

ZERONA®

FREQUENTLY ASKED QUESTIONS

1. What is Zerona?

Zerona is a patented low-level laser system specifically designed to contour the body by losing inches in circumference off specific body areas (waist, hips, thighs) without any pain, downtime, needles or surgery.

2. What is the action mechanism behind Zerona?

The 635 nm wavelength of the Zerona is specifically absorbed by the mitochondria (the cell's energy generator), temporarily weakening the structure of the cell membrane. This creates a temporary opening allowing for the fat contents to seep out from the fat cell into the interstitial space from where it is processed by the lymphatic system.

3. What results can I expect?

In a double blind, randomized, placebo controlled study, patients were treated 6 times over a 2 week period and lost on average 3.5 inches in combined circumferential measurements of their waist hips and bilateral thighs.

4. Can all patients benefit?

Our clinical research has shown that patients, on average, lost 3.5 inches in circumference off hips, waist and thighs. To maximize the chances of every patient responding as significantly or better, three things are important to consider:

1. The general health of the patient. As a rule, do not treat sick patients. Wait until their condition has improved. Do not treat patients who have a condition listed in the contraindications document.
2. Hydration is critical. Make sure your patient drinks plenty of water (ideally at least 8 glasses of 8 oz of water) spread out throughout the day. Diuretics (coffee, alcohol, etc) should be discouraged.
3. The lymphatic system should be mobilized. The patient should be encouraged to be active and walk for 30 minutes every day.
4. Use Curva. Curva is a proprietary blend of supplements designed to assist the body in processing the liberated fat. Curva should be taken twice daily with meals.

Please refer to the Zerona protocol for more detailed information.

5. What areas of the body can I treat?

Essentially all parts of the body where subcutaneous deposits of fat can be found may be treated with Zerona, especially those resistant to diet and exercise. Most patients start with treating their waist, hips and thighs as these can be treated simultaneously with the 5 lasers of Zerona.

6. Once liberated, what happens to the fat?

Once liberated, triglycerides are absorbed by the lymphatic system where they are transported to lymph nodes. Macrophages (immune cells) release liposomal acid lipases (LAL) which break down the triglycerides into free fatty acids and glycerol. These are then small enough to enter the blood stream. Once in the blood stream, several things may occur:

- a. Some of the free fatty acids are readily available to be used as fuel by the body.
- b. What does not get consumed as energy will get to the liver where it will either be oxidized or re-processed for storage. More research is underway to determine exactly how much gets oxidized versus re-stored, but clinical evidence suggests that fat does indeed get oxidized (no visible or measurable redistribution of fat, either in the treated areas or at the systemic points).

7. What happens to cholesterol and triglyceride levels post Zerona?

A study was performed using Zerona to check cholesterol and triglyceride levels. None of the patients demonstrated a statistically elevation in their triglycerides and cholesterol levels. In fact a statistically significant reduction in both low density lipids (LDL) and cholesterol levels was observed. More research is underway to assess if Zerona may be a useful medical therapy in reducing LDL and cholesterol levels.

8. Do you treat obese patients (BMI>30) differently than other patients?

Clinically obese patients will benefit from Zerona. To show a significant benefit, we recommend doing 2 series of 6 treatments back to back (12 treatments total). Note that Zerona will provide a circumferential reduction to the treated areas, but will not treat their obesity. However, many centers treating obesity will combine Zerona with a program of weight loss and exercise. The significant improvement in body shape over a short period of time is used to motivate patients to comply with their diet and exercise program.

9. Is it safe?

Yes. Zerona works on the principle of photochemistry whereby laser light is used to accelerate naturally occurring processes within cells. The treatment is painless and normal activities can be resumed immediately.

10. How deep does Zerona affect fat cells?

Penetration depth of the 635 nm wavelength is:

- 2mm in skin

- Almost no absorption in fat, which means that provided we get photons through the skin barrier, we will be able to achieve the required bio-chemical reaction within the mitochondria of the fat cell.

