Cryolipolysis for Noninvasive Fat Cell Destruction: Initial Results from a Pig Model

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Abstract

Background: Liposuction is one of the most frequently performed procedures in the United States, though it is declining in popularity[1]. This decline has led to the development of noninvasive methods to reduce localized fatty deposits.

Objective: Determine whether Cryolipolysis™ (cooling fat cells to induce lipolysis) can selectively damage and reduce subcutaneous fat without damaging the overlying skin or causing a meaningful change in lipid levels or liver function.

Methods: Three Yucatan pigs were treated in one session using the Zeltiq cooling device at 22 treatment sites set to an average heat extraction rate of 41 mW/cm^2 for either 45 or 60 minutes. Treated areas were evaluated by photography, ultrasound, and by gross and microscopic pathology. Lipid levels were tested at baseline and at regular intervals during a 3-month follow-up period. One additional pig was treated at a heat extraction rate of 37 mW/cm^2 for 15 minutes per site at various days prior to sacrifice.

Results: The treatments resulted in a significant reduction in thickness of the superficial fat layer without damage to the overlying skin. The reduction in the fat layer was preceded by a gradual inflammatory response triggered by cold-induced apoptosis of adipocytes. Post-treatment lipid levels remained within normal limits[2].

Conclusions: Cryolipolysis has been shown to significantly decrease subcutaneous fat without damaging the overlying skin or causing meaningful changes to blood lipids or liver function.

Introduction

Several noninvasive modalities (e.g. radiofrequency and ultrasound) show great promise for reducing fat, but rely on traumatic heating or shock waves to achieve an effect. In contrast, a new method called Cryolipolysis uses precise cooling to cause apoptosis rather than acute trauma to eliminate fat cells and reduce the adipose layer.

Studies indicate that fat cells are more susceptible to cold than are other types of cells[3,4]. The controlled exposure of adipocytes to cold can decrease the viability of fat cells without affecting surrounding structures[5,6]. Therefore, the controlled extraction of heat may be used as a noninvasive approach to reducing the superficial fat layer.

Methods

A proprietary tissue cooling device was used to treat 25-30% of total body surface area. Treated areas were evaluated with ultrasound and histological samples were assessed for damage to the fat layer, dermis, and epidermis. Blood lipid levels were evaluated pre-treatment and at regular intervals post-treatment.

Two prototype cooling applicators used in study

The Zeltiq non-invasive cooling device is not cleared for use by FDA for lipolysis; it is limited by United States law to investigational use.
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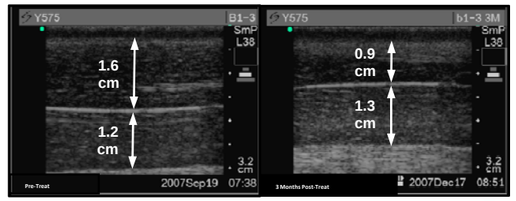
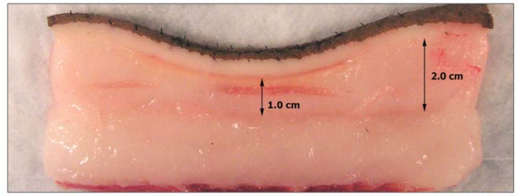
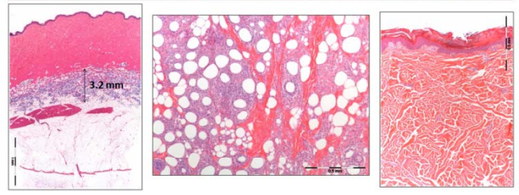
Results – Measured Fat Layer Reduction



Pre-treatment (left) and 3-months post-treatment (right) ultrasound images of the subcutaneous fat in Pig 1 showed that a 0.6 cm decrease in the thickness of the fat layer occurred over a 90 day period.



Gross pathology from the same treatment site in Pig 1 showed that the superficial fat layer at the center of the treatment site was reduced by 1 cm at 90 days post-treatment as compared to an untreated region.



Histological analysis of samples taken from Pig 1 showed ongoing lipolysis in the upper fat layer (left). High magnification photos of this image showed changes in the shape and size of the fat cells (center), and a healthy dermis with no sign of damage or inflammation noted in the blood vessels or nerve bundles (right).

