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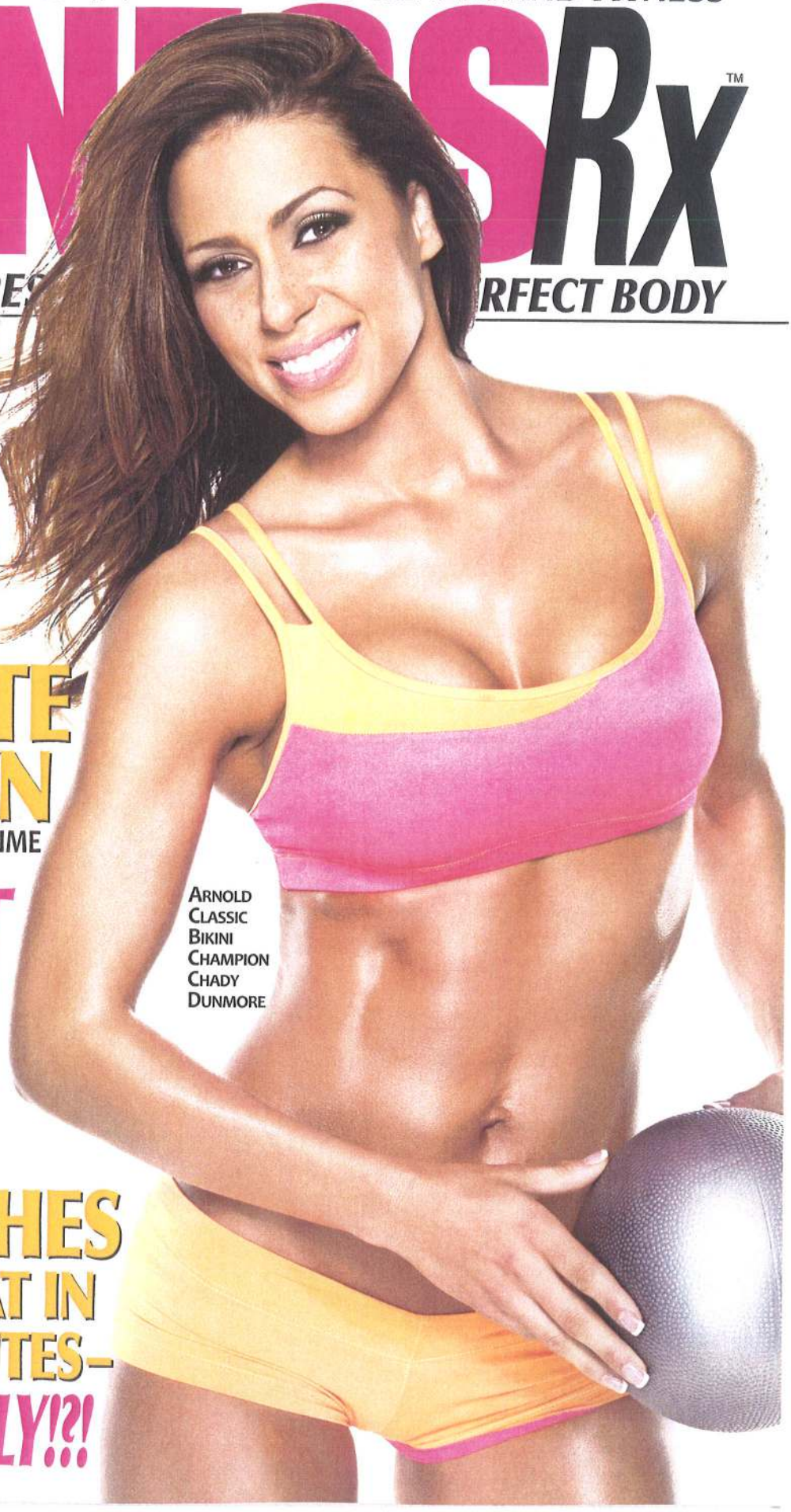

