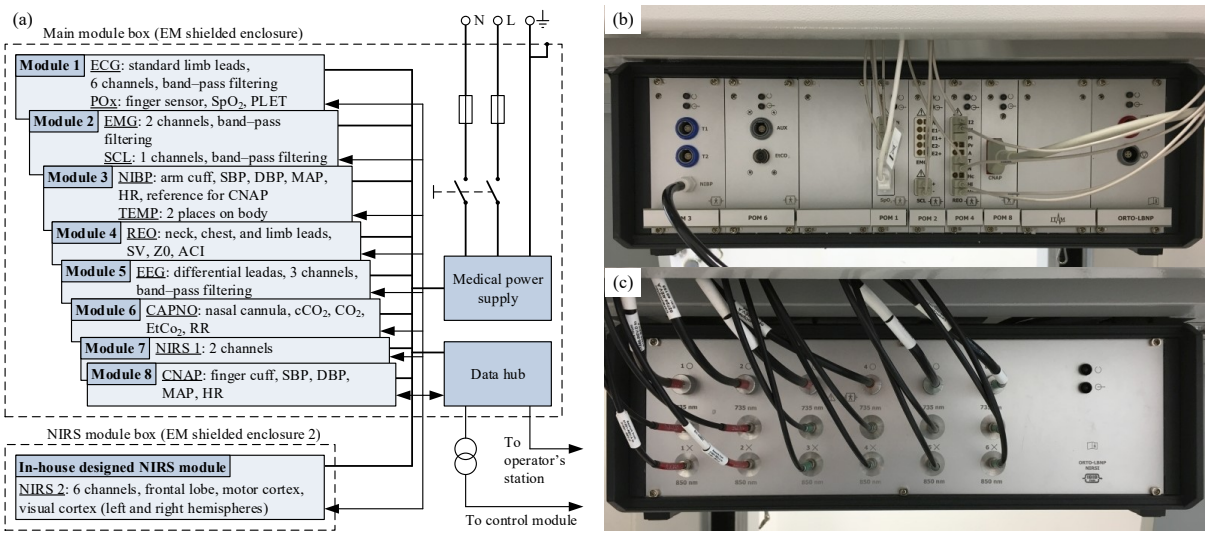

Fig. 4. Medical monitoring subsystem: the (a) block diagram, (b) main module box by the Institute of Medical Technology and Equipment, Poland, (c) in-house-designed NIRS module box by the Nałęcz Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences.

Software

A computer application for controlling the tilt table and LBNP chamber, as well as receiving, analysing and presenting data from the medical modules during examination was developed during construction of the prototype system. The software runs on the Microsoft .Net Framework 4.0 platform. It was prepared in the C # language using the Visual Studio environment. The source code was developed according to the applicable design principles and software engineering principles. A set of tests for the individual software units and integration tests were also prepared. Similar to the medical monitoring subsystem, the computer

application complies with the requirements of the standards harmonised with Directive 93/42/EEC and has been certified with a CE marking.

The prototype system developed at technology readiness level 9 was deployed in a room with medical approvals, and prepared for pilot-based studies. A photograph of a subject being examined with the prototype of the ORTHO-LBNP system is shown in Fig. 5 (a). A neoprene skirt similar to those used in kayak sports was applied to seal the space between the subject and the edge of the LBNP chamber. The sealing skirt was customised by the manufacturer so that two ropes can be attached to it to prevent the skirt from sliding off the hips when negative pressure is applied. The ropes were fastened on the other side to the stands mounted at the head of the table. For a continuous recording of arterial pressure acquired from the subject's finger at the heart level, an adjustable handrest was designed and installed on top of the LBNP chamber.

A unique feature of the prototype system is the ability to carry out experiments with a saddle on which the patient is placed for minimising the impact of the footboard (Fig. 5 (b)) on the subject's legs. In this way some researchers tried to reduce the leg muscle tension and weaken the blood pushing out toward the upper part of the body [20]-[22]. Thus the seat may intensify the effect of blood pooling in the lower extremities and we decided that the prototype system would be equipped with a removable saddle as an option for research applications, as shown in Fig. 5 (c).

