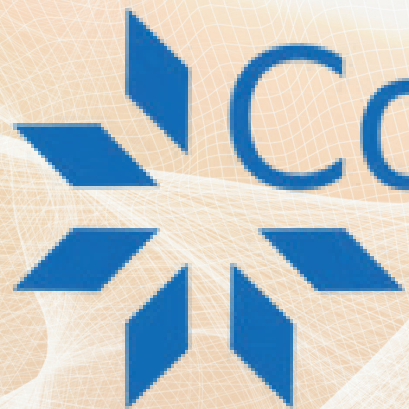




# CoolSlimming

Ultimate  $360^{\circ}$

## Consultation Guide



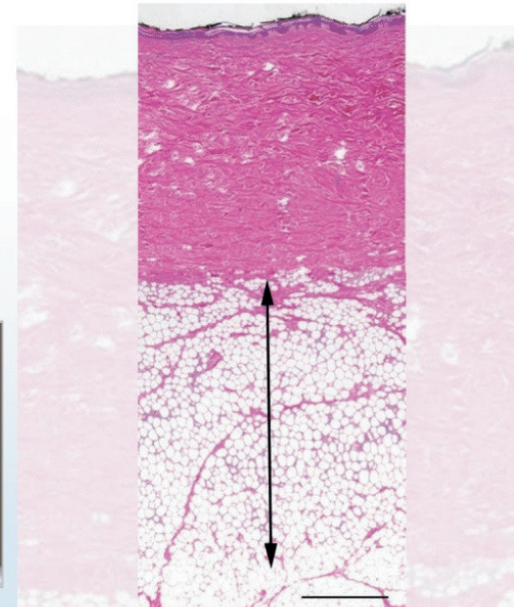
# Background to the Discovery of Cryolipolysis



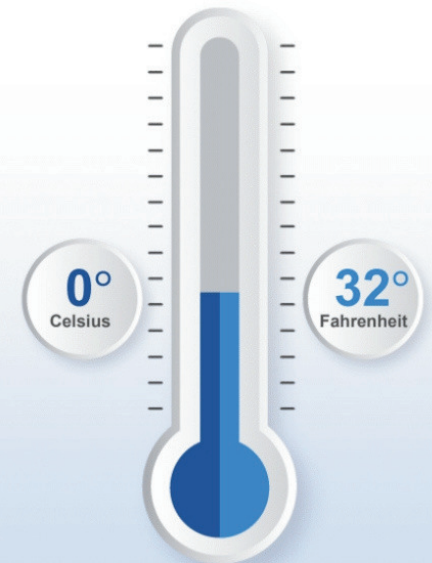
Popsicle<sup>1</sup> and equestrian cold<sup>2</sup> panniculitis observed



Dieter Manstein, MD, PhD and Rox Anderson, MD hypothesized that tissue-specific cold injury could be used for reduction of subcutaneous fat without injuring the overlying skin<sup>3</sup>



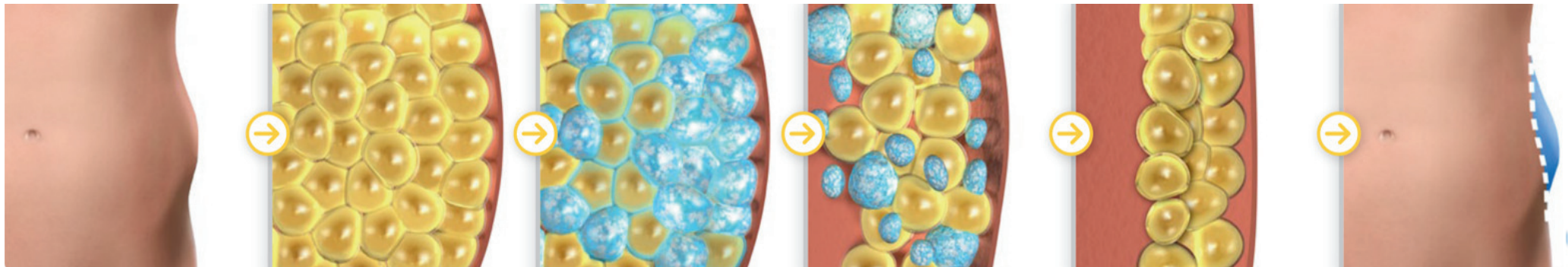
Adipose tissue is preferentially sensitive to cold injury compared with surrounding tissues (eg, skin, muscle, and nerves)<sup>3</sup>



