Review Article

Intermittent Pneumatic Compression as a Regulator of Physiological Processes: A Conceptual Framework

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Introduction. We propose the concept of intermittent pneumatic compression (IPC) as a systemic regulatory intervention whose therapeutic potential is currently deeply underutilized. This study aims to demonstrate the consistency of this concept with modern data, systematize disparate findings, and identify new research directions for the future development of IPC.

Materials and Methods. The proposed concept posits that IPC acts through the movement of vascular fluids and the activation of mechanoreceptors. These initial local actions systemically trigger regulatory and integrative processes mediated by humoral transport and reflex arcs. To validate the conceptual model, a qualitative simulation was performed using two independent Large Language Models (LLMs) to provide expert-level scrutiny and refine the relative contributions of physiological pathways.

Results. A comprehensive review of the evidence demonstrates that IPC yields significant benefits, including the reduction of pain and sympathetic activity and the enhancement of nerve regeneration and parasympathetic tone. Furthermore, IPC positively influences cerebral blood flow, mental quality of life, and night sleep. At the biochemical level, IPC supports factors of fibrinolysis, angiogenesis, proliferation, and repair and notably reduces blood glucose and HbA1c while preserving aerobic metabolism and reducing oxidative stress risk. The LLM simulation confirmed the local-mechanical pathway as the primary contributor and the neural pathway as a significant modulator, while the endocrine-humoral and immune pathways were deemed secondary beneficiaries.

Discussion. The consistency of findings supports the view of IPC as a systemic regulator capable of modulating metabolic, anti-inflammatory, and neuroplastic effects. Future research should prioritize explorations into mechanotransduction, metabolic modulation, CNS effects, and oncology. The

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development of a multi-layered database mapping procedure parameters to biological responses is necessary for the transition toward personalized IPC treatments and the design of new, adaptive devices.

Conclusion. The concept is not presented as a definitive statement but as a catalyst for research, identifying new therapeutic and technological frontiers and prompting a systemic re-evaluation of IPC's potential.

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Introduction

Intermittent pneumatic compression (IPC) is not a unitary intervention but a family of therapeutic techniques aimed at preventing, correcting, or compensating for circulatory and partly neurogenic lesions. This perspective reveals a wide variety of possible settings and configurations, challenging any simple view of its application.

Our analysis of 200 consecutive PubMed results (search date: July 1, 2025; query: 'intermittent pneumatic compression' [Title/Abstract]) revealed the following topic distribution: 49% focused on thromboprophylaxis, 9.5% on other venous disorders, 17% on lymphedema or other edemas, 4% on other peripheral vascular diseases, 4.5% on blood and hemodynamics, 5.5% on muscle recovery and regeneration, and 2.5% on the brain, nerves, and pain. The remaining 7.5% addressed non-clinical aspects.

This narrow focus is contrasted with the empirical landscape. Appendix 1 presents a comparative analysis of clinical indications: the list generated by a Large Language Model (reflecting common knowledge) includes approximately 30 conditions, while our own list, compiled from decades of Ukrainian clinical observations, contains over 50 interventions that were actually attempted. While definitions of a valid indication may vary, it is clear that the therapeutic potential of IPC is currently deeply underutilized.

This paper, however, addresses entire domains still absent from the clinical agenda.

Objective. This work builds on the concept of IPC as a systemic regulatory intervention. We aim to:

a. demonstrate its consistency with modern empirical data;

b. show how this framework systematizes and integrates disparate findings;

c. identify new research directions and clinical prospects; and

d. outline the necessary requirements for the future development of IPC technology.

Materials and Methods

The core of the Tarshinov model

Intermittent pneumatic compression acts through two primary mechanisms: the movement of vascular fluids along a compression gradient and the activation of mechanoreceptors. These initial actions trigger processes that extend far beyond the treated area, mediated by humoral transport and reflex arcs. Via the nervous system and humoral transport (including oxygen, endocrine agents, and immune agents), IPC indirectly and systemically stimulates regulatory (adaptive) and integrative (compensatory) processes. This effect manifests from the organismal level down to the subordinate molecular level.

The concept's genesis. In 1992, based on the Soviet-era device APKU-5, Ukrainian engineer Ihor Tarshinov (1943–2013) modeled the "Bioregulator-004M," an IPC device for lymphatic drainage. Due to limited modern communication channels, the development of IPC in Ukraine remained isolated from international trends until roughly 2012.

Tarshinov developed his theoretical framework based on practical observations and extensive consultations with diverse physicians who used his device. His ideas were also significantly influenced by the works of A. Chizhevsky, A. Zalmanov, and L. Nikolova. Tarshinov's personal vision for therapy was defined by his focus on restoring the body's self-regulation through a systemic approach, explaining the mechanism via biophysics and hydrodynamics, and targeting the capillary system. The theoretical views on the method were formally documented in the early 2000s by I. Sukharev (2001) [1] and V. Lyseniuk (2002) [2]. At that time, their conceptual framework included these core tenets:

- IPC primarily acts as a non-invasive intervention on the body's physiological self-regulation, operating on all levels. While its initial effects are a result of direct mechanical action, the primary therapeutic changes occur at the level of microcirculation.
- The method normalizes cellular and systemic processes. It activates cellular metabolism by stimulating aerobic processes, reduces trophic disorders, accelerates tissue regeneration and detoxification, and improves the function of the autonomic nervous system, leading to sedative and hypnotic effects.

Thus, the fundamental concept of IPC as a regulatory therapy was largely formed approximately 25 years ago. It was subsequently refined through a deeper understanding of its neural mechanisms by A. Chuprikov and the author. This theoretical perspective provided a foundation for applying IPC to nearly 50 pathological conditions (a list is provided in Appendix 1). In turn, these clinical observations consistently supported and refined the fundamental value of the theory.

Tarshinov's team received recognition from the World Intellectual Property Organization for the first portable IPC device for personal use [3] and the introduction of IPC in the treatment of asthenic syndrome in patients with erectile dysfunction [4]. A more detailed summary of our team's experience before 2015 is provided in [5].

In our opinion, the views and clinical observations from Tarshinov's team are not only supported by contemporary foreign research but also provide a framework to harmonize and systematize these disparate findings, enabling the synthesis of a new meta-concept.

Our practical specifics. The Ukrainian IPC method differs significantly from common protocols used for lymphedema or phlebothrombosis. While we do not claim this approach is universally superior, its safety has been empirically demonstrated with responsible clinical use.

We frequently used a fast compression cycle. With chambers inflating and holding for only 1–2 seconds, our method was an order of magnitude faster than some lymphedema protocols with chamber cycles lasting 10–15 seconds. This approach produced approximately five compression waves per minute—a much larger "dose" of mechanical influence per unit of time. We theorized this 1 Hz frequency was close to the heart rate, allowing for potential synchronization with the body's natural vascular oscillations. If validated (as, for example, in [6]), this principle could pave the way for future biofeedback systems that adjust compression frequency to correct specific physiological imbalances.

Another feature was the frequent use of alternating wave direction, particularly for ischemic conditions. Pressure on a limb would first move from the fingers to the trunk (drainage) and then reverse (hyperemic effect). This empirical technique was developed to directly mobilize blood flow. The a posteriori physiological hypotheses are that the reverse wave creates transient hyperemia, while the drainage wave removes excess fluid, leaving vascular walls ready to receive more arterial blood. Furthermore, the mechanical stimulation of occluded arterial walls may have a direct therapeutic effect.

The strictly sequential and non-overlapping arrangement of chambers in our cuffs created "pockets" of reduced compression between them. While this is suboptimal for lymphedema treatment, in other

pathologies, these pockets could act as compensatory cushions, absorbing part of the load.

We placed a strong emphasis on procedural zoning. In an ideal clinical scheme, the entire body was treated sequentially. However, the physician always prescribed specific parameters for each individual body region. This high degree of individualization meant no fixed "suit" or single "protocol" could be considered acceptable. A more detailed summary for making prescriptions is provided in [7].

Results

Neural effects

The nervous system is fundamentally responsive to external stimuli, including mechanical ones, so the idea of neurotropic effects of intermittent pneumatic compression is a logical premise. IPC—when consciously experienced—also produces psychotropic effects in the broad, non-pharmacological sense of the term. In recent years, research into the neurotropic effects of IPC has intensified, but this field of research remains strikingly underexplored [8]. Viewing IPC as a psychophysiological technique opens new research directions in neuroplasticity and mind–body integration.