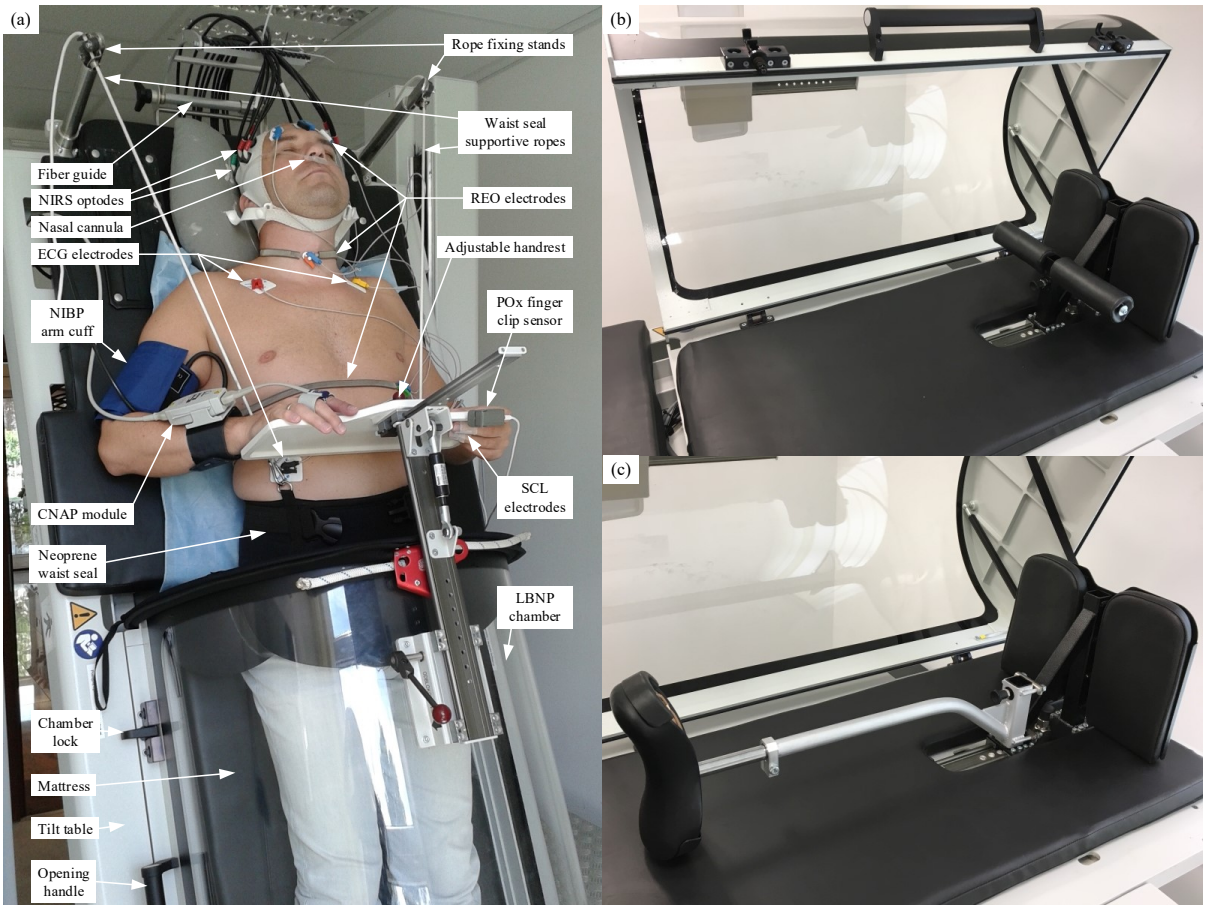

Fig. 5. Photographs of the prototype system: a (a) subject during an examination, the (b) open LBNP chamber with the footboard, (c) optionally mounted saddle.

Research scenarios

Scenario I

Scenario I will be composed of seven phases, shown in Fig. 6, which can be characterised as: (1) 300-s check before the stimuli, (2) LBNP is applied stepwise with 11.1 mmHg/15 s decrement to -100 mmHg, and then this value is sustained for 120 s, (3) 180-second phase of rest between stimuli, (4) 75°-HUT (5°/s) for 120 s after a 15-s reversing of the gravity vector (-30°), (5) 180-second phase of rest between stimuli, (6) 75°-HUT (5°/s) accompanied by an exposure to an LBNP of -60 mmHg increased linearly by -4 mmHg/s, and then this value is sustained for 120 s during HUT, and (7) 120-s check after the stimuli.

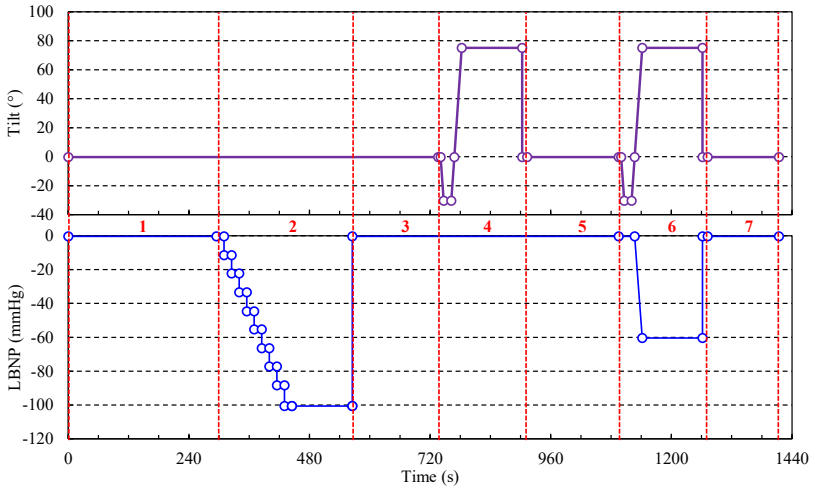

Fig. 6. Tilt and LBNP profiles in 24-min Scenario I.

Scenario II

Scenario II will be composed of seven phases, shown in Fig. 7, which can be characterised as: (1) 120-s check before the stimuli, (2) 75°-HUT (45°/s) for 60 s after a 3-s reversing of the gravity vector (-30°), (3) 180-second phase of rest between stimuli, (4) LBNP decreases linearly by -20 mmHg/s to -100 mmHg, and then this value is sustained for 60 s, (5) 180-second phase of rest between stimuli, (6) push-pull, i.e., 3 × 75°-HUT (45°/s) preceded by -30°-HDT (45°/s) and accompanied by an exposure to an LBNP of -60 mmHg decreased linearly by -20 mmHg/s, and then this value is sustained for 30 s during HUT, and (7) 120-s check after the stimuli.

