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The Concept of Fractional Fat Reduction with the ilipo Low Level Laser Device

D Freeman
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Introduction

Low level laser therapy (LLLT) for fat reduction treatments uses a mechanism where laser energy targets the mitochondria of the adipose cell, temporarily stimulating the electron transport mechanism within this organelle. The primary outcome of this action is the temporary increase in the production of ATP (energy) within the cell. Secondary effects of this cascade acceleration is the increase of H^+ ions migrating across the mitochondrial membrane into the cell interior, decreasing the pH. Since the body strives for homostatis, the cell responds to this increased concentration of H^+ ions by opening transport channels or pores in the cell membrane allowing the re-distribution of ions across the cell wall to redress the pH imbalance. In addition to H^+ concentration increase, there is also an increase in Ca^{2+} ions passing into the main cell interior from the mitochondria which triggers the release of a lipase enzyme [(1)(2)]. This enzyme breaks certain chemical bonds on the stored triglyceride molecules to create 3 free fatty acids and 1 glycerol molecule from each triglyceride unit. The smaller metabolites are then able to pass through the pores in the cell wall [(3)(4)], out into the extracellular matrix, where they will be transported away from the area by the lymphatic system for re-distribution to the body's tissues, and metabolism during post treatment exercise.

The ilipo has been in use for almost 3 full years in aesthetic practices around the world with great success, supporting patients to specifically reduce chosen or troublesome fat storage zones. In conjunction with a healthy diet and exercise lifestyle the treatment provides long term non-invasive and pain free body reshaping.

The aim of this document is to answer two of the most frequent questions that are posed with regards to the treatment and explain the benefits of fractional fat reduction.

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1. Is the fat released by ilipo dangerous?

During ilipo treatment the stored triglycerides are broken down into free fatty acids and glycerol before being released from the cell. Once outside of the cell they are transported by the lymphatic system, which drains into the body's circulatory system, thus introducing the contents of the cell into the blood supply. These fatty acids and glycerol would then be taken up and re-esterified (made back into triglyceride molecules) unless burned by the body to provide energy. This is why the post treatment exercise is so important, without suitable amounts of this, some or all of the freed fatty acids could be restored back into fat cells. A randomised controlled study published by Caruso-Davis et al [(5)], in 2010, detailed the effect of a LLLT device on circumference reduction of the abdominal region. Data show statistically relevant effect, with an average of 0.4-0.5cm reduction in each treatment session but observed that while this treatment offered statistically viable reduction of waist circumference, the mobilised fat would either be burned for food or be distributed into the fat depots typical of that person's fat distribution and without periodic treatments, the body would redistribute fat to its original patterns.

It is understandable to see why some patients might be concerned about the idea of fat cell contents getting into their circulatory network, with so much emphasis from the medical community as to the cardiac and circulatory risks of high cholesterol/triglyceride levels and fat 'furring' of the arteries. Ideally they need to be educated on the facts that firstly; ilipo treatment does not release triglycerides into the body's circulatory systems, it releases fatty acids, which are a normal metabolite transported around the body on a daily basis and secondly; the movement of higher concentrations of fatty acids and glycerol around the circulatory system occurs after every meal that they eat as well as after ilipo treatment, thus ilipo poses no increased risk on the body than eating a normal daily meal. Fat eaten as food is processed into chylomicrons in the gut and absorbed through the gastrointestinal tract into the lymphatic system, which subsequently drains them into the venous (circulatory) system, i.e. fat released by ilipo and fat eaten in the diet, both enter the circulatory system in a similar manner, just from two different sites and are processed from that point in a similar manner.

2. What limits are there to ilipo treatment and reducing fat?

While it would be nice to think that we could have a whole body treatment and remove any excess fat in one sitting, it simply isn't achievable because of the limits placed on us by the human body not by the device itself.

First of all, the human body is not designed to eliminate stored fat or calories unless needed to meet a demand for energy either by increased exercise or reduced daily

calorie intake. Therefore, after an ilipo fat reduction treatment, there needs to be a period of exercise to cause the 'freed' energy to be metabolised or burnt off and thus be permanently removed from the body's reserves. If this is not completed effectively, the unused energy will simply be restored into the body's fat cells for future use.

Would this restoring occur in the cells that have just been emptied? This, unfortunately, is an unknown factor that would be hard to identify conclusively. It would be easy to assume that the newly empty cells would be the most attractive re-storage point at that time but at the end of the day, the body could choose to store them any where within the subcutaneous tissue that it normally prefers to store fat in. Each patient can probably identify a zone of the body where they most quickly notice fat gain – their bodies preferred area of storage, and this would still continue to be a zone of concern after ilipo treatment if the patient continues to mismanage their diet vs. exercise balance.

