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INSTITUT INTERNATIONAL DU FROID  
INTERNATIONAL INSTITUTE OF REFRIGERATION

## WHOLE BODY CRYOTHERAPY/ CRYOSTIMULATION



OCTOBER 2020

**39<sup>th</sup> Informatory Note  
on Refrigeration  
Technologies**



**“ The use of  
cryostimulation is growing  
exponentially.  
However, solid scientific  
evidence of its benefits  
remains to be provided. ”**

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## Summary

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Whole-Body Cryotherapy (WBC) and Partial-Body Cryotherapy (PBC) – grouped under the term Cryostimulation – are new techniques consisting in exposing the whole body (head excluded for PBC) to extreme cold for a short period of time (typically 3 minutes at -110 °C).

After exposure, patients experienced decreased soreness, oedema and inflammation, as well as musculoskeletal relaxation and increased range of motion. Cryostimulation is also effective in alleviating symptoms of anxiety and depression and accelerating muscle recovery in athletes.

However, solid scientific evidence of these benefits has yet to be provided. An intensification of research is necessary to identify the key variables inducing the benefits of cryostimulation and to define and adapt treatment protocols (frequency and exposure parameters in particular).

In addition, safety issues related to the use of cryostimulation are essential, in particular the consideration of medical contraindications and physical risks such as anoxia. This also requires certification of the operators and cryogenic devices used.

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*The note was also reviewed by several other experts in this Working Group as well as by Judith Evans (President of IIR Section C), Laurie Huget (Cryogenic Society of America) and other experts on the editorial board of Cold Facts magazine, under the supervision of Jean-Luc Dupont (Head of the Scientific and Technical Information Department). It was proofread by Nathalie de Grissac and designed by Aurélie Durand (IIR head office)*

## Introduction

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The objective of this Informatory Note is to provide general information about cryotherapy, and especially the whole-body (WBC) and the partial-body (PBC) cryotherapy. For ease of reading, the two methods will be grouped in the text under the word “cryostimulation”.

## History

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The effects of cold-water swimming on well-being and pain are well documented [1, 2]. New cryotherapy techniques (WBC, PBC) have recently been developed and consist of exposing the whole body (head included for WBC and excluded for PBC) to extreme cold for a short period [3]. The first device was made in Japan in 1979 by Professor Yamauchi to treat rheumatoid arthritis [3]. WBC was subsequently used in Europe, especially in Germany, Russia, and Poland. Currently, WBC and PBC are used to relieve pain, accelerate recovery after physical exercise and sport and increase well-being and health [3]. According to such potential effects, the use of these techniques presents an exponential development. For the time being, Poland is the only country in the world that has organised the reimbursement of cryotherapy sessions through its social security system for patients suffering from some chronic diseases.

## Basic principle

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Local and systemic cold therapies are widely used to relieve symptoms of various diseases including inflammation, pain, muscle spasms, and swelling, especially chronic inflammatory ones, injuries, and overreaching/overtraining syndrome [4, 5].

Based on the common practice, an individual, minimally dressed (e.g., bathing suit, socks, clogs, headband, and surgical mask to avoid direct inhalation of humid air), is exposed to very low temperatures (-40 to -180 °C) for a short time (1-4 min) in order to induce the expected physiological reactions.

At present, the exposure protocols (temperature vs exposure duration, number, and frequency of sessions) are consensually and empirically defined but are not based on rigorous scientific studies. More specifically, the anthropometrical features of the patient (e.g., body mass index (BMI), fat mass) or the purpose of the session (e.g. well-being, sport recovery, pain removal) are not clearly considered. For example, a generic and typical protocol is “3 minutes at -110 °C”, regardless of the patient and the purpose of the session. Indeed, several studies have applied different protocols, especially in terms of temperature [6].

The basic principle underlying the benefits of cryostimulation in inflammatory syndrome mainly relies on the activation of the nervous system and the direct effects on the inflammatory mediators. Briefly, cryostimulation leads to a peripheral vasoconstriction, a decrease in pro-inflammatory cytokine concentrations and an increase in anti-inflammatory cytokine concentrations in blood [7]. Cryostimulation is also somehow able to mimic physical activity, at least in determining certain molecular changes in a way that is comparable to that observed consequently to physical activity (reviewed in [6]). Particularly, the pulsed and temporarily limited induction of pro-inflammatory cytokines (e.g. IL-1, IL-6) and the induction of irisin expression (a recently discovered myokine produced by the contracting skeletal-muscle and stimulating thermogenesis at the adipose tissue level) suggest that the sympathetic activation induced by extreme cold can elicit such an exercise-mimicking response.