In physics, depth of penetration is defined as 66.66% of all photons being absorbed, with 33.33% going deeper into tissue. In fact, statistically, some photons will go extremely deeply (through a combination of scatter and refraction). To verify this, just shine a laser pointer at your finger. You will be able to see light shine through your finger, demonstrating that some photons go deep enough for you to see them.

From a thermal laser interaction standpoint, using depth of penetration to define the limits of laser-tissue interaction makes sense as one considers that, when 66.6% of all photons have been absorbed, the energy density has become too low to have any significant thermal impact on the irradiated tissue. However, from a bio-chemical standpoint, the number of photons required to achieve mitochondrial stimulation is very low, and the 33.33% of remaining photons will be sufficient to effectively target the mitochondria. Clinical evidence (Dr. Neira) demonstrates that the 635nm wavelength is capable on interacting with fat cells to a depth of at least 5 cm.

11. What is the systemic effect?

A systemic effect was first noticed on patients getting treated with LLLT for chronic pain. Patients reported a reduction in pain in areas that had not been directly irradiated with the laser. Since then, several studies have demonstrated that LLLT has a paracrine effect on fat cells, where cellular inter-communication (much like what happens with histamines) leads to fat cells responding to treatment even though they were not directly irradiated with laser light. Our retrospective study on 567 patients has shown that patients can expect an improvement in non-irradiated areas (neck, chest, arms, knees, etc.). This improvement however, is more modest than that achieved with directly irradiated areas.

12. Why is there only a 2-week follow-up in the study?

Whenever conducting a study looking at improvement in body contouring, weight stability is critical in order to determine the benefits derived from the technology used in the study. This is particularly important when treating patients with a BMI > 25, as these patients have a propensity to store extra fat through a metabolic imbalance (they are overweight because they burn less calories than they ingest).

This has far reaching implications with regards to the length of follow-up and leaves but 2 options:

1. Either stabilize the food intake of the patients through a diet and have a long follow-up, or
2. Instruct patients to maintain their pre-treatment dietary and exercise routine and have a short follow-up

Stabilizing food intake of patients through a diet may be used by critics to suggest that the results achieved were not solely due to the benefits of the technology and, for this reason, was rejected.

With this in mind, patients were specifically required to (and signed an affidavit to this effect) maintain their pre-treatment dietary and exercise routine (a requirement of the FDA to ensure that benefits to patients derived solely from the effect of the laser). This implied however, that the follow-up had to be limited to 2 weeks in order to ensure that results were not mitigated by excessive food consumption.

13. What is the Zerona guarantee?

SBMI guarantees that patients will see a minimum improvement. If patients do not experience a 3.5 inches improvement across the 5 standard measurement points, they are eligible to get 3 to 6 more treatments at no cost to help further their results.

14. Why should diode be parallels?

Saying that diodes should be parallel to the skin is a bit of a misnomer. What really needs to happen is for the beam to be PERPENDICULAR (at 90°) to the skin. When a laser beam comes in contact with the skin, 2 things happen: Absorption, which is what is required for the biological processes to take place, and reflection which is light that bounces back from the skin. If your laser is exactly at 90°, then there is no reflection and all your laser energy is absorbed. The more angled your laser beam is (i.e. the less perpendicular it is), the more reflection there is, hence wastage. And if less energy is absorbed, then your results won't be as good.

15. Where are measurements taken?

The measurement points are as follow:

- a. Directly below the rib cage
- b. Middle abdomen below the umbilicus
- c. Lower abdomen (2 to 3 inches below the umbilicus)
- d. Hips at the widest point
- e. Thighs: 2 to 3 inches below the crotch.

