

## Intercurrences And Complications Of The Use Of Cryolipolysis: Series Of Cases And Treatments.

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### **Abstract:**

The cryolipolysis technique uses selective and controlled cooling based on the principle that lipid-rich tissues are more susceptible to cold damage than surrounding water-rich tissues. Cryolipolysis stands out as a non-invasive method for body contouring without damaging subcutaneous tissue, becoming a popular treatment to non-invasively address localized fat accumulation and tone the dermis. The complications previously reported in the literature are mostly paradoxical adipose hyperplasia (HAP), but there has been a large increase in unreported injuries in recent years, with several complications such as frostbite, panniculitis, HAP and hyperchromia post-inflammation.

**Objective:** This study aims to describe the authors' experience guiding professionals in the management and treatment of several cases of complications resulting from the application of the Cryolipolysis technique. We guided more than 10,000 complications in 12 years, and made a brief review of the world literature on the subject.

**Materials and Methods:** An exploratory study was conducted, presented in a narrative review, to demonstrate the action of the Cryolipolysis technique used in the treatment of aesthetic dysfunctions. The review explored scientific articles published and available in the following databases: MEDLINE (Medical Literature Analysis and Retrieval System Online), PubMed (National Library of Medicine), SCIELO (Scientific Electronic Library Online), LILACS (Latin American and Caribbean Literature in Health Sciences), and Google Scholar. In addition, a series of cases of complications from the use of the cryolipolysis technique that occurred in a multicentric manner and developed with the use of various commercially available equipment were added to this study.

**Results:** when using techniques based on scientific studies, respecting time and temperature, in addition to associations with equipment, drugs and techniques that inhibit cellular precursor factors, we will reduce possible interurrences and complications. The most common complications described in this study are neuropathic lesions in sympathetic innervation, paradoxical adipose hyperplasia, frostbite, frostnip and hemosiderin hyperpigmentation.

**Conclusion:** The scientific literature demonstrating the lesions and their possible causes with the cryolipolysis technique is robust, but it did not prevent serious complications secondary to the use of Cryolipolysis, which has become common in aesthetics in Brazil and worldwide. Therefore, it deserves full attention for the adoption of appropriate application techniques to minimize such complications, among them: greater temperature control with machines that show the skin temperature on the panel, correct time control, without exaggeration, high-quality antifreeze membrane and mandatory use of the "liner" (plastic) as occurs throughout the world, protection of sympathetic innervation through microcurrent and completion of the techniques with inhibition of factors that lead to cell multiplication such as PPAR gamma and CD 68 through shock waves or 40 kHz ultrasound, in addition to not performing vigorous massage on hard frozen tissue.

**Keywords:** cryolipolysis, adipose tissue, aesthetic complications, Panniculitis, adipose hyperplasia, frostbite, Frostnip

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## **I. Introduction**

The cryolipolysis technique uses selective and controlled cooling based on the principle that lipid-rich tissues are more susceptible to cold damage than surrounding water-rich tissues.

These dead cells trigger an inflammatory response and are metabolically eliminated through phagocytosis, a natural digestive process of the body, leading to reduced fat deposition in the treated area (Ferraro, 2012; Pugliese, 2020).

Technological advances have led to several treatments to treat localized fat, with cryolipolysis standing out as a non-invasive method for body contouring without damaging subcutaneous tissue (Loap, 2018). Initially validated as a stand-alone technique for localized fat reduction through controlled freezing, cryolipolysis has been enhanced with adjunctive approaches, such as contrast cryolipolysis, which incorporates periods of heating at the beginning or end of the application, producing promising results. Furthermore, cryolipolysis has been combined with other therapeutic modalities to promote lipolysis and increase efficacy (Jones, 2018; Ruiz-Silva; 2024).

Cryolipolysis has become a popular treatment to noninvasively address localized fat accumulation, bypassing the risks associated with reconstructive surgeries, such as complications related to anesthesia, bleeding, contour irregularities, scarring, altered sensitivity, infections, or fat embolism (Wu, 2020; Lopes-Martins, Ruiz-Silva et al, 2024)

The use of cryolipolysis has gained popularity as a frequent cosmetic procedure in the United States, according to the Aesthetic Society. In Brazil, despite Professor Dr. Carlos Ruiz teaching courses since 2012 and teaching how to avoid occurrences and complications, due to the wide variety of equipment that is not similar to the North American ones with FDA, there are dozens of techniques and a lack of standardization of the procedure in most cases, without basis or foundations based on the current literature, which has led to the incidence of several post-treatment complications, which have generated thousands of injuries in recent years (Ruiz-Silva, 2023; 2024).

This study aims to describe the authors' experience through several cases of complications resulting from the application of the Freezing technique in Brazil and which gave rise to some important complications after the procedure, as well as a brief review of the world literature on the subject.

## **II. Material And Methods**

This study is characterized by exploratory research, presented through a narrative review, to highlight the action of the Cryolipolysis technique, used in the treatment of aesthetic dysfunctions and its possible adverse effects and/or complications. The review explored scientific articles published between 2008 and 2024, and available in the following databases: MEDLINE (Medical Literature Analysis and Retrieval System Online), PubMed (National Library of Medicine), SCIELO (Scientific Electronic Library Online), LILACS (Literature from Latin America and the Caribbean in Health Sciences), and Google Scholar. As inclusion criteria, sources that mentioned cryolipolysis treatments for reducing adipose tissue through apoptosis and lesions resulting from this treatment were selected. Sources that did not present physiology and lesions and journals that were not scientific were discarded. In addition to the bibliographic review, a survey of several cases of complications after the use of Cryolipolysis that occurred in Brazil in a multicentric manner was added to this study, in order to describe the authors' experience in approaching and managing these adversities after the treatment of localized fat using various commercially available equipment.

## **III. Result And Discussion**

### **Intercurrences, Complications and Adverse Effects**

Intercurrence is the term that defines the occurrence of an unexpected event in a procedure, which could not generally be foreseen or warned to the patient. Any and all procedures, from the simplest to the most complex, are subject to unexpected complications, which do not necessarily incur an error (Oliveira, 2024).