Analgesia. IPC can reduce the intensity or shorten the duration of pain of various genesis, namely, that caused by sports training [9], static work [10], sprains, posttraumatic edema, bone fracture [11], and arthroplastic surgery [12]. Its analgesic effects are also well-documented in treating peripheral vascular diseases like diabetes [13] and intermittent claudication [14]. In these cases, IPC's rapid pain relief is mainly due to its anti-edematous and anti-inflammatory vascular effects. This is important for considering neural effects not in physiological but in practical terms.

Nerve functioning. IPC's long-term effects can directly influence nerve endings, for example, by accelerating their regeneration after injury [15]. K. Zaitsev (2015) showed that a single IPC session increases the strength and speed of impulse conduction through neuromuscular contacts, while a full course improves conduction through nerve fibers and boosts the overall neuromuscular response. IPC has also been shown to enhance motor and sensory nerve conduction velocities after two weeks of treatment [16]. Additionally, in patients with peripheral neuropathy due to chemotherapy, IPC improved foot sensation and balance control within the first day of observation [17]. The inclusion of IPC in a comprehensive rehabilitation program for hemiplegia increased the effectiveness of motor [18] and sensory function recovery [19].

Autonomic regulation. Early concepts regarding IPC's neural effects were primarily speculative, yet they prompted further research. Bezpalyi et al. (1999) proposed that IPC stimulates segmental reflexes and vegetative-vascular reactions [20]. Later, we performed IPC under heart rate variability monitoring. A single session led to an increase in overall regulatory activity. The first 10–15 minutes involved adaptive fluctuations in the sympatho-parasympathetic balance. This was followed by a sustained dominance of parasympathetic tone with low sympathetic influence. This ratio progressed for about 10–15 minutes, gradually shifting to a plateau. Analysis showed a reduction in the tension of regulatory systems, indicated by a greater role of the segmental level and reduced influence from higher brain centers [21]. Throughout a course of treatment, patients (combat veterans) exhibited distinct adaptive phases of HRV. The body's highest sensitivity to the IPC procedure occurred around the fourth day of the rehabilitation course. The most significant changes, when compared to the first day, were established by the sixth or seventh day [22].

It's still unclear whether IPC primarily reduces sympathetic activity while enhancing parasympathetic tone—or whether its effect is more about harmonizing autonomic balance in general by lowering overactivity in either direction. Perhaps the former is typical of a single session (a fast-acting effect), while the latter develops over a longer course (a slow-acting effect). This duality complicates intuitive recognition and makes it difficult to study using standard protocols.

Circadian rhythms. Currently, data on the potential influence of IPC on the correction of circadian rhythm disruptions are limited. While such an effect is expected, albeit an indirect one, its development is likely so slow that it would coincide with the natural resolution speed of these processes (e.g., in cases of jet lag). Although IPC has been used in individuals exposed to prolonged circadian rhythm disruption (such as during the polar night), its direct impact on these disorders has not been studied. At the same time, an incomplete correction of general desynchronosis syndrome and chronic stress symptoms was observed [23]. Furthermore, IPC's influence on age-related circadian rhythm disorders also remains unstudied.

In this context, a promising research direction could be the study of IPC's effect on "peripheral clocks." Overall, and similar to its role in managing the consequences of chronic stress, IPC should be explored not as a means for pathogenetic treatment of the disorder but rather as a method for the prevention of vascular and other long-term consequences of desynchronosis.

Reception. Our stabilographic study on head and back IPC procedures indicated that muscle relaxation and cerebral inhibition are a pronounced leading reaction. This is accompanied by a decreased role of visual control and an increased reliance on proprioception for body balance [24]. Beyond its vascular effects, IPC can trigger a rapid "release" response that includes thermoregulation (via hyperemia and localized heat accumulation) and a reduction in perceived tension. The rhythmic, slow tactile input across large surface areas or targeted stimulation of highly sensitive zones (e.g., feet, hands, or ears) makes IPC a multisensory event capable of activating a wide spectrum of neuropsychological mechanisms associated with safety, recovery, embodied well-being, interpersonal interaction, and a sense of groundedness.

Quality of life. The muscle-relaxing impact of IPC, comparable to a warm bath, along with the rapid reduction of swelling, heaviness, or pain, can noticeably influence mood, motivation, and even self-image. In addition, there are some observations of a favorable effect of long-term use of IPCs on the mental component of quality of life, in particular, according to the Lymph-ICF-LL [25] and ShortForm-36 [26] questionnaires. This effect is secondary and depends on the success of specific therapy for the underlying disease.

The CLOTS 3 trial found that while IPC improves survival in immobile stroke patients, it did not improve health-related quality of life as measured by the EQ-5D-3L [27]. By improving survival in the most severe cases, IPC increased the number of survivors with significant disability in the cohort, thereby lowering the average quality-of-life score for the entire group. In the future, randomized clinical trials that do not incorporate a subsequent stage of cluster analysis will be hard to justify as possessing a sound methodological design. This remark does not question the excellence of the CLOTS 3 trial; rather, it reflects a methodological consideration that the study has helped to bring into focus.

Cerebral blood supply. Introducing IPC to treat ophthalmological patients led to improvements in visual function, suggesting a positive effect on the retinal and optic nerve vasculature [28]. IPC applied to the lower limbs can enhance cerebral blood flow and cerebral tissue oxygenation without affecting intracranial or cerebral perfusion pressure [29]. In patients with cerebral infarction, IPC can promote bilateral cerebral circulation in the prefrontal, sensorimotor, and temporal cortex and have a positive effect on functional rehabilitation in case of their damage [30]. We performed a short, single-time IPC procedure on the scalp under rheoencephalography control. Our preliminary observations, while requiring confirmation in a larger and more controlled setting, hint at a potential reflex effect of IPC on cerebral vascular tone, leading to rapid changes in hemodynamic balance (correction of asymmetry,

harmonization of blood distribution in arterial basins) and arterial blood filling (fluctuations in vascular volume) [31]. Should future studies substantiate these early findings, a compelling yet speculative avenue would emerge: to explore whether IPC could, even minimally, influence cerebrospinal fluid dynamics, meningeal lymphatic flow (the glymphatic system), and cross-basin circulatory interactions.

Sleep and relaxation. The drowsiness commonly observed during IPC sessions requires characterization: is it true sleepiness or dissociation (rest without sleep)? Clinically, patients demonstrate varying depths of sleep, from simple cortical inhibition to advanced sleep signs (e.g., apnea), which probably depends on fatigue or lack of daily sleep. A preliminary study on the effect of IPC on night sleep showed an improvement in patients' morning well-being, decreased exhaustion, enhanced subjective sleep quality, and reduced daytime drowsiness. This also corresponded to a decreased subjective need for nighttime sleep [32].

Cognitive modulation and neuroplasticity. IPC should also be assessed as a rapid-recovery tool during work breaks. Reports from an athlete indicated that the hypnagogic state facilitated the absorption of verbal instructions in athletes, akin to imprinting them into muscle memory rather than cognitive memory. This suggests a form of neuroplasticity where somatic input creates new body–brain templates. This parasympathetic dominance, characterized by slowed mental activity, may support theta-wave synchronization and activation of the Default Mode Network. Repetitive sensory input minimizes prefrontal cortex engagement, freeing resources from conscious and somatic processing and redirecting them toward limbic and visceral demands.

Psychotropic and neuro-corrective effects. Preliminary reports from clinical practice suggest that IPC may influence psychoneurological states. Specifically, observations indicate positive changes in the manifestations of asthenia, anxiety, and depression in patients [33]. However, these reports stem from small, complex clinical groups, making it difficult to isolate the precise contribution of IPC to the overall therapeutic outcome. Similarly, A. Chuprikov's work attributed the reduction of anticonvulsant dosages in epilepsy to the use of IPC [34], which aligns with theoretical expectations of cortical modulation but requires broader investigation. These early findings necessitate objective research using advanced neuroimaging techniques, such as functional near-infrared spectroscopy [35] and electroencephalography, to provide verifiable data on the method's central effects.

Biochemical effects

The biochemical effects of intermittent pneumatic compression are well-known. They include factors of fibrinolysis [36][37], angiogenesis and chemotaxis [38], proliferation and repair [39][15][40][41], as well as aerobic metabolism [42][43]. The classical model of IPC evolved from a purely mechanical therapy through the incremental accumulation of fragmented observations of biochemical effects. While Tarshinov's model was primarily biophysical, its core principle of IPC as a systemic regulator led to the expectation of hormonal and humoral reactions. However, systemic biochemical effects are not immediately demonstrable and require rigorous proof of causality. Without such evidence, the very idea of regulation remains hidden and undervalued.