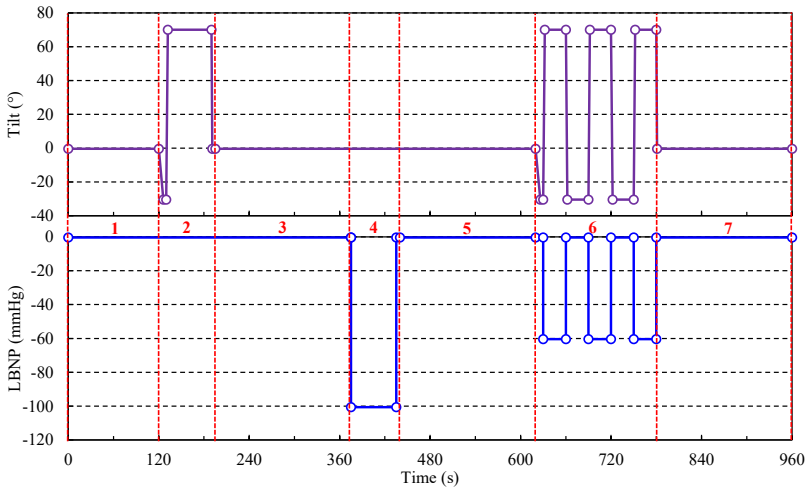

Fig. 7. Tilt and LBNP profiles in 16-min Scenario II.

The pilot study will be carried out in an isolated room in the presence of a physician (physiologist), a paramedic and an ORTHO-LBNP system operator. The paramedic will prepare the subject for the study by placing on his/her body electrodes and measuring sensors that will be removed after completion of the study. The subject will be asked to close his/her eyes during the tests and to place his/her hands on the rest. In order to cause the least disturbance, no conversation will be held with the subject. Only if disturbing symptoms will occur, will the subject immediately report this to the personnel. The physician will systematically be observing the subject's cardiogram, his/her HR, CNAP wave, and systolic and diastolic blood pressure (SBP and DBP, respectively) in comparison with the changing tilt of the table and negative pressure in the chamber. Any time, at the request of the subject or on the instruction of the doctor, the operator will interrupt the tests. The tilt table then will return to the Trendelenburg position if interruption occur during HUT and/or LBNP stimuli, or horizontal position if interruption occur during HDT stimulus. At the same time atmospheric pressure will be resumed in the chamber.

Safety Considerations

The subjects will be informed of possible presyncope symptoms that may occur during the tilt and/or LBNP exposure, with an emphasis on the prompt notification of any symptoms. Prior to the exposure, a shortened medical survey will be performed, including a subjective examination for possible contraindications to the exposure, and a physical examination, i.e., RR and HR measurements in sitting and standing positions. Once the subject is placed in the LBNP chamber, their resting ECG as well as SBP and DBP will be assessed.

Both tilt and LBNP tests are relatively safe, but complications in the form of ventricular arrhythmias or asystole are known. Therefore, at the time of the study, the presence of trained medical personnel, consisting of a physician and paramedic, shall be provided. The following rescue equipment will be available:

1. Ambu self-inflating bag with connector to supply oxygen.
2. Oxygen cylinder with reducer. Check the filling status before exposure!
3. Automatic defibrillator. Check the battery charge before exposure!
4. Anti-shock kit in accordance with the Executive Regulation of the Minister of Health of 24 September 2013 on the guaranteed benefits in the area of primary healthcare (Journal of Laws, 2013, item 1248) and Law of 6 September 2001 - Pharmaceutical Law (Journal of Laws, 45, 2008, item 271) with amendments. The detailed composition of the anti-shock kit is presented in **Appendix A** to this research protocol.

If presyncope syndromes are present, immediately stop the HUT and/or LBNP exposition and move the tilt table to the Trendelenburg position (tilt angle of -16°). There is a difference in the way of handling push-pull simulations. The procedure depends on the study phase. For $+G_z$ exposures, i.e., HUT and/or LBNP, immediately stop the LBNP exposure (if used) and move the tilt table to the Trendelenburg position. In the event of any feeling of discomfort by the subject during $-G_z$ exposures, i.e., HTD, the orthostatic exposition should be discontinued and returned to the horizontal position of the tilt table (tilt angle of 0°).

In case of asystole or ventricular arrhythmias in the form of ventricular tachycardia or ventricular fibrillation, the resuscitation procedure should be implemented in accordance with the adult advanced life support (ALC) algorithm:

1. Check whether the victim reacts, whether breathing or not, or does not have single sighs.

2. Inform the MIAM resuscitation team at the Intensive Care Unit - tel. 621-852-654.
3. Start a cardiopulmonary resuscitation according to scheme 30:2, i.e., provide 30 chest compressions, followed by two breaths.
4. Supply oxygen to the self-inflating bag used for resuscitation.
5. Connect the defibrillator/monitor, minimise resuscitation intervals.
6. Rate the heart rhythm.
7. Perform defibrillation if there is a ventricular fibrillation (VF) or ventricular tachycardia (VT) without pulse. Follow the procedure given by the automatic defibrillator.
8. Immediately take cardiopulmonary resuscitation (CPR) for 2 minutes, minimise resuscitation intervals.
9. Rate the heart rhythm, continue ALC.