It is not uncommon for a technically correct health treatment, but whose outcome caused harm to the patient, to be labeled as an error by the health professional.

Iatrogenesis consists of adverse effects or pathological changes caused by or resulting from a correct health treatment performed within the recommended limits, which are predictable, expected or unexpected, controllable or not, and which can sometimes occur. These are problems that are often predictable and easy to resolve, often avoidable when we know the causes and should not be seen as complications (Oliveira, 2024).

They are usually mild, transient and technically dependent. Allergies are another good example. It is absolutely impossible to prevent or predict the appearance of allergies when the patient does not report to the doctor that he/she has already had them to some substance, since allergies are completely impossible to avoid unless the cause is known in advance. Therefore, a patient who takes a medication that he/she has never taken and is allergic to it presents a "medical complication"; a variation in the reaction of his/her own organism (Oliveira, 2024). This also applies to the healing process of a patient. When undergoing plastic surgery or aesthetic procedures, even if performed correctly, the aesthetics of the scar (such as the appearance of keloids, hypertrophic

or atrophic scars) depends much more on the organic reactions of the patient than on the techniques used, and if the professional observes the appropriate conduct when performing the procedure, they are also classified as a medical complication (Oliveira, 2024). In the medical field, such complications are also called iatrogenesis. The term iatrogenesis comes from Greek and refers to any pathological change caused in the patient by poor medical practice. In legal terms, not all iatrogenesis can be considered a medical error, but rather a predictable consequence in the literature as a predictable intercurrent within the spectrum of treatment (Tafelli, 2017).

More serious and difficult-to-resolve injuries are called complications and we must avoid them and know how to treat them.

Cryolipolysis stands out for being a procedure with a high rate of effectiveness for reducing and modulating adipose tissue, in addition to cryoweight loss.

It is a safe, effective procedure, with a low rate of adverse effects and that offers satisfaction to patients. The greatest fear of professionals who work with Freezing are the dreaded intercurrents and complications, we must know how to avoid them, but it is extremely important to know what to do when they occur.

#### Adverse events

This is an unfavorable event that occurs during or after therapy. It is important to emphasize that to be considered an adverse event, Cryolipolysis does not necessarily have a causal relationship with the event.

#### Adverse effect

A harmful or undesirable effect that occurs during or after an intervention, in which there is a reasonable possibility of a causal relationship between the treatment and the effect. Adverse effects are considered mild, transient, and self-limiting. However, they are susceptible to adverse events and complications (de Faria et al., 2023).

An adverse reaction is any harmful or undesirable, unintentional response.

#### Side effect

It is an unintended effect (adverse or beneficial) caused by the therapy. The word “side” denotes something of secondary importance. Thus, the use of this expression can minimize the perception of harm when the effect is harmful. As this term is often used inappropriately, we consider it outdated and the literature recommends abolishing its use (Oliveira, 2024).

Post-cryolipolysis injuries have a multifactorial pathophysiology, involving soft tissue damage resulting from prolonged cooling. The peripheral nerves are the most sensitive. The first symptoms are paresthesias of the affected tissues.

Initially, the skin is anesthetized, with intense pain after reperfusion and a phase of hyperemia. Edema begins after a few hours, possibly with the formation of blisters in more severe cases.

The literature says that “burns” that are actually frostbite (figure 1) are not common, and usually happen when professionals make technical errors because they are not trained to perform the technique; they handle the device improperly (Ribas, 2021), they do not check how many degrees Celsius the machine is delivering using thermometers or if it is out of calibration.



**Figure 1: Frostbite and its evolution with necrosis, hyperchromia and hyperchromia**

**Incidents due to machine malfunctions**



**Figure 2 and 3: Equipment working on only one side, with only one side having thermometers**



**Figure 4 and 5: uncalibrated machine, according to INMETRO it should reach -11 degrees**



**Figure 6: The machine heated up on the sides and burned the patient, in addition to not cooling the central region.**

**Panniculitis, “Geladura” (in Portuguese) Frostbite, Frostbite**

Many cases of evident skin chelation have arisen in the clinical practice of Cryolipolysis in Brazil. Given the current situation, our understanding leads us to believe that the lack of control over exposure time in addition to the lack of temperature control has been causing injuries. Most professionals responsible for these cases of Frostbite (“geladura” in Portuguese) report that they followed the rules established by the companies that sold the machines or technical training provided by the rental companies. In addition, we see many professionals neglecting to control skin temperature, in addition to not using a good quality antifreeze protective membrane and the lack of the mandatory Liner (plastic) (Zelickson, 2009).

Cryolipolysis promotes apoptosis (Ruiz-Silva, 2024), time and temperature of current articles do not exceed -11 degrees for a maximum of 35 minutes (Kania, 2024; Michon, 2021; Azab, 2021; Jain, 2020; Pugliese, 2020; Kilmer, 2020; Abdel, 2020; Few, 2020; Putra, 2019; Palauro, 2025)

To generate apoptosis via hypoxia, the intracellular lipid enters a solid state around 10°C (Stevens 2013) and the Adipocytes around 3°C to 10°C, this is the key to the results (Pinto, 2013; 2014; Jane, 2014; Sasaki, 2014). However, cell death by necrosis at -2°, 0° and 2°C; excessive periods at low temperatures generate necrosis in addition to apoptosis.

Cold-induced panniculitis is a common lesion in cold regions, and was extensively studied by Harvard University in the United States in the 1970s and 1980s, studying Popsicle Panniculitis, Equestrian Panniculitis and Trench Foot (Hong, 2022; Manstein, 2008; Zelickson, 2009), and defined it as hardened red nodules followed by transient necrosis.

In 1970, the term “popsicle panniculitis” emerged after the presence of a hardened red nodule followed by transient necrosis of adipose tissue on the face of a child who had sucked on a popsicle, which evolved to generate a dimple on the face. Buttocks of children exposed to ice cubes after vaccinations also had the same lesions (Jalian, 2013).



**Figure 7: Cold panniculitis**

Cold panniculitis is a form of panniculitis with an idiosyncratic response to exposure to cold. It affects people who have spent prolonged periods in the cold, affecting areas of the skin that have been exposed to the environment.