Systemic endothelial effects. While many of the biochemical effects of IPC have been studied only at a local level, a shift to a systemic perspective is possible through two distinct avenues. First, by investigating systemic effects as a primary outcome, such as the transport of nitric oxide [44] or oxygen [45][46] to distant tissues. Second, by applying local procedures over the largest possible surface area of the body, which transforms isolated local effects into a mass-scale systemic response.

The endothelial products of IPC are triggered as a "package" response to the physical stimulus, rather than being specific to the device's settings. Yet, this relationship requires further investigation, as certain hemodynamic frequencies can influence the inflammatory phenotype of endothelial cells [47]. We propose that the endothelial response to IPC-induced shear stress is heterogeneous and context-dependent. While an inflamed endothelium may produce pro-inflammatory factors, a healthy one will produce anti-inflammatory ones. If this is correct, then in cases of localized vascular inflammation, the procedure could be applied to healthy areas to elicit a beneficial, systemic anti-inflammatory response via paracrine-scale effects.

Data on the potential influence of IPC on the hormonal system are limited.

Insulin and glucose. However, IPC has been used for some time in small patient cohorts with diabetes mellitus. While most studies focus on vascular complications, there are reports of reduced blood glucose levels [48][49], decreased HbA1C [50], and a reduced need for medicinal insulin [51]. In our practice, it was considered normal for patients with diabetes to experience a transient increase in glycemia around the fifth day of daily procedures. The mechanism of this phenomenon needs to be studied.

Thyroid and other hormones. In our clinical observations of patients with hyperthyroidism, we noted a temporary increase in symptoms, which returned to baseline after therapy. This effect could typically be

avoided by excluding procedures on the arms, shoulders, and upper back. Conversely, patients with hypothyroidism experienced temporary improvement. Future studies with serial hormone level measurements are needed to elucidate the precise dynamics and mechanisms of these phenomena and therefore to formulate definitive tactical recommendations.

Regarding other glands accessible to regional hemodynamic influence — such as the adrenals and gonads — clinical observations are sporadic and uncertain.

Proposed principles for hormonal correction. This set of observations suggests that one mechanism by which IPC influences the functional activity of an endocrine gland is through a hypothetical feedback loop: by enhancing hormone delivery and efficacy in peripheral tissues, IPC could potentially trigger a compensatory downregulation of the gland's activity via classic endocrine feedback mechanisms.

It can be hypothesized that in the short term, IPC increases the gland's activity, likely by enhancing its blood supply:

- The functional activity of the glands can be enhanced through the transport of mediators (for example, thyroid-stimulating hormone).
- In addition to slow synthesis, a rapid effect is possible through secretion ("washing out" of deposited hormones from the gland parenchyma, especially in its hyperfunction).
- Increased blood flow mimics certain conditions, such as the stress response or systemic inflammation, and can itself become a specific mechanical stimulus for the adrenal glands, pancreas, and thyroid glands.

It seems that healthy glands exhibit significant resistance to stimulation and only react noticeably in patients with pre-existing endocrine pathology. It remains unclear how secretion, synthesis, trophic, and regulatory influences actually coexist. We can predict the forces, but only well-designed clinical trials will indicate their balance and therefore pave the way for specific clinical applications for IPC.

It is likely that IPC can stimulate both physiological and pathological (e.g., autoimmune and neoplastic) processes in the glands. Such ambivalence is typical for a regulator. We should learn to strike a balance between the desired and undesirable effects; this will make the therapy specific. Perhaps the localization of procedures and the duration of the course will be key parameters here.

Immune effects

There is strong reason to believe that intermittent pneumatic compression does not affect the immune system as a direct stimulator or suppressor but rather as a facilitator. Theoretically, IPC may serve an immunotropic role as a suprasystemic modulator. It may help suppress excessive immune responses (e.g., in autoimmune or para-inflammatory conditions), while also supporting secondary immunity by reducing systemic inflammation — essentially unburdening the immune system from the load of edema, hypoxia, and sympatho-stress. The effects of IPC in this area are not yet well studied and require targeted investigation.

Drainage. There are conflicting data on whether IPC affects the transport of edema proteins [52] or only water [53]. However, since IPC helps form compensatory drainage pathways [54][52], the local area of swelling remains connected to the body's overall fluid network. It seems reasonable that improved drainage during IPC may accelerate the transport of inflammatory mediators [55][56], enhance antigen presentation to the immune system, and help initiate immune responses. If IPC effectively supports lymphatic outflow [6] — which is known to play a role in immune cell transport and immune system function [57] — it is logical to assume that IPC may have an indirect but meaningful influence on immune dynamics through this pathway. This connection goes beyond fluid regulation and suggests a deeper impact on immune behavior.

Inflammation. Mechanically, IPC supports the synthesis of anti-inflammatory mediators such as interleukin-10 and nitric oxide (NO) [58].

Maintaining active microcirculation — by limiting the exudative phase of inflammation [59] — helps preserve aerobic metabolism and lowers the risk of oxidative stress [60].

After IPC, the balance of T cells changes: inflammatory CD4+ T cells go down, while CD34+ progenitor cells go up. This suggests less inflammation and more lymphatic vessel repair or growth [61]. The combination of edema reduction and enhanced microcirculation can reshape the local immune environment. By lowering interstitial fluid volume, IPC shortens the distance between infiltrating immune cells and their targets, while reduced tissue pressure eases pain and supports mobility. These changes enable better leukocyte access and function, ultimately promoting repair rather than chronic inflammation.

Improved blood flow can also facilitate the delivery of leukocytes to inflamed tissue. There was uncertainty about whether increased flow might interfere with leukocyte adhesion. However, recent findings suggest that physiologically accelerated flow may actually support leukocyte extravasation [56].

Immune cells are inherently mechanosensitive — capable of detecting and responding to mechanical stimuli such as tension, compression, and shear stress [62]. These signals can influence gene expression, migration, activation, and polarization patterns, particularly in macrophages [63]. Although this mechanotransduction pathway has not yet been directly studied in the context of IPC, its presence in related modalities (e.g., stretching, acupuncture) warrants consideration. It is plausible that IPC, through its mechanical action, might directly modulate immune cell behavior. This hypothesis remains to be systematically explored.

Clearance. With increased central venous pressure, IPC creates a physiological conflict: on one hand, it stretches atrial myocytes, promoting the release of atrial natriuretic peptide, diuresis, and improved cardiac output and renal perfusion; on the other, it reduces the renal perfusion gradient and adds mechanical resistance to filtration. The net effect on clearance remains uncertain. A review [64] summarized data on IPC and lactate clearance in athletes: two studies showed enhancement, two showed no change, and one showed a neutral or decreased effect. The possible influence of IPC on renal clearance requires further investigation.

Stress. Stress-related suppression of immunity may be alleviated due to reduced sympathetic tone, allowing the immune system to respond more actively — sometimes even excessively, especially in cases where it was previously overinhibited. In such cases, a brief proinflammatory activation may occur as part of the rebalancing process.

IPC may also engage neuroimmune mechanisms — for example, by activating the inflammatory reflex through the vagus nerve, as a consequence of enhanced parasympathetic activity. When applied to the abdominal region, IPC may improve gut motility, potentially reducing endotoxemia, a known risk factor for systemic inflammation.

Precautions. Still, IPC cannot be assumed to act on the immune system with intentions for all the good and against all the bad. Potential risks include immune overactivation, cytokine storm, toxemia, pathogen dissemination, and sepsis. Autoimmune responses require special caution. While IPC may sometimes provide relief under stable conditions, the therapeutic regimen must remain gentle and conservative — shortened sessions, breaks between treatments, and limited body areas (e.g., limbs only)

may be preferable. Even then, the intervention balances on the edge of provoking autoaggression. Unfortunately, the path to a clinically safe protocol in such cases may be challenging. Exacerbations of myasthenia gravis and rheumatoid arthritis we have witnessed have made it clear how strong and rapid the immune response to IPC can sometimes be.