Follow-Up

After the study, on the same day, it is advisable not to drive or fly an aircraft.

Data Management

MIAM is both a research institute and medical centre, where data management and information security are provided in accordance with the ISO IEC 27001 standard. A copy of the certificate is included as **Appendix B**.

Statistical Analysis Plan

The statistical analysis of the results will be performed in two aspects:

1. Differentiation of the study phases (scenario I).
   The statistical analysis will be directed toward estimating how separate tilt and LBNP stimuli and the complex stimulus affect basic physiological parameters, i.e., HR, inter-beat interval (IBI), SBP, DBP, mean arterial pressure (MAP), stroke volume (SV), cardiac output (CO), left ventricular ejection time (LVET), rate pressure product (RPP), and total peripheral resistance (TPR), calculated using the ECG and CNAP signals. The mean values of the individual parameters for the test group (experimental arm 1), along with standard deviations and standard errors, will be determined for each experiment phase, and their changes will be described in relation to the check before the stimuli (phase 1). Finally, significances of these changes will be shown.

2. Differentiation of the study phases and differentiation of subjects with various level of flight experience (scenario II).
   The statistical analysis will be directed toward estimating how separate tilt and LBNP stimuli and the combined stimulus as well as the level of flight experience affect HR, IBI, SBP, DBP, MAP, SV, CO, LVET, RPP, and TPR, calculated using the ECG and CNAP signals, base transthoracic impedance (Z0_T), first derivative of transthoracic impedance (dZ/dt_T), base transcephalic impedance (Z0_H), and first derivative of transcephalic impedance (dZ/dt_H), calculated using the REO signals, changes in oxygenated haemoglobin (ΔC_HbO2), changes in deoxygenated haemoglobin (ΔC_Hb), and changes in total haemoglobin (ΔC_tot), calculated using NIRS signals. The mean values of the

individual parameters for the test group (experimental arm 2), along with standard deviations and standard errors, will be determined for each experiment phase, and their changes will be described in relation to the initial level in phase 1. Additionally, descriptive statistics of the above-mentioned physiological parameters obtained by the subjects with flight experience in relation to the parameters obtained by the subjects without flight experience, will be performed Finally, significances of changes in physiological parameters along with the subsequent phase of the research work and the level of flight experience will be presented.

We do not have a preferred statistical method at the time of preparing the research protocol and planning the pilot study. However, we expect negative results of the normal distribution test and hence the use of nonparametric statistical tests, e.g., the Friedman-Kendall analysis of variance for multiple dependent samples. A more detailed description of the used statistical analysis and level of significance will be included in publications, and the PRS record will be complemented with the results.

Quality Assurance

MIAM has a quality management certificate based on the ISO 9001:2008 and AQAP 2120:2009 requirements. Moreover, high quality of the research carried out at the institute has been confirmed by the certificates issued by the US Air Force in the following areas:
- aerospace physiology and centrifuge training program,
- acceleration physiology and centrifuge training program.

Copies of the certificates are included as **Appendix B**.

Expected Outcomes of the Study

During the implementation of both research scenarios, all signals/parameters that can be acquired by the medical monitoring subsystem will be recorded. However, in scenario I the main emphasis will be placed on the analysis of basic physiological parameters, i.e., HR, inter-beat interval (IBI), SBP, DBP, mean arterial pressure (MAP), stroke volume (SV), cardiac output (CO), left ventricular ejection time (LVET), rate pressure product (RPP), and total peripheral resistance (TPR), calculated using the ECG and CNAP signals. The latest literature shows that the analysis of basic physiological parameters, e.g., heart rhythm and blood pressure, enables for predicting orthostatic hypotension [23] and reveals precursory signs of syncope [24]. Our intention is to verify the behaviour of a group of cadets experiencing accelerations on a regular basis who are subject to tests in a device of a novel design. We expect that a stronger stimulus will cause greater changes in the values of the analysed physiological parameters. Among the stimuli used, the strongest one should be HUT accompanied by LBNP. The analysis should indicate these physiological parameters that should be taken into account in the development of an orthostatic tolerance index (OTI).

The results of scenario II will be focused not only on the impact of the stimuli, but will also be analysed in terms of the distinguishing of subjects with different level of flight experience and quantifying an examined person's propensity to endure gravitational stimuli. Both analysis of basic physiological parameters as well as analysis of indices determining the level of oxygenation of brain areas acquired with the in-house-designed NIRS module will be

performed. It is expected that greater changes in brain oxygenation indices will be seen in the subjects without flight experience than in active pilots that have undergone a training improving their G-tolerance.

We anticipate that new indicators will be proposed to enable an objective assessment of the predispositions to pursue a military pilot career. Finally, this should make the selection procedures in military aviation easier.

At least two manuscripts, one containing the results of scenario I, the other containing the results of scenario II, will be submitted for publication.