16. When are measurements taken?

Measurements are taken:

1. Before the first treatment
2. At the end of the 6th treatment
3. 1 week after the final treatment

17. When can patients start noticing results?

This depends on how effectively their lymphatic system processes the liberated fat. Age and lifestyle are but a few parameters that may influence the rate of improvement. To optimize processing, it is recommended that patients stay optimally hydrated (by drinking 64 ounces of water spread throughout the day and cutting back on diuretics) and that they mobilize their lymphatic system through gentle physical activity (daily 30 minute walk or mild exercise). The ideal patient should begin to notice a difference in how their clothes fit at the time of their 4th treatment.

18. How long will results last?

Zerona does not destroy fat cells but empties them of their content which means that fat cells are capable of re-storing fat should the patient have a chronic caloric imbalance. A balanced diet

is the only way to ensure long-term improvement. Patients who eat more calories than they burn will see their improvement decrease over time.

19. Is the fat simply redistributed?

Once liberated, triglycerides are broken down into free fatty acids and glycerol and enter the blood stream. Once in the blood stream, several things may occur:

- a. Some of the free fatty acids are readily available to be used as fuel by the body.
- b. What does not get consumed as energy will get to the liver where it will either be oxidized or re-processed for storage. More research is underway to determine exactly how much gets oxidized versus re-stored, but clinical evidence suggests that fat does indeed get oxidized (no visible or measurable redistribution of fat, either in the treated areas or at the systemic points).

Clinical evidence from our retrospective study on 567 patients across the U.S. clearly demonstrates that Zerona is effective not only in the irradiated areas, but also at systemic points, demonstrating that there is no measurable re-distribution of fat.

20. Would longer treatments be more beneficial?

No. Early clinical work demonstrated that the fat cells begin to open after only 6 minutes of laser exposure and that most of the fatty material is excreted after 15 minutes. Increased benefits will only result from an increased number of treatments, not increased exposure during each individual treatment.

21. Why does it not work as well on patients with previous liposuction?

Patients with previous liposuction have had their fat cells mechanically removed. Zerona works by emptying fat cells of their content, so Zerona will not be effective with patients that have only a few fat cells left. Liposuction also creates a lot of fibrotic tissue which further hampers results.

22. Why do you need to treat every 2 days?

Clinical research shows that the pore created by the laser only remains open for 24 to 72 hours. To maintain the pore open over a period of time sufficient to get optimal results, treatments every 48 hours are considered optimal.

23. Why 6 treatments?

It was felt that 6 treatments were required to keep the pore in the fat cells open long enough for the majority of triglycerides to seep out into the interstitial space. Based on 6 treatments delivered over a 2 week period, our randomized, double-blind, placebo-controlled study demonstrated that patients experienced an average circumferential loss of 3.5 inches across their waist, hips and thighs.

24. Would more treatments lead to better results?

Yes, additional treatments will lead to improved results. An additional series of Zerona treatments can begin immediately after the first series. We also recommend additional treatments (see the Zerona guarantee) for patients (either because of a sluggish lymphatic system or poor lifestyle choices) that do not respond appropriately to the original series of 6.

25. Why don't patients lose weight?

The study performed to validate the efficacy of Zerona focused on circumferential measurements of hips, waist and thighs and did not include monitoring the weight of the patient. SBMI never makes claims that cannot be evidenced in a clinical study. This does not mean that patients do not lose weight however, just that we have no clinical evidence to back a weight loss claim. Anecdotal evidence from centers using Zerona who have been monitoring weight have noticed that patients saw a reduction both in their weight and in their total fat percentage.

26. What is Curva and why should it be used with Zerona?

Curva is a proprietary blend of supplements containing Niacin, L-carnitine, Omegas 3&6, Ginkgo biloba and Green tea extract. Curva increases blood flow, promotes cell motility and facilitates the breakdown of fat. Curva has been specifically formulated to assist the body in processing the fat liberated by the Zerona treatment.

27. What are the side-effects of Curva?

Curva contains Niacin which may cause flushing. This should not be mistaken for an allergic reaction such as hives. The flushing can be mediated by taking Curva during meals (it is recommended to take Curva twice a day, at breakfast and dinner). If a patient still experiences flushing, this can be resolved by taking 300mg of aspirin daily.