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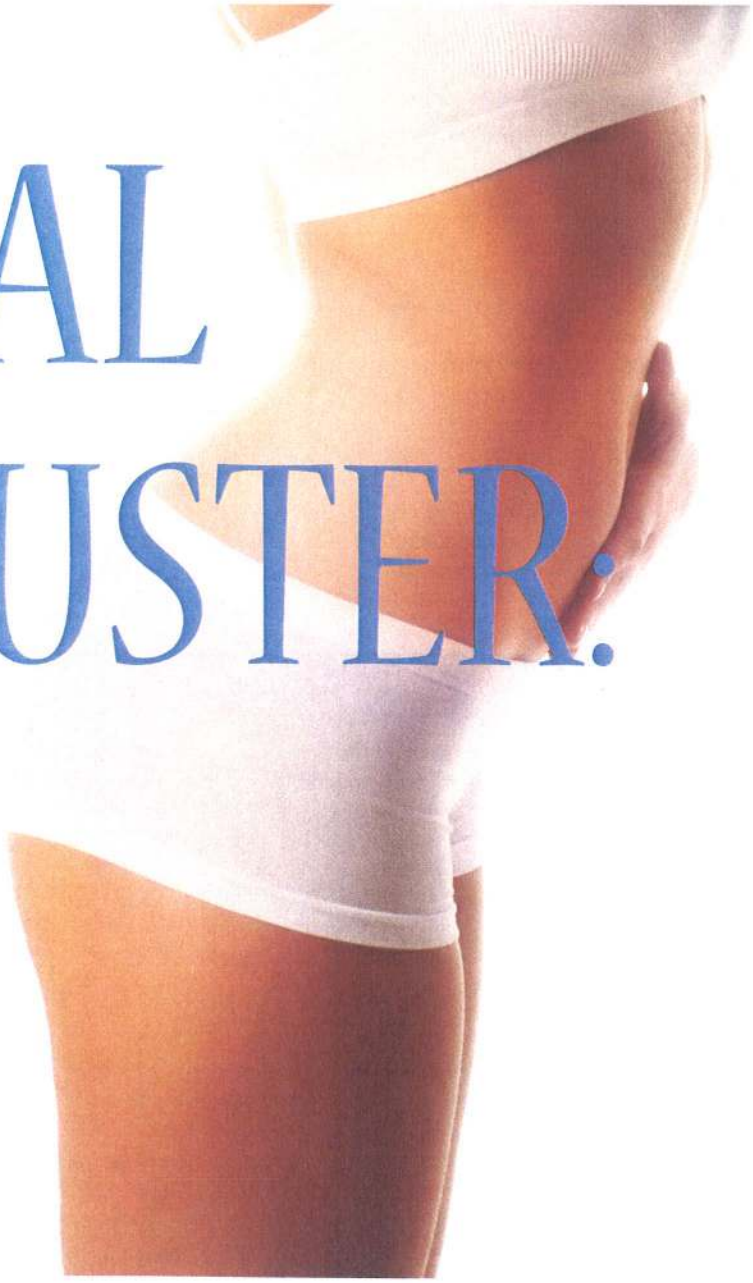


By Dan Gwartney, M.D.

Liposuction is one of the most popular cosmetic procedures for removing fat, and advancements have improved the ease and effectiveness. Among these advances, which include cannulas, tumescence, etc., is the application of external energy modalities to break up the fat cells prior to attempting to suction out the contents/tissue— among the methods used to do so are heat, cold, ultrasound and lasers.[1] Despite these improvements, liposuction still carries the disadvantages noted above.

The Holy Grail for fat-loss procedures would be to find a non-invasive method that would have no downtime, procedural or healing complications (ideally, it would be cheap and guaranteed as well). One company is making the claim that its method does just that. Erchonia Medical, Inc. is a privately-held company that has developed several FDA-approved devices that use low-level laser therapy to aid in diverse conditions (some indications are awaiting FDA approval) such as acute and chronic neck and shoulder pain, acne, burn and wound healing, bone healing, reducing pain and swelling during breast augmentation, affecting capsular contracture associated with breast implants, and laser-assisted liposuction.[2]

Numerous clinical trials and basic research articles support Erchonia's claims of efficacy and safety. It now offers the Zerona laser, a non-invasive laser treatment awaiting FDA approval— but employed throughout the United States in clinics as an off-label use of an existing FDA-approved technology.

