

The Balneology Research Institute, state enterprise (CZ: Výzkumný ústav balneologický, státní podnik, 1952-1991, abolished 1993) was a research institute of European importance. Since 2011, **the newly established Balneology Research Institute, a public research institution** (hereinafter referred to as BRI) **is its successor** (www.balneologie.eu). Today, BRI has use more than 20 scientific and professional specialists with multi-disciplinary capacity. Its capacity grows every year. The members of the Board and the Supervisory Board of the BRI represent a high scientific and professional level.



The BRI mission is focused on approach of the evidence-based medicine. Clinical evaluation of biomarkers and immunomarkers changes due to the effect of selected procedures is practically not applied in usual spa practice. BRI is only one in the Czech Republic to promote examples of good practice in Europe and Asia in double-blind clinical studies of the effect of peloid or curative mineral water on knee arthrosis. In 2018 we published a successful publication *The Future of Spa Industry*. The publication predicts spa developments in the world, in Europe and in the Czech Republic for the next fifteen years, until 2033. The publication outlines the consequences of the so-called Fourth Industrial Revolution "Industry 4.01" and its Health 4.0 derivative in therapeutic spa. It has excellent reviews of leading Czech and Slovak forecasters.

In April 2019, we signed a Memorandum of Cooperation in research, development and innovation in water therapy in the field of micro and nano bubbles. The partner is the leading European manufacturer Rudolf Koller s.r.o. from the Koller Group, <https://whirl.rkoller.com/>. We are at the beginning of the development of a new treatment technology usable for innovation of balneological procedures. After the initial hesitation of the Czech spa environment, interest in this technology has arose in Marienbad and Franzensbad.

The opening study „Identification of Possibilities and Procedures of Preclinical Analysis and Clinical Evaluation of the MILK Program (BRI, April 2019), is the first result of this collaboration. The study identified micro and nano bubbles (MNBs) as a revolutionary technology that could fundamentally change the world of rehabilitation medicine. The simplified systematic information research describes selected results of research and technical solutions in the world, especially in Europe and USA, which are using technology comparable to Program MILK (PM). The simplified systematic research described selected results of research and technical solutions in the world, especially in Europe and USA, which are using technology comparable to PM. The dynamically growing interest in MNB applications in incredibly different sectors such as wellness, medical treatment, wastewater treatment, veterinary care, washing and washing in personal hygiene, cleaning activities and many others has been described. However, the main interest was focused on the competencies of the Program MILK KOLLER (PMK) competitors. Some of which have excellent results and great prospects. Worldwide development is directed to the use of this technology as a medical device based on clinical trials. The first observation-level clinical investigations (USA, Taiwan, South Korea and other Asian countries) are clearly moving towards this. Rudolf KOLLER Ltd. has a good opportunity to gain a marketing advantage.

The second result of cooperation with Rudolf Koller Ltd. is a case study „**Preclinical Research of Case Reports of the MILK Program**“

Preclinical analysis of PM effect precedes clinical trials, which are more expensive both in time and cost. It has to provide the first basis for the formulation of the methodology and the commissioning of the clinical trial at the medical device level. Based on an updated search and our investigation, the study first briefly described a possible interpretation of the Program MILK device's operation.

- Physical explanation of formation and properties of microbubbles. Different views in the world. The interpretation that characterizes the "microbubble cloud" as dispersed gas particles in an aqueous environment is best suited. It is a form of “wet foam” where the gas content can generally be up to 85% of the total dispersion mixture volume. Physical BRI hypothesis: The microbubble cloud created by the PM device contains dispersion particles in the range of a low dispersion fraction up to 10%. BRI intends to continue its research focused on physical interpretation and is currently looking for the necessary financial resources. The aim is to verify the existing knowledge supplemented by hypothetical opinion in cooperation with an academic workplace equipped with a certified device for the necessary measurement of the dispersion particle size (hereinafter referred to as microbubbles for simplicity) based on measurement of coherent source interference of known wavelength.

- The technical description of the hydromassage bathtub is to be described in the assembly instructions with the illustration of the units: high-pressure pump, compressor, UV disinfection. The operation of the bathtub is described in the Operating Instructions. Both documents were provided by the manufacturer Rudolf Koller sro, where they are available.

- We have formulated a hypothesis of how microbubbles affect the body through a huge area of skin pores - cavitation, thermal effects, mechanical, chemical, etc. PM helps to leach deposits in pores, including microbial agents and toxins. According to the literature, they have a positive charge and thus can interact with the negatively ionized microbubbles that are attracted to them when they enter the pores and sebaceous glands.

The preclinical research of the casuistic effects of PM in the selected six cases examined the tendencies of support the overall feeling of health, respectively. alleviation of disease symptoms, supportive effect in the area of current blood pressure (BP), pulse (P) and changes in heart rate, plus input and output self-assessment of each case. The time of exposure of PM to the measured case in each case was the same in all cases. All case probands were subjected to the procedure every day from 16 to 25 January 2020, so that the time lag between each procedure entry allowed drying, clothing and then the immediate first daily measurement.

Preclinical research met expectation that were based on:

- i. By observing the manufacturer and distributor Rudolf Koller s.r.o. effects on its users and its promotional press and paper materials for PM.
- ii. Data on search results in Medline and Google Scholar databases on the effects of competing technologies. Simplified meta-analysis of clinical observations or preclinical analyzes.

Main preclinical findings:

- No case of deleterious effect on the case study participant was found.
- The treatment with PM should last longer than applied to increase the effect, ie 30 min. daily, at the same water temperature and daily exposure for at least three weeks (eg at a contracted spa treatment facility). It is recommended to review it with context of potential future measurement.
- The hypothesis that PM may have a positive effect on the cardiovascular system was confirmed by a case study. Higher BP has a tendency to decrease (in 4 cases), very slight changes or stagnation in 1 case, one case was characterized by a change in trend from lower BP to higher towards the standard level. The pulse readings showed a tendency to slightly increase the frequency, but a longer measured time (at least 21 days) would be needed to evaluate the pulse.
- PM has a positive effect on the nervous system. In three cases there was a positive effect on the psyche.
- As a secondary benefit for 2 individual cases, warning recommendations for pulse failure control were formulated, which were detected in selected

probands before the measurement started. Recommendations will be discussed separately in the form of information for subsequent targeted examination. One of these cases has already been warned, given the fact that two measurements a day account for nearly 50% of pulse disturbances. Proband knew the problem, but did not find it restrictive. Recommendations for 24-hour Holter ECG for online diagnosis monitoring.

- The PM bath has a general positive effect on the feeling of a slight improvement in physical and mental condition. After an initial 5 days of sleep improvement, sometimes even increased sleepiness, there is a positive adjustment in terms of sleep time and quality.
- The PM bath has a general positive effect on the feeling sustained softening the skin, in one case demonstrated the effect of removing itchiness, respectively to eliminate symptoms prior to the development of varicose ulcer.
- PM bath generally has a positive effect on the feeling of permanent skin softening, in one case it demonstrated the effect of removing itching, respectively elimination of symptoms prior to foot ulcers.

Conclusion

Preclinical analysis of the effect of PM supported the hypothesis whether and partly in which parameters a positive effect on the human body there is. This finding can have a strong impact on the marketing instrument. The current use of microbubble technology in the world is more in the area of wellness (mostly two- and multi-seat whirlpools), but also in the areas of veterinary or even industrial use (sewage treatment plants, etc.). Therapeutic use has so far been rather marginal. This situation has changed in recent years. Supporting application research with the possible use of grants in the Czech Republic and the EU is an opportunity to participate in innovations in rehabilitation and balneological medicine.

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