28. What can I do to optimize my Zerona results?

To optimize results, it is recommended that patients stay optimally hydrated (by drinking 64 ounces of water spread throughout the day and cutting back on diuretics) and that they mobilize their lymphatic system through gentle physical activity (daily 30 minute walk or mild exercise). We also recommend that patients wear a compression garment (Spanx or Armour) throughout the process. For more information, please refer to Zerona's clinical protocol.

29. Why should patients avoid alcohol during the Zerona process?

There are three main reasons why alcohol should be avoided with Zerona:

- a. Alcohol is a diuretic and it is critical that the body stays optimally hydrated throughout the treatment program.
- b. Alcohol also contains a lot of calories: a 5-ounce glass of red wine packs 100 calories! This directly conflicts with the recommendations of the program which calls for a balanced diet and a healthy lifestyle.

- c. Third and most importantly, alcohol is processed as fat by the liver which directly restricts the body's ability to process the newly liberated fat. Once liberated by Zerona, the fat that is not used up as energy to fuel the body's normal metabolic needs fat is processed by the liver using enzymes. The total amount of fat being processed at any given time is limited by the amount of enzymes produced by the liver. Alcohol is processed as fat by the liver using the same enzymes. So, when the liver is busy processing alcohol, it is not able to process the fat liberated by Zerona. Hence more time/treatments are required to achieve results.

30. Is Zerona effective in treating obese patients?

Yes. However, many centers treating obesity will combine Zerona with a program of weight loss and exercise. Zerona will not significantly address their excess weight but will provide a circumferential reduction to the treated areas in a relatively (4 weeks) period of time. The significant improvement in body shape over a short period of time is used to motivate patients to comply with their diet and exercise program. Most physicians combining Zerona with a weight loss program prescribe 2 series of 6 treatments back to back (12 treatments total).

31. How does Zerona compare with other body slimming technologies?

Zerona is the only technology that has been clinically validated in peer-reviewed journals to consistently produce a 3.5 inch circumferential reduction in waist, hips and thighs. Zerona is the only truly non-invasive device that safely achieves significant results over a short period of time.

32. How long has Zerona been in use?

The laser tissue interaction behind Zerona was identified over 6 years ago. LLLT has been used routinely as an adjunct to liposuction for 6 years. Zerona was introduced in the U.S. over 123 months ago and is being routinely used by over 650 practices across the country.

33. Is there a risk of fat embolism?

No. Fatty embolism occurs when clumps of fat cells enter the bloodstream after trauma (typically from a long bone fracture). Zerona does not rupture fat cells. With Zerona, triglycerides are first processed by the lymphatic system where they are broken down by lipases into free fatty acid and glycerol before entering the blood stream, so there are no risks of fat embolisms with Zerona.

34. Should we begin a treatment on a patient who is currently menstruating?

Zerona does not have any effect on menstruation, so this is not a contraindication. However, a majority of women experience water retention during their period, which may negatively affect measurements. We recommend female patients begin their treatment one week after their menstruation cycle.

35. What is the FDA approval status of Zerona?

Until recently, Zerona was used off-label as “a device reducing pain and inflammation as an adjunct to liposuction”. However, in August 2010, the FDA approved Zerona for the specific indication of circumferential reduction. The FDA ruled that:

- a. Zerona is a device using low level laser light for the disruption of adipocyte cells within the fat layer for the release of fat and lipids from these cells for non-invasive aesthetic use.
- b. Zerona is indicated for use as a non-invasive dermatological aesthetic treatment for the reduction of circumference of waist, hips and thighs.
- c. The clinical data submitted by Erchonia (the manufacturer of Zerona) provides reasonable assurance of the safety and effectiveness of the product.

