Research observations on the susceptibility to lesions in lipid-rich tissues when exposed to cold led Manstein et al. to perform an in vitro examination of the adipocyte response to cold. Their assay showed that cooling adipocytes at temperatures above -11°C resulted in apoptosis-mediated cell death and that the subsequent inflammatory response enhanced cell damage to adipocytes that had not been exposed to cold.³⁴

The selective cryolipolysis was then introduced in 2007 as a technique non-invasive to skin cells, nerves or muscles which eliminates exclusively fat cells. The tissue to be treated is sucked into the applicator with moderate vacuum, thus, coming into contact with two cooling plates at an average temperature ranging from -11°C to -13°C.³⁴

The technique is similar for all different apparatus, being necessary the use of a protection blanket on the skin before the tip is placed. At the end of the cycle, right after the removal of the applicator, the area should be massaged for two minutes, a practice that has a direct impact on the final result.³⁴ The restoration of oxygenated blood stimulated by the massage is believed to produce a series of free radicals of oxygen which could potentially increase tissue loss. Reheating cooled adipose tissue after cryolipolysis may promote additional adipose cell damage by ischemic reperfusion during the recovery period.³⁴

Possible side effects include mild to moderate pain, erythema, edema, hematoma, and transient neuralgia, being all of them resolved spontaneously within two to four weeks.³⁴ There were no changes observed in cholesterol and triglyceride levels or hepatic function, as well as no lasting sensory changes.³⁴

Studies have reported that the average fat reduction, considering perimeter measurements of the treated area, ranges from 14.67% to 28.5%.³⁴

The number of treatment cycles depends on the volume of the area. Nevertheless, the same area can only be submitted to a new treatment session after eight weeks, time required to resolve the inflammatory process. It is important to inform patients that results take from two to three months to be seen, which is the time necessary for the lipids to be eliminated by macrophage phagocytosis.³⁴

CASE REPORT
CASE REPORT 1
A 45-year-old female from Rio de Janeiro had localized fat in the lower abdominal region. At the beginning of the study the patient weighed 54.0 kg and her waist circumference measured 78 cm. The cryolipolysis procedure (Coolsculpting® - Zeltiq Aesthetics, Inc., Pleasanton, CA) was performed with a single CoolMax tip, using commercial parameters and maintaining the temperature at -10°C for 60 min. Local massage was performed immediately post-procedure, in addition to three sessions of manual lymphatic drainage, once a month. The procedure was carried out without complications. Side effects, such as erythema and numbness were typical, mild, and resolved with no need for intervention. Clinical photographs documented the subjects before and three months after treatment. (Figure 1)

Weight fluctuations and perimeter measurements were documented during the follow-up visit in the third month following the procedure. The patient had a 1 kg weight loss (53.0 kg) and a 4 cm reduction (74 cm) in her abdominal perimeter.

INTRODUCTION
Among men and women one of the main dissatisfaction towards their bodies is the difficulty for localized fat loss. In Brazil, liposuction surgery is the second most performed cosmetic surgery, according to data from the latest Brazilian Society of Plastic Surgery's Census of 2017.³ Despite the cosmetic benefits to the body contour, as with any procedure, surgery involves risks of complications, such as skin irregularities, infections, pulmonary thrombembolism, deep venous thrombosis, fatty embolism, sepsis, and death.³

Less invasive approaches for removing localized body fat have been developed to minimize patients’ recovery time. Among these alternatives is cryolipolysis, which functions as a cold-induced inflammatory mechanism that gradually reduces fat thickness for 90 days after a 30- to 60-minute skin surface exposure.³

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Weight fluctuations and perimeter measurements were documented during the follow-up visit in the third month following the procedure. The patient had a 1 kg weight loss (53.0 kg) and a 4 cm reduction (74 cm) in her abdominal perimeter.
CASE REPORT 2
A 50-year-old female from Porto Alegre weighing 68.1 kg had localized fat in the upper and lower abdominal region. Two sessions of cryolipolysis (Coolsculpting ® - Zeltiq Aesthetics, Inc., Pleasanton, CA) were performed. In the first session, a CoolMax tip was used during a one-hour cycle in the lower abdomen. In the second session, after 10 days, two CoolCore tips were used in the upper abdomen. Each tip was used for a one-hour cycle and local massage was done immediately post-procedure, as well as three sessions of manual lymphatic drainage (in 30, 60, and 90 days). The procedure was carried out without complications. (Figure 2)

CASE REPORT 3
A 37-year-old female from Porto Alegre weighing 59.8 kg had localized fat in both arms. A cryolipolysis procedure (Coolsculpting ® - Zeltiq Aesthetics, Inc., Pleasanton, CA) with a CoolFit tip was performed on each arm. A one-hour cycle was carried out with each tip and the areas were massaged immediately post-procedure. Patient presented hypotension, severe pain, and ecchymosis on her left arm after post-procedure massage, with improvement of symptoms after being in the supine position. (Figure 3)

EVALUATION
In order to quantify the efficacy of the treatment, photographs of the three cases in two moments (pre-treatment and 3 months after treatment) were evaluated by three blind peer reviewers, who were physicians certified in dermatology or plastic surgery. Post-treatment photographs were randomized with pre-treatment images and presented to reviewers. Subsequently, they were invited to assess the abdominal contour and the arm region of the subjects and to identify the pre-treatment image. The three reviewers correctly identified the images (pre- and post-treatment) of all patient cases and at both treatment times.