Hypothesized that crystallization of cytoplasmic lipids in adipocytes occurs at temperatures well above the freezing point of water<sup>3</sup>

1. Epstein EH, Jr. and Oren ME. N Engl J Med. 1970;282(17):966-967. 2. Beacham BE, et al. Arch Dermatol. 1980;116(9):1025-1027.  
3. Manstein D, et al. Lasers Surg Med. 2008;40:595-604.

# The CoolSlimming Process



**1. Genetics and lifestyle create our body shape.**

**2. Stubborn, unwanted fat bulges are assessed and treatment plan created.**

**3. Controlled cooling is applied to desired areas to freeze & crystalize fat cells. 30% of fat cells are affected on average.**

**4. Crystallized fat cells go through apoptosis & eliminate out of the body through the lymphatic system over the next 12 weeks.**

**5. Remaining fat cells condense, shrinking the fat layer. The skin also tightens with the reduction of volume.**

**6. Stubborn fat is eliminated permanently, leaving area contoured and smooth. Multiple sessions may be required for desired results.**

# What Areas Can Be Treated?

- The CoolSlimming 360° System is indicated for cold-assisted lipolysis (breakdown of fat) in areas of subcutaneous fat such as of the upper arm, bra fat, back fat, banana roll, submental area, thigh, male chest, abdomen, and flank, or “love handles” in individuals with a Body Mass Index (BMI) of 30 or less.
- In addition, the device is intended for cold-assisted lipolysis of the submental and submandibular areas in individuals with a BMI up to 46.2.



# CoolSlimming 360 Applicators





# How Many Treatments Are Required?

- Most clients require 1–3 CoolSlimming treatments, depending on their body, lifestyle, and the level of sculpting they wish to achieve. During your consultation, your therapist will assess the area, discuss your goals, and recommend the most effective treatment plan for you.
- Each CoolSlimming session destroys approximately 25–30% of the fat cells within the treated area. Because every body responds differently, results will vary from person to person.
- Treatments are performed once every 4 weeks to allow the body time to naturally eliminate the targeted fat cells.

## **Factors That Influence Results:**

- Lifestyle habits such as diet, exercise, hydration, and sleep
- Medications or hormonal changes
- Weight gain following treatment

CoolSlimming is designed for body sculpting, not weight loss. We will guide you through realistic, achievable expectations during your consultation to ensure you feel informed, confident, and supported throughout your treatment journey.

# Post-Treatment Care & What to Expect

CoolSlimming requires no downtime, and you can return to normal daily activities immediately. Light movement such as a gentle walk or a light gym session is perfectly fine.

## **It is normal to experience:**

- Swelling and tenderness in the treated area for 4–7 days
- A bruise (rare, but more likely if you are prone to bruising) even if not visible, the area may feel bruised
- Numbness or reduced sensation, which can last several weeks before gradually returning to normal

These responses are expected and part of the body's natural elimination process.



# Post-Treatment Care & What to Expect

## Aftercare Guidelines

- First 24 hours: avoid carbohydrates, alcohol, and caffeine to support treatment efficiency
- Hydration: drink a minimum of 2 litres of water daily for 12 weeks to assist the body in flushing out the destroyed fat cells
- Nutrition: maintain a balanced, healthy diet to support long-lasting results

## When You'll See Results

Most clients begin noticing changes around 3 weeks post-treatment, with optimal results visible at 12 weeks. This timeframe allows your lymphatic system to naturally clear the targeted fat cells and for the remaining fat cells to condense.

