

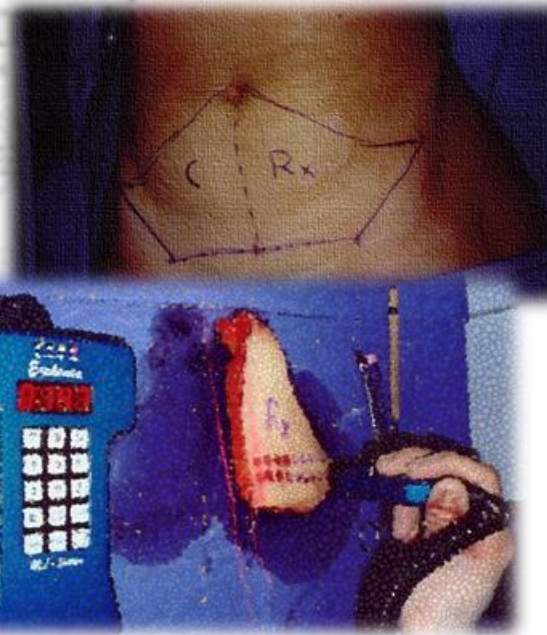
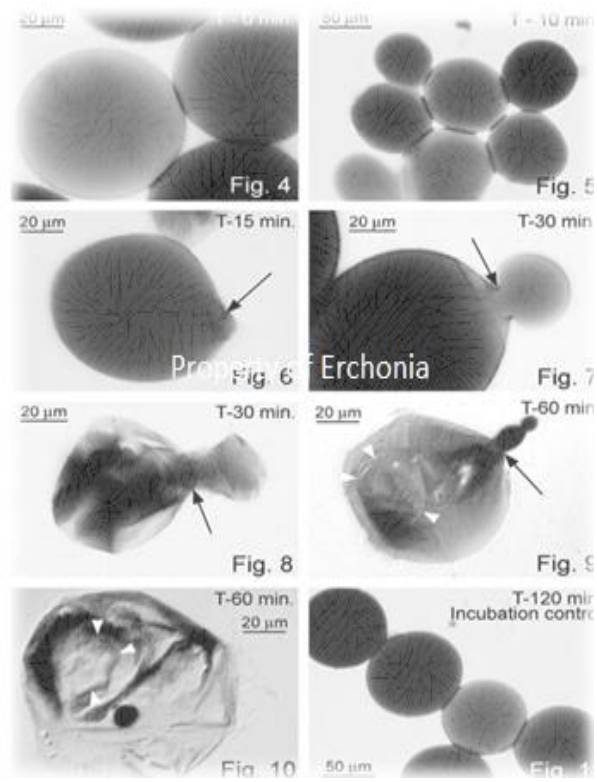
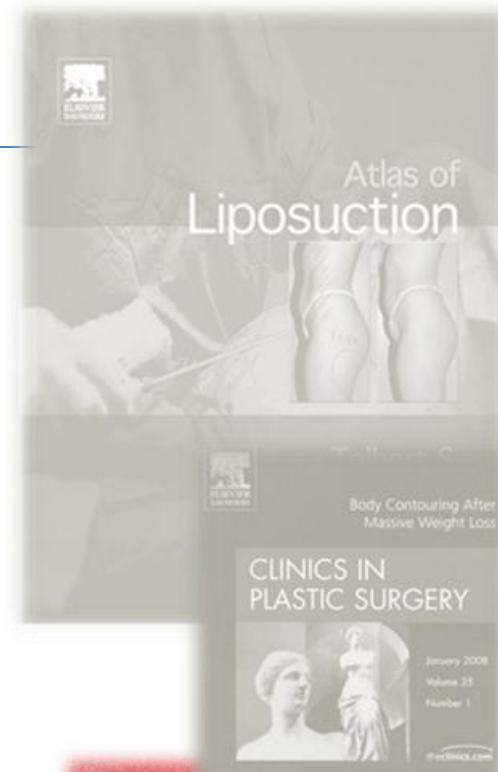
# The Commitment to Research:

Since 1996 Erchonia, the manufacturer of the Zerona has been committed to fully elucidating the medical utility of low-level laser therapy through rigorous clinical studies.

The Zerona has been examined extensively from *in vitro* and *ex-vivo* analyses to *in vivo* clinical investigations.

Presently, Erchonia remains steadfast to unlocking the potential benefits of the Zerona by exploring subtle changes within adipocyte function that could modulate DNA expression, protein and hormone synthesis, ultimately affecting the endocrine and immune systems.

As you will quickly learn, the Zerona was built on a solid foundation of histological and clinical evidence and should reassure you and your clinic that the Zerona will provide patients with a reliable, safe, and effective non-invasive slimming of the waist, hips, and thighs.