## Expected benefits

The main physiologic effect of cryostimulation is related to the reduction of skin, muscle and core temperature, which reduces cell activity and the need for nutrients and oxygen. Due to the therapeutic effect linked to temperature decline, cryostimulation was used to relieve rheumatoid arthritis symptoms [7]. Following exposure, patients experienced decreased soreness, œdema, and inflammation, as well as musculoskeletal relaxation and increased range of motion [3]. In patients with multiple sclerosis, WBC mitigated oxidative stress [8]. This cold modality was also effective in alleviating symptoms of anxiety and depression [9,10]. These results suggest that cryostimulation could be used as a complementary, non-pharmacological therapy to relieve the symptoms of depression and multiple sclerosis.

Regarding athletic performance, cryostimulation can be effective before exercise, as well as between and after training sessions to accelerate short- and long-term muscle recovery. It is common for athletes, after torn muscles or sprain during the training or game, to undergo cryotherapy exposure to relieve pain [11].

A cryostimulation session performed immediately after physical training can enhance strength recovery, reduce delayed muscle soreness and swelling, improve anti-inflammatory response, reduce the concentration of muscle enzymes in blood related to muscle injury, and improve the quality of sleep [12-18]. Additionally, it has been suggested that daily cryostimulation sessions during weeks of high intensity training can prevent overreaching syndrome [19]. All of these studies indicate that cryostimulation could be used after training sessions or competitions to improve both short- and long-term muscle performance and to induce faster recovery periods.

## Controversies/ Challenges

The main difficulty in the research design for cryostimulation studies is the lack of opportunities for double-blind experiments. Therefore, the randomized control trials that are conducted will never be considered high quality trials and the suspicion of a placebo effect may remain. Some other problems are also present as many biological factors may interact with short and long-term cold-induced physiological adaptations. Among others, body size, body surface area/mass-ratio, fatness, physical fitness, gender, age, state of cold adaptation, health status have been shown to be important factors that may influence the outcome of the studies [3]. Therefore, due to this very large inter-individual biological variation, it is more difficult to determine statistical significance due to the impact of cryostimulation in a series of data unless very stringent inclusion criteria are used and large numbers of volunteers are recruited. Globally, in the scientific literature there are many studies with a limited number of participants, some have problems with procedure standardization. Altogether, in the literature, results are too often divergent and there are nowadays reports expressing that cryostimulation is of no use or even detrimental [20].

It is therefore complicated to have a clear picture of the real impact of cryostimulation. The use of meta-analysis can address this problem when



sufficient data are available and fairly similar investigations have been conducted (even though meta-analysis also has drawbacks). A recent meta-analysis showed positive impacts of the use of cryotherapy/cryostimulation after physical exercise on delayed onset of muscle soreness [16].

Another issue concerns dangerous scientific shortcuts that are sometimes used to propose cryostimulation as a panacea. A recent example involved some cryo-centers claiming that cryotherapy may help obese patients and/or overweight individuals lose weight after irisin (a marker of higher oxidation in adipocyte lipids) was found to be released after exposure in a cryotherapy chamber [6].

## Used technologies

In addition to immersion in ice-cold water, various technologies can be used for WBC/PBC.

### USE OF CRYOGENICS - LIQUEFIED GASES

The use of a liquefied gas (usually liquefied nitrogen, and possibly liquefied air) can be found in so-called cryosaunas (direct injection of cryogenic gas) or in cryochambers (indirect injection) as shown in figures 1 & 2 [21].

Cryosaunas appear to be the simplest equipment, which could explain the success and the wide use of this technology (low investment costs). This type of equipment is used for PBC, the head of the patient remaining outside the equipment so that the person can avoid anoxia due to the vaporized gas. Thus, special care must be taken when using this type of equipment (anoxia, and cold burning of the the patient's skin due to the direct injection of cryogenic gas).

The anoxia concern can be solved by indirect devices, the liquefied gas being injected in the pipes of an adapted heat exchanger, exhausting the vaporized gas outside the equipment (and preferably outside the building). With this type of devices, the atmosphere inside the cryochamber always remains in normal operation and filled with breathable air. This technology makes it possible to have simultaneously one or many patients in the cryochamber. By using two heat exchangers, it also makes it possible to propose a front/pre-chamber at -30/-50 °C where the patients acclimatize for the forthcoming chamber at very low temperature. Anyways, and whatever the technology, the removal of any sweat before entry is mandatory in order to avoid the risks of skin burning and necrosis.