# Common Side Effects

The following effects can occur in the treatment area during and after a treatment. These effects are temporary and generally resolve within days or weeks.

| During Treatment                                                                                                                                                                                                                          | Immediately After Treatment                                                                                                                                                                      | 1–2 Weeks After Treatment                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Sensations of pulling, tugging, and mild pinching at the treatment site</li><li>• Intense cold, tingling, stinging, aching, cramping. These sensations subside as the area becomes numb</li></ul> | <ul style="list-style-type: none"><li>• Redness and firmness</li><li>• Transient blanching and/or mild bruising around the edges of the treatment area</li><li>• Tingling and stinging</li></ul> | <ul style="list-style-type: none"><li>• Redness, bruising, and swelling</li><li>• Tenderness, cramping, and aching</li><li>• Itching, skin sensitivity, tingling, and numbness. Numbness can persist up to several weeks after a treatment</li><li>• Sensation of fullness in the back of the throat after submental area treatment</li></ul> |



# Contraindications

**Localised skin cooling is contraindicated in patients who have:**

## **Cryoglobulinemia**

- Presence of abnormal proteins (called cryoglobulins) that clump together in the blood at temperatures below 37 °C, which can impede blood circulation and damage skin, joints, nerves, and organs.

## **Paroxysmal Cold Hemoglobinuria**

- Very rare subtype of autoimmune hemolytic anemia (AIHA), caused by the presence of cold-reacting autoantibodies in the blood and characterised by the sudden presence of hemoglobinuria, typically after exposure to cold temperatures.

## **Cold Agglutinin Disease**

- Rare type of autoimmune hemolytic anemia in which the body's immune system mistakenly attacks and destroys its own red blood cells.

# Considerations

CoolSlimming 360 System use has not been studied in children, those who are pregnant or lactating, or patients with:

- Known sensitivity to cold such as cold urticaria, Raynaud's disease, or Chilblains (pernio)
- Known sensitivity or allergy to fructose, glycerin, isopropyl alcohol, or propylene glycol
- Impaired peripheral circulation in the area to be treated
- Neuropathic disorders such as post-herpetic neuralgia or diabetic neuropathy
- Impaired skin sensation
- Open or infected wounds
- Bleeding disorders or concomitant use of blood thinners
- Recent surgery or scar tissue in the area to be treated
- Hernia in or adjacent to the treatment site
- Skin conditions such as eczema, dermatitis, or rashes in the area to be treated

# Important Safety Information

Cryolipolysis technology has been widely studied and used globally, and CoolSlimming 360 operates on the same scientific principles as well-known systems like CoolSculpting. While CoolSlimming 360 itself has no reported cases of the rare side effects occasionally documented in CoolSculpting studies, we believe in full transparency. For this reason, we outline these uncommon risks so clients have a complete understanding of the broader cryolipolysis landscape, even though they have not been associated with CoolSlimming 360 to date.

| Rare Event <sup>1</sup>        | Description <sup>1</sup>                                                                                                                                                                            |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Paradoxical hyperplasia</b> | (About 1 per 3,000 treatment cycles, 0.033%) Visibly enlarged tissue volume within the treatment area, which may develop two to five months after treatment. Surgical intervention may be required. |
| <b>Late-onset pain</b>         | (About 1 per 6,000 treatment cycles, 0.017%) Late-onset pain may begin several days after a treatment and usually resolves within several weeks.                                                    |
| <b>Severe pain</b>             | (About 1 per 6,000 treatment cycles, 0.017%) Patients may experience pain of varying severity, which more commonly can be described as mild to moderate, and in rare instances, can be severe.      |

1. Allergan Inc. US CoolSculpting® Important Safety Information. November 2021. Available at: <https://www.coolsculpting.com/pdfs/CSC125713-v3-CoolSculpting-Important-Safety-Information.pdf>.