Zerona is the only aesthetic device specifically cleared for the reduction of circumference of multiple areas. The FDA has also deemed appropriate not to make use of the word temporary in the approval, suggesting that, provided patients adhere to a healthy lifestyle (whereby they balance their food intake with their energy expenditure), results should be permanent. Finally, the FDA agrees that Zerona is not only safe but also effective for the indication. It is very atypical for the FDA to make statements regarding the effectiveness of products and is testament to the strength and quality of the clinical data submitted by Erchonia.

36. Is Zerona a class II or a class IIIb laser?

The answer is both. The FDA and ANSI both have their own classification system which may lead to confusion. Below is an explanation of the difference between the two classifications that regulate lasers:

- a. ANSI (American National Standards Institute) regulates laser safety and classifies lasers from I to IV, based on how much damage to tissue (specifically eye and skin) specific wavelengths, power levels and exposure times can cause. The Zerona device is a class IIIb device. See below for a complete description.

"Lasers and laser systems are assigned one of four broad Classes (I to IV) depending on the potential for causing biological damage. The biological basis of the hazard classes are summarized in [Table III:6-4](#).

- Class I: cannot emit laser radiation at known hazard levels (typically continuous wave: cw 0.4 μW at visible wavelengths). Users of Class I laser products are generally exempt from radiation hazard controls during operation and maintenance (but not necessarily during service).

Since lasers are not classified on beam access during service, most Class I industrial lasers will consist of a higher class (high power) laser enclosed in a properly interlocked and labeled protective enclosure. In some cases, the enclosure may be a room (walk-in protective housing) which requires a means to prevent operation when operators are inside the room.
Class I.A.: a special designation that is based upon a 1000-second exposure and applies only to lasers that are "not intended for viewing" such as a supermarket laser scanner. The upper power limit of Class I.A. is 4.0 mW. The emission from a Class I.A. laser is defined such that the emission does not exceed the Class I limit for an emission duration of 1000 seconds.
- Class II: low-power visible lasers that emit above Class I levels but at a radiant power not above 1 mW. The concept is that the human aversion reaction to bright light will protect a person. Only limited controls are specified.
- Class IIIA: intermediate power lasers (cw: 1-5 mW). Only hazardous for intrabeam viewing. Some limited controls are usually recommended.

NOTE: There are different logotype labeling requirements for Class IIIA lasers with a beam irradiance that does not exceed 2.5 mW/cm² (Caution logotype) and those where the beam irradiance does exceed 2.5 mW/cm² (Danger logotype).

- Class IIIB: moderate power lasers (cw: 5-500 mW, pulsed: 10 J/cm² or the diffuse reflection limit, whichever is lower). In general Class IIIB lasers will not be a fire hazard, nor are they generally capable of producing a hazardous diffuse reflection. Specific controls are recommended.
- Class IV: High power lasers (cw: 500 mW, pulsed: 10 J/cm² or the diffuse reflection limit) are hazardous to view under any condition (directly or diffusely scattered) and are a potential fire hazard and a skin hazard. Significant controls are required of Class IV laser facilities."

This classification affects who is allowed to operate a laser system and changes from state to state.

b. The FDA has a different classification system which regulates products in 3 classes:

- Class 1 regulates products that do not pose any health risks. Products falling under this category typically are non-therapeutic devices (diagnostic equipment, medical furniture, etc.). These products do not need to seek an approval, but simply need to file for registration with the FDA.
- Class 2 regulates products that have a therapeutic purpose and are non life-threatening - which must be backed by a predicate device. A predicate device is a device already approved which has similar specifications and indications for use to the device for which approval is being sought. Class 2 devices benefit from an expedited process known as 5-10K, which requires minimal (if any) clinical data and is typically processed within 90 days from filing. All thermal laser devices are considered class 2 based on a previously approved predicate (or a predicate of a predicate). The predicates can all be traced back (either directly or indirectly) to a CO2 laser device from Coherent Medical (now defunct) initially approved in 1969!
- Class 3 devices are considered potentially life threatening and are subject to intense scrutiny from the FDA. Devices falling under this category typically include pacemakers, drugs, etc., but also any devices for which a predicate cannot be found, i.e. Zerona. However, upon reviewing the information submitted by Erchonia as part of its FDA submission, FDA reclassified Zerona as a class 2 device

37. Who can operate the device?

As a class IIIb laser Zerona must be operated under the supervision of a medical professional (typically an MD or DO). Rules regulating the actual operation of Zerona vary from state to state.