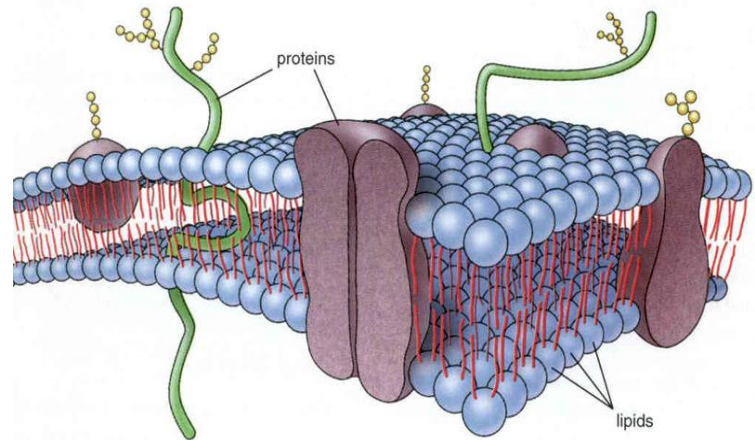


# Zerona Histological Evidence Summary:

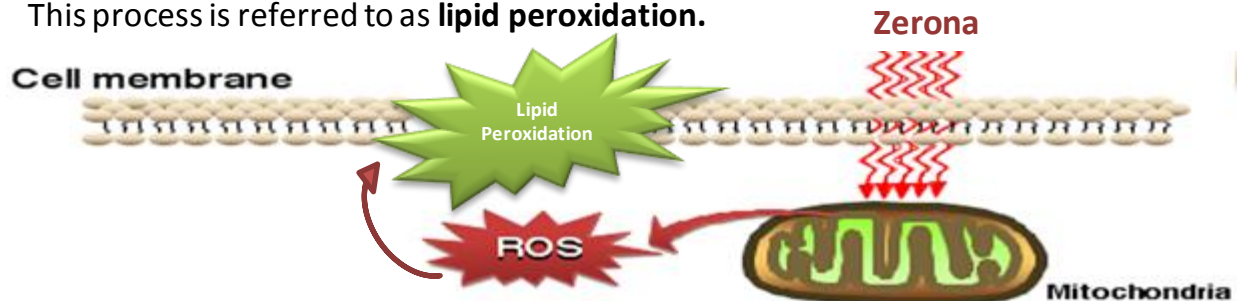
## Proven at four independent cytology laboratories

- University of Chicago
- University of Singapore
- University of Colombia
- University of Mexico

Membranes are highly fluid, dynamic structures with selective permeability acting as a barrier to preserve intracellular and extracellular composition.

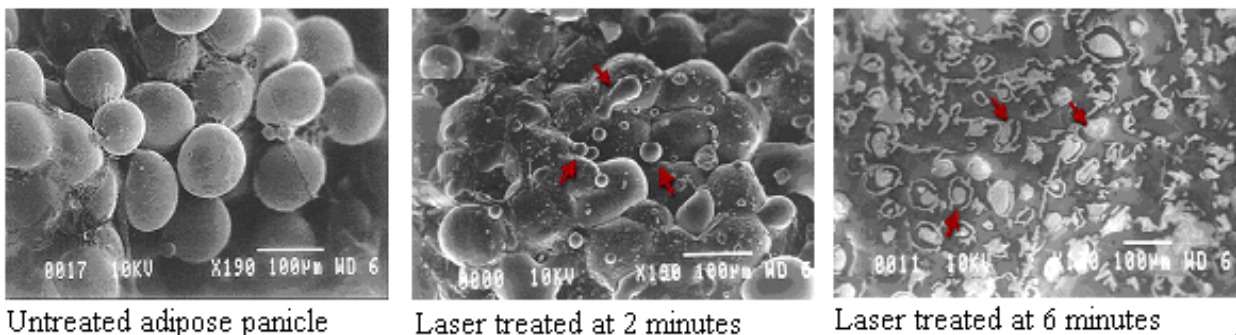


Subsequent to 635nm low level laser therapy, a transient rise in reactive oxygen species (ROS) is observed. This highly-reactive free radical has been shown to react with membrane-bound cholesterol creating transitory pores or openings within the membrane. This process is referred to as **lipid peroxidation**.



The creation of the transitory pore has been confirmed at each research site and is responsible for the liberation of the stored lipids and fatty material promoting cell collapse.

Figure 1: Emulsification of adipose panicles subsequent to laser irradiation



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

Neira, R., Arroyave, Ramirez, H., et al. Fat liquefaction: Effect of low-level laser energy on adipose tissue. *Plast. Reconstr. Surg.* (2002): 110; 912-22.

Neira, R., Arroyave, J., Solarte, E., et al. In vitro culture of adipose cells after irradiating them with a low-level laser device. *Congreso Bolivariano de Cirugia Plastica Reconstructiva*. (2001).

Solarte, E., Reyes, A., Montoya, J., et al. Effects of irradiation with low-level laser in the optical transmittance of adipocytes. *Revista Colombiana de Fisica* (2002):

Neira, R., Jackson, R., Dedo, D., Ortiz, C.L. and Arroyave, A. Low-level-laser assisted lipoplasty: apearance of fat demonstrated by MRI on abdominal tissue. *Am. J. Cosmet. Surg.* (2001).

# Zerona Clinical Trial Summary:

A Placebo-controlled, randomized, double-blind, multi-centered clinical study (n=67)



35 Subjects Randomized to "Active" Group



32 Subjects Randomized to "Sham" Group

Patients signed an affidavit stating that **no personal lifestyle changes** could be made throughout the study.

Patients were **required to track** daily physical activity, daily caloric intake, and participation in any program or consumption of dietary supplement that could promote slimming.

**FDA determined** that a cumulative reduction of **at least 3.0 inches** was **clinically meaningful**.

Patients received treatment every-other-day for two weeks for a total of just 6 treatments.