Current synthesis

While the Tarshinov model posits four distinct pathways of action, we wanted to assess the potential contribution of each. We performed a conceptual simulation built on the following assumptions:

- The mechanism of intermittent pneumatic compression is based on the mechanical stimulation of fluid movement.
- The primary impact is local, triggering three secondary pathways: neural, endocrine-humoral, and immune.
- IPC is a systemic regulatory therapy with both specific and nonspecific effects, applicable to a wide range of conditions.

This conceptual model was submitted to two independent large language models (LLMs) to simulate expert-level scrutiny. We employed LLMs for three key methodological reasons: their inherent lack of human bias, their ability to synthesize a vast, cross-disciplinary knowledge base, and their capacity to perform a structured, controlled analysis of the proposed model. Both were instructed to be critical, to avoid desired positive responses, and to respond with "unknown" when appropriate. This conceptual exercise does not substitute for clinical trials; rather, it serves as a heuristic for assessing the extent to which various elements of the model merit further study.

The simulation results confirmed that the four proposed pathways logically contribute to the systemic response to IPC, albeit to varying degrees. The models agreed that the local-mechanical pathway is the primary contributor, initiating the entire physiological cascade. The neural pathway was identified as a significant modulator and integrator of the overall effect, though with a moderate risk of overemphasis, particularly in long-term therapy or specific cases. The endocrine-humoral pathway was considered indirect and systemically relevant, especially in cases of broad physiological disturbances, but was also deemed technically difficult to study due to the complexity of long-term outcomes. Both models viewed the immune pathway as a secondary beneficiary rather than a primary mechanism of action, noting that while long-term immune changes are possible, proving a causal link to IPC is difficult.

Crucially, the simulation indicated that the relative contribution of each component might be more or less relevant depending on the type of disorder being treated. The relative activity of each pathway may also change over time. This conceptual exercise suggests that the Tarshinov model — which accounts for these multilevel and time-dependent interactions — provides a logically consistent framework for understanding the systemic effects of IPC.

Discussion

Limitations and criticism

Conventional contraindications. Intermittent pneumatic compression, while not a panacea, has inherent limitations and contraindications, which are comprehensively reviewed in the international consensus statement [65]. Although this guideline covers medical compression broadly, it specifically highlights side effects and contraindications unique to IPC. Critically, many historical contraindications are now being reclassified as manageable limitations, a change driven by continuous advancements in device design and growing clinical experience [66]. This shift suggests practitioners must view contraindications as part of a changing knowledge system, not as immutable rules.

Regulatory limitations

§1. We observed that some effects—such as drowsiness or hypotension—are caused by the procedure itself, not by variations in its parameters. We suggest classifying these unavoidable outcomes as non-specific effects: IPC triggers them, but they are difficult to control accurately, making them essentially side effects. When these effects benefit a patient, they can be viewed as non-specific indications; however, this intrinsic lack of precision is also considered a core limitation.

§2. IPC cannot remedy organs that are anatomically destroyed or no longer exist. While the method may support regeneration or tissue remodeling, fundamentally disrupted anatomy is a hard limit that persists: it casts a shadow even when the light of therapy is switched on. Therefore, therapeutic expectations must remain realistic in the face of irreversible damage.

§3. The body's determined self-destructive trajectory presents a critical limitation. We cannot intervene when the organism is locked into pathological homeostasis, which we define here as a reorganized, stable state of illness that actively maintains pathology. In this state, IPC becomes a mere stimulus rather than a corrective force. If we blindly stimulate this reorganized regulation, such as during an acute

autoimmune reaction or cachexia, we are likely to accelerate self-damage much faster than we can facilitate a beneficial resolution. Therefore, IPC is generally ill-suited for conditions defined by aggressive, self-perpetuating pathology.

§4. The mechanical energy enters the body like a ripple in water: the farther the wave travels, the fainter its effect becomes. Consequently, the most reliably coupled therapeutic effects manifest on a macro-scale, typically within the centimeter to decimeter range. This suggests that we must focus our attention on systems-level effects, acknowledging the limited precision available for molecular targeting or for directly improving complex outcomes like quality of life. Crucially, regulatory therapy is a duet; its outcome depends not only on the stimulus but critically on the organism's individual and situational response. Because of this variability, the more distant the wave, the harder it is to predict if it will reach its target, or in what form.

§5. The core limitation—or intrinsic weakness—of IPC is its relatively slow action. When the timing of intervention is measured in minutes or hours, IPC is often unsuitable (excluding specialized tools like antishock suits). IPC accelerates biological time, but not to the infinite speed required for acute, life-threatening scenarios.

Supposing that IPC accelerates biological time, it becomes necessary to define the functional limits of this acceleration. We propose that future research should aim to quantify this boundary by establishing a coefficient of acceleration (K) for biological processes under IPC. This conceptual coefficient would represent how much faster a given physiological process proceeds under the influence of IPC compared to its natural speed. Tentatively, we hypothesize that the value of K would be highly variable and would ultimately depend on the specific organ system or task being studied (e.g., the immune or nervous systems).

Lack of evidence. Why discuss a concept with such limited direct evidence? First, the model is internally consistent and does not contradict the fundamental principles of medicine and biology. Second, this concept has shown significant heuristic potential. Retrospectively, the systemic approach provides the most comprehensive explanation for diverse clinical applications. It predicted, and now explains, the effectiveness of IPC in sports medicine, which is difficult to attribute to simple fluid displacement alone. Similarly, observed neural responses to IPC—from subtle vagotonia to the common drowsiness during sessions—cannot be fully justified by classical local mechanics.

Simplicity for safety, complexity for efficiency. The question often arises: is the complexity of IPC being overestimated? A few simple rules may prove sufficient to perform the procedure safely. For example:

- If the case involves solid lymphedema, pressure should exceed diastolic pressure, and compression duration should be longer than 3 seconds. Otherwise, lower pressure and shorter compression are preferable.
- If edema or the risk of it is present, the pneumatic wave must move from the periphery toward the heart. Otherwise, a bidirectional mode can be used.
- An intensive approach involves an energetic local procedure, while a gentle approach achieves a prolonged general effect. [7]

However, how many factors must be considered to guarantee results for a specific patient? A technology designed to influence the body's fundamental regulation cannot remain simple, especially when effective individual treatment demands a comprehensive knowledge of IPC's full "alphabet" of settings.

The central question is how a simple mechanical intervention can produce such a wide range of systemic physiological effects. IPC fundamentally mimics movement—the body's essential, evolutionary challenge to homeostasis. Compression acts as a primal regulatory signal. Yet, when analyzed, IPC is defined by specific pressure, duration, and frequency—the critical difference between striking keys at random and playing a score. Furthermore, as the cascade of clinical effects develops, the resulting response becomes highly individual and context-dependent.

Potential directions for further exploration

We will now turn to some of the most promising and potentially transformative avenues for research and investigation in the field of intermittent pneumatic compression as a regulatory therapy.

An attempt to systematically organize these topics reveals that their relationships and clusters form a dynamic network or cloud with multiple entry points, which highlights the challenge rather than simplifies it. For instance, some topics require both fundamental and applied research, or they decompose into stages that can be executed in an arbitrary order. Some topics generate new sub-themes and establish vital interdisciplinary connections.

Foundations. Since these studies explore fundamental biomechanical mechanisms shared across living systems, some findings may later extend beyond medicine—to veterinary practice, agriculture, or even plant biotechnology.

§1. *Mechanotransduction and mechanosensitive ion channels.* IPC's effects at the molecular level remain largely theoretical. Key directions include: how repeated compression alters activation thresholds and

expression of Piezo1/2, TRPV4, ENaC in endothelial, smooth muscle, fibroblast, and immune cells; differences between cell types and types of mechanical stimuli (shear, stretch, compression); cellular "mechanical memory" and preconditioning; selective activation of different channels to achieve specific vascular, lymphatic, or neural effects; modulation of intercellular signaling via gap junctions; and defining measurable pressure/frequency windows for maximal channel response. These studies could enable "molecularly dosed" IPC, moving beyond empirical protocols toward targeted, physiologically optimized compression therapy.

§2. *Metabolic modulation and ATP dynamics.* Quantifying ATP and related metabolic indicators (ATP/ADP, NAD^+/NADH, lactate/pyruvate, AMPK activity, citrate synthase activity, MDA) before and after IPC could reveal whether compression merely improves microcirculation or truly alters cellular energy status. Both intracellular and extracellular ATP (as a purinergic signal) should be considered. Such studies may clarify tissue-specific and dose-dependent metabolic responses to IPC and determine whether it can act as a mild "passive exercise," enhancing mitochondrial efficiency in patients with metabolic disorders. If confirmed, these findings would support IPC as a method of targeted metabolic modulation rather than a purely mechanical intervention.