The application of low-level laser assists in traditional liposuction by disrupting the membrane of fat cells in the target area, making it easier to vacuum out cell contents (stored fat) and cell fragments. It is like eating applesauce, rather than biting off the apple with your teeth and swallowing without chewing.[3] Whereas Zerona directs a laser held above the treatment site several minutes prior to surgery, other procedures (e.g., SmartLipo) use lasers of different wavelength and power contained within the cannula itself (the cannula is the suction tube that is inserted under the skin during liposuction).[1]

Lose 7 Inches of Fat in 20 Minutes—*Really!?!*

Zerona: The Laser That Blasts Fat

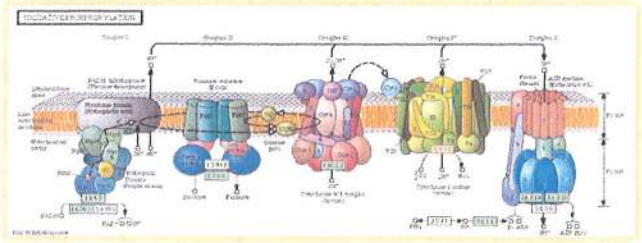
Proponents of the cannula-contained laser believe it is more precise to have the laser lead the cannula under the skin; additionally, there is a skin-tightening benefit reported.[4] However, the technique is still dependent upon a skilled hand, guiding the cannula to avoid passing the tip too quickly past the just-lasered fat cells— or angling too sharply toward the surface. Zerona is automated and covers a broad area, with no guidance or intervention required during treatment once the beam is targeted.

According to findings presented in conferences and published in the medical literature, up to 90 percent of fat is emulsified within 12 minutes of the superficial (outside the skin) laser treatment.[5] This contrasts with a study showing no effect— this study may not be a relevant comparative, as it used a laser with different properties and the model (300-pound Yucatan pigs) may have confounded the issue, due to having skin thickness greater than humans.[6]

An Erchonia laser similar to the Zerona was first used as a pretreatment adjunct to liposuction; the FDA granted approval for this use in 2004.[7] In order for the laser to have any effect (otherwise,

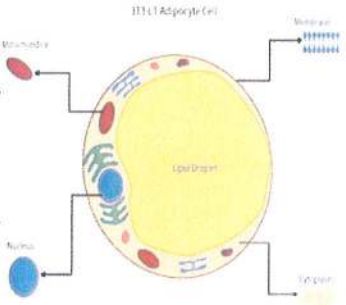
Location of Cytochrome c oxidase

- Cytochrome c oxidase is a multicomponent membrane protein that contains a binuclear copper center (Cu_A) along with a heme binuclear center (a_3-Cu_B) both which facilitate the transfer of electrons from water soluble cytochrome c to dioxygen.
- Metal prosthetic groups (heme structures) allows for this enzyme to operate as a photoabsorbing structure.
- Absorption of light of a specific wavelength stimulates electrons to enter an excited state, allowing for more electrons to participate in the redox reaction and participate at an accelerated rate.
- An electrochemical gradient is established quicker, and more ATP is manufactured.



The Fat Cell

- The arrow is indicating that the fat cell possesses a mitochondria; thus, a target for laser therapy.
- The application of 635nm (red light), which has been shown to be photoreactive, can therefore alter adipocyte bioenergetics.