Dissemination of Results and Publication Policy

The results will be first reported via the National Centre of Research and Development, Poland, to the Ministry of National Defence, Poland. The Ministry will decide whether to implement the ORTHO-LBNP system into the selection process of candidates for military pilots.

The publications will be prepared under the leadership of the PI. The PI decides on the author lists. Only persons who gave the conception of the prototype system, modelled the tilt table and LBNP chamber, designed and constructed the prototype system, coordinated certification procedures, programmed the tilt and LBNP profiles, designed the experimental protocol, coordinated the pilot study, processed data for analysis, analysed and verified data, and interpreted the results, can be included on the author lists. The person who contributes the most to the preparation of the manuscript will be its first author. If the PI is not the author of the largest contribution, he will be acknowledged as the last author of the article.

All authors will review the manuscripts and accept their final version.

Duration of the Project

Duration of the project is December 2012 - February 2018.

Realisation of the research scenarios is scheduled for February 2017 - February 2018.

Problems Anticipated

A comprehensive risk analysis has been developed for the project, identifying the following hazard areas:

1. Energy threats (39 risks).
2. Biological and chemical hazards (7 risks).
3. Environmental hazards (8 risks).
4. Risks arising from the release of energy, substances and the selection of subassemblies (8 risks).
5. Risks associated with the use of the product (27 risks).
6. Risks related to usability (16 risks).
7. Hazards of damage and malfunction (11 risks).
8. Risks associated with embedded software (8 risks).
9. Risks associated with SOUP software (2 risks).
10. Risks associated with PC software (7 risks).

Each of the identified risks can be minimized to an acceptable level. None of them is a risk determined as certain.

The risk analysis is not part of this document due to its extensiveness.

Project Management

The project is managed in accordance with the PRINCE2 methodology. The PI manages the Team Leaders who come from the member institutions implementing the project listed in the General Information section. The PI shall consult and report the results of the project to the Steering Committee, in which each of the member institutions has one representative.

Ethics

Tilt and LBNP test are recognised as relatively safe interventions, however ventricular arrhythmias or asystole can appear. For decades, research works involving military pilots have been conducted at MIAM. Most of these studies have been interfered with the cardiovascular system to a greater or lesser extent. Therefore, the institute has qualified personnel to conduct such a research, an advanced rescue team and the ethics committee that deals with studies in real or simulated conditions.

Potential subjects will be informed on the study at least 30 days before the planned study. Those who are initially interested in the study participation will receive a copy of the research protocol for acquainting. They should decide at least 15 days before the beginning of the planned study and inform the PI or a study coordinator appointed by the PI. Just before the study, the subjects will receive two copies of the informed consent form to acquaint and sign. One of the signed copies is for the subject and the other is for the sponsor.

Informed Consent Forms

A copy of the informed consent form in English is included as **Appendix C**.

Literature

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Budget

The project is supported by the resources of the National Centre of Research and Development (NCRD), Poland, within the framework of the Program for National Defence and Security.

Information on the budget level is not available due to a military character of the project.

Other support for the Project

No other funds.

Collaboration with other scientists or research institutions

Medical University of Warsaw
1. Maciej Śmietanowski, M.D., Ph.D. (physiologist)
2. Liana Puchalska, M.D., Ph.D. (physiologist)

Links to other projects

ID	Project No.	Title	Source of funding	Duration	Publications
1.	03/WNiI/2007/IWSZ	Improvement of examinations in real flight conditions of physiological and psychological parameters in cadets and pilots retrained on new types of aircraft for the assessment of environment and training progress	Ministry of National Defence, Poland	2007–2013	1. DOI: 10.3357/AMHP.4087.2015

Curriculum Vitae of investigators

PI's Curriculum Vitae

Personal information

Forename and family name:	Łukasz Dziuda
Date of birth:	November 21, 1976
Nationality:	Polish
ORCID:	0000-0003-1816-4604
URL for web site:	http://www.wiml.waw.pl/?q=pl/Lukasz_Dziuda https://www.researchgate.net/profile/Lukasz_Dziuda

Education

2014	D.Sc.:	Nałęcz Institute of Biocybernetics and Biomedical Engineering (IBBE) of the Polish Academy of Sciences (PAS), Poland
2007	Ph.D.:	Department of Electronic and Electrical Engineering, University of Strathclyde, UK Supervisor: Professor Sir Jim McDonald, BSc, MSc, PhD, DSc, CEng

2000 M.Ss.: Department of Electrical Engineering, Lublin University of Technology, Poland

Current position
2017– Associate Professor, Head of the Department of Flight Simulator Innovations, Military Institute of Aviation Medicine (MIAM), Poland

Previous positions
2015–2016 Associate Professor, Head of the Creative Neuro Science Laboratory (CNS Lab), IBBE PAS, Poland
2013–2014 Research Fellow, Head of the LBNP Laboratory, Technical Department of Aeromedical Research and Flight Simulators, MIAM, Poland
2008–2013 Research Fellow, Leader of the Medical Electronics Group, Department of Aviation Bioengineering, MIAM, Poland
2005–2007 Research Assistant, Leader of the Medical Electronics Group, Department of Aviation Bioengineering, MIAM, Poland
2004 – 2005 Temporary Assistant, Department of Electronic and Electrical Engineering, University of Strathclyde, UK