Each treatment consisted of concurrent stimulation of waist, hips, and thighs for 20 minutes anterior and 20 minutes posterior (Total treatment time of 40 minutes)

Evaluation points were at baseline, weeks 1 and 2, along with a 2 week post-procedure follow-up.



**"Active" Group Averaged 3.54" in two weeks**  
Twenty-two (63.0%) demonstrated the 3.0" reduction

Area	Inches	Centimeters	P value
Waist	-0.98	-2.5	<0.0001
Hip	-1.05	-2.7	<0.01
Left Thigh	-0.65	-1.7	<0.01
Right Thigh	-0.85	-2.2	<0.01
Total	-3.52	-9.1	<0.01

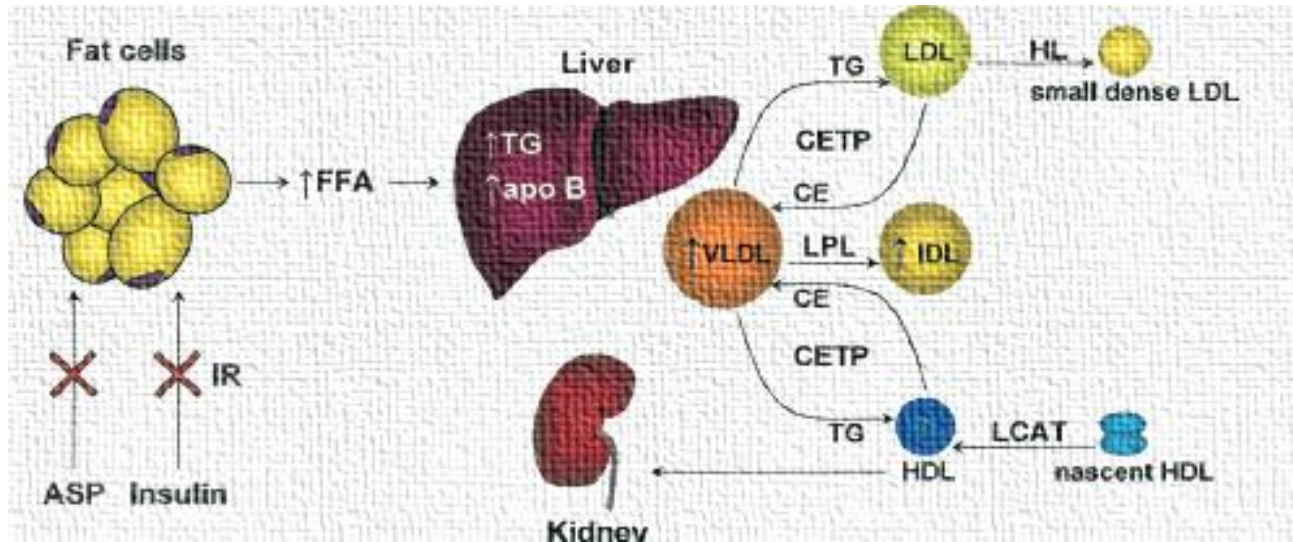
**"Sham" Group Averaged 0.68" in two week**  
Two subjects (6.28%) demonstrated a reduction of 3.0"

Area	Inches	Centimeters	P Value
Waist	-0.25	-0.63	>0.05
Hip	-0.21	-0.53	>0.05
Left Thigh	-0.17	-0.4	>0.05
Right Thigh	-0.05	-0.12	>0.05
Total	-0.68	-1.68	>0.05

Between treatment groups, the difference in inch reduction was statistically significant (**p<0.0001**)

# Potential Medical Benefit of Zerona:

Most cosmetic devices are absent of an underlining medical benefit; however, with the percentage of overweight and obese Americans expected to reach 86% by 2030, it is essential to evaluate multidimensional technologies.



Hypertrophic adipocytes are associated with cardiovascular conditions including hypercholesterolemia and hyperlipidemia.

Furthermore, enlarged fat mass is directly associated with the nearly 200 million individuals worldwide with diabetes mellitus.

By reducing adipose tissue mass, the Zerona has demonstrated unprecedented medical benefits as illustrated in the following charts.

Independent research clinics have examined serum cholesterol, LDL, HDL, triglyceride, fasting glucose, and hemoglobin A1C following Zerona.

Total cholesterol (n=80)	Baseline	Study end
Average	191.11	178.79
Std. dev.	43.34	36.46

LDL (n=80)	Baseline	Study end
Average	103.88	91.83
Std. dev.	32.27	29.00

HDL (n=19)	Baseline	Study end
Average	65.53	64.63
Std. dev.	18.07	16.52

Study conducted by Dr. Paul Nassif (n=10)			
A1c	5.3	5.17	-0.19
Glucose	113.45	103	-10.5

Leptin (n=22)	Baseline	Study end (6/1/09)
Average	29.49	14.60
Std. dev.	16.54	11.53