# Important Safety Information

**Very Rare Adverse Events may happen less than 1 out of 10,000 treatment cycles (less than 0.01%)<sup>1</sup>**

| Very Rare Event <sup>1</sup>      | Description <sup>1</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Freeze burn</b>                | (About 1 out of 14,000 treatment cycles, 0.007%) First- and second-degree freeze burn may occur during treatment. It typically resolves without sequelae with proper care.                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Vasovagal symptoms</b>         | (About 1 out of 30,000 treatment cycles, 0.003%) Dizziness, lightheadedness, nausea, flushing, sweating, or fainting might occur during or immediately after the treatment.                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Subcutaneous induration</b>    | (About 1 out of 30,000 treatment cycles, 0.003%) Generalised hardness and/or discrete nodules within the treatment area can develop after the treatment and might present with pain and/or discomfort.                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Hyperpigmentation</b>          | (About 1 out of 11,000 treatment cycles, 0.009%) Hyperpigmentation can occur after treatment and usually resolves spontaneously.                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Hernia</b>                     | (About 1 out of 185,000 treatment cycles, 0.001%) Treatment might cause new hernia formation or exacerbate a pre-existing hernia, which can require surgical repair.                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Treatment area demarcation</b> | (About 1 out of 20,000 treatment cycles, 0.005%) An aesthetic outcome of treatment in which the patient experiences excessive fat removal in the treatment area, resulting in a visible disruption to the continuous contour of fat, or unwanted indentation in the treated area.                                                                                                                                                                                                                                                                                             |
| <b>Cold panniculitis</b>          | (About 1 out of 60,000 treatment cycles, 0.002%) Cold panniculitis results from injury to adipose tissue exposed to cold and may result in a mild to severe inflammatory response. In mild cases, the symptoms are self-resolving and may include redness, swelling, skin nodules, warmth, tenderness, and possible low-grade fever. These cases typically resolve without long-term sequelae. In more severe cases, an intense inflammatory response may result in more extensive tissue damage, including fat necrosis, which may require medical or surgical intervention. |

1. Allergan Inc. US CoolSculpting® Important Safety Information. November 2021. Available at: <https://www.coolsculpting.com/pdfs/CSC125713-v3-CoolSculpting-Important-Safety-Information.pdf>].

# Extra Clinical Studies

| Reference                                                                                                                                                    | Title                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| Zelickson 2009. <i>Dermatol Surg.</i> 35(10), 1462-1470                                                                                                      | Cryolipolysis for Noninvasive Fat Cell Destruction: Initial Results from a Pig Model                   |
| Manstein 2008. <i>Lasers Surg Med</i> 40(9), 595-604.                                                                                                        | Selective Cryolysis: A Novel Method of Non-Invasive Fat Removal                                        |
| Jimenez Lozano, JN. Presented at the 139th <i>Annual Conference of the American Society for Laser Medicine and Surgery (ASLMS)</i> , Inc. March 27-31, 2019. | Assessment of Subcutaneous Fat Injury, Depth of Injury, and Temperature Threshold After Cryolipolysis  |
| Zachary C, et al. <i>Lasers Surg Med.</i> 2021;53: 70-78.                                                                                                    | Clinical Study Demonstrates that Electromagnetic Muscle Stimulation Does not Cause Injury to Fat Cells |

# Cryolipolysis and Inflammatory Response

- **Cryolipolysis** is a nonsurgical fat reduction method that relies upon the greater susceptibility of lipid-rich adipocytes to cold injury compared with surrounding water-rich cells.<sup>1</sup> Cryolipolysis may trigger apoptosis and a subsequent gradual inflammatory and clearance response.<sup>2,3</sup>

## Histopathology Observations After Cryolipolysis<sup>2</sup>

### Apoptosis

Evident within 3 days post-treatment

- Influx of inflammatory cells

### Inflammatory Phase

14-30 days

- Few neutrophils, lymphocytes, and other mononuclear cells
- Macrophages, foam cells, and other phagocytes
- Adipocyte size reduction

### Clearance and Resolution

60 days +

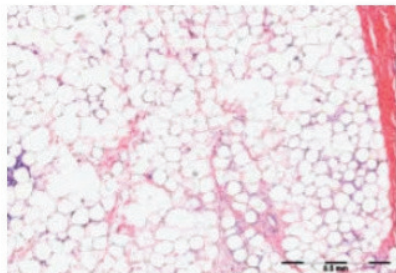
- Apoptotic digestion
- Reduction of inflammatory infiltrate

1. Skin Experts. <https://www.asds.net/skin-experts/skin-treatments/cryolipolysis>. Published 2020. Accessed February 4, 2021. 2. Jimenez Lozano JN. Presented at: 139th Annual Conference of the American Society for Laser Medicine and Surgery (ASLMS); March 2019; Denver, CO. 3. Manstein D, et al. *Lasers Surg Med*. 2008;40:595-604.