Fellowships
2000–2004 Academic Visitor, Department of Electronic and Electrical Engineering, University of Strathclyde, UK

Institutional responsibilities
2000– Representative of MIAM, Polish Technological Platform on Photonics, Poland

Commissions of trust
2014– Scientific Council, MIAM, Poland (Deputy Chairman since 2016)
2014– Ethic Committee, MIAM, Poland
2012– Reviewer of Project Applications, National Centre for Research and Development, Poland

Web of Science
h-index 10
Publications: 27
Citations: 168 (without self-citations)

Other
Patents: 3
Scholarship of the Foundation for Polish Science
PRINCE2® Foundation certificate

Other investigators

Military Institute of Aviation Medicine
1. Franciszek W. Skibniewski, Ph.D. (expert in the field of aviation bioengineering)
2. Krzysztof Kowalczuk, M.D., Ph.D. (expert in the field of aviation medicine)
3. Paulina Baran, Ph.D. (psychologist)
4. Mariusz Krej, M.Sc. (programmer)
5. Sylwester Guzowski, M.Sc. (programmer)
6. Marcin Strojek, M.Sc. (paramedic)

Institute of Medical Technology and Equipment
1. Adam Gacek, D.Sc., Ph.D. (biomedical engineer)
2. Aleksander Sobotnicki, M.Sc. (electronic engineer)
3. Mariusz Sobiech, M.Sc. (constructor)

Nałęcz Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences
1. Adam Liebert, Full Professor, D.Sc., Ph.D. (expert in the field of biomedical engineering)
2. Roman Maniewski, Full Professor, D.Sc., Ph.D. (expert in the field of biomedical engineering)
3. Anna Gerega, Ph.D. (constructor)
4. Stanisław Wojtkiewicz, Ph.D. (constructor)
5. Piotr Sawosz, Ph.D. (constructor)

Polish Air Force Academy
1. Jan Rajchel, D.Sc., Ph.D. (pilot)
2. Marek Bylinka, Ph.D. (pilot)
3. Michał Burek, Ph.D. (pilot)

ETC-PZL Aerospace Industries Sp. z o.o.
1. Anna Brzozowska, M. Sc. (constructor)
2. Piotr Kwaśny, M. Sc. (constructor)
3. Janusz Gajda, M. Sc. (constructor)

Research activities of the PI

ID	Project No.	Title	Source of funding	Duration	Involvement
1.	DOBR/0052/R/ID1/2012/03	Development of the ORTHO-LBNP system for research and training of Polish Air Force pilots under conditions of ischemic hypoxia and orthostatic stress	NCRD	2012–2018	60%
2.	PBS3/B9/41/2015	Optoelectronic patient monitoring in magnetic resonance	NCRD	2015–2018	20%
3.	PBS3/B9/29/2015	Detector of early fatigue symptoms as an element of improved driving safety	NCRD	2015–2018	10%
4.	PBS3/B9/37/2015	System of evacuation and rescue of victims in natural disasters	NCRD	2015–2017	10%

Financing and Insurance

All diagnostic surveys and pilot studies performed at MIAM are insured.

Appendix A

List of medicinal products being part of the anti-shock kit, which may be given by a physician

1. Aminophyllinum 0,25 g - 10 amp. a 10 ml.
2. Antazolini hydrochloridum 50 mg/ml - 5 amp. a 2 ml.
3. Aqua pro inj. - 5 amp. a 5 ml.
4. Atropini sulfas 1 mg - 10 amp. a 1 ml.
5. Calcii chloridum or Calcii gluconas - solutions 10% - 10 amp. a 10 ml.
6. Clonazepamum a 1 mg - 10 amp. a 1 ml.
7. Dopamini hydrochloridum 4% - 10 amp. a 5 ml.
8. Epinephrinum a 1 mg - 10 amp. a 1 ml.
9. Furosemidum 20 mg - 5 amp. a 2 ml.
10. Glucosum 40% 2 - 10 amp. a 10 ml.
11. Glyceroli trinitras aerosol - 1 pack.
12. Hydrocortisonum 250 mg - 5 phial a 250 mg + 5 amp. diss. a 2 ml or Methylprednizolonum 40 mg -1 phial a 40 mg + 1 amp. diss., Methylprednizolonum 125 mg - 1 phial a 125 mg + 1 amp. diss., Methylprednizolonum 250 mg - 1 phial a 250 mg + 1 amp. diss., Methylprednizolonum 500 mg - 1 phial a 500 mg + 1 amp. diss., Methylprednizolonum 1000 mg - 1 phial a 1000 mg + 1 amp. diss.
13. Lidocaini hydrochloridum 2 % - 10 amp. a 2 ml.
14. Metamizolum natricum 2,5 g - 5 amp. a 5 ml.
15. Metoprololi tartas 1 mg/ml - 5 amp. a 5 ml.
16. Morphini sulfas 20 mg/1 ml - 2 amp. a 1 ml.
17. Naloxoni hydrochloridum 0,4 mg/1 ml - 10 amp. a 1 ml.
18. Natrii chloridum 0.9% - 10 amp. a 10 ml.
19. Natrii hydrocarbonas 8.4-% solution for intravenous injection - 5 amp. a 20 ml.
20. Salbutamoli sulfas aerosol 100 mcg/dose - 1 pack.
21. Salbutamoli sulfas a 0,5 mg - 10 amp. a 1 ml.
22. Thiethylperazini dimaleas a 6,5 mg/ml - 5 amp. a 2 ml.
23. Tramadoli hydrochloridum 50 mg/ml - 5 amp. a 2 ml.
24. Verapamili hydrochloridum 2,5 mg/ml - 5 amp. a 2 ml.