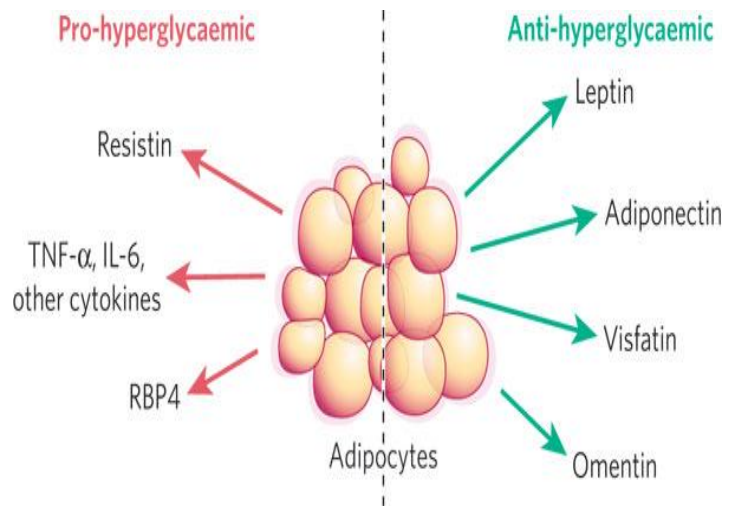
# Importance of the fat cell:

Histological evidence shows that the clinical outcome of the Zerona is achieved without inducing cell death.

Most applications for non-invasive slimming depend on the destruction of this endocrine organ cell. However, the adipocyte is responsible for the synthesis of bioactive peptides which participate in autocrine, paracrine, and endocrine pathways.

The storage capacity of adipocytes remains a key component of its function but recent data has shown fat cell expansion modulates the synthesis of adipose-derived hormones.

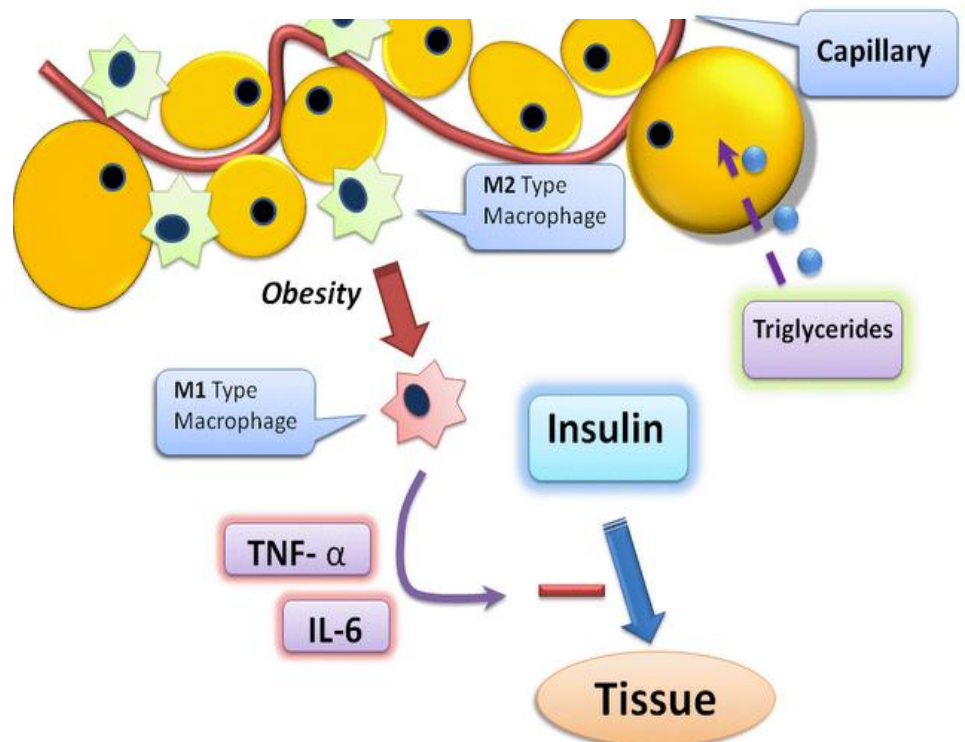
Studies have revealed a correlation between deregulated adipose tissue function and excessive fat mass having deleterious effects on the endocrine and immune systems.



Significant adipocyte expansion is believed to interrupt the interplay of transcriptional factors and other intracellular components yielding pathological consequences (i.e. insulin resistance, inflammation).

The Zerona is the first device to appreciate the endocrine function of the adipocyte by delivering an aesthetic treatment designed to provide patients with a meaningful slimming without inducing cell death.

Furthermore, the reduction in adipocyte size perhaps restores appropriate functionality by modulating bioactive synthesis upregulating beneficial hormone levels.



