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Zerona LLLT Receives Industry-First FDA Clearance

For the past several years Zerona low-level laser therapy (LLLT) for body contouring has had its fair share of critics. However, with sound science and clinical outcomes supporting the mechanism of action, industry experts are praising Zerona's strong foundation of rigorous research backing its fat reduction and body contouring applications. With this foundation and a recent, industry-first FDA clearance for the reduction of upper arm circumference, these critics may at last be silenced.

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Scientifically Proven Technology Now Offers Arm Circumference Reduction

By Kevin A. Wilson, Contributing Editor

Developed by Erchonia Corporation (McKinney, Texas), and marketed exclusively by Primcogent Solutions (Dallas, Texas), Zerona utilizes a patented 635 nm diode laser, which delivers five rotating, line-generated coherent laser beams for non-invasive, safe and effective circumference reduction of the waist, hips and thighs. Now, a new device using this proven core technology, Zerona AD, has been granted an industry-first FDA clearance for circumference reduction of the upper arm, another innovative milestone for the brand.

Like its predecessor, Zerona AD utilizes the same proprietary method of delivering the 635 nm wavelength and applies a similar protocol: a series of six, 20 minute treatments per arm over a two week period. "The Zerona technology is very easy to use," said Jamé Heskett, M.D., founder and medical director of Wellpath (New York, N.Y.). "There are no parameters to adjust related to energy delivery, as there would be with a thermal laser or other light-based therapy." Recently, Dr. Heskett was featured on *The Dr. Oz Show* demonstrating the ease of use and safety of the original Zerona body system. "The only preparation for the patient is that they must be well hydrated, which improves the overall result," she noted. The outcome is fully realized within just a few weeks, she added. "People who come properly hydrated and follow the treatment with a healthy lifestyle will be very satisfied with the results."

Ease of use is one of the big advantages with Zerona. According to Patricia Ogilvie, M.D., an aesthetic dermatologist in Munich, Germany, "In aesthetic medicine it's always good when a therapy does not require

much attention to safely and effectively use it. This frees ancillary personnel to do other tasks. Zerona is so safe and easy to use that there are no worries with treatment. Once you set up the device properly and turn it on, you walk away for the required amount of time and the lasers automatically complete the treatment. Any properly trained staff member can perform the treatment. There is no risk of burns or side effects because Zerona is what we call a cold laser."

One unique aspect of the Zerona treatment that patients love also increases critics' skepticism. Since the modality's mechanism of action is photochemical and causes no thermal or acoustic effect, there is no pain or physical sensation, which makes some question whether Zerona is really working. "It is important to manage this by educating patients properly," said Dr. Ogilvie. "Patients, and practitioners as well, seem to have a deeply ingrained idea that if there's no pain, nothing can be happening. The clinical results refute this but it is still difficult for some people to accept."

R. Stephen Mulholland, M.D., plastic surgeon and medical director of SpaMedica Cosmetic Surgery and Laser Skin Care Spa (Toronto, Ontario, Canada), agreed. "I think the general attitude that if a therapy isn't producing pain it can't be doing anything, has been pervasive in our field, and was an obstacle to the initial acceptance of Zerona LLLT. Zerona also seems to have been a victim of its own press as well. There was a lot of hype about what it could do, inflating expectations beyond the realistic, which was not entirely the responsibility of the company marketing the technology at the time."



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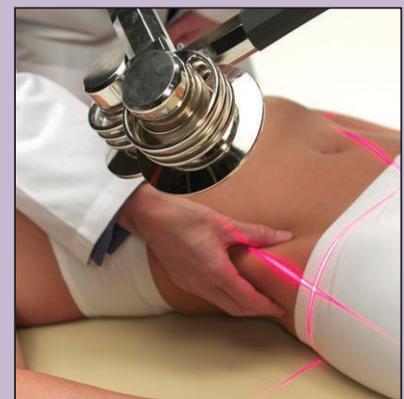
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Zerona Tx

Photo courtesy of Primcogent Solutions



Before Tx



After Zerona Tx

Photos courtesy of R. Stephen Mulholland, M.D.

"I carefully select my patients and see satisfaction rates as high as other prominent aesthetic treatments such as injectables, breast implants or liposuction. It's undeniable that it works."

Dr. Mulholland says this phenomenon is common in the industry, and many currently popular technologies are going through this right now. "Additionally, as with all devices, patient selection is still important to the success of a therapy within your practice, as well as within the industry as a whole." According to the company, obese patients will get the same results as anyone else, but they may desire additional treatments to achieve more meaningful results.

Another misunderstanding associated with Zerona was the supposed lack of science supporting its technology. However, Dr. Mulholland stressed that the science was always there. "The initial marketing of the device did not successfully emphasize the scientific story to the physician audience, to the detriment of the technology. In fact, studies have shown that Zerona produces not only clinically significant outcomes, but also meaningful results the patient can see. No other FDA cleared technology for circumferential reduction has the magnitude of academically rigorous, evidence-based, peer-reviewed research supporting its safety, efficacy and mechanism of action. There have been over 1 million Zerona treatments performed to-date throughout North America. I carefully select my patients and see satisfaction rates as high as other prominent aesthetic treatments such as injectables, breast implants or liposuction. It's undeniable that it works. The question is; how does it work?"