38. How do you account for the bad press you have been receiving on the internet?

In this day and age, the digital media provides disgruntled individuals with the perfect tool to be vociferous. This invariably happens with any device or product on the market. SBMI is committed to the success of both providers and patients alike:

- a. Providers have the option to return their Zerona device for whatever reason if they choose to stop providing treatments.
- b. Customers benefit from the Zerona guarantee whereby they get additional free treatments if they do not meet specific success criteria.

While committed to their success, SBMI has no control over the quality of the treatments provided by its customers. Inappropriate diode positioning or failure to follow protocol may lead to a small number of dissatisfied patients who, thanks to the digital media, can blow this issue

out of proportion. It is unfortunate that happy patients are far less likely to post comments about their positive experience!

39. How is it different than liposuction?

Liposuction is an invasive procedure involving the mechanical removal of fat cells. By contrast, Zerona is completely non-invasive and only affects fat cells temporarily. Zerona does not compete with liposuction; it is simply a body shaping option available to patients who do not wish to undergo a surgical procedure.

40. Does Zerona help with loose skin?

There have been no studies specifically looking at the effect of Zerona on loose skin and SBMI never makes claims that cannot be evidenced in a clinical study. Anecdotal evidence suggests that patients undergoing Zerona have noticed an improvement in skin tone and texture.

41. Does Zerona improve the appearance of cellulite?

There have been no studies specifically looking at the effect of Zerona on cellulite and SBMI never makes claims that cannot be evidenced in a clinical study. Anecdotal evidence suggests that patients undergoing Zerona have noticed an improvement in the appearance of cellulite.

42. Can Zerona cause cancer?

No. Zerona uses low levels of light in the visible spectrum (635nm) to stimulate our cells to be more efficient and accelerate the rate of naturally occurring processes. Low level light therapy has been evaluated for over 40 years and there has never been any indication that it may cause cancer. However, patients with cancer should not be treated. For more information, please refer to our list of contraindications.

43. What is a Level 1c trial and why should Physicians and consumers care?

A level 1c clinical trial is described as: "Evidence from at least one moderate-sized randomized controlled trial". In our case, the trial was also multi-centric. The benefits of such a study are:

- Multi-centric: eliminates the potential bias from a single investigator
- Randomized: Ensures that patients are not selected to be included in a group that the treating physician feels they will respond better, hence potentially skewing results
- Double-blind: neither the Physician nor the patient knows which device (real or sham) is being used to perform the treatment: eliminates bias.
- Placebo controlled: having a placebo group allows to compare results from the treated group to placebo, thereby ensuring that a true, relative comparison can take place.

The benefits to the physician (when partnering with us) and the patient (when considering paying for a series of treatments) is that the data provided to support our claim is without bias and that all efforts have been made to ensure that what was achieved in the study will be matched (or exceeded) in real life.

Results from our study are also highly statistically significant: This means that:

- Results achieved had nothing to do with chance
- The number of patients included in the study was sufficient: once statistical significance is achieved, including more patients in the study would not significantly alter results: it would only increase the statistical significance of the study (which is already statistically significant).

Against this background, most (if not all) competitors perform level 4 studies: "evidence from at least one high quality case series". This means that there are no controls in place to eliminate bias and no way to compare results to placebo. It explains why, in many cases, Marketing claims made by companies based on such studies are, more often than not, impossible to duplicate in the real world.