# An Outcome Only Achieved by Zerona:

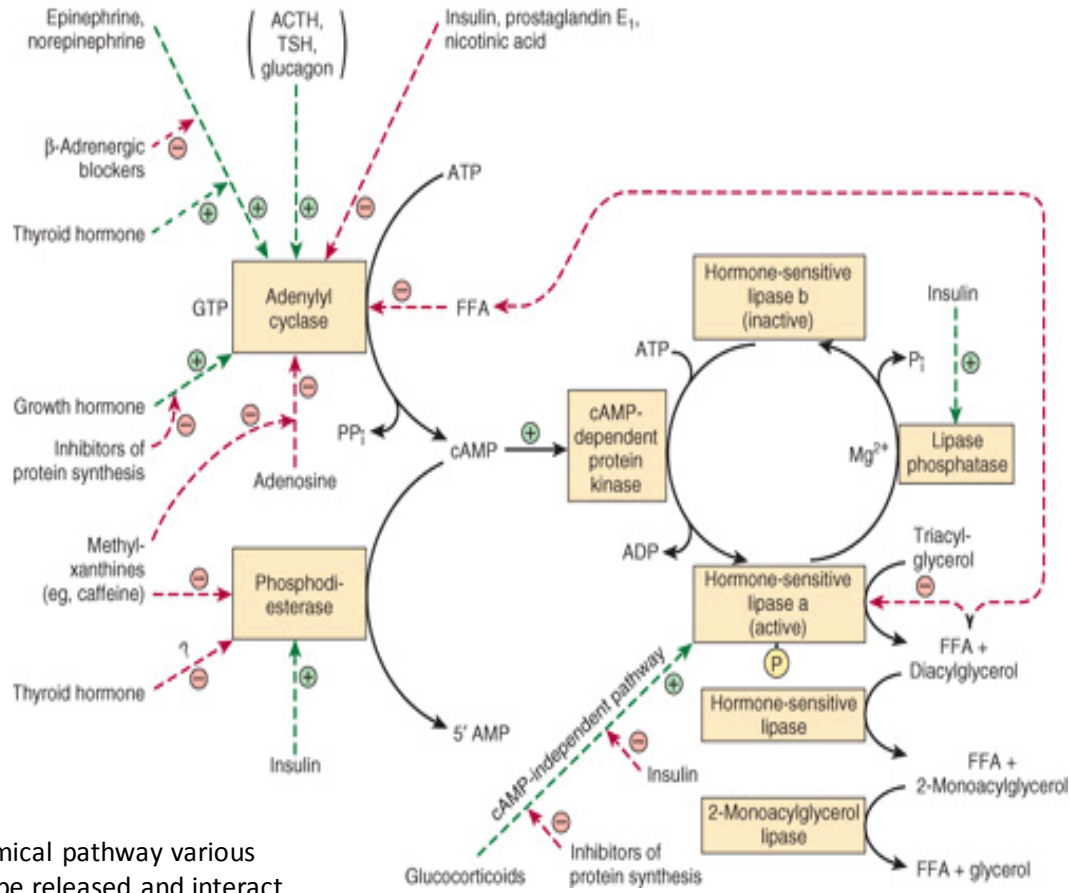
Fat catabolism is a tightly regulated process, requiring an orchestra of proteins, enzymes, and hormones to promote adipose tissue lipolysis.

Adipocytes predominately store fatty material as triglycerides, three fatty acid chains all connected by a single glycerol backbone.

In order to mobilize triglycerides it must first be degraded by specialized enzymes referred to as hormone-sensitive lipase.

This process known as lipolysis all takes place within the adipocyte.

In order to modulate this biochemical pathway various hormones and/or proteins must be released and interact with membrane-bound receptors.



## Bioactive substances include:

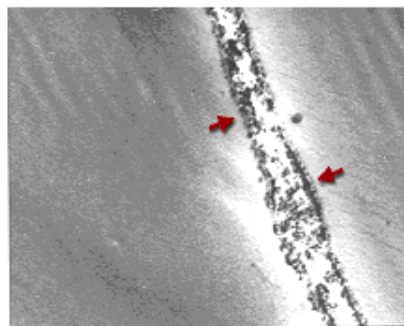
Substance	Affect
ACTH	(Inhibit)
Epinephrine	(Activate)
Glucagon	(Activate)
Growth Hormone	(Activate)
Insulin	(Inhibit)
Nicotinic Acid	(Inhibit)
Norepinephrine	(Activate)
Thyroid Hormone	(Activate)
TSH	(Activate)

The Zerona avoids this complex network by forming a transitory pore within the protective membrane of adipocytes.

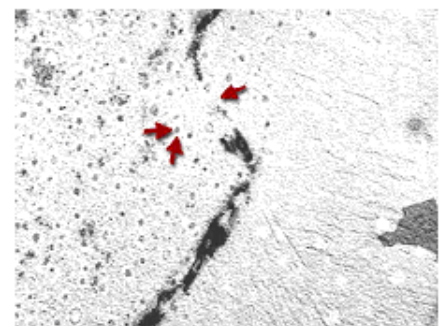
Stored lipids and fatty material traverse the membrane via the transitory pore entering the interstitial space where the lymphatic system is readily capable of removing the fatty debris.

The formation of the transitory pore enables the Zerona to bypass a key fat catabolism step by photochemically liberating the fatty material.

Figure 2: Formation of a transitory pore within the membrane of an adipocyte.



Untreated adipocyte



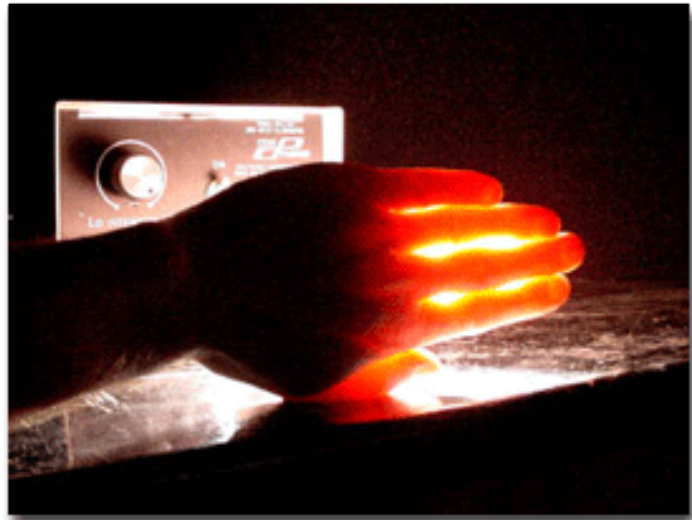
Laser treated adipocyte- aperture identified

# Depth of Penetration:

The biggest criticism of Zerona is whether or not light is able to penetrate down to sub-dermal tissue. This question is rather easy to address by using the literature that has been peer-reviewed published.