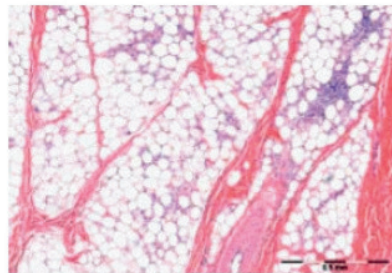


# Proposed Mechanism of Action of Cryolipolysis

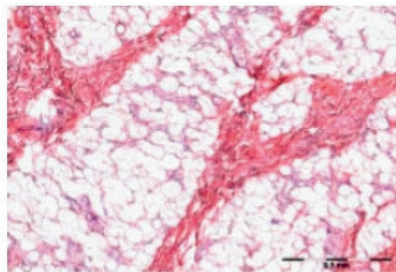
- Histologic analysis at various time points following cryolipolysis demonstrated death of adipocytes which are subsequently engulfed and digested by macrophages<sup>1,2</sup>
  - Death of adipocytes could be due to crystallization of cytoplasmic lipids and appears to occur through a process of apoptosis rather than necrosis<sup>2,3</sup>



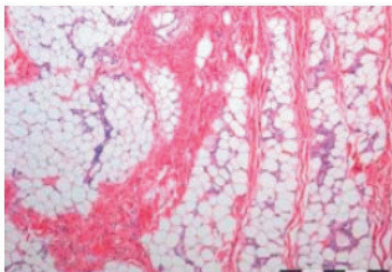
3 days†



14 days†



30 days†

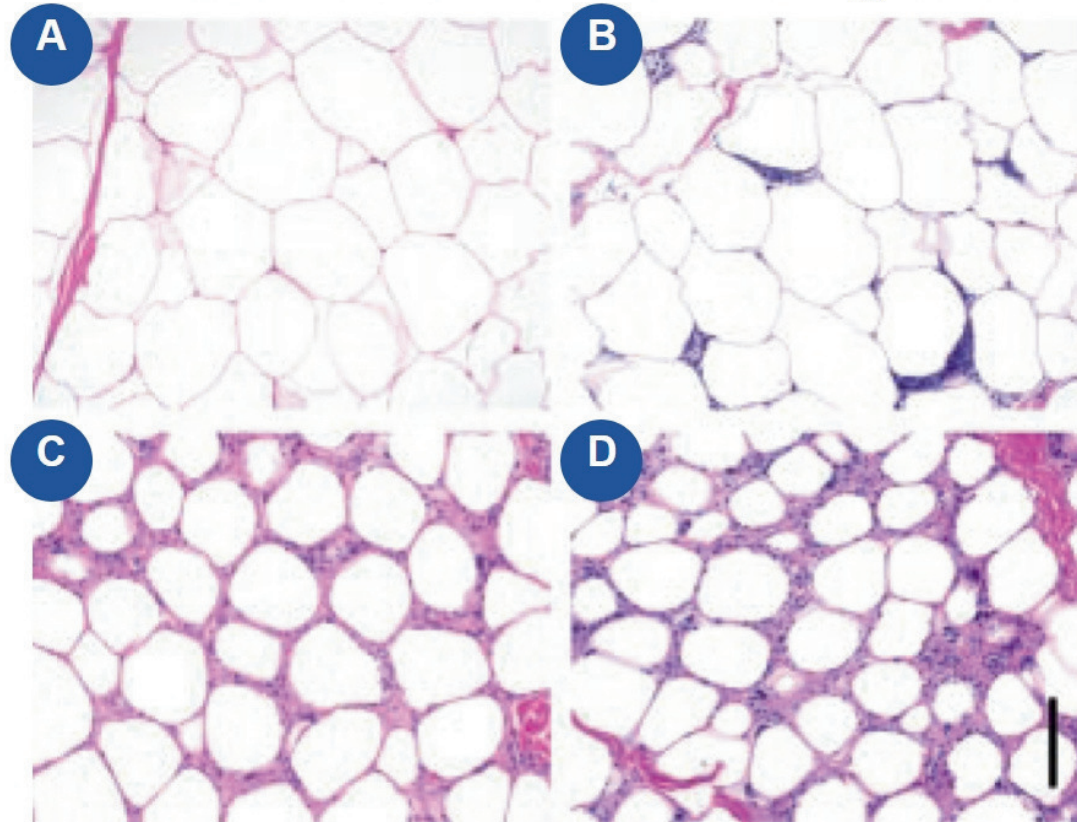


60 days†

- **3 days** after treatment: evidence of an inflammatory process and influx of inflammatory cells<sup>1</sup>
- **14 days:** inflammatory process becomes more apparent<sup>1</sup>
- **30 days:** inflammatory process has begun to decline; thickness of interlobular septa has increased<sup>1</sup>
- **60 days:** inflammatory process declines further, increase in thickness of septa more pronounced, with substantial loss of fat cells in treated area<sup>1</sup>

1. Zelickson B, et al. Amer Soc Derm Surg. 2009;35:1462-1470. 2. Avram MM and Harry RM. Lasers Surg Med. 2009;41:703-708. 3. Manstein D, et al Lasers Surg. Med 2008;40:595-604.

# Results: Timeline of Histological Grading



A single cold exposure was applied (-7°C, 10 min, flat cold plate). Bar represents 100  $\mu$ m.

**(A) Within first hour:** normally shaped and sized adipocytes, no inflammatory cells.

**(B) 2 days:** clusters of inflammation (mainly neutrophils) embracing individual adipocytes.

**(C) 14 days:** dense lymphocytic infiltrate, occasional macrophages, some reduction of adipocyte cell size

**(D) 30 days:** similar to 14 days, however in addition multinucleated giant cells (macrophages) and further reduction of adipocyte cell size



# Injury in Adipose Tissue After Cryolipolysis

## Objective

- To investigate the cellular and molecular changes that occur after cryolipolysis