The histological aspects of cold panniculitis are similar to those of panniculitis caused by Lupus erythematosus and dermatomyositis (which are contraindications for Cryolipolysis), remembering that they are inflammatory diseases.

In some cases, cold panniculitis is characterized by particularly dense chronic inflammation at the interface of the subcuticular dermis (Rivitti, 2014). Also called hypodermatitis, panniculitis is an inflammatory process of the hypodermis (adipose tissue). There is no universally accepted classification of panniculitis, many pathologists classify it by dividing panniculitis into septal and lobular forms (Delgado 2009; Rivitti, 2014). "Septal" meaning inflammation confined predominantly to the septa, was classically associated with erythema nodosum (EN) and "lobular" indicating inflammation predominantly involving the fat lobule itself, similar to most other types of panniculitis (Lupus).

#### Supportive care

- Anti-inflammatory drugs
- Avoid any excess that can cause Panniculitis.
- There is no specific definitive treatment.
- Several strategies are used with moderate results, including AINEs and antimalarials: Diclofenac, Ibuprofen, Naproxen, Nimesulide, Indomethacin, Ketoprofen, Mefenamic acid, Piroxicam, AAS (acetylsalicylic acid)

Local application I suggest topical ointment and cream contains 0.64 mg of betamethasone dipropionate (equivalent to 0.5 mg of betamethasone)

Diprogenta Cream is the most indicated; each gram of DIPROGENTA Cream and 1 mg of gentamicin, in the form of sulfate, has a rapid onset of action, being indicated for the relief of inflammatory manifestations sensitive to corticosteroids. It has anti-inflammatory, antipruritic and vasoconstrictive action, and has a prolonged duration of action, allowing application twice a day.

Gentamicin, a broad-spectrum bactericidal antibiotic, is effective against a wide spectrum of common skin pathogens.





**Figure 8 And 9: Paniculitis After Double Freezing Technique With Two Massage Maneuvers In Region That Has Compartment**



**Figure 9 And 10: Panniculitis In A Region With Little Localized Fat And Close To The Ribs Where Blood Reperfusion Is Much Greater**



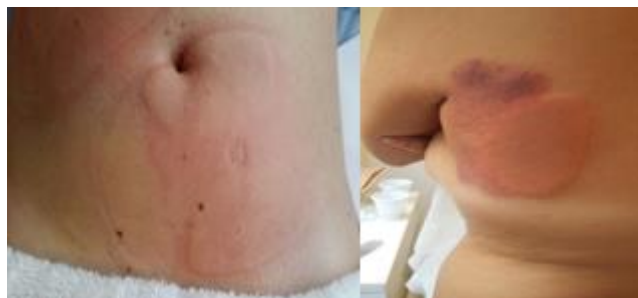
**Figure 11 And 12: Paniculitis After Double Freezing Technique With Two Massage Maneuvers In Region That Has Compartment**

### **Subcutaneous edema**

Subcutaneous edema consists of the accumulation of clear liquid in the subcutaneous tissue, which appears gelatinous. Edema occurs when there is an accumulation of liquid under the skin, which normally appears due to inflammation and hypoxia (Kumar, 2005).

In clinical practice, we have seen that it frequently occurs when professionals use techniques that heat the dermal tissue before cryolipolysis, for example, the contrast technique that heats before freezing, the use of high-frequency ultrasound of 1 and 3 MHz, where the thermal effect predominates.

The big mistake, widely publicized by internet influencers, is to use radiofrequency or cryofrequency before freezing, in addition to using a thermal blanket.



**Figure 13 and 14: subcutaneous edema after previous use of Radiofrequency and after cryolipolysis**



**Figure 15 and 16: subcutaneous edema after using 3MHz ultrasound before cryolipolysis**

### **Frostnip superficial cold injuries**

Frostnip occurs when the top layer of your skin is slightly injured due to exposure to cold. When your body is exposed to cold, blood vessels constrict, diverting blood away from the skin to maintain core body temperature. After prolonged exposure to cold temperatures, we have superficial hypoxia. If we do not have antifreeze blankets or excessive exposure, dermal injury may occur in the cooled areas, presenting numbness, edema and redness. (Valente, 2018; Dow, 2024).

With reperfusion, the region may hurt or burn intensely. Remember that we will usually have injury to nerve endings of the sympathetic system due to freezing of the myelin sheath. No permanent damage occurs, although the area sometimes remains particularly sensitive to cold for a few months (Starink, 2024; Dow, 2024). It can generate hemosiderin hyperchromia



**Figure 17 and 18: Frostnip with improvement after use of Betamethasone**



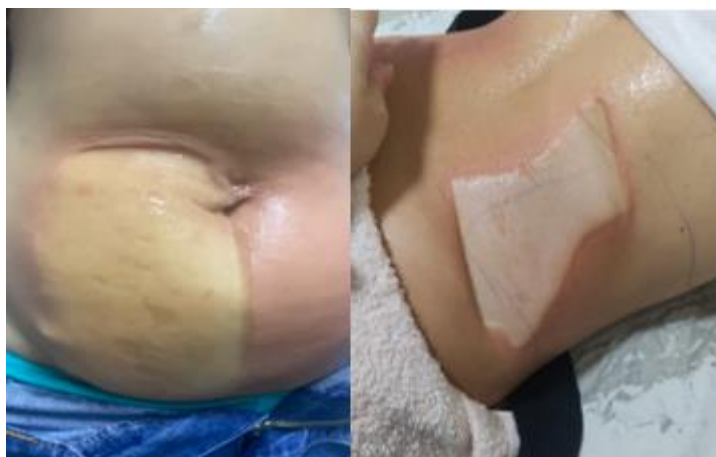
**Figure 19: Frostnip with spontaneous improvement after 2 hours**

### **Frostbite**

Frostbite is the destruction of tissue by direct action of cold and the development of reperfusion injury. Injuries occur when the skin temperature is  $<0^{\circ}\text{C}$  for a long period. It is important to note that the risk of burns

increases from 5% to 95% when the temperature on the skin surface decreases from  $-4.8^{\circ}\text{C}$  to  $-7.8^{\circ}\text{C}$ . (Essien, 2024)

After exposure to temperatures below zero, ice crystals are formed in the extracellular medium and, if freezing is rapid, this can even occur in the intracellular medium. The fluxes of ions such as sodium and potassium cause damage to cell membranes and, subsequently, apoptosis. An endothelial inflammatory process mediated by the arachidonic acid cascade may occur with release of thromboxane A<sub>2</sub>, prostaglandins, bradykinins and histamine vasoconstriction, platelet aggregation, leukocyte adhesion and erythrocytosis, which results in venous and arterial thrombosis and subsequent tissue ischemia, necrosis and dry gangrene (Wibbenmeyer, 2024).