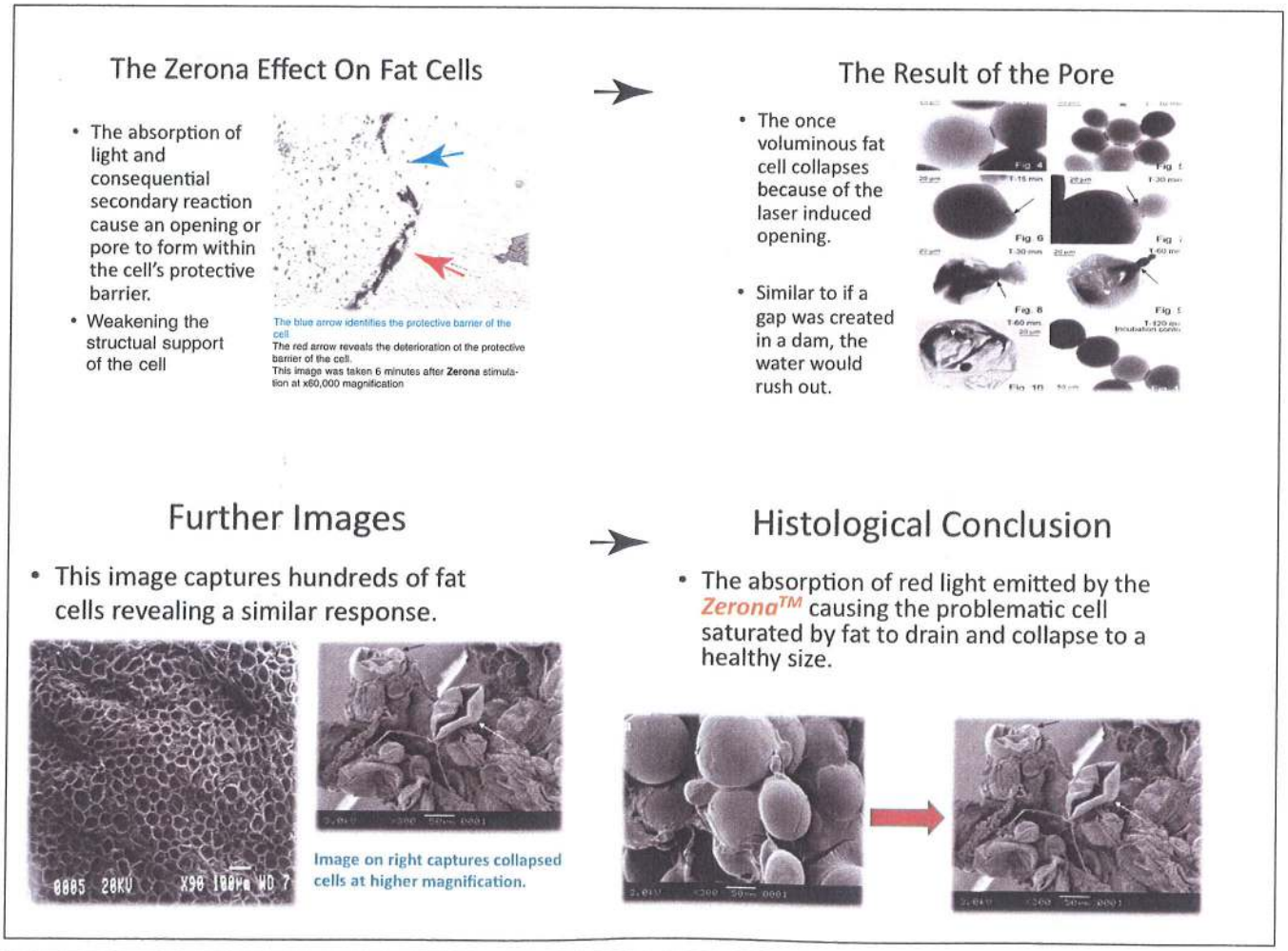
why go to the time and expense?), it must penetrate the skin and have sufficient energy to create a hole in the membrane of the fat cell. It must also be controlled so the experience doesn't resemble James Bond's in "Goldfinger" (1964), where he was nearly bisected by a laser beam. The first step in proving Zerona's claim is to demonstrate that the laser can in fact "burn" a hole in a fat cell.

The "defining" experiments were performed by Dr. Rodrigo Neira, a plastic surgeon in Cali, Colombia. As reported at the Congreso Bolivariano de Cirugía Plastica Reconstructiva (2001), when exposed to the 635 nm laser, cultured adipocytes (fat cells grown in a lab) were emulsified, or in simpler terms, liquefied.[8] The experiment was repeated, looking at tissue removed during surgical lipectomy (cutting fat from the body with a scalpel). After just six minutes of exposure to the laser, the fat tissue was similarly affected.