Infusion fluids:

1. Calcii chloridum + Kalii chloridum + Natrii chloridum (Ringer's fluid) - 1 pack a 250 ml.
2. Glucosum 5 % - 1 pack a 500 ml.
3. Glucosum 10 % - 1 pack a 500 ml.
4. Mannitolum 20 % - 1 pack a 250 ml.
5. Natrii chloridum 0,9 % - 2 pack a 500 ml.

List of medicinal products being part of the anti-shock kit, which may be given by a paramedic

1. Antazolini hydrochloridum 50 mg/ml - 5 amp. a 2 ml.
2. Aqua pro inj. - 5 amp. a 5 ml.
3. Atropini sulfas 1 mg - 10 amp. a 1 ml.
4. Calcii chloridum or Calcii gluconas - solutions 10% - 10 amp. a 10 ml.
5. Hydrocortisonum 250 mg - 5 phial a 250 mg + 5 amp. diss. a 2 ml or Methylprednizolonum 40 mg -1 phial a 40 mg + 1 amp. diss., Methylprednizolonum 125 mg - 1 phial a 125 mg + 1 amp. diss., Methylprednizolonum 250 mg - 1 phial a 250 mg + 1 amp. diss., Methylprednizolonum 500 mg - 1 phial a 500 mg + 1 amp. diss., Methylprednizolonum 1000 mg - 1 phial a 1000 mg + 1 amp. diss.
6. Epinephrinum a 1 mg - 10 amp. a 1 ml.
7. Glucosum 20% - 10 amp. a 10 ml.
8. Natrii chloridum 0.9% - 10 amp. a 10 ml.

Infusion fluids:
1. Calcii chloridum + Kalii chloridum + Natrii chloridum (Ringer's fluid) - 1 pack a 250 ml.
2. Glucosum 5 % - 1 pack a 500 ml.
3. Glucosum 10 % - 1 pack a 500 ml.
4. Natrii chloridum 0,9 % - 2 pack a 500 ml.

Appendix B

(Copies of certificates)

CCJ

CERTYFIKAT

Potwierdza się, że system zarządzania bezpieczeństwem informacji w organizacji

WOJSKOWY INSTYTUT MEDYCYNY LOTNICZEJ

ul. Krasińskiego 54/56, 01-755 Warszawa

spełnia wymagania

ISO/IEC 27001:2013

(ISMS)

Zakres certyfikacji:

Badania lotniczo-lekarskie i medycyny pracy. Szkolenia lotniczo-lekarskie. Sterylizacja narzędzi i materiałów. Diagnostyka laboratoryjna. Zabezpieczenie techniczne badań i szkoleń.

Ocenę wykonano w odniesieniu do Deklaracji Stosowania, wersja 2.0 z dnia 20.07.2015 r.
Spełnienie wymagań ISO/IEC 27001:2013 jest równoznaczne ze spełnieniem wymagań PN-ISO/IEC 27001:2014. Integralną częścią niniejszego certyfikatu jest potwierdzenie, w którym zawarto informacje dotyczące warunków ważności certyfikacji. Dodatkowo informacje na temat ważności certyfikacji można uzyskać telefonicznie/faxem lub na stronie www.ccj.wat.edu.pl
Certyfikat wydano po raz pierwszy: 14.03.2013.
Certyfikat nr 816/I/2015 ważny od 01.10.2015 do 30.09.2018.
Wersja: A, data wydania: 01.10.2015.
WOJSKOWA AKADEMIA TECHNICZNA
ul. gen. Sylwestra Kaliskiego 2, 00-908 Warszawa 49
CENTRUM CERTYFIKACJI JAKOŚCI
ul. Duchnicka 3, 01-796 Warszawa

DR INŻ. WITOLD POKORA

PCA
AC 057
ISMS

CCJ

CERTYFIKAT

Potwierdza się, że system zarządzania jakością w organizacji

WOJSKOWY INSTYTUT MEDYCYNY LOTNICZEJ

ul. Krasińskiego 54/56, 01-755 Warszawa

spełnia wymagania

ISO 9001:2008

Zakres certyfikacji:

Badania lotniczo-lekarskie i medycyny pracy. Szkolenia lotniczo-lekarskie. Sterylizacja narzędzi i materiałów. Diagnostyka laboratoryjna. Zabezpieczenie techniczne badań i szkoleń.

Spełnienie wymagań ISO 9001:2008 jest równoznaczne ze spełnieniem wymagań PN-EN ISO 9001:2009. Informacje na temat ważności certyfikatu zawarte są w potwierdzeniu, na stronie www.ccj.wat.edu.pl oraz można je uzyskać w CCJ.
Certyfikat wydano po raz pierwszy: 08.10.2012.
Certyfikat nr 816/S/2015 ważny od 01.10.2015 do 14.09.2018.
Wersja: B, data wydania: 07.04.2017.