Accounting for circadian metabolic rhythms may allow IPC to become a precisely timed metabolic intervention.

§3. *Anti-inflammatory and immunomodulatory effects.* IPC may act not as a simple anti-inflammatory stimulus but as a harmonizer of immune balance. The primary mechanosensitive targets are cells of the innate immune system—neutrophils, monocytes, and macrophages—together with the endothelium. Repetitive mechanical loading could reduce neutrophil overactivation and NET formation, promote macrophage polarization from M1 to M2 phenotypes, and downregulate endothelial adhesion molecules (ICAM-1, VCAM-1), thus limiting leukocyte adhesion. On the molecular level, IPC might suppress NF-κB and NLRP3 activation, shift the IL-10/TNF-α ratio toward an anti-inflammatory profile, and accelerate lymphatic clearance of cytokines rather than merely reducing their synthesis. Through these effects—and possibly via vagal, cholinergic anti-inflammatory pathways—IPC could restore the physiological equilibrium between inflammatory and reparative phases, offering a mechanistic explanation for its broad clinical benefits.

Physiology

§4. *Infections, clearance, and allergy.* A worthy achievement would be to reduce the number of contraindications for IPC through a better understanding of its action in infectious diseases. The prerequisite research must be a definitive safety assessment: do standard IPC protocols increase the risk of pathogen dissemination, either lymphogenous or hematogenous? This risk-benefit analysis should stratify infections by dissemination potential (e.g., low-risk chronic versus high-risk uncontrolled acute).

IPC should also be discussed in the context of enhanced clearance of metabolites and inflammatory products. Studies should quantify the transport and clearance of bacterial toxins (e.g., LPS), cytokines and their fragments, and products of tissue catabolism, as well as PAMPs and DAMPs entering systemic circulation. Furthermore, high-priority research should investigate the systemic impact of IPC on hepatic and renal blood flow, as this could indirectly benefit organ function in conditions like systemic inflammatory response syndrome or sepsis. A key question is whether IPC can improve splanchnic perfusion, potentially reducing gut barrier dysfunction and subsequent endotoxemia in critical illness. We should also optimize guidelines on combining IPC with antibiotic therapy.

The identified mechanisms should be explored for possible application in allergic disorders.

§5. *Stem cells.* The potential relationship between IPC and stem cell activity should be approached cautiously. IPC is unlikely to act as a direct stimulator of stem cell proliferation; rather, its main role may lie in improving the microenvironment that supports reparative processes. By enhancing local perfusion, oxygenation, and clearance of metabolites, IPC may help maintain the functional integrity of stem cell niches. Mechanical shear stress and nitric oxide–mediated signaling could facilitate limited mobilization of progenitor cells (e.g., $CD34^+$, endothelial, or mesenchymal) from the bone marrow into circulation, similar to natural physiological responses. Mechanical cues may also influence the differentiation of resident mesenchymal stem cells within damaged tissues, guiding them toward appropriate repair lineages. These effects may contribute indirectly to tissue recovery or the integration of transplanted regenerative cells. However, potential risks such as unwanted stimulation of dormant clonal populations require careful study before any clinical application.

§6. *Oncology.* Using IPC in oncology requires individualized ethical and clinical judgment. Safety decisions should balance the risk of harm with the risk of withholding potential benefit. The theoretical risks stem from changes in tissue perfusion, oxygenation, and mechanical stress that could, in certain tumor types, alter growth-factor gradients, vascular permeability, or migration potential. Whether IPC

could activate dormant tumor cells or promote micrometastases remains unknown; such effects must be explored in preclinical models. The biological response of neoplastic tissue likely depends on its vascularity, invasiveness, and metabolic profile—thus, identifying biomarkers of tumor sensitivity to IPC (e.g., VEGF expression, angiogenic potential, interstitial pressure) is a key research goal.

Importantly, these same mechanisms may also be harnessed therapeutically. By improving microcirculation and reducing high interstitial pressure, which acts as a physical barrier to drug penetration, IPC could enhance drug delivery or immune-cell infiltration, potentially acting as a physical adjuvant to chemotherapy or immunotherapy. The interplay between improved oxygenation, reduced oxidative stress, and tumor metabolism represents a dynamic equilibrium rather than a simple "benefit or harm" dichotomy.

Furthermore, research must address the dichotomy between risk and benefit by linking IPC use to long-term progression-free survival and overall survival in post-treatment patients. An equally important question is whether IPC, by accelerating antigen transport to lymph nodes, can amplify the antitumor immune response, potentially synergizing with modern immunotherapy (e.g., checkpoint inhibitors).

§7. *Pharmacokinetics.* IPC may become a physical modulator of pharmacokinetics by influencing microcirculation, lymphatic flow, and tissue perfusion. The key hypothesis is that IPC improves peripheral drug delivery—overcoming the major limitation of pharmacotherapy in patients with edema, ischemia, or fibrosis, where blood flow is poor. By enhancing local and systemic circulation, IPC can accelerate absorption from subcutaneous or intramuscular depots, increase peak plasma concentration (Cmax), shorten time to peak (Tmax), and modify distribution between plasma and tissues. For lipophilic agents, nanomedicines, and biologics that rely on lymphatic transport, IPC may promote faster systemic appearance. Improved renal perfusion can alter clearance (Cl) and elimination half-life (T½), especially for drugs with narrow therapeutic windows. These effects could explain interindividual variability in patients undergoing IPC and highlight the need for dose adjustment studies. Conceptually, IPC might enable "personal pharmacology"—timed mechanical modulation of perfusion to direct drugs toward underperfused targets and reduce systemic exposure. This approach could transform IPC from a rehabilitation tool into an adjunct to pharmacotherapy, particularly in conditions with compromised circulation. Controlled pharmacokinetic studies, including plasma and tissue concentration monitoring, are required to define IPC parameters that safely optimize drug absorption, distribution, and elimination.

§8. *Pregnancy-related conditions.* The most immediate and plausible application lies in alleviating pregnancy-induced edema and venous stasis, where IPC's mechanical action offers a direct, non-

pharmacological rationale. For more complex conditions like preeclampsia, the central hypothesis is whether IPC's documented endothelial-modulating effects could translate into improved systemic vascular function and, crucially, uteroplacental perfusion. Due to the high sensitivity of this patient group, research must be rigorously controlled and primarily focused on maternal and fetal safety.

§9. *CNS and neuroplasticity.* Beyond its peripheral circulatory effects, IPC generates a rhythmic somatosensory input whose impact on the central nervous system (CNS) remains insufficiently characterized. Studies using EEG to capture rapid changes and fMRI to assess long-term network organization are needed to clarify how peripheral mechanical stimulation is processed centrally. Research should explore whether IPC's afferent input can modulate central sensitization and pain processing through spinal and supraspinal mechanisms, and whether it can influence autonomic nervous system regulation via viscerosomatic integration, measurable both by changes in functional connectivity and by heart rate variability. Potential clinical applications include supporting neurorehabilitation and promoting neuroplasticity after neurological injury, as well as managing central sensitization syndromes such as fibromyalgia. A key question is whether observed CNS effects merely reflect improved peripheral circulation or represent an active neuromodulatory phenomenon.

§10. *Borderline physiology.* IPC efficacy appears closely linked to the body's homeostatic reserve. At the threshold of pathology, regulatory systems become unstable—a domain that includes chronic fatigue, overtraining, and post-stress exhaustion. In such borderline states, IPC may cease to act as a normalizing signal and shift from beneficial to either [1)] neutral or even [2)] counterproductive.

1) This phenomenon reflects the paradox of "panacea poisoning"—when a system operating near its homeostatic maximum becomes physiologically deaf to subthreshold external stimuli such as IPC. The intervention may regain efficacy only after partial restoration of reactivity. Future studies should investigate whether IPC can help restore autonomic balance and receptor sensitivity (e.g., β-adrenergic responsiveness) impaired by chronic stress, with monitoring via proxy markers of vegetative regulation such as heart rate variability.