The treated fat tissue from Dr. Neira's research was submitted for two types of electron microscopy (a microscope so powerful— 60,000x magnification— it can see the smallest parts of the insides of a cell; way more detailed than the most powerful light microscope). The electron microscopy confirmed that 99 percent of the contents of the fat cells were released.[9] The extrusion of the fat was caused by the formation of a "transitory pore," or a temporary hole, which allowed the fat globule to be squeezed out like a popped zit. No other tissue was affected, such as the capillaries or stromal cells— which allows the stored fat in the area to be released without destroying the structure, function, or health of any tissue in the treated area.[8,9] This is a fairly unique feature, as most other techniques rely on adipocyte necrosis (immediate death of the fat cell), apoptosis (programmed or reactive death of the fat cell), or mechanical destruction.

After confirming the effect of the laser in the laboratory setting, Dr. Neira performed the procedure on test subjects who were "lasered" for six minutes; he obtained MRI images of the areas immediately before and shortly after the treatment.[10] The MRI revealed that the fat in the area was not as organized, as would be expected if the cells remained intact. Instead, the area developed a homogenous appearance in the MRI scans, suggestive of the fat being extruded into the intercellular space, which is referred to, anatomically, as the interstitial space. Interestingly, the change was even seen in the deep subcutaneous fat, beyond the reach of the laser, which only penetrates a few centimeters. This suggests that the laser-induced evacuation of the treated fat cells triggered similar fat-releasing through biochemical messengers in fat cells beyond the laser's reach.

It is important to clarify that the Zerona does not "burn a hole" into the fat cells. It is not like holding a magnifying lens over a leaf, and watching it burst into flames when sunlight is



focused into a tiny area. Without clarifying the cellular process, readers may be imagining smoke curling from their belly button as the nurse stands by with a fire extinguisher. In fact, what is happening in the fat cell is, well... boring by comparison.

Going Inside the Fat Cell

The photonic energy of the laser stimulates two metal atoms, copper and iron, in an enzyme contained within the mitochondria of the fat cell called cytochrome c oxidase.[11] When stimulated, this enzyme drives energy production, ramping up the burning of fatty acids to produce ATP, the energy molecule. In addition to generating ATP, the process also creates reactive oxygen species (ROS).[12] ROS travel through the cell, attaching onto vulnerable molecules, creating oxidative damage. This process occurs in nearly all cells, as energy is produced by burning calories, but the rate is markedly elevated in the fat cells, due to the excitation created by the laser beam. The ROS attach onto the membrane of the fat cell, creating tiny perforations called transitory pores, through which the fat globule can pass. The hole is called a transitory pore because the fat cell will eventually heal and close the defect.

Zerona does not kill the fat cell; killing or removing the fat cell is not preferable. When fewer fat cells are present, and the need to store fat is not decreased, the fat cells become grossly distended. These are called hypertrophic adipocytes, and research has shown that they release metabolically-harmful adipokines, and do not release stored fat as readily.[13] Maintaining fat cell number may be as important metabolically as reducing fat cell volume.

With Zerona use, the regional stem cell population is maintained, and treatment does not induce an inflammatory response.[14] This greatly improves patient comfort and healing. The lymphatic vessels (the "sewer" of the circulatory system) are not harmed, as can happen with tissue-damaging techniques. This is critical, as the lymphatics clear the released fat— transporting the load to the lymph nodes, where macrophages (a type of white blood cell that is like a garbage disposal) break down the released triglycerides to free fatty acids. It is presumed that the free fatty acids are transported to metabolically-active tissue (i.e., muscle, liver, heart), where they are burned as calories.

As an interesting side note, the treatments are scheduled 48 hours apart, as the transitory pore heals fairly quickly. With frequent treatment, the fat cell remains "open" and the membrane is not allowed to fully restore its integrity. There are no reported side effects or risks to exposure to the Zerona laser, so daily treatments can even be used, or longer-term therapy might be an option. Of course, cost and inconvenience would factor in.