## Study Design

- 7 patients with healthy tissue (average age = 41.2 years; BMI = 27.7) and planned for abdominoplasty were enrolled in cryolipolysis treatments with a small cup applicator at -11°C for 35 or 45 min
- Tissue samples harvested at 3, 7, 21, and 84 days after treatment
- RNA-sequencing used to examine differential gene expression of endocrine/metabolic and macrophage associated genes and to identify appropriate markers
- Immunohistochemistry used to confirm gene expression results and to quantify extent and depth of injury after treatment
- Transient bioheat transfer modeling conducted to estimate temperatures within treated tissue

## Results

- 3-days post-treatment, **Caspase-3** positive adipocytes were detected
- 1-3 weeks post-treatment, differentially expressed endocrine/metabolic genes were downregulated while macrophage CD genes were upregulated
- **Perilipin-1** and **CD68** shown to be suitable markers for assessing extent of injury
- Perilipin-1 +/- quantified to determine relative count of dysfunctional (dead) and functional (untreated) adipocytes
- CD68 positive staining allowed measurement of maximal extent of injury into treated fat layer, with average depth of 10.46 mm (modeling temperature threshold = 4.59°C)

Clinical significance of preclinical data has not been established.

**Caspase-3**: part of protease ~~enzyme~~ family that plays a role in cell apoptosis<sup>2</sup>. **Perilipin-1 (PLIN1)**: modulator of adipocyte lipid metabolism. **CD68**: typical marker for macrophages (which clear cellular debris and promote phagocytosis)

1. Jimenez Lozano, JN. Presented at the 139th Annual Conference of the American Society for Laser Medicine and Surgery (ASLMS), Inc. March 27-31, 2019.

2. Porter AG, et al. Cell Death Differ. 1999;6(2):99-104.