We are also limited to how much fat reduction can be done in a single sitting. If too large an volume of fat is mobilised from the fat cells, there might well be an amazing instant inch loss to congratulate the patient over, but would be so much available energy requiring metabolism that the patient would be exercising for the next 8+ hours to use it all up! For the majority of patients this is unlikely to happen, leaving the majority of the freed fatty acids to be restored and result in some of those amazing 'inches-lost' to creep back on again before the next treatment.

There is also a limitation on how many free fatty acids can be transported by the blood at any one time, since the fatty acid molecules need a transporting carrier molecule to enable the insoluble fat to solubilise in the water based blood serum (think of it like when you pour fat into water, the two do not mix until you add some dishwashing soap, which assists the fat to disperse or solubilise in the water). Once all of these carrier molecules spaces are filled, no new fatty acids will be picked up and transported by the blood until some of the previous molecules have been removed from the circulation. This will limit the amount of fatty acids that can be mobilised around the body after each treatment session prior to the post treatment exercise taking place.

3. What is the Fractional Fat Reduction (FFR) effect with the ilipo and why is it important?

The design of the ilipo is such that small pockets of adipose cells are irradiated and stimulated to release their stored fat contents rather than stimulating fat cells to empty in a continuous layer across the whole surface area being treated. This Fractional Fat Reduction (FFR) results in the creation of a porous 'sponge-like' structure in the targeted fatty tissue.

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The skin is made up of various discrete layers with the thin epidermis outermost, the dermis beneath it and then the subcutaneous adipose/fat layer sandwiched between the dermis and the muscle facia underneath the skin (see Fig 1. below).

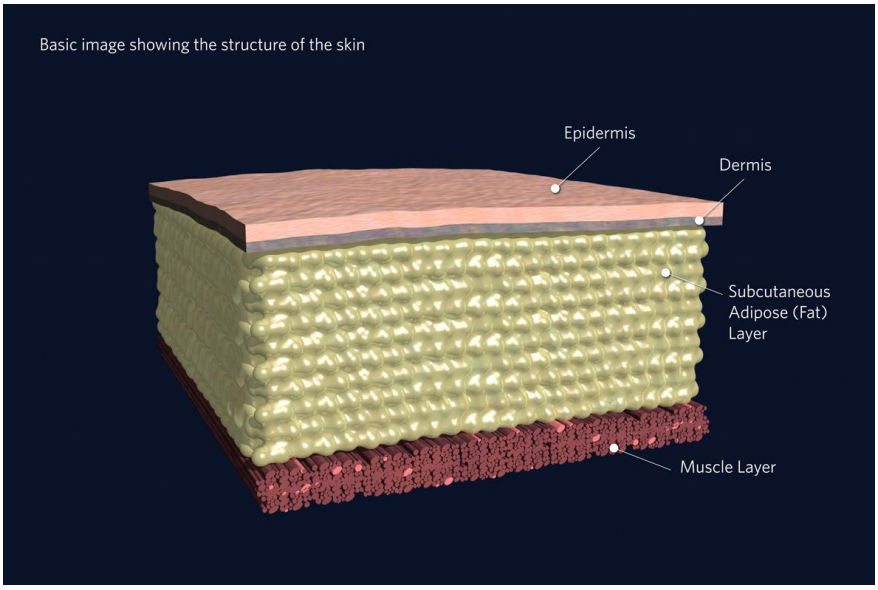


Fig 1. Structure of the skin

Many LLLT devices often describe their laser light distribution to be even across the entire skin surface to provide a uniform treatment. This is even used as a marketing point (see Fig 2. below).

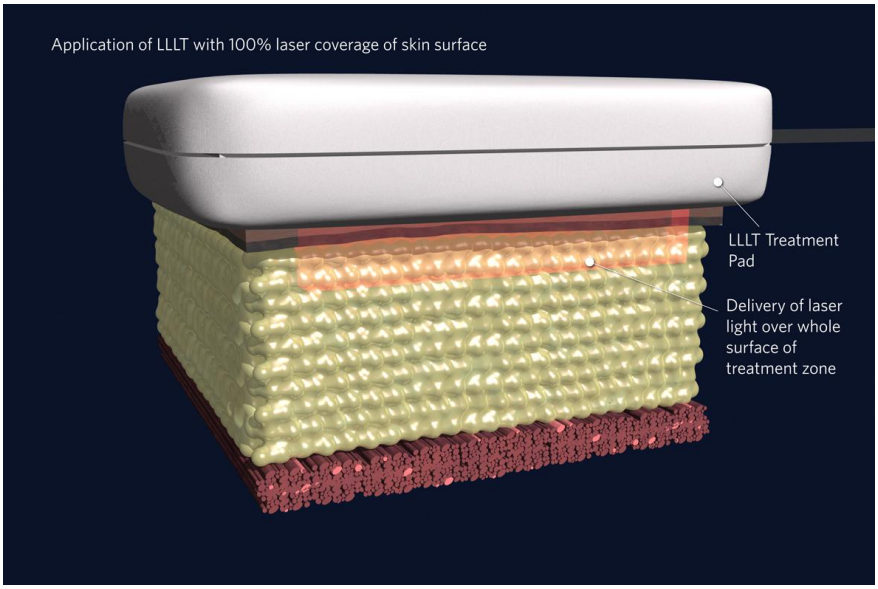


Fig 2. aApplication of 'other' LLLT with 100% laser coverage of skin surface under the treatment pad

If the laser treatment was to target and empty a whole layer of fat cells under the skins surface of the targeted treatment area it could create a large area void directly under the epidermis/dermis (see Fig 3. below).