**Figure 20 and 21: Frostbite subcutaneous tissue in a solid state, with ice formation where subcutaneous edema was generated.**

#### **Frostbite (“geladura” in Portuguese)**

“Heat burns and ice or cold freezes”. It is an injury resulting from the freezing of tissues. Initial presentations may be deceptively benign, the skin appears white or blistered and numb; rewarming causes severe pain and may result in the development of gangrene.

Ice crystals form within or between tissue cells, freezing them and causing their death. Adjacent non-frozen regions are at risk, as vasoconstriction and local thrombosis can cause ischemic damage due to reperfusion during rewarming, inflammatory cytokines are released (e.g., thromboxanes, prostaglandins), exacerbating tissue injury.

The depth of tissue loss depends on the duration and depth of freezing (Dow, 2019; 2024).

The affected area is cold, hard, white and numb. When warmed, the area acquires erythematous patches and becomes edematous and painful. Blisters form within 4 to 6 hours, but the full extent of the lesion may not be apparent for several days. Blisters filled with clear serum indicate superficial injury; this heals without residual tissue loss.

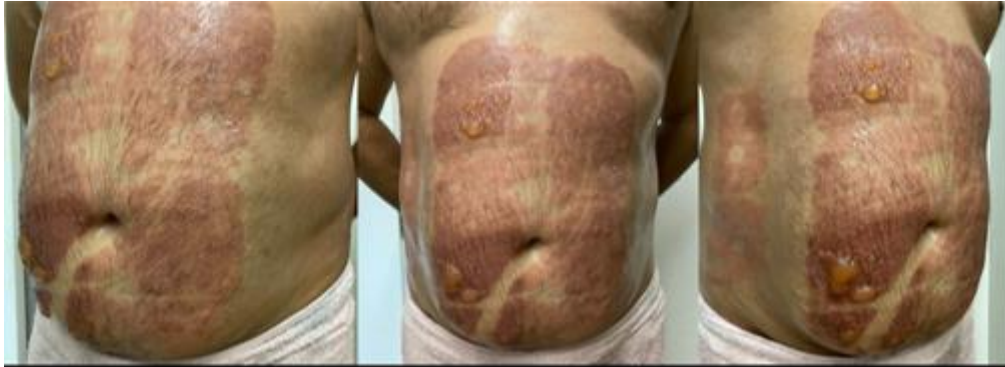
Blisters with blood proximal to the lesion indicate deep injury and probably tissue loss. Freezing of the deep tissues causes dry gangrene with a hard black carapace over the healthy tissue; wet gangrene, gray, edematous and soft, is less common (Dow, 2019; 2024).

Wet gangrene can become infected, but dry gangrene probably does not.



**Figure 22 and 23: Frostbite of subcutaneous tissue in a solid state, with ice formation where subcutaneous edema was generated, do not massage or force reperfusion.**

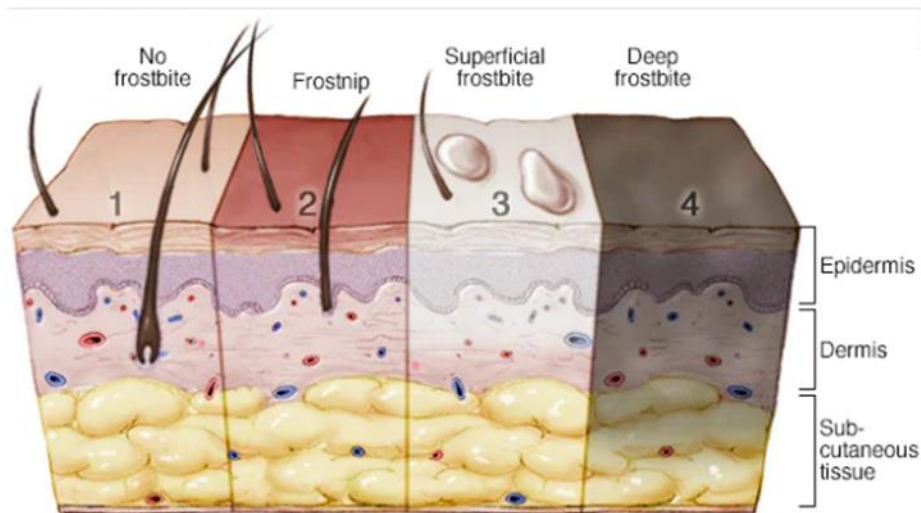




**Figure 24, 25 and 26: initial appearance of frostbite after reperfusion massage in an attempt to eliminate the ice formed in the subcutaneous tissue.**

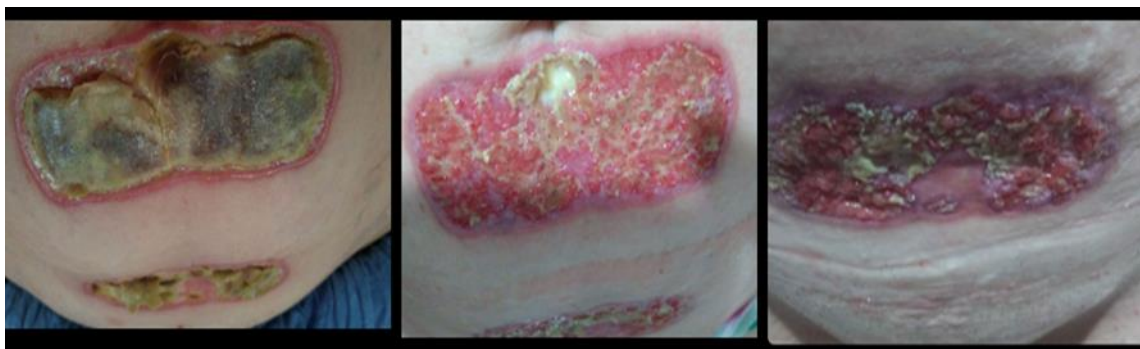
Local action of cold Injuries very similar to burns and classified into degrees:

- 1) First degree, injury characterized by local pallor or redness and anserine appearance of the skin (erythema)
- 2) Second degree, erythema and formation of blisters or blisters with clear, hemorrhagic content;
- 3) Third degree, necrosis of soft tissues with formation of blackened, adherent and thick crusts;
- 4) Fourth degree, by gangrene or disarticulation.