A 2011 review of body contouring technologies¹ by Dr. Mulholland thoroughly describes the mechanism of action of Zerona's proprietary 635 nm low-level laser. "The laser light penetrates through to the superficial layers of fat," he started, "stimulating a photochemical reaction by which a transitory pore is created within the membrane of

adipocytes. Lipid material is liberated through the pore, into the interstitial space and taken up by the lymphatic system for use or disposal."

Dr. Mulholland's description of the mechanism of action stems from numerous peer-reviewed publications reporting the formation of transitory pores within the cell membranes of adipocytes directly within the target area following LLLT at 635 nm. Stored intracellular lipid material then leaks into the interstitial space through the newly formed openings. Following their release, the lipids are naturally removed by the lymphatic system and metabolized by the body, leaving behind drained and collapsed fat cells. This process has been documented through scanning electron microscopy and published in peer-reviewed journals such as *Lasers in Surgery and Medicine* and *Plastic Reconstructive Surgery*.

This well-documented outcome is believed to be the result of photochemical mechanisms stimulated by Zerona's 635 nm wavelength at the therapeutic dosage of 0.95 J/cm². Photochemistry is defined as a subtle mechanism that targets a photoreceptor with a distinct wavelength administered at a therapeutic dose, a concept that has been studied extensively in literature. Studies have assessed the concept of therapeutic dosage and have defined a therapeutic dosage window; thus any wavelength delivered at a dose outside of this window will not achieve the desired clinical effect.

The 635 nm wavelength, administered at a dose amenable to the therapeutic window, allows the technology to effectively target and activate cytochrome c oxidase (CCO), a

photoreceptor that plays a key role in cellular respiration. Activation of CCO increases the production of adenosine triphosphate (ATP) and reactive oxygen species (ROS). It is the increased ROS that is capable of reacting with the fat cell's membrane, causing the formation of transitory pores.² This outcome is accomplished without the generation of heat or vibration.

Robert F. Jackson, M.D., a cosmetic surgeon in Indianapolis, Ind. and lead author on numerous peer-reviewed published clinical trials with Zerona, assessed blood chemistry following Zerona treatment and reported no elevation in lipid levels, and in fact, the study showed a significant reduction.³ "This study adds to the fact that not only is this device effective, it does not result in untoward changes in blood chemistry," he explained.

"Like other body contouring therapies, Zerona is not a weight loss treatment," Dr. Heskett pointed out. "The fat itself doesn't weigh much in comparison to its volume. The remaining cellular material makes up most of the weight." While that fact may initially seem like a disadvantage, Dr. Heskett said the opposite is true. "Fat cells have an inherent hormonal role in the body, and we need them. The mechanism of action of Zerona mimics the body's natural metabolic mechanisms and creates a cascade effect in fatty tissue."

Mark S. Nestor, M.D., Ph.D., a dermatologist and director of the Center for Cosmetic Enhancement and the Center for Clinical and Cosmetic Research (Aventura, Fla.), served as lead investigator for the FDA directed multisite upper arm trials for Zerona. He feels the rigorous clinical research that Zerona has undergone

is another distinct quality. "Zerona technology lends itself well to rigorous clinical study, more so than other devices," he said. "For example, one can easily perform reliable sham treatments because there is no sensation involved. Therefore we can mimic the appearance of treatment by using light emitting diodes (LEDs), so that neither the physician nor patient knows if active treatment was delivered. This allows us to perform truly blinded studies as well as control for the placebo effect."

Data from Dr. Nestor's trials were recently assembled, examined and published.⁴ In the randomized, double-blinded, sham-controlled study, otherwise healthy subjects (n=40, body mass index 20 to 35 kg/m²) underwent three sessions of Zerona LLLT (635 nm) or sham treatment (20 patients per group) per week for two weeks. In addition, subjects agreed not to deviate from their current dietary and exercise habits. "The goal was to develop a protocol independent of confounding factors," Dr. Nestor explained.

Clinical evaluation of outcomes included pre- and post treatment circumference measurements, as well as a subjective rating of patient satisfaction. The active group showed an average combined arm circumference reduction of approximately 3.7 cm compared to average combined reduction of 0.2 cm for the sham group. "What is more impressive to me," Dr. Nestor noted, "is that the strong statistical significance of these outcomes is backed by patient perception that upper arm appearance improved and results exceeded their expectations. The bottom line is that patients see and feel the difference with Zerona."



Before Tx



After Zerona Tx

Photos courtesy of R. Stephen Mulholland, M.D.

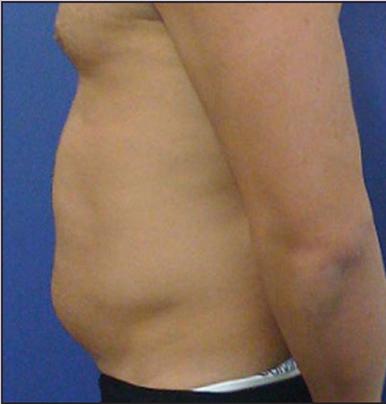


Before Tx



2.5" reduction after Zerona Tx

Photos courtesy of Mark S. Nestor, M.D., Ph.D.