Dr. Maloney speculated that treating the health effects of obesity may be an indication for prolonged treatment schedules, but any claims in that regard await clinical trials. A pilot trial described on the Erchonia website demonstrated a significant reduction in the adipocyte hormone leptin, as well as LDL cholesterol (bad cholesterol).[15] At first glance, a reduction in leptin may seem counterproductive, as leptin is an appetite-suppressing hormone. However, human clinical trials have shown that leptin, a signaling hormone that notifies the brain of the stored energy (fat) stores, is elevated in obese individuals. The metabolic paradox is explained by the conclusion of trials using pharmaceutical leptin in a weight-loss trial, showing that obese persons with elevated leptin are in fact leptin-resistant. By lowering leptin, the Zerona treatment may allow the body to recalibrate and respond appropriately to the appetite-suppressing hormone.

Fat cells communicate with the body and brain through hormones and adipokines. The sudden influx of fat cell hormones and signaling adipokines into the circulation may explain the findings of an early study submitted to the FDA during the approval process. In this study, individuals who were treated on one side of the body experienced fat loss on the opposite side as well, even though the laser beam was shielded from affecting that area.[13,14] The systemic effect of the Zerona treatment led the research team to recom-

mend changing the FDA-suggested study design to a placebo-controlled trial using two groups— test subjects and a control group— matched by age, gender and BMI. The results of that trial will be described shortly.

The early findings of Dr. Neira were designed to affirm the utility of laser treatment prior to liposuction to "liquefy" the fatty area prior to attempting to "suction away" the adipose. Like many other techniques, it was readily demonstrated that pre-treating an area with the laser made the procedure easier and better tolerated by the patient.[6-10] The laser used in the non-invasive Zerona treatments is the same that has received FDA-approval for use in laser-assisted liposuction. This allows the Zerona to be used "off-label" at this time, with a reasonable assurance of safety, even though Erchonia cannot yet market the device for this purpose.

Waiting for FDA Approval

According to Ryan Maloney, Ph.D., medical director of Erchonia Medical, Inc., the data for FDA approval has been submitted and accepted, but as this approval would establish a new category, the process is delayed as the committee must decide what criteria must be met not only by Erchonia, but also any competing technology that wishes to make similar claims. The process is called "de novo classification."[14]

To prove the efficacy of the Zerona laser for non-invasive body contouring, a multi-site study analyzing data collected on 67 healthy, overweight subjects (BMI between 25-30) was undertaken.[16] The subjects were randomly assigned to either receive the Zerona treatment or a visually similar treatment using a simple, low-power, red beam (635 nm is a very specific wavelength of light in the red spectrum). The FDA assigned a threshold of three inches as the "reduction total" from three measurements (waist, hips and bilateral thighs) as proof of Zerona's effect; this was felt to be similar to what could be achieved through a single liposuction procedure. The subjects were measured and told not to alter their diet or exercise for the two-week period— confirmed through logs kept by the subjects.

After two weeks of treatment, consisting of six appointments lasting 40 minutes per appointment, the subjects were re-measured. The Zerona-treated group met the cut-off established by the FDA, losing an average of 3.51 total inches from waist, hips and thighs, doing nothing— literally. The control group lost 0.68 inches, a non-significant change from their starting measure. A third measure was taken two weeks following treatment, showing a regain of only 0.31 inches. This was done to investigate whether the loss was just a redistribution of fluid, or if the loss was indeed due to a reduction in fat tissue volume.

These findings demonstrated that the claims of Erchonia held up to the scientific scrutiny of a double-blinded, placebo-controlled study. Reports from clinics offering the treatment are supportive. As with any technique, satisfaction is not 100 percent, but it is high.

Erchonia takes the rare stand of offering additional treatments at no cost to people who do not achieve the three-inch threshold. Many patients exceed the three-inch reduction, with reports of five inches or greater being reported following a single treatment.

Where Does the Fat Go?

This leads to the one question raised by many, "Where does the fat go?" Could the sudden dumping of fat (triglycerides) into the bloodstream be unhealthy?

A study collected data on the change in triglycerides and cholesterol following two weeks of treatment with the Zerona. Contrary to what logic would dictate, serum (blood) levels of triglycerides decreased in 60 percent of treated subjects; 85 percent of subjects experienced a reduction in total cholesterol, with an improvement in the HDL:LDL ratio; liver enzymes (a sign of liver stress) were unchanged.[14]

Dr. Maloney reported that skin tone was typically unchanged or improved. This is another benefit of laser therapy. The fibroblasts, which give the dermis of the skin structure, are also stimulated— resulting in skin tightening. Recall, the technology is used in treating wounds and aiding in skin healing.[12,14]

Dark-skinned individuals may require additional sessions, based on random observations from clinics using Zerona. A larger patient-based experience in the Atlanta area showed a similar response in African-American patients, compared to the general population.[14]

The Zerona field can be extended to any area, save near the eyes, allowing a person to target the arms, upper back or chest.[14]

It will be interesting to see if the FDA does finally grant approval to Erchonia, as that will offer the gold standard of legitimacy to the procedure. As it stands now, all reported research and patient experiences support the reports that this could offer the Holy Grail of body contouring. ■

References:

1. Mann MW, Palm MD, et al. New advances in liposuction technology. *Semin Cutan Med Surg*, 2008 Mar;27(1):72-82.

2. Erchonia Medical, Inc. Laser Applications. Available at: http://www.erchonia.com/laser-applications, accessed February 9, 2009.

3. Neira R, Ortiz-Neira C. Low-level laser-assisted liposculpture: clinical report of 700 cases. *Aesthetic Surg J*, 2002;22:451-5.

4. Dudelzak J, Hussain M, et al. Laser lipolysis of the arm, with and without suction aspiration: clinical and histologic changes. *J Cosmet Laser Ther*, 2009 Jun;11(2):70-3.

5. Neira R, Arroyave J, et al. Fat liquefaction: effect of low-level laser energy on adipose tissue. *Plast Reconstr Surg*, 2002 Sep 1;110(3):912-22.

6. Brown SA, Rohrich RJ, et al. Effect of low-level laser therapy on abdominal adipocytes before lipoplasty procedures. *Plast Reconstr Surg*, 2004 May;113(6):1796-804.

7. Witten CM. Department of Health & Human Services. Food and Drug Administration. Available at: http://www.erchonia.com/files/pdf/FDA_Clearance_K041139_EML.pdf, accessed February 9, 2009.

8. Neira R, Solarte E, et al. Effects of the electric laser diode beam on in vitro human adipose tissue culture. Congreso Bolivariano de Cirugia Plastica Reconstructiva 2001.

9. Neira R, Arroyave, et al. Fat liquefication: Effect of low-level laser energy on adipose tissue. *Plast Reconstr Surg*, 2002;110:912-922.

10. Neira R, Jackson R, et al. Low-level laser-assisted lipoplasty appearance of fat demonstrated by MRI on abdominal tissue. *Am J Cosm Surg*, 2001;18(3):133-40.

11. Konev SV, Beljanovich LM, et al. Photoreactivation of the cytochrome oxidase complex with cyanide: the reaction of heme a3 photoreduction. *Membr Cell Biol*, 1998;12(5):743-54.

12. Alexandratou E, Yova D, et al. Human fibroblast alterations induced by low power laser irradiation at the single cell level using confocal microscopy. *Photochem Photobiol Sci*, 2002 Aug;1(8):547-52.

13. Vázquez-Vela ME, Torres N, et al. White adipose tissue as endocrine organ and its role in obesity. *Arch Med Res*, 2008 Nov;39(8):715-28.

14. Personal communication with Ryan Maloney, Ph.D., medical director of Erchonia Medical, Inc., via telephone on February 8, 2009.

15. Erchonia Medical, Inc. Study Shows Fat Reduction Laser Reduces Hunger and LDL Levels. Available at http://www.erchonia.com/news/press-releases/study-shows-fat-reduction-laser-reduces-hunger-and-ldl-levels, accessed February 9, 2009.

16. Jackson RF, Dedo DD, et al. Low-level laser therapy as a non-invasive approach for body contouring: a randomized, controlled study. *Lasers Surg Med*, 2009 Dec;41(10):799-809.