2) In maladaptive conditions like overtraining syndrome or chronic fatigue—characterized by autonomic dysregulation and neuroendocrine imbalance—IPC's stimulatory input could be misinterpreted as interference, potentially worsening the imbalance. This underscores the need to delineate physiological states and to develop simple functional tests (e.g., heart rate recovery or O_2 re-saturation dynamics) to identify individual "windows of reactivity" before treatment. Safety remains paramount, since IPC-

induced mobilization of metabolites may overload compromised systems. The central question is when and for whom IPC is appropriate—a matter of physiological readiness rather than diagnosis alone.

§11. *Anti-aging.* IPC may help counteract several hallmarks of vascular and tissue aging by acting as a controlled, repetitive endothelial stimulus that maintains nitric oxide synthesis, endothelial reactivity, and tissue perfusion. Acting as a passive mechanical analog of exercise, IPC can support microcirculation, muscle metabolism, and lymphatic drainage in older adults with reduced mobility, potentially alleviating endothelial dysfunction, sarcopenia, and low-grade inflammation ("inflammaging"). Improved clearance of interstitial metabolites and modulation of local cytokine balance may contribute to healthier immune and metabolic aging. Since age-related tissue stiffness and altered vascular responsiveness affect the transmission of mechanical stimuli, IPC parameters should be adjusted accordingly—using lower pressure gradients and longer inflation–deflation cycles to ensure both efficacy and safety in elderly individuals.

The philosophical premise of IPC as "passive exercise" invites research into its potential to counteract age-related decline. Fundamental studies should explore IPC as a possible geroprotective factor at the molecular level, assessing its influence on the clearance of senescent cells and their pro-inflammatory secretome, epigenetic regulation, and telomerase activity. If confirmed, such effects could make IPC a preventive tool for preserving functional independence and improving quality of life in old age.

Clinical frontiers

§12. *Sports recovery.* Current evidence on IPC and athletic recovery remains inconsistent, likely due to small, heterogeneous samples and confounding by combined therapies. Most research has focused on short-term performance metrics, whereas IPC's true potential may lie in cumulative effects and long-term adaptive support. The focus should therefore shift from outcomes to the conditions under which those outcomes are achieved. A critical objective is to build consensus on interpretation by prioritizing contextual factors over isolated performance data. Future studies should stratify participants more clearly—distinguishing non-elite individuals from peak-performing athletes, who may exhibit a "panacea poisoning" effect. The most promising applications of IPC likely concern the management of specific recovery phases rather than the enhancement of maximal performance.

§13. *Skin.* Beyond anecdotal claims in cosmetology, IPC may warrant serious dermatological investigation. One direction involves improved capillary density and tissue oxygenation, enhancing skin color and regeneration. Another, less explored, concerns barrier function: mechanical stimulation may

influence keratinocyte differentiation and lipid synthesis in the stratum corneum, potentially strengthening epidermal integrity and reducing transepidermal water loss — a clinically relevant possibility for dry and atopic skin. Occasional reports also mention partial hair repigmentation after prolonged IPC courses; whether this reflects coincidence or a reproducible effect remains uncertain. Finally, the rapidly expanding market of cosmetic and wellness procedures targeting cellulite and lipodystrophy deserves evidence-based evaluation: future studies should quantify structural changes in dermal and subcutaneous layers using ultrasound or elastography and relate them to patient-reported outcomes.

§14. *Preventive perspectives.* IPC is usually considered a therapeutic modality, yet its potential as a preventive tool may be equally important. Many vascular disorders develop gradually through preclinical stages — characterized by venous or lymphatic stasis, endothelial dysfunction, and low-grade systemic inflammation ("inflammaging"). Regular IPC could, in theory, modify these risk factors by enhancing microcirculation, supporting lymphatic drainage, and improving endothelial reactivity. Such effects may translate into reduced incidence of deep vein thrombosis, chronic venous insufficiency, and other stagnation-related conditions among sedentary or occupationally constrained individuals.

Beyond circulation, IPC might also facilitate lymphatic clearance and immune cell trafficking, contributing to more efficient immune surveillance in mucosal and peripheral tissues. Whether this translates into lower rates or milder courses of seasonal infections remains to be tested in controlled cohorts. Similarly, sustained vascular support may have indirect relevance to cognitive aging and vascular dementia — a hypothesis deserving cautious exploration.

The most distant yet conceptually intriguing prospect is oncological prevention: by mitigating chronic tissue hypoxia and inflammation, IPC could theoretically reduce microenvironmental factors that favor oncogenic transformation, though this remains speculative and requires long-term validation.

To assess these possibilities, large-scale observational data are needed. A prospective registry of healthy or occupational IPC users — even in a pilot format within rehabilitation or workplace programs — could provide real-world evidence on adherence, safety, and health correlations. Such an initiative would bridge preventive medicine with public health economics, testing whether protecting many might ultimately cost less than treating a few.

§15. *Mechanical post-conditioning.* Studies are required to quantify the duration of sustained benefits, such as prolonged endothelium-dependent vasodilation, and monitor the time-dependent cascades of molecular events. This includes monitoring the delayed gene expression of inflammatory and angiogenic

factors and the migration patterns of mobilized immune and progenitor cells hours after the session ends. The therapeutic potential of IPC may not lie in its direct effect but in its ability to induce a systemic state of enhanced self-regulation. This cumulative adaptive response suggests that IPC throws a metaphorical "stone into the water," creating long-period waves of reactivity that ultimately guide the organism toward homeostasis. A critical line of inquiry must shift focus to the post-effects—the delayed, complex, and underrecognized adaptive responses that persist for hours, days, or even weeks or months after a treatment course. Understanding these dynamics is essential to explain IPC's efficacy in situations where acute benefits are minimal, or where the therapy "shouldn't" work.

Organization and methodology

§16. *Prediction.* Further research must focus on defining the precise temporal profile of IPC's effects: the onset of action, time to peak benefit, and, most critically, the duration of remission for specific conditions. This will enable a shift from empirical, fixed treatment schedules to physiology-guided regimens. Conversely, if the length of the planned course is fixed, we should be able to estimate likely outcomes. Understanding these temporal dynamics is essential for clinical planning, allowing practitioners to inform patients not just about expected benefits, but about the minimum time required for those benefits to emerge and the optimal timing for repeat treatments to prevent relapse. The ultimate goal is to develop predictive models that bring IPC into the domain of strategic long-term care. This requires research integrating individual physiologic biomarkers with machine learning analytics.

§17. Another direction is dynamic mapping of tissue stress, shearing, and pressure gradients during IPC sessions. Using elastography, we could visualize tissue-layer displacement and evaluate the depth of mechanical effect in real time.

The overconcentration of IPC research on deep vein thrombosis prevention has created a misleading impression of its narrow scope. It is now evident that we are poised on the verge of 12-15 years' worth of discoveries waiting to happen.

The Alphabet

One of the most promising yet underdeveloped areas in intermittent pneumatic compression research is what we call the "alphabet" of IPC. By this, we mean a structured and hierarchical map of all parameters that influence the clinical outcomes of an IPC procedure — as well as the expected biological responses associated with specific parameter values across different levels of physiological organization. A

“parameter” here refers to any feature of IPC that can be expressed in measurable units, unambiguous qualitative descriptors, or binary “yes/no” properties — and which can be practically used to distinguish devices or techniques.

This is a systemic gap in the development of IPC. Today, the idea of an “alphabet” remains a working concept on the desks of a few dozen researchers worldwide. No attempt so far has resulted in a public, broadly accepted, or even conditionally complete document. The reason is simple: such a task demands an unusually high level of interdisciplinary coordination. It creates a paradox — we develop treatment protocols without a fully defined coordinate system. Like writing a driving manual without being entirely sure how many wheels the vehicle is supposed to have.

Tables are not enough. The current evidence is insufficient for establishing standardized IPC protocols due to profound heterogeneity in study designs, patient populations, devices, and therapy settings. Yet this very heterogeneity shows that different factor combinations yield different outcomes. The goal is not to eliminate this methodological noise, but to understand and use it as the true expression of human physiological diversity.

Comparative tabulation of IPC parameters and corresponding outcomes is an established methodology, commonly used in systematic reviews and device evaluations. These matrices catalog parameters, their values, and observed effects, forming the basis for subsequent meta-analysis.

However, constructing a comprehensive matrix quickly reveals its fundamental limitation. Each cell demands a detailed narrative explanation, resulting in a structure that is massive, multidimensional, and resistant to standardization — a structure nearly impossible to publish in a traditional format. It ceases to be a mere table and becomes a reference system: an encyclopedic or multi-layered database.