30 year old male before Tx



8.74" reduction after Zerona Tx

Photos courtesy of Rafael Acra, M.D.

"In the multicenter study we went as far as eight months after completion of the course of treatment and found virtually no change in circumference for either group. This suggests a long-term effect."

In addition, Dr. Nestor believes his study has a powerful impact on the overall scientific picture of Zerona. "The FDA directed trial for the original Zerona device was, of course, tightly controlled or it would never have garnered clearance, but perhaps the only criticism that had any real merit was the ability to accurately measure abdominal circumference while fully controlling confounding variables," he said, "so that was a partial goal of more recent investigations. Confounding variables are easier to control when evaluating change in upper arm circumference. The arm treatment model, free from confounding variables like bloating due to gas or food consumption and even hydration, is so great because we bypass all that, making it easier to demonstrate that the treatment itself does indeed reduce circumference. We're simply reinforcing the outcomes seen with previous trials."

Another question surrounding Zerona has been the long-term follow-up. "In the multicenter study we went as far as eight months after completion of the course of treatment and found virtually no change in circumference for either group," Dr. Nestor reported. "This suggests a long-term effect, not simply just a temporary or short-lived response like those seen with other devices." With this recent study, Dr. Nestor has demonstrated that results are not only seen at two weeks, but that they are sustained for at least eight months.

A multi-center retrospective evaluation of 689 patients is the latest peer-reviewed publication on Zerona body treatment.⁵ This study was performed to evaluate criticism that Zerona's results were caused by fluid redistribution. As Dr. Jackson, the lead investigator explained: "It had

been purported that the Zerona treatment may have caused redistribution of fat and fluid to other body areas, and we had to make certain this was not a valid claim." Data was not pre-selected, but assembled wholly of patients who received the standard two-week course of six treatments and whose treatment records included circumference measurement for all treated (waist, hips and thighs) and non-treated areas (arms, knees, neck and chest). For waist, hips and thighs, a statistically significant combined reduction of 3.27 inches was reported, which is consistent with the published results of the FDA directed clinical trial. When assessed separately, the waist, hips and thighs each demonstrated a statistically significant circumferential reduction as well.

When the circumferential losses reported for the waist, hips and thighs was combined with those of the systemic non-treated areas, an overall 5.17 inch loss was observed. According to the study authors, these data dispute the notion that fluid or fat redistribution is the cause of Zerona's clinical outcome, and in fact, these results indicate a possible fat reducing systemic effect that warrants further research. Dr. Jackson added, "The size of the study population, coupled with the results, further substantiates the effectiveness of Zerona."

According to Dr. Mulholland, the market for Zerona is also there. "When you look at the U.S. market, roughly two-thirds of the population would like to slim down, he began. "Liposuction is about 4% of the overall market for elective surgeries, a number that is expected to double by 2015. The market is obviously big, but for every person willing to undergo liposuction

there may be upwards of 20 people who would strongly consider a non-surgical option if the price was right. In addition, the proliferation of various body contouring technologies is more proof. Zerona stands by itself as effective, non-invasive laser body contouring that's safe and scientifically sound. However, it's not without commitment – you still have to take care of yourself – but there is truly nothing else like Zerona on the market today."

Furthermore, it's not just contouring the waist, hips and thighs concurrently; it's also capable of spot reduction, which Dr. Heskett explained is a huge benefit. "This market is comprised mostly of women, and women desperately want to spot reduce troublesome areas. You cannot spot reduce with diet and exercise, but you can with Zerona."

Dr. Nestor has high hopes for the future of Zerona technology. "This is very exciting. We have proven results without pain, side effects or downtime. There is much work to be done for different applications beyond body shaping as well."

Bob Gerberich, senior vice president of global sales and field development for Primcogent Solutions reinforced Dr. Nestor's thoughts: "Zerona has more peer-reviewed, published science and pre-clinical (human) research supporting its mechanism of action than almost any other non-invasive technology on the market," he stressed. "Now with the Zerona body device and the new Zerona AD, providers can offer their patients non-invasive full circumferential fat reduction of the waist, hips, thighs and upper arms in one concurrent 40 minute treatment. Furthermore, this core technology has

a multitude of potential clinical applications. Advanced protocols and many new applications are in the works. Simply put, we believe we've only seen the tip of the proverbial iceberg with 635 nm LLLT."

Dr. Mulholland believes not only in the future of LLLT, but in the longevity of Zerona body shaping itself. "This is not a technology that's going to be great for two years and then disappear. I've been saying from day one that with the right approach, Zerona would rise above the skepticism and competition. It's a great product and a promising technology. Low-level laser slimming is here to stay. I see every physician who is serious about non-surgical, generalized laser slimming looking for a standard and the unquestioned leader is Zerona." ■

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Before Tx



After Zerona Tx

Photos courtesy of Dr. Ringwald

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