Before giving examples from the literature we can use a simple example to illustrate the penetrative capacity of red 635nm light.

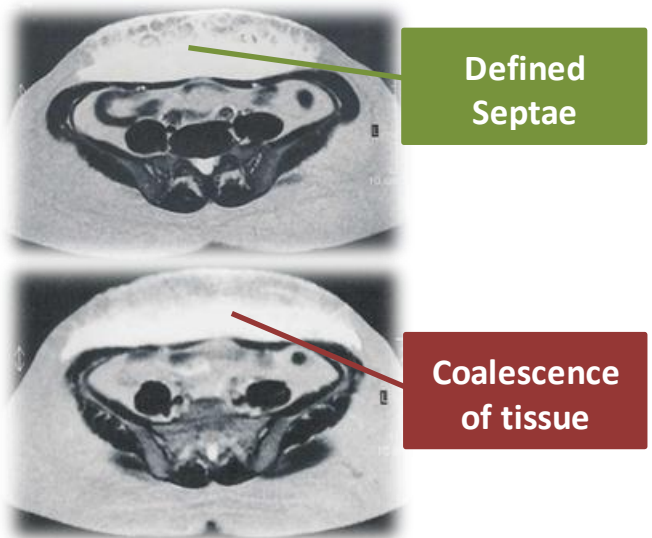
When lying out on a nice summer day while we enjoy the sun with our eyes closed the color that dominates our vision is red. Why is that? The reason is, all the other colors of the visible spectrum are absorbed, leaving our photoreceptors to absorb only the red photon.



There is no question light is heavily attenuated in tissue, but simplistic remarks that light cannot penetrate tissue are inappropriate. Physicists have formulated complex equations that define the penetration of light through various tissue compositions with respect to the light's applied geometry.

Kolarova et al (2000) applied a 632.8 nm laser through skin samples obtained from 11 men observed that approximately 7% of laser light penetrated subdermal tissue. With nearly 1% of light recorded at depths beyond 19 mm. Above 80% of light penetrated the epidermis stimulating the dermal layer.

A similar finding was observed by Dr. Rodrigo Neira following the completion of an *in-vivo* assessment of the Zerona's light parameters. The MRI study exhibited a recorded depth of penetration as determined by radiological changes of ~5cm (50mm).



In addition to the penetration of photons, laser therapy has been shown to promote a systemic effect within viable tissue, modulating non-irradiated cells.

# Biochemistry of the Zerona Protocol:

Metabolism is a complex network of reactions working to support organism growth, reproduction, structure stability, and environment adaptability.

The Zerona is clinically proven to promote the release of stored lipids and fatty material through the creation of a transitory pore within adipocyte membranes.

Since this process does not promote cell death or require an immunological response it depends directly on the catabolism of lipids to achieve a slimming outcome.

The image to the right depicts the natural mechanism of fat catabolism, the process in which the body acquires energy from stored lipid material.

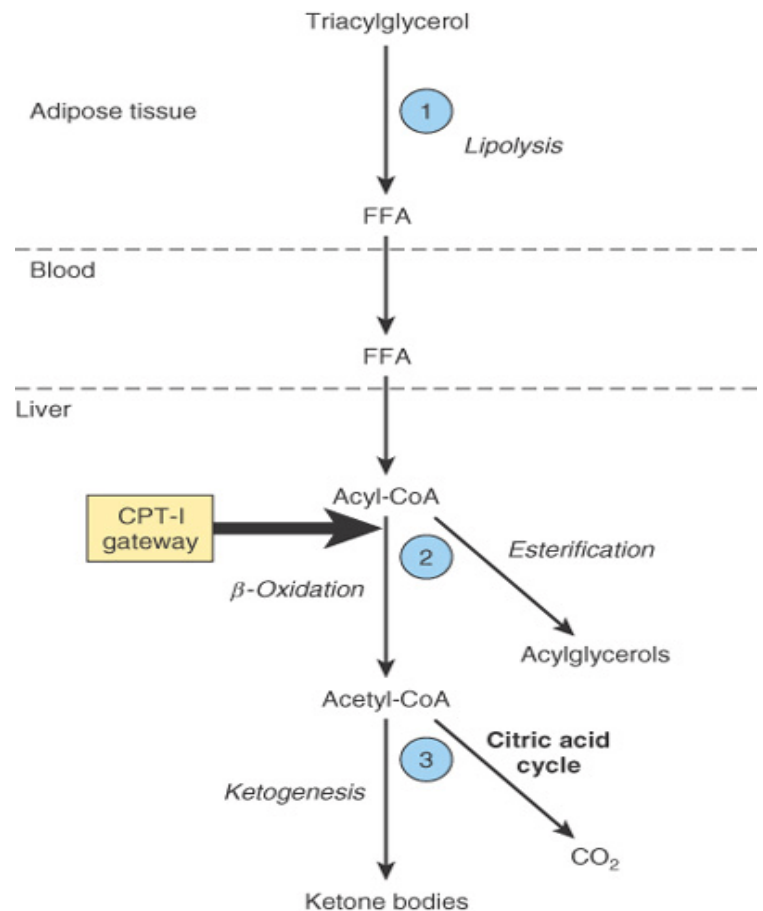
There are **three important regulation steps** in this process (depicted by blue circles). Under favorable conditions, the body will utilize the Zerona-liberated lipids to produce acetyl-CoA in order to synthesize adenosine triphosphate (ATP).