In this light, the development of an IPC ″alphabet″ is both a prerequisite for standardization and a research challenge in its own right. It deserves recognition as a standalone scientific agenda. We hope this conceptual outline serves as an initial stimulus for its deeper exploration.

Unknown parameters. At present, our understanding of which IPC parameters are clinically significant remains fragmented. While a few—like pressure, duration of inflation and pause, and total session time—are commonly discussed, many others, such as wave direction or frequency, are overlooked. That gives only six commonly discussed parameters, while there could be up to twenty (see Appendix 2). The primary challenge is to encompass the complete spectrum of IPC parameters; only then can we begin to establish their clinical hierarchy (fundamental, secondary, indifferent) through practice. The next steps would include developing systems for measurement and evaluation—especially for subjective sensations,

multivector relationships, nonlinear biological effects, derived parameters, ratios, and integrated indices. For instance, pressure alone means little without time. We need to understand which combinations or ratios actually matter for clinical outcomes.

Personalization. A sign that we are moving in the right direction will be when the IPC community starts discussing different types of people, not just different pressure levels in the cuff. Compression is not about force per se but about how tissues respond to it. This means the same pressure value may produce very different physiological effects in different patients. To personalize the compression level, we could introduce empirical coefficients, hypothetically such as: $P = (P_0 + Pmax) \times K_1 \times K_2$, where P is the target compression for a specific patient; K_1 reflects tissue compliance—how soft and deformable the tissue is; and K_2 reflects tissue rigidity—how tense or fibrotic it is. The optimal area for IPC has high compliance and low rigidity. Areas with low compliance and high rigidity may be painful and less responsive and require caution. Mixed profiles often lead to unstable or unpredictable results.

Interdisciplinary imperative. Building a corresponding Big Data system is theoretically feasible but extremely challenging. Crucially, its application in clinical routine would be infeasible without artificial intelligence support. Such a project requires deeply interdisciplinary expertise—mathematical modeling that typically lies beyond the skills of the physicians, biologists, or biomedical engineers who currently dominate IPC research. Ironically, these same professionals would be the main users of such a system—yet they are least equipped to create it. This complexity leads to the risk of "Tarshinov's IPC collapse". High-quality solutions are rarely cheap—and low-quality ones are rarely worth paying for.

An alternative approach would be to build the "alphabet" not through computational modeling but by conducting a series of direct clinical studies, using large and carefully selected representative groups. While costly, this could yield a practical parameter "alphabet" within a few years but would still necessitate a dedicated hardware-software platform.

The ideal device

IPC is a device-dependent procedure. Let's consider a situational (ad hoc) classification of medical pneumatic compression devices and divide them into three groups, organized along two axes: the device complexity and capability, and the clinical tasks and usage context:

- Class I: Personal or home-use devices—simple interface, preset modes, high safety margin, compact form, support for unsupervised use and long-term compliance.

- Class II: Routine clinical devices—adjustable settings, diverse treatment protocols, durable construction, designed for supervised use and full medical compliance.
- Class III: Research platforms—full parameter control, support for experimental designs, capable of emulating virtually any IPC scenario.

What we need is a Class III system—a tool that allows the simulation of any IPC procedure with any parameters. This would be a specialized development, not intended for mass production, commercial sale, or routine clinical use.

Research-to-practice gap. Building such a system is a challenge—but its existence might create an even greater problem: the fundamental research-to-practice gap. On what equipment would regular doctors be expected to reproduce the findings of researchers working on a Class III device?

How can we convert a complex, poorly formalized technique into something that can be mathematically modeled and made broadly accessible? Here, we face the problem of an interface mismatch: engineers lack clinical thinking; clinicians don't speak the language of mathematics; and mathematicians often disregard the biopsychosocial context. Much of the technical workload could be managed by artificial intelligence, but the price would be a "black box" phenomenon—where a doctor receives a decision without a transparent rationale. Even if the "alphabet" of IPC appeared tomorrow, most clinicians would not be able to use it. It would require new interfaces, new visualizations, and new forms of education. This is not only an interdisciplinary issue—it is also a technological and pedagogical one.

The best device. Let's take another look at the market. For years, the most troubling question observed in clinical practice and device distribution has been: 'Which device is the best?' There is no universally best device—only the best match between its capabilities and your clinical goals. A Class III platform is just an expensive pump without a clinical 'alphabet'; a simple unit can be effective in skilled hands.

We once gave a talk at a rehabilitation event focused on limb injuries, presenting a comparative table of IPC devices. The audience was asked to name the best and worst models. None of the market leaders met our predefined ideal. Ironically, the lowest-rated device was the one optimized for DVT prevention. It was the best certified and most extensively studied—but it lost because we asked the right clinical questions.
If clinicians don't define the demand, the market will. A device that looks good in a catalog may not be best for a patient. Clinical reasoning must set the terms—only then will manufacturers produce real solutions, not just devices.

Optimized versus universal device. Now consider the market from another angle. Many devices are well-optimized—but only for narrow tasks. The lack of a universal system limits the translation of research into practice. We have many specialized devices but no universal ones to unify the methodology.

If each device only realizes 10% of the method's potential, the market doesn't recognize the core idea of IPC as a systemic regulatory method. It sees tools, not a methodology. The devices themselves are not bad—but they don't give freedom to think. There is no Class 2.5 device—one built for understanding IPC. The pedagogy of the method is not yet articulated in technical terms.

One such universal system ("Bioregulator-004M", Ukraine, 1992-2015) was developed and hand-assembled in just 101 units, some of which remain in service. In our view, it is still one of the most advanced and complicated IPC systems ever built, and this made it commercially unpopular. So, if this heavyweight were to be revived, it would evolve: one version would become a modern research-grade platform; another would degrade into a clinical-grade model—likely splitting into a family of devices tailored to specific clinical tasks.

Modular environment. It's plausible that some IPC parameters are mutually incompatible. One device may allow control over pressure, while another permits precise timing. Therefore, a research-grade IPC platform may end up being a modular environment—a sandbox, an incubator—with interchangeable components (cuffs, control units) configured for the task at hand. Not a single device, but a design system for any IPC configuration. From this research rig, simplified, evidence-based commercial models could be derived, effectively transforming the platform into a template for generating market-ready devices. Moreover, the results wouldn't just apply to IPC, but could inform related domains—such as counterpulsation therapy.

Biofeedback. Biofeedback and sensor systems would be indispensable in such a platform. In everyday practice, in home settings, this could support self-regulating, personalized IPC sessions, minimize user error, and enable remote monitoring. One solution might combine IPC with tensometric sensors to assess absolute pressure and distribution. We believe that integrating IPC with bioimpedance analysis (M.I. Kayes, 2021) is not only unconventional but scientifically justified. It enables individualized session timing based on real-time tissue hydration and offers dynamic visualization of patient status.

Depending on the IPC "target" in each case, biofeedback could rely on rheography, pulse oximetry, skin temperature monitoring, noninvasive brain potential registration, heart rate variability analysis, blood pressure, or, in some cases, spirometry. Psychophysiological self-assessment scales (e.g., fatigue, pain, work capacity, and quality of life) could guide session frequency.

Big data. The future of IPC may lie in a world where its clinical effectiveness is no longer demonstrated through individual case reports, but through medium or big data: thousands of procedures, patients, and parameters analyzed in real time, with consideration of genetic, biochemical, behavioral, and environmental factors.

In this future, IPC is not merely a therapeutic tool—it becomes part of a system of regulatory analytics, where algorithms search for response clusters, predictors of efficacy, and optimal parameter settings. At that point, IPC moves beyond classical physiotherapy toward a mathematically guided intervention that requires systems thinking and models grounded in population-level dynamics.

Conclusion

Intermittent pneumatic compression, across its different device architectures and parameter settings, produces a wide range of cascading clinical effects. This suggests its potential utility extends far beyond traditional applications, reaching into anti-aging, infectious diseases, and neurological disorders. To realize this potential, we must reconstruct parameter logic on new methodological grounds and develop devices with fundamentally new control architectures.

We do not present this concept as a definitive answer, but as a practical tool for organizing disparate data and broadening the view of IPC. It is our hope that this framework will interest researchers and developers in these new directions.

The motivation behind this work has always been simple: to make IPC available to every patient who needs it. The Ukrainian history of IPC began when an oncologist told Ihor Tarshinov: “Why are you taking your device home? What are you thinking about? It is needed by thousands of patients.” Decades of clinical practice have since made it clear that the number of patients who could benefit is measured not in thousands, but in hundreds of thousands.