The 90-day gross pathology (middle image) and physical examination of pig tissue confirmed an obvious reduction in fat volume in the treated area compared with adjacent control areas. These apparent contour changes correlated with a decreased thickness of the ultrasound-measured fat layer at 90 days post-treatment (top ultrasound images). Compared to controls, the greatest reductions were in areas exposed to greater cooling intensity.

Histological analyses of the treated tissues (lower images) illustrated that the natural phagocytosis process in response to cold was ongoing and resulted in adipocytes that were smaller on average, and irregularly shaped, with respect to a control. Upon removal of the damaged cells and lipids by macrophages and other inflammatory mediators, the treated area contained a lower number of adipocytes relative to controls. The histological samples also confirmed clinical observations at all post treatment time points that the epidermis and dermis were free of inflammation and that the nerves and blood vessels were undamaged.

References

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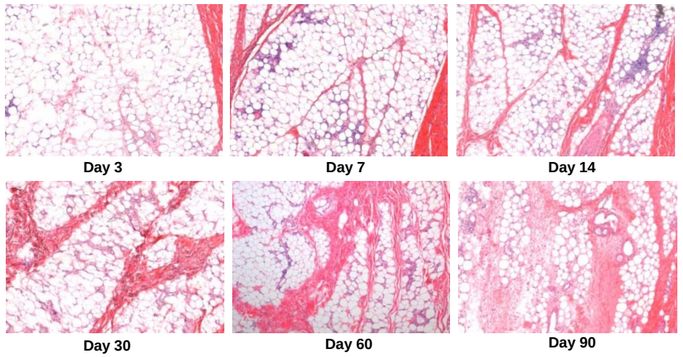
Results – Progressive Inflammatory Response

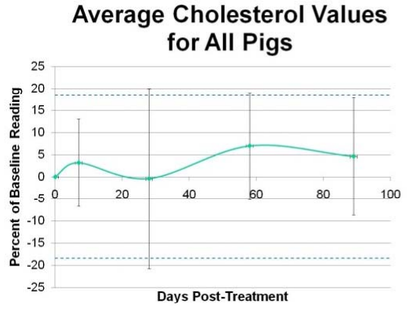
Controlled cooling exposure resulted in death of adipocytes and their subsequent removal by a progressive inflammatory response as seen in the images below. At Day 3, inflammatory cells (primarily neutrophils) had infiltrated the treatment area and surrounded the adipocytes. This infiltration increased through Days 7 and 14. At Day 14, macrophages and multi-nucleated giant cells were present. At Day 30, the population of macrophages had declined and the septae appeared thickened. The inflammation had diminished further by day 90. The selective removal of adipocytes resulted in a change in the relative proportions of adipocytes and septae. The increased variation in size and shape of adipocytes from Day 14 onward reflects their targeted removal as a result of controlled cooling.

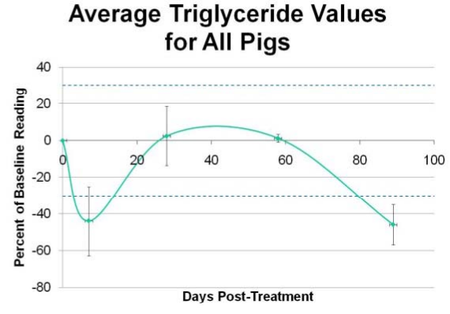


Sequenced histology of treated tissue from Pig 4 showed the progression of changes in the fat layer post-treatment.

Results – Lipid Level Response

Assessment of triglycerides and cholesterol (HDL, LDL and total) over the 90-day follow-up period demonstrated some variation over time, but any rise seen from baseline did not exceed normal bounds reported for these animals[2]. Normal bounds are represented on the graphs as dashed lines.





Conclusion

Cryolipolysis, a new method of controlled energy extraction (cooling) from adipose tissue, was evaluated as a means to predictably destroy adipocytes while preserving the skin and surrounding structures. This noninvasive procedure achieves fat loss by controlled application of heat extraction for an extended predetermined period of time. These results indicate that Cryolipolysis treatment merits further study as it has the potential to result in significant improvements in body contour. Cryolipolysis can decrease subcutaneous fat without causing harmful changes to blood lipid levels and without damaging ~~to~~ the overlying skin or surrounding structures.