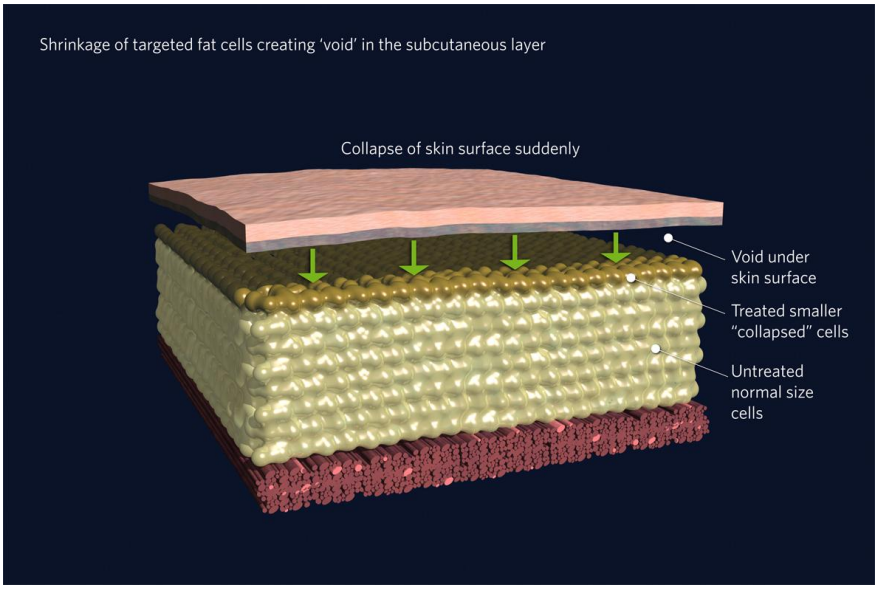


Fig 3. Shrinkage of targeted fat cells, creating 'void' in the subcutaneous layer under the epidermis/dermis surface that would theoretically cover the entire area under the treatment pad

This might result in the formation of unsightly wrinkles or mini folds of excess skin tissue as the surface collapses into this void since the natural skin elasticity would requires some time to 'contract' and tighten across the area (see Fig 4. below). This unwanted effect could be longer lasting in older patients or patients with significantly reduced elasticity in their skin tissue.

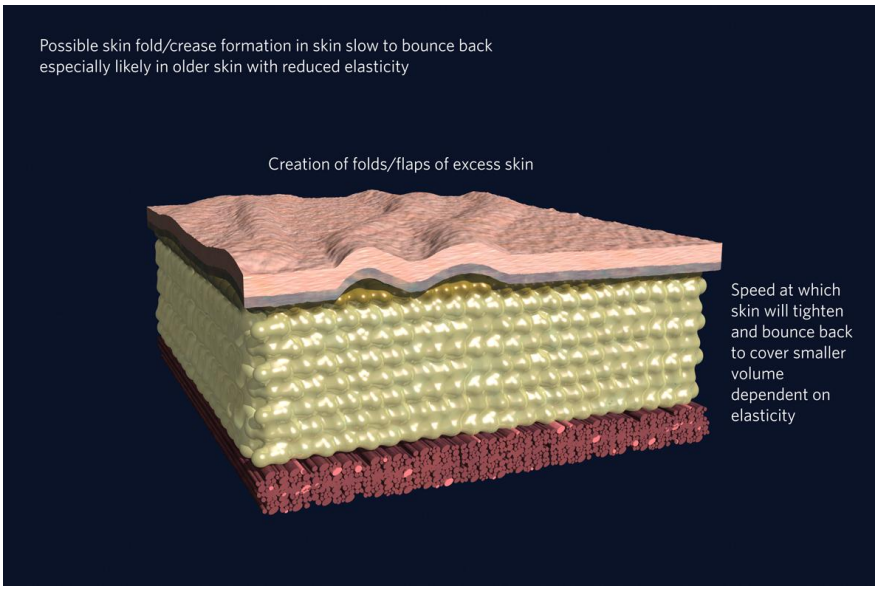


Fig 4. The possible skin fold/crease formation when the epidermis/dermis collapses into the void underneath it

By creating a fractional fat reduction effect with low divergent laser diodes we see the production of channels of stimulated fat cells within the fat layer.