**Figure 27: representation of injuries due to exposure to cold**

([https://www.mayoclinic.org/-/media/kcms/gbs/patient-consumer/images/2014/10/14/09/41/r7\\_frostbite.jpg](https://www.mayoclinic.org/-/media/kcms/gbs/patient-consumer/images/2014/10/14/09/41/r7_frostbite.jpg))



**Figure 28: 4th degree frostbite after 60 minutes of suction cryolipolysis at -11 degrees and maximum vacuum**

### **Chilblains**

Chilblains are characterized by inflammatory skin lesions caused by prolonged exposure to cold. Symptoms are precipitated by acute exposure to cold. The first symptoms are paresthesias of the affected tissues that may progress to itching and burning pain.

Painful bluish nodules may form, which may persist for several days. Skin manifestations, which appear up to 12 to 24 hours after acute exposure, include localized edema, erythema, cyanosis, plaques, nodules and, in rare cases, ulcerations, vesicles and blisters. The best treatment is the use of topical corticosteroids (0.1% triamcinolone cream) (Dow, 2019; 2024).



**Figure 29, 30, 31 and 32; 2nd degree frostbite, evolution occurred as chilblains.**

**Flictena**

Flictena is an elevation covered by epithelium containing liquid and measuring more than 1 cm, it is synonymous with a blister.

When a frostbite occurs, our lymphatic system sends a liquid to help the body contain the burn, thus preventing the loss of mineral salts and water.



**Figure 33 and 34: 4th degree frostbite with Flictena**



**Figure 35 and 36: Frostbite with Flictena**

### **Cold Allergy**

Cold allergy is a condition that can cause very uncomfortable injuries and have serious consequences for those affected if they are exposed to extreme temperatures. It is very important to diagnose it in order to avoid these damages and to know why the body reacts when it comes into contact with cold (de Albuquerque, 2024).

Cold allergy is the popular name for a condition known scientifically as cold urticaria. Its episodes are more common in the coldest periods of the year, autumn and winter, and usually involve the appearance of red patches, swelling and itching in areas exposed to cold temperatures. These situations occur due to hypersensitivity of the dermis when receiving this type of stimulus, the so-called induced urticaria, which causes hypersensitivity crises and, consequently, the manifestation of the symptoms of the condition, is the excessive release of histamine by the body when receiving the stimulus of exposure to cold.



**Figure 37 and 38: Cold allergy after cryolipolysis and improvement with the use of Prednisone**

### **Cold-associated urticaria**

Cold-associated urticaria is part of the so-called cholinergic urticaria, representing a characteristic example of hypersensitivity to cold. Most cases are idiopathic, but it can also be associated with increased affinity of immunoglobulin E for mast cells. The diagnosis can be confirmed by exposing the patient to cold.

The greatest danger, however, is the risk of anaphylaxis. This generalized reaction is normally caused by intense exposure to cold, such as when entering the sea or a cold pool, and can cause a drop in blood pressure, loss of consciousness, nausea, vomiting, and swelling of the throat and tongue, impairing breathing (Geller, 2013).

Cold-associated urticaria is treated in a similar way to urticarial lesions. Antihistamines are recommended for acute cases. We recommend Fernegam, Histamim, Loratadine, 10 mg, Clarintin or Prednisone, 20 mg.



**Figure 39 and 40; Cold allergy caused by freezing with Gelox and improvement with the use of Prednisone**

### **Pernio erythema or perniosis.**

Pernio erythema is more related to vasoconstriction than to an allergy itself, resulting in lesions in the affected areas.

Symptoms: lesions usually appear 12 to 24 hours after exposure to cold environments and improve in 2 to 3 weeks, presenting symptoms such as: Swelling; Pain; Itching; Burning sensation; Ulceration or fissure.



Erythema nodosum is a specific form of panniculitis characterized by sensitive, red or violet subcutaneous nodules that are palpable (Mendes, 2026).



**Figure 41 and 42: erythema perninium that evolved into panniculitis and hyperchromia**

### **Bruises and Ecchymosis**

After suction with excessive pressure, it is common for a purple spot to appear, probably an ecchymosis, but often mistakenly called a hematoma.

Both ecchymosis and hematoma can appear after cryolipolysis. Ecchymosis is formed when superficial blood vessels are damaged and a small hemorrhage occurs. It appears after the rupture of the blood vessel and over time, its color changes from greenish to yellowish before disappearing naturally. It appears in irregular, diffuse and flat spots, without causing elevations in the area (Silva, 2021; Mota, 2024).

The treatment for ecchymosis and hematoma are also different.

While ecchymosis is a rupture of the most superficial blood vessel, hematoma is a deeper rupture that can cause elevations in the skin and dark spots.

Treatment for bruises resulting from injuries and contusions usually disappears spontaneously within days or weeks. To relieve pain in the affected area, you can apply 500 mg of mucopolysaccharide polysulfate in a 40-gram ointment; gel with 100 grams of escin with diethylamine salicylate, and use anti-inflammatories such as ibuprofen.

Hematomas are also caused by ruptured blood vessels, but blood accumulates in the tissue, causing a raised bump. Depending on the size and location, the hematoma may require surgical intervention to drain the blood. Initially, we must reduce inflammation by using anticoagulant ointments based on heparin, which are indicated and reduce inflammation, relieve pain and reduce swelling and purple spots in the injured areas. Thrombofob 200 u gel with 40 grams of sodium heparin

Perform ultrasound, microcurrent and LED with anti-inflammatory parameters at the site of the injury after 24 hours and accelerate the hematoma absorption process, to prevent skin pigmentation and help eliminate the hematoma.



**Figure 43 and 44: Hematoma after cryolipolysis of plaques, evolving into inflammatory hyperpigmentation**

### Excessive suction

Excessive suction can cause injuries due to tissue stretching, causing subcutaneous edema, as shown in figures 45 and 46

Vacuum cryolipolysis causes a series of injuries, which has led most companies to modify the vacuum system to minimum vacuum cryolipolysis and central freezing, thus avoiding areas of poor contact without freezing and without apoptotic effect, compartment injuries in upper and lower limbs, as well as injuries to nerve endings (Nikolis, 2021; Stefani, 2015)

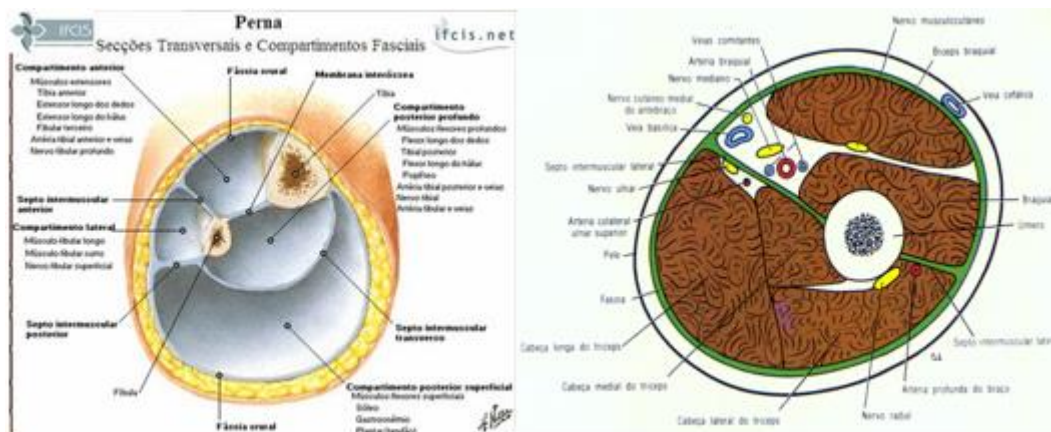


**Figure 45, 46 and 47: Lesion with subcutaneous edema after Suction cryolipolysis in compact tissue**

### Compartment syndrome

consists of increased tissue pressure within a tight fascial compartment, resulting in tissue ischemia. The first symptom is exaggerated pain, proportional to the degree of injury; it is a self-perpetuating cascade of events. It begins with tissue edema that typically occurs after injury (from soft tissue edema or hematoma).

If edema occurs within the fascial compartment, typically in the anterior or posterior compartment of the lower limb, there is little room for tissue expansion; thus, interstitial (compartmental) pressure increases. As compartmental pressure exceeds the normal capillary pressure of about 8 mmHg, cellular perfusion slows and may eventually stop. It generates reperfusion injury after vascular injury and repair (Lopes, 2024)



**Figure 48 and 49: Compartments in arms and thighs**

### Innervation injury and paresthesia

Suction generates compression of the innervation, generating paresthesia.

Lipids are more susceptible to cold injury than water-rich tissues (Suh, 2019; Savacini, 2018). Possible damage to the peripheral nervous system during cryolipolysis represents an important issue to be considered. It is important to know the distribution of nerves and their types throughout the body in order to assess their different thermal sensitivities and take them into account when positioning the cryolipolysis applicators.

Cold produces a decrease in the conduction velocity of peripheral nerves and a reduction or blockage of their synaptic activity. Nerve fibers vary in sensitivity to cold according to their diameter and degree of myelination.

It has been shown that the most sensitive nerves are the most myelinated and of small diameter, since the demyelinated ones require lower temperatures to be blocked. Since the temperature of action of cryoadipolysis is not lower than -10 ° C, we will only have first-degree and transient injury; Neuropraxia (+10 to -10 ° C), (Marmol, 2019)



The lack of axonal nerve transmission generates injury and blockage of the electrical bioconductivity of the SNS, activating hyperplasias, we need stimulation of nerve endings of the sympathetic system to generate beige or brown adipose tissue. Transient decrease in sympathetic neural stimuli can activate preadipocytes (Ho, 2017) Paradoxical adipose hyperplasia.

Repetitive cryotherapy can result in further injury to the sympathetic nerve dysfunction causing spots on the skin (Duarte, 2028), clinically the pain is intolerable in this neuropathy (sympathetic) and we have somatic focused pain. This neuropathic sensitivity to cold is also called "cold-sensitive syndrome" (Goldberg; 1959)

Muscle functions are governed by nerve activity. Nerve activity (motor and sensory) is anesthetized due to the reduction in nerve conduction speed by cold, muscle activity in the area will also be temporarily paralyzed (Marmol, 2019).

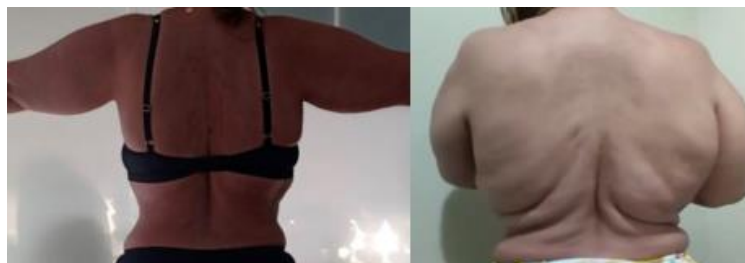
### **Paradoxical adipocyte hyperplasia (HAP)**

Adipogenesis is the hyperplasia of adipose tissue (increase in localized fat) and can be activated after cryolipolysis by activation of transcription factors, in addition to increased fibroplasty with generation of fibrosis, adhesions and nodules.

PPAR gamma is the main receptor of the adipocyte nucleus responsible for cell division and differentiation. They are potent activators of adipogenesis, which convert fibroblasts into adipocytes (Silva, 2016). Blocking this receptor combats adipose tissue hyperplasia. PPAR gamma and C/EBP are responsible for adipose tissue hyperplasia (Sorisky, 2000).

Block: Reduction of adipocyte hypertrophy and recurrence of adipose tissue (Ruiz-Silva, 2024)

There is an increase in hyperplasias worldwide 100 times more than reported in articles or underreported (Ho, 2017; Khan, 2019; Michon, 2021), due to the difficulty of diagnosis (Vogel, 2018) generating a worldwide underreporting (Ho, 2017), however most machines do not require notification.



**Figure 50 and 51: case of post-freezing hyperplasia that lasted 8 hours, Brazilian single-session method**

Increase in the rate from 0.0051% (Jalin, 2014) to 1% (Jain, 2020; Strounza, 2018)

Michon, 2021; reports that it is predominant in suction machines that do not freeze the center, they suck excessively, especially in those who used the excessive time of 60 minutes.

Nikolis, 2021; reduction in the incidence of 75% with central freezing.

Negative pressure may be a factor (Stefany, 2015).

The possible cause is the transient decrease in sympathetic neural stimuli that can activate preadipocytes (Ho, 2017), understanding that the paradoxical response is part of the natural selection of adipocytes for survival (MC Keown, 2021; Ho, 2017; Wang, 2018; Khan, 2018; Franzoni, 2024).

The non-injured generate a rebound and multiplication effect, a survival effect (Stefany; 2015; Ho, 2017).

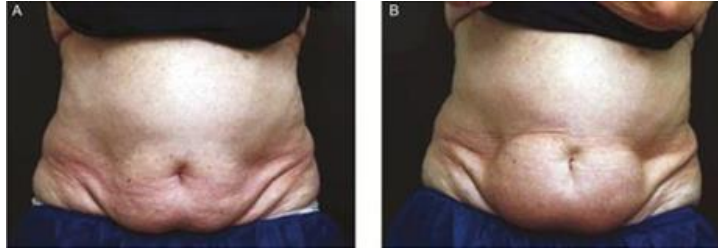
### **Massage with the tissue still “SOLID” Frozen, generates injury.**

Another hypothesis is that the massage performed at the end of the cryolipolysis session, with the aim of increasing lipolysis, causes trauma to the adipocyte membranes, resulting in inflammatory adipocytolysis. Cookson described this phenomenon as pyroptosis and reported that it resembles apoptosis, but is inflammatory (Strounza, 2018)

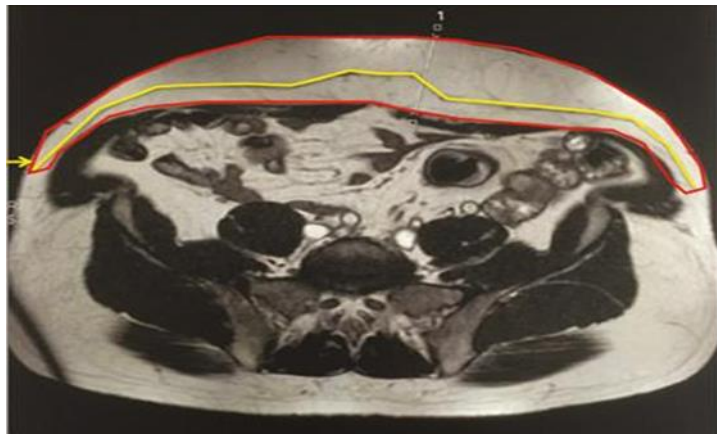
The inflammatory adipocytolysis process is dependent on caspase-3 and leads to the formation of holes in the adipocyte membranes, leading to an inflammatory repair process; However, some holes are irreparable and, thus, the adipocytes become necrotic (Seaman, 2016).

The region presents a large, painless swelling in the treated area, post-mild abdominal nodular panniculitis with spontaneous regression in one month, paresthesia in the treated area for a few weeks, and may present hematoma after abdominal cryolipolysis.

In the tomodensitometry (figure 53), we have the presence of a non-necrotic parietal pseudomass, with a fatty appearance, without signs of necrotizing fasciitis or fluid effusion (seroma or hematoma). Abdominal magnetic resonance imaging (MRI) confirmed these findings and revealed hypertrophy of the superficial abdominal adipose tissue, above the superficial fascia (Strounza, 2018).

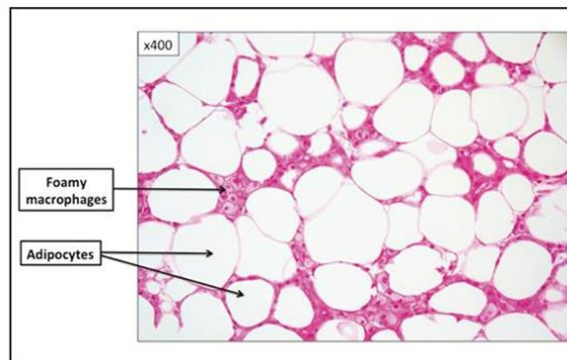


**Figure 52: Adipose hyperplasia (Strounza, 2018)**

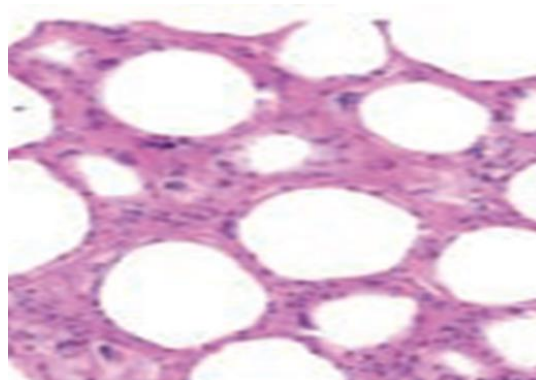


**Figure 53: tomodensitometry demonstrating hyperplasia**

Histological analysis of the pathological adipose tissue performed after surgery revealed nonspecific lobular panniculitis, septal thickening, interstitial infiltration of foamy macrophages and foci of adiponecrosis. In addition, adipocytes of variable size were present.



**Figure 54: Foamy macrophages, adiponecrosis and replication of new adipocytes, characteristics of suction freezing followed by vigorous massage.**



**Figure 55: Note that in 2008 Masten already demonstrated the presence of interstitial infiltration of foamy macrophages and foci of adiponecrosis. Presence of new adipocytes replicating.**

It is worth noting that in lipedema and in post-cryolipolysis followed by solid tissue massage, there is an increase in the CD68+ differentiation cluster (Ruiz-Silva, 2024).

Immunohistochemical analyses indicated degenerative and regenerative changes in lipedema tissue, characterized by crown-like structures (necrotizing adipocytes surrounded by infiltrating CD68+ macrophages), a feature commonly seen in obese adipose tissue. These findings suggested increased adipogenesis in lipedema tissue, which may further lead to hypoxia similar to that observed in obesity, resulting in adipocyte necrosis and macrophage recruitment (Wiedner, 2028; Morgan, 2024).

Genetic research has not found a specific relationship to dysfunction of a specific transmission gene (Sousky, 2000). An important insight into lipedema and cryolipolysis is to consider that Brazilian researchers found these same cells when investigating freezing with suction cryolipolysis for 30 minutes followed by massage (Palauro, 2024; 2025). Preadipocytes that undergo excessive apoptosis as they differentiate acquire relative resistance to apoptosis (Jain, 2020). Inhibitors of apoptosis (IAPs) act to suppress apoptosis via inhibition of caspase activity, extracellular survival factors inhibit apoptosis in several pathways and bind to cell surface receptors, and suppress apoptosis; stimulate an increase in the production of antiapoptotic Bcl2 proteins, such as Bcl2 and Bcl-XL; activated by multiple adipogenesis, which is the case of lipedema (Seaman, 2016).



**Figure 56 and 57: Classical paradoxical adipose hyperplasia**

Some authors suggest that the increase in volume is due to the fact that preadipocytes, whose fat content is lower, will not be lysed by the application of cold, unlike mature adipocytes. These preadipocytes will then be able to proliferate later, leading to an increase in tissue volume.

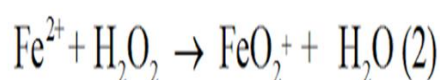
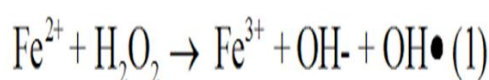
Other hypotheses include adipocyte hypertrophy, changes in the expression of receptors associated with adipocyte metabolism, reduced sympathetic innervation or hypoxia (Cox, 2022).

Another explanation is that, after cooling, hypoxia can trigger a response that includes hypertrophy and fibrous cells (Vargas, 2021; Gonzalez, 2025)

### **Hyperchromia due to hemosiderin**

One of the most common causes of cold panniculitis, which is accompanied by an inflammatory process that generates hyperchromia, is the use of the double or triple reperfusion technique, which consists of double freezing followed by massage. When performed in regions that have a compartment, they generate an increase in hemosiderin due to the Fenton reaction, causing iron stains. Remembering that the abrupt increase in O<sub>2</sub> and Ca, activates Superoxide with lipid peroxidation, a large amount of Hydroxyl is generated (Bitu-Moreno, 2020). Superoxides undergo dismutation by SOD, receive another hydrogen and become a Hydroxyl radical that influences the membrane and Nucleic Acid (Pinho, 2014), promotes the increase in the concentration of Malondialdehyde, Myeloperoxidase (presence of H<sub>2</sub>O<sub>2</sub>) (Costa, 2022) generated lipid peroxidation and oxidative stress. Hemosiderin is a pigment resulting from the destruction of hemoglobin, being a consequence of the excess deposit of iron. Red blood cells are rich in hemoglobin, which is rich in iron ions that give the blood its red color. When death occurs by extravasation, hemoglobin is retained in this space, releasing iron. The iron then undergoes oxidation when it receives heat, giving rise to a pigment called hemosiderin, which is responsible for the rust-colored stains.

- Suggested treatment is to use a hemosiderin depigmenting serum gel with Hemaline 2% and Haloxyl 2%



**Figure 58: Fenton reaction**



**Figure 59 and 60: Hemosiderin hyperchromia**

### **Hypopigmentation**

Loss of pigment after a skin injury. The skin may lose its pigment after recovering from frostbite. In this case, it is not as white as in vitiligo and, over time, it may return to its normal pigmentation.

We suggest using a skin repigmentation cream, Pigmerise" represents a major advance over the current first-choice treatments for Vitiligo, such as psoralens and chelin. It is a natural phytocomplex, derived from black pepper extract (*Piper nigrum* L.), in resin oil, standardized with a high concentration of alkaloids and volatile oils. Pigmerise" does not contain alcohol in its composition and can be applied to sensitive areas, such as the mouth, eye area and genital region, thus increasing patient adherence to treatment.

Pigmerise" stimulates the proliferation of melanocytes that are located deep in the epidermis and increases melanogenesis. Pigmerise" protects cellular DNA and, therefore, does not trigger the risk of developing melanoma. Pigmerise" is safe and effective with or without exposure to UV radiation. The formulation of Pigmerise" in Fitalite" favors a deeper absorption of the phytocomplex, actively reaching the melanocyte. Suggested formulation is Pigmerise™ 20%, Fitalite™ qsp 50 g



**Figure 61, 62,63 and 64: hyperchromia followed by hypochromia**

### **Asymmetries and irregularities**

Only the frozen areas undergo apoptosis due to hypoxia. Even in lesions, we can observe that vacuum machines with freezing through lateral Peltier are ineffective.



**Figure 65,66, 67, 68, 69, 70, 71, 72, 73: Injury caused by machine that does not freeze the center**



#### IV. Conclusion

Although reported in the world literature, serious complications secondary to the use of Cryolipolysis have become common in Brazil and worldwide, therefore deserving full attention to the adoption of appropriate application techniques to minimize such complications, among them: greater temperature control with machines that show the skin temperature on the panel, correct time control, without exaggeration, high-quality antifreeze membrane and mandatory use of the “liner” (plastic) as occurs throughout the world, protection of sympathetic innervation through microcurrent and completion of the techniques with inhibition of PPAR gamma through shock waves or 40 kHz ultrasound, not making it necessary to perform the technique.

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