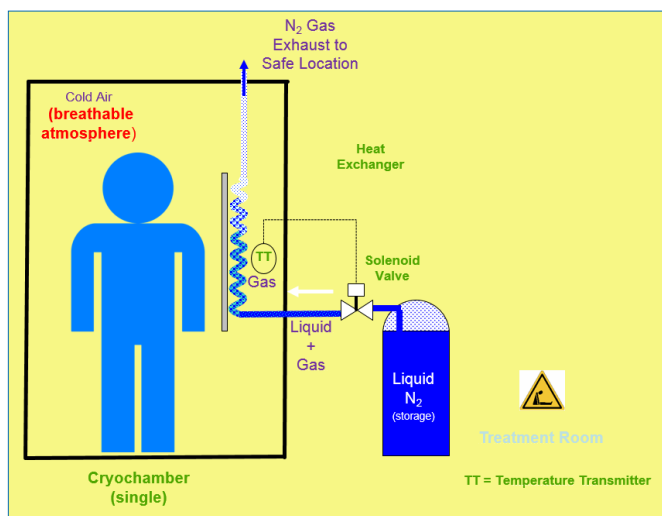
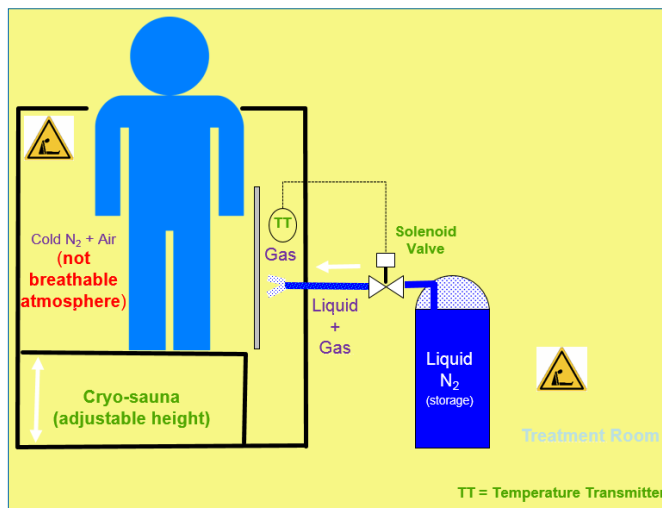


Figure 1

Top: Cryosauna: Principle with liquid N<sub>2</sub> / Direct injection / PBC / Individual

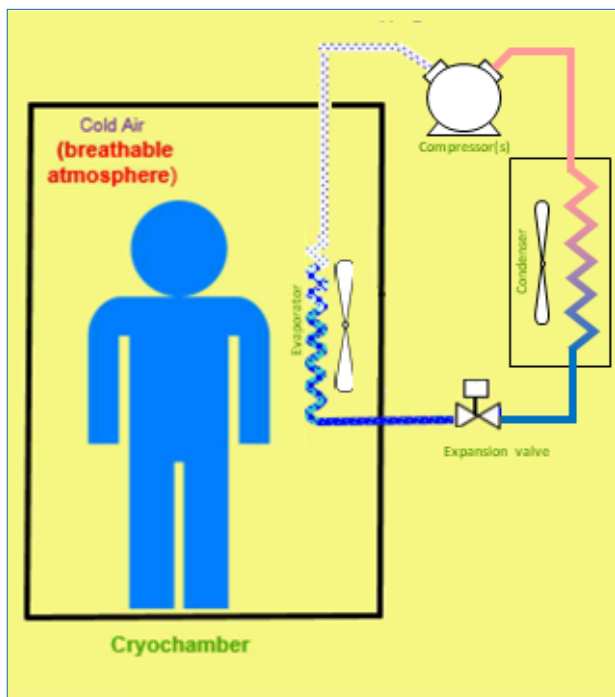
Bottom: Cryochamber: Principle with liquid N<sub>2</sub> / Indirect injection / WBC / Individual or Collective

For these technologies, the mentioned temperature often refers to the temperature of the liquefied gas at the outlet or at the vicinity of the expanding device, explaining the advertised very low temperature values (-110 °C/-180 °C) for cryosaunas. With cryo-chambers, air temperature is usually regulated and can be adjusted to the needs. It is important to emphasize that this equipment mainly operates in natural convection conditions (static cooling), that could reduce the cooling effect of the patient's body.

### USE OF MECHANICAL REFRIGERATION

The use of vapour compression refrigeration cycles is also an interesting option due to low operating cost despite their higher capital cost.

These techniques are easily applied to the front/pre-chamber and main cryochamber adapted for one or many individuals. The refrigeration cycles are traditional low temperature cycles: direct expansion, two step compression (compound compressors) or cascades (two stages, multistage or integrated cascades). For these technologies, the refrigerant remains confined in the refrigeration loop, preventing the problem of breathability of the atmosphere in the cryochamber (figure 2).