WOJSKOWA AKADEMIA TECHNICZNA
CENTRUM CERTYFIKACJI JAKOŚCI
ul. Gen. Sylwestra Kaliskiego 2, 00-908 Warszawa

DR INŻ. WITOLD POKORA

IAF

PCA
AC 057
QMS

CCJ

CERTYFIKAT

Potwierdza się, że system zarządzania jakością w organizacji

WOJSKOWY INSTYTUT MEDYCYNY LOTNICZEJ

ul. Krasińskiego 54/56, 01-755 Warszawa

spełnia wymagania

AQAP 2120:2009

Zakres certyfikacji:

Badania lotniczo-lekarskie i medycyny pracy. Szkolenia lotniczo-lekarskie. Sterylizacja narzędzi i materiałów. Diagnostyka laboratoryjna. Zabezpieczenie techniczne badań i szkoleń.

Integralną częścią niniejszego certyfikatu jest potwierdzenie, w którym zawarto informacje dotyczące stosowania AQAP zgodnie z wymaganiami STANAG 4107. Dodatkowo informacje na temat ważności certyfikacji można uzyskać telefonicznie/faxem lub na stronie www.ccj.wat.edu.pl
Certyfikat AQAP wydano po raz pierwszy: 01.10.2015.
Certyfikat nr 816/A/2015 ważny od 01.10.2015 do 30.09.2018.
Wersja: A, data wydania: 01.10.2015.

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CENTRUM CERTYFIKACJI JAKOŚCI
ul. Duchnicka 3, 01-796 Warszawa

DR INŻ. WITOLD POKORA

UNITED STATES AIR FORCE

Certificate of Recognition

to

Poland's

Military Institute of Aviation Medicine

Aerospace Physiology and Centrifuge Training Programs

For the period 1 June 2015 through 31 May 2020

DAVID A. WELGE
Lt Col, USAF, BSC, CAsP
Chief, Physiology Program Branch

JOHN A. CHERREY
Brigadier General, USAF
Director, Intelligence, Operations and
Nuclear Integration

UNITED STATES AIR FORCE

Certificate of Recognition

to the

Military Institute of Aviation Medicine

Polish Air Force

Acceleration Physiology and Centrifuge Training Program

For the period 1 November 2012 through 31 October 2017

ANDREW D. WOODROW
Lt Col, USAF, BSC
HQ AETC/A3FM

TIMOTHY M. ZADALIS
Major General, USAF
Director, Intelligence, Operations,
and Nuclear Integration

Appendix C

(Informed consent form in English)

INFORMED CONSENT FORM

Forename and family name, age: ……

Address: ……

Protocol title: Evaluation of a prototype system for generating conditions of orthostatic hypotension and blood pooling in the lower body.

I hereby declare that I have been informed on the purpose of the intended research and the manner in which it is carried out. I understand what it is supposed to be and what my consent is for. I have been informed that I may refuse to participate in the study or withdraw the consent at any time, also during the study.

I express my informed consent to participate in the study, which is described on the back of this form. Additionally, I agree that in the case of accidental detection of irregularities during the study, the information about the need to repeat the case study will be forwarded to the Military Medical Aviation Commission.

I gave this consent in the presence of the witness.

Place and date: .....

....

Subject's signature PI's signature

INFORMATION ON THE STUDY

Protocol title: Evaluation of a prototype system for generating conditions of orthostatic hypotension and blood pooling in the lower body.

Purpose of the study: Checking how the tilt and LBNP stimuli affect the cardiovascular system and cerebral oxygenation.

Study design:
1. Shortened medical survey including a subjective examination for possible contraindications to the tilt and/or LBNP exposures and a physical examination, i.e., respiration rate and heart rate measurements in sitting and standing positions.
2. Study using the ORTHO-LBNP system, i.e., a prototype device consisting of a tilt table to generate orthostatic stress and an underpressure chamber to extort pooling of blood in the lower extremities, as during +Gz accelerations.

Study description:
The study is carried out in an isolated room in the presence of a physician (physiologist), a paramedic and an ORTHO-LBNP system operator. The paramedic prepares the subject for the study by placing on his/her body electrodes and measuring sensors that will be removed after completion of the study. The subject is asked to close his/her eyes during the study and to place his/her hands on the rest. In order to cause the least disturbance, no conversation is held with the subject. Only if disturbing symptoms will occur, will the subject to immediately report this to the personnel. The physician is systematically observing the subject's cardiogram, his/her heart rhythm, continuous blood pressure wave, and systolic and diastolic blood pressure in comparison with the changing tilt of the table and negative pressure in the chamber. Any time, at the request of the subject or on the instruction of the doctor, the operator will interrupt the tests. The tilt table then will return to the Trendelenburg position or horizontal position, depending on the study phase, and atmospheric pressure will be resumed in the chamber.

Additional information:
All devices used in the study meet the applicable safety standards and are approved for testing in humans. A short-term psychological survey with the use of the UWIST Mood Adjective Checklist (UMACL) is allowed to be performed before and after the ORTHO-LBNP exposure. After the study, on the same day, it is advisable not to drive or fly an aircraft.

Place and date: .....

.....
Subject's signature