This case report was approved by the Research Ethics Committee of the Veiga de Almeida University (UVA, Rio de Janeiro) under the CAAE protocol number 02789118.1.1001.5291.

DISCUSSION
The objective of this study was to evaluate the safety and efficacy of cryolipolysis for localized fat reduction in the short term. The participants of the study had follow-up periods ranging from 1 to 3 months. The post-treatment period has also been evaluated in other clinical studies. 1

The cryolipolysis mechanism of action has been elucidated by researchers worldwide. What has been shown so far is that exposure to cold results in apoptosis of adipocytes, followed by an inflammatory infiltrate, which peaks after 30 days, that leads to phagocytosis. From 60 to 120 days after the procedure a decrease in the inflammatory response and in the infiltration is shown, as well as the mobilization of adipocytes. The exact mechanisms of adipocyte sensitization to cold and adipocyte apoptosis have not yet been clarified. 4,5,6,7

In this study, all participants had a median excess of localized fat and were treated with Coolsculpting ® (Zeltiq Aesthetics, Inc., Pleasanton, CA) using the following protocol: thermal blanket application and temperature extraction of the treated area for 60 min at a cooling temperature of -10°C (cooling intensity factor) using either small (CoolFit), medium (CoolCore) or large (CoolMax) vacuum pressure applicators for the extraction of heat from both sides of a skin fold and reduction of blood flow by tissue compression and cold-induced vasoconstriction.

Immediately at the end of the cycle and after the removal of the applicator, manual massage was performed for two minutes. One study has demonstrated that the incorporation of manual massage immediately after the procedure increased the reduction of the fat layer of the massaged area by 68% when compared to an unmassaged area after two months. 7

The total treatment time was of 60 minutes for each treated area. Each subject received treatment in two areas: upper and lower abdomen, right and left arm, according to their individual needs. Treatments were performed in either one or two sessions. The subjects of this study did not change their diet and maintained a constant body weight during the period of one to three months after the procedure. There were no significant changes in their body weight or BMI. However, when comparing to pre-treatment measurements, abdominal circumference was significantly reduced at 90-day follow-up of the individual mentioned in Case Report 1. She had a four-centimeter circumference reduction, result which is consistent with previous studies performed on 50 individuals who also indicated an average reduction of the abdominal perimeter from 3.53 to 4.45 cm at the end of treatment. 7,13

Previous studies have shown more visible results in patients with low to medium localized fat. Results are not as effective in patients who are obese or have excessively flaccid skin. Thus, cryolipolysis does not appear to be indicated for patients who want to reduce fat on a large scale, these goals being better achieved with liposuction surgery. 7,14

The patient described in Case Report 3 also achieved a good response to treatment, having a significant fat reduction in the triceps region in both arms. The results were assessed at a follow-up visit only one month post-procedure and compared to the pre-treatment photographs.

In spite of the limitation of this study, in which a long-term effect of the cryolipolysis could not be evaluated, a longitudinal study by Bernstein on long-term follow-up of two individuals treated unilaterally in the flanks showed a reduction in the thickness of fat in the treated flank two years after the procedure, even with a gain of 10 pounds (4.5 kg) in their body weight. The same subject also presented fat reduction after 6 years on the treated left flank when compared to the untreated right flank. This demonstrates the long-lasting effect of the procedure, since there was no new adipose tissue deposition over time. 7,14

No patient reported persistent erythema, burns or necrosis of the skin. Even though there were reports, side effects were mild and limited to erythema, edema, bruising, numbness, and tingling on the treated area, having the conditions spontaneously cleared within two weeks. These events are consistent with the findings reported in literature. 7,14

Patients also demonstrated that the cryolipolysis procedure is well tolerated for subcutaneous fat reduction. During the procedure, all three patients reported only minimal discomfort.

The cryolipolysis treatment using the Coolsculpting ® device (Zeltiq Aesthetics, Inc., Pleasanton, CA) is approved in Brazil by ANVISA (Brazilian Health Regulatory Agency) and in the United States by the FDA (Food and Drug Administration). This type of procedure is appealing because it is non-invasive; the patient has to take a short or no sick leave; and there is no need for local anesthesia. Further studies may help elucidate the full potential and effectiveness of this procedure.

CONCLUSION
Cryolipolysis is an option of selective, effective, and non-invasive treatment for excess adipose tissue. The technique is currently approved by the FDA (Food and Drug Administration, USA) and ANVISA (Brazilian Health Regulatory Agency, Brazil).

CONFLICTS OF INTEREST
No potential conflict of interest relevant to this article was reported.

NOTES
Patient consent: Patients provided written informed consent for the publication and use of their images.

Figure 1

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