**Figure 2**

**Cryochambers: Principle with Mechanical Refrigeration (Single stage) / WBC / Collective**

Classically, these techniques use ventilation devices to activate the cold transfer from the evaporator to the cryochamber. Thus, they work in forced convection conditions, increasing the cooling effect on the patient's body: even if the evaporating temperature of the refrigerant is higher than the temperatures encountered with cryogenic gases (evaporation temperature around  $-50\text{ }^{\circ}\text{C}/-100\text{ }^{\circ}\text{C}$ ), the cold effect on the patient remains as intense – and possibly more effective thanks to ventilation.

Air cycle based on turbo compression of air and its expansion in an adapted device can also be used. In this case, expanded air can reach very low temperatures (down to  $-70\text{ }^{\circ}\text{C}/-110\text{ }^{\circ}\text{C}$ ) and can be directly expanded in the cryochamber.

## Risk assessment

Two categories of risks for the patient must be considered. Minimizing these risks requires some basic rules, such as never performing a cryotherapy session alone, and being assisted by a trained and competent operator.

### Medical contraindication:

Some individuals should refrain from using cryostimulation until evidence of limited risks is provided. For instance, people with serious hypertension, serious cardiopathies, cold allergy, Raynaud syndrome, sickle cell anemia, cryoglobulinemia, claustrophobia, skin problems, frostbites, severe hypothyroid disease should not be exposed to cryostimulation. In some countries, medical check of the subjects who are going to be exposed is compulsory and in some other countries it is not. Also, blood pressure is sometimes measured but there is no agreement on the cut-off values for allowing subjects access the chamber or not. In Poland, the cut-off value is rather strict and subjects over a systolic blood pressure of 130 mmHg (17,332 Pascals) are not allowed to be exposed. Protocols should be defined and validated in order to limit the risks of health problems during and after exposure. Unfortunately, some rare cases with significant health problems occurred during and after exposure [23-24].

### Physical risks:

For cryosaunas, the major risk is the potential problem of anoxia due to the direct use of liquid nitrogen. Even if the head of the patient is not exposed to nitrogen vapor, the unbreathable atmosphere is only a few centimeters below chin level. For this type of equipment, some rare cases of freeze burning of patients have been reported. For all techniques, skin freezing by direct contact with very low temperature metal, alloys and floor should be limited by the wear of adequate equipment (e.g. gloves, socks).

# Conclusion

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More information and data should be available to justify and understand the benefits of cryostimulation. The diversity of the cold chambers used, the various protocols used, the data that have been obtained under very different circumstances retain to provide good robust evidence of the benefits.

Several issues need to be investigated:

- Temperature in the main cold chamber and impact on the subject;
- Dose effects of treatments;
- Safety issues.

Optimal protocols should be defined depending on the exposure, the desired effect, and the patient's characteristics. These issues are urgent and must be worked on rapidly.

In Pubmed, the number of papers concerning WBC and PBC is around 700. This number is globally quite low but interestingly, one third of the articles have been published in the five past years reflecting growing understanding of the importance of the field. With the help of the IIR and through the working group on WBC, new links with researchers involved in the field are being developed. This may help in solving some issues by stimulating collaborative multicenter work and encourage sharing of information and knowledge. This should lead to studies with a higher number of subjects, with enhanced design and statistical approaches in publications with high impact.



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## IIR recommendations

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To develop scientific evidence on the benefits of cryostimulation, researchers, and operators must adopt a dual strategy.

- The IIR Working group encourages the development of research to demonstrate when and how cryostimulation is beneficial to humans. Effects of gender and anthropometrics should be studied. Frequency of exposure is a key parameter, but the number of sessions to enhance the beneficial effects of cryotherapy is still to be established, as well as the exposure scale (time/temperature).
- The key variables inducing the benefits of the cryostimulation must/shall be identified. This includes skin temperature variation and temperatures achieved with different cryostimulation devices. It will be necessary to develop a recognized conformity certification for cryogenic technology devices and operators. There are many cryo-manufacturers with different technologies and each technology has its own temperature measurement method (e.g. thermal sensor, location of measurement). Thus, it is important to define a standardized method of measurement of the actual temperatures inside each device.

Safety issues related to the use of cryostimulation require that the risks of medical contraindications and the prevention of anoxia in cryosaunas and, in general, frostbite be better considered through appropriate measures.

The skills of the operators (physician, physiotherapist, kinesiologist, trainer), as well as the necessary specific training and possible certification of these operators must be also developed.



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