Respecting human physiology, Erchonia has developed a program to facilitate the body's natural means of catabolizing the Zerona-liberated lipids.

**It is estimated that nearly 75% of American's are chronically dehydrated with nearly 80% not consuming an adequate amount of minerals and nutrients.**

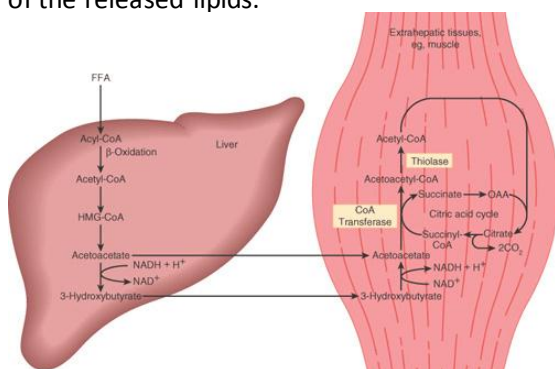
In order to function properly, human cells require abundance of nutrients and with most American's lacking these essential elements, the Zerona protocol was developed to prevent a non-response based on a patient's inappropriate dietary habits.

The purpose of the Zerona protocol is aid the body in the natural degradation and metabolism of the released lipids.



## Two ways human physiology can be supported to facilitate greater mobilization and metabolism of the Zerona-Liberated Lipids:

- 1.) Curva – blend of unique supplements to directly support fat catabolism
- 2.) Lymphatic Stimulation- mechanical and fluid activation of the lymphatic system can accelerate lipid removal to enhance the outcome



# Retrospective Studies of Zerona:

The Level 1 clinical investigation properly evaluated the efficacy of the Zerona as a stand-alone application for non-invasive body slimming.

As outlined in the Zerona Clinical Trial Summary no adjunctive components were used during that study. However, several follow-up studies have been performed to assess the effectiveness of Zerona when coupled with nutritional support, lymphatic stimulation, diet, and adequate patient hydration.

Incorporating very simple additives such as hydration and lymphatic stimulation has propelled Zerona to nearly a 90% satisfaction rating among physicians. As outlined in the Biochemistry of the Zerona Protocol Summary, this process highly depends on the body's ability to metabolize the Zerona-liberated lipids, and when enhanced, the results are exceptional!

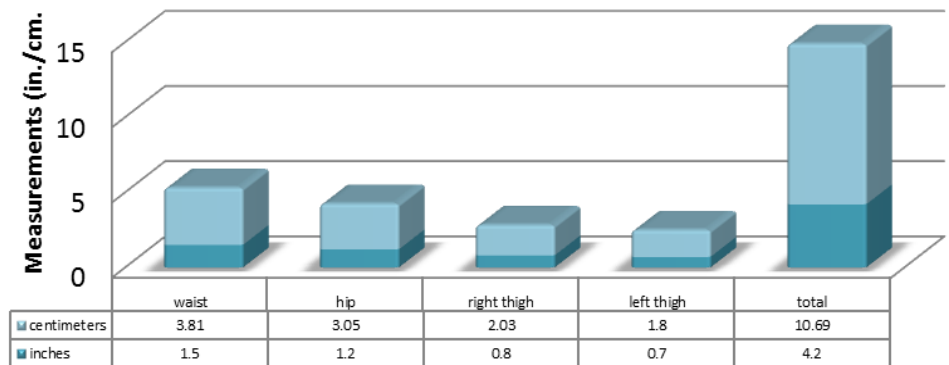
The two graphs to the right represent a random selection of patients treated domestically by Zerona clinicians.

These two studies illustrate an average circumferential reduction above the 3.5 inch reduction the clinical trial exhibited.

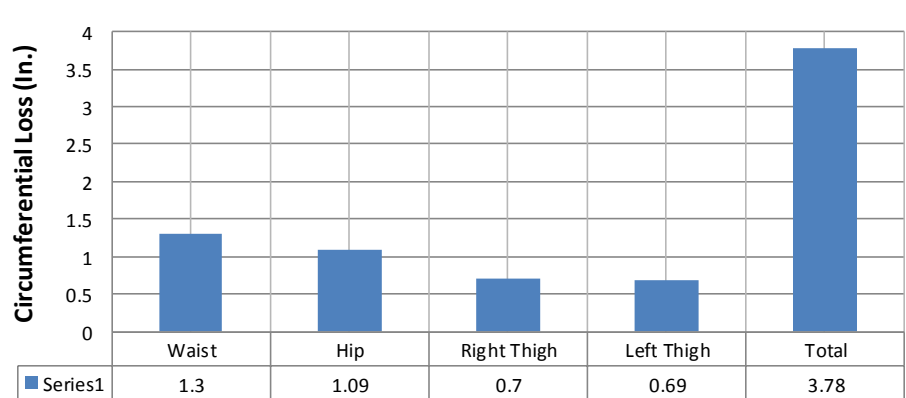
The patient data represents patients who consumed nutritional support and followed a strict hydration protocol. No dietary recommendations were made to these patients.