Appendix 1. Comparison of empirical experience

The purpose is to highlight the divergence between formalized global knowledge and locally derived empirical practice. We compared two lists of diagnoses:

- Compiled by ChatGPT-4o (2025): This list, derived from a Large Language Model (LLM) trained on publicly available data, represents a quasi-consensus view—a generalized, encyclopedia-like

compilation of globally accepted (or strongly hypothesized) indications. This artificial source is deliberately chosen to avoid the critique of any specific published author's work.

- Compiled by Author (2017): This list reflects indications derived from the Ukrainian clinical environment during a period when its publication ecosystem was often disconnected from global research. These data points, though foundational to local practice, were often not formalized to current international standards [7].

Conditions with strong consensus (widely accepted indications) are excluded for clarity. Asterisked conditions (in both columns) indicate those that remain doubtful but where the potential benefit likely justifies the risk or requires further clinical validation.

Diagnoses, ICD-10 code	LLM, 2025	Author, 2017
Deep vein thrombosis I80.2. Varicose veins during pregnancy O22. Spinal cord injury S14, S24, S34.	Present	Not listed
Chronic heart failure I50. Thromboangiitis obliterans I73.1. Pelvic venous congestion syndrome I86.2. Multiple sclerosis G35. Rheumatoid vasculitis M05.2. Systemic lupus erythematosus M32. Systemic scleroderma M34. Chronic kidney disease N18	Present*	Not listed
Cerebral palsy G80 [67][68]. Arterial hypertension I10–I15 — mainly cohort studies [69][70][71].	Present*	Present
Angiotrophoneurosis G90.9, trophic ulcer of the lower extremities L97, lipodermatosclerosis I83.1 — non-randomized controlled trials [1][72]. Hyperglycemia R73 — different designs [48][51][73][74]. Macular dystrophy H35.3, diabetic retinopathy H36.0, glaucoma H40, myopia H52.1 — mainly non-randomized controlled trials [28][75][76][77]. Asthenic syndrome F48.0 — non-randomized controlled trial [33][78]. Sleep disorders F51 — quasi-experimental study [32]. Post-traumatic stress disorder F43.1 — longitudinal observational studies [21][22][24]. Attention deficit disorder F90, epileptic syndromes G40 — case series and case reports [79][80][81][82]. Unspecified neuropathies G62.9, dorsalgia, osteochondrosis, radiculopathies M54 — case series and case reports [67][68][83]. Somatoform autonomic dysfunction F45.3 — institutional report [20]. Different designs cited in [5]: Cellulitis L74.9 — institutional report, *p.* 204. Arthritis M13, osteoarthritis M15–M19 — mainly reports and cases, *pp*. 151–153, 203, 204. Joint contracture M24.5 — mainly reports and cases, *pp*. 152, 181–182, 205. History of myocardial infarction Z86.7 — cases, *pp*. 224, 229. Diabetic encephalopathy E11.9 — expert opinion.	Not listed	Present

Diagnoses, ICD-10 code	LLM, 2025	Author, 2017
Baroacoustic trauma of the ear H83.3, sensorineural hearing loss H90.3 — quasi-experimental study [84]. Intellectual disability F70–F79, childhood autism F84.0, childhood enuresis F98.0 — case series and case reports [79][80][81][82]. Psychogenic erectile dysfunction F52.2 — non-randomized controlled trial [33][78]. Different designs cited in [5]: Chronic sinusitis J32.0 — cohort study, *pp. 177–178.* Chronic nonspecific pneumonia J18.9 — case series, *pp. 178–180.* Chronic cerebrovascular disease I67.8 — case report, *pp. 164–167.* Post-burn skin conditions T95.0 — institutional report, *pp. 181–182.* Meteopathy syndrome T75.2 — expert opinion, *p. 104.*	Not listed	Present*

Appendix 2. Potential IPC parameters

This appendix provides a structured list of parameters that constitute the proposed IPC "alphabet." The present version of this taxonomy is deliberately scoped to the physico-technical core of IPC. Key dimensions for future expansion include adaptive control algorithms, clinical scenario integration, and the quantification of subjective perception.

Topographical

- Anatomical location: visible body parts, with attention to lateralization and segmental zoning.
- Projection-based location: areas that correspond to internal organs or pathological processes.
- Target location: preparatory, primary, compensatory, or indirect zones of action.
- Area of influence. Since “area ≠ significance,” it might be helpful to propose a weighted scale (e.g., based on the number of receptors, volume, or vascular accessibility) with a weighted unit like cm^2 × sensitivity coefficient. The shape of contact (flat or circular compression) and relative area (percentage of the available surface) may also be considered.

- Compression dose: an integrated index combining pressure, area, and time—to reflect the energetic or neurophysiological impact.

Pressure. Much of this data is better visualized via pressure curves or cyclegrams, allowing synchronized analysis of multiple zones or types of pressure:

- Phase pressure dynamics: contact force (P_0, compression from strap only), baseline compression pressure (P_{min}, before inflation), peak or plateau pressure (P_{max}), and inflation/deflation gradients.
- Peak pressure kinetics: screen value (nominal pressure), actual internal chamber pressure, effective pressure on the skin (depends on body position, fit, and tightness), subjective pressure perception (often used to gauge "dose"), and tissue-depth gradient.
- Anisotropic pressure in tissue layers: includes shear, stretch, local gradients (in fascia), directional shifts (in muscles and fascia), tensor deformation (at receptor or interface zones), hydro-mechanical gradients (in fluids), and cellular-level tension gradients.
- Dynamics of the pressure pattern during the session.

Time

- Segment-level base timings: inflation time (t_1), plateau time (t_2), deflation time (t_3), pause time (t_4).
- Derivatives: relative ratios of these phases.
- Cuff-level parameters: duration of compression and pause phases, full cycle length, and total procedure time. Derived: compression wave speed.
- Session-level and treatment plan timing: duration per session, interval between sessions, course length, interval between courses. Derived: time ratios.
- Phase-based parameters: intersegmental phase shifts and overlap; positional mapping of active segments.

Frequency

- Absolute activity metrics: number of inflations and plateaus per minute; duration of inflation, plateau, deflation, and pause.
- Relative metrics: percentage of time spent in each phase (e.g., plateau) within a cycle or full session; phase-time ratios.

Cuff Construction

- Chamber properties: material (elastic or inelastic), wall thickness, thermal conductivity, absolute and relative size, shape, and skin contact conformity.
- Multichamber layout: number of chambers, relative overlap, and size gradients.
- Pneumatic tubing: length (resonant or not), pressure control mode (global or per-chamber).
- Cuff tailoring design: type of closure (single or sectional), adaptability.
- Working medium (air inside the chamber): temperature, vibration, containment (sealed or open circuit).

Statements and Declarations

AI Use

Generative Large Language Models (LLMs)—specifically ChatGPT-4o (OpenAI), Gemini 2.5 Flash (Google LLC), and DeepSeek (Beijing DeepSeek Technology Co., Ltd.)—were used by the author. The specific tasks for which the LLMs were utilized include:

Conceptual Assistance: Obtaining quasi-reader feedback and controlled critical remarks on the research substance, as well as controlled generation of ideas and data (particularly in the "Potential directions for further exploration" section).

Generation and Synthesis: In places explicitly noted within the text (particularly in the "Current synthesis" section and "Appendix 1"), LLMs were used for model building and the generation of definitions and generally accepted knowledge.

Language and Style Correction: Controlled translation of the Ukrainian text into English, controlled text volume reduction, and correction of the academic style.

All output generated by the LLMs was thoroughly reviewed, corrected, and approved by the author. The author assumes full responsibility for the article's content, methodological justification, conclusions, and the accuracy of all data generated and utilized within the manuscript.

Conflicts of Interest

The author reports a past association that could be viewed as a potential conflict of interest. The author's family was a founder of ETO “New in medicine”, Ltd., the manufacturer of the products discussed herein.

The author also holds relevant patents. Nevertheless, ETO “New in medicine”, Ltd. ceased operations in 2019, and the maintenance of the aforementioned patents has been discontinued. Consequently, the author declares no current competing financial interests related to this work.

Declaration on Bibliographical Sourcing

In adherence to national ethical guidelines concerning the ongoing full-scale invasion of Ukraine, the citation of works by authors affiliated with Russian Federation institutions was limited. For essential conceptual contributions, authors were mentioned by name only, omitting direct bibliographic references.

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