Please see the Medically Supervised Weight Loss Summary to see the results when Zerona is coupled with a diet.

**Independent and combined circumferential reduction of waist, hip, and thighs (n=567)**



**Mean Circumferential Reduction Following Zerona (n=2,000)**

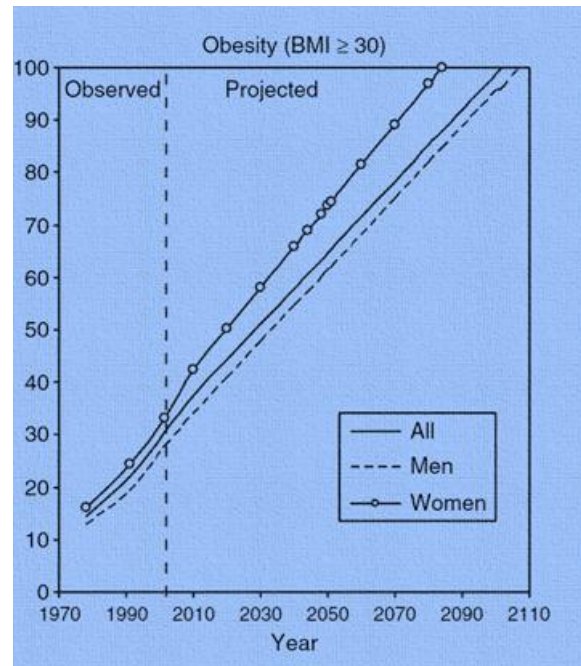


# Medically-Supervised Weight Loss with Zerona:

By 2030 nearly 87% of the US population will be overweight or obese. The comorbidities of this epidemic will create a nearly 1 trillion dollar burden on the health care system.

Treating obesity is an interdisciplinary responsibility, necessitating that all practitioners assume responsibility to impede or reverse this disturbing trend.

Diet and exercise are the two logical steps to dramatically change the ever-expanding direction of our population; yet, these two simple steps have continued to fail and will inexorably continue to fail.



The leading contributor to poor compliance is motivation, without immediate results patients become disenfranchised abandoning their new healthy lifestyle.

Zerona, when coupled with a diet has produced significant and meaningful outcomes, providing patients with an immediate visual slimming instilling the motivation necessary to adopt a healthy living.

## Dr. Capasso Data: Coupling Zerona with Low-Calorie Diet (n=88)

	Inches	BMI	% Fat	Number of Treatments
Average	11.9	29	1.48	8
Range	3.75-26.8	21-45	0-5.9	6-18

The results illustrated to the right demonstrate a clinically meaningful response for patients with a BMI as little as 20 as well as with patients exceeding a BMI of 35.

By modulating the use of free fatty acids, Zerona is synergistic with all diets whether low-calorie or low-sugar high protein diets.

## Dr. Hinnman Data: Zerona Coupled with Ketogenic Diet after two weeks (n=10)

Wt	BMI	WAIST	BB	waist	DATE	Wt	BMI	BB	WAIST	Average Difference (n=10)
213.6	35.5	43	50		27-Feb	203	33	40	43	
228	35	46	49		1-Mar	221		43	48	
176.4	26.8	36	35		28-Feb	169	25	33	34	Waist -4 inches
240.5	32.6	49	48.5		27-Feb	229	31	47	43	
232	40	48	53		28-Feb	220	39	40	45	Hip -6 inches
157.4	27.9	39.75	41.25		5-Mar	149	26	38	39	
149	30.1	38	42		27-Feb	139	28	34	39	BMI -2
184.7	33	42	48		1-Mar	178	32	39	46	
175.7	31	48	44		1-Mar	167	28	35	41	
154	26	36	39		4-Mar	147	24	33	36	
					5-Feb	141		26	34	
191	32	43	45			178	30	37	41	

# Clinical Trial Level Summary:

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The terms ‘**clinical study**’ or ‘**clinically test**’ are often used but seldom practiced. A clinical trial is designed and performed to serve a single function, to demonstrate the safety and efficacy of a device and/or product.

There are numerous levels of trials that are used under specific circumstances, but the only acceptable trial that can support the sale of a therapeutic strategy is a **level 1 or Randomized Controlled Trial (RCT)**.

Any trial short of a level 1 can only predict trends under the unique circumstances taking place at the time of the trial. There is no definitive way to determine whether the device or procedure being analyzed is responsible for the observed clinical outcome.

An equally valid theory for the clinical result could be based on environmental influences or a placebo effect. Grade B trials are necessary to determine whether a level 1 RCT is warranted.

The Zerona is presently the only device to undergo a level 1c RCT trial to evaluate the efficacy and safety of this non-invasive slimming application.

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## Grade A

- Level 1a Evidence from large randomized controlled trials (RCTs) or systematic reviews (including meta-analyses) of multiple randomized trials
- Level 1b Evidence form at least one high-quality cohort study
- Level 1c Evidence from at least one moderate-sized randomized controlled trial (RCT) or a meta-analysis of small trials that collectively has only a moderate number of patients
- Level 1d Evidence from at least one RCT

## Grade B

- Level 2 Evidence form at least one high-quality study of nonrandomized cohorts that did and did not receive the new therapy
- Level 3 Evidence from at least one high-quality case-control study
- Level 4 Evidence from at least one high-quality case series

## Grade C

- Level 5 Opinions from experts without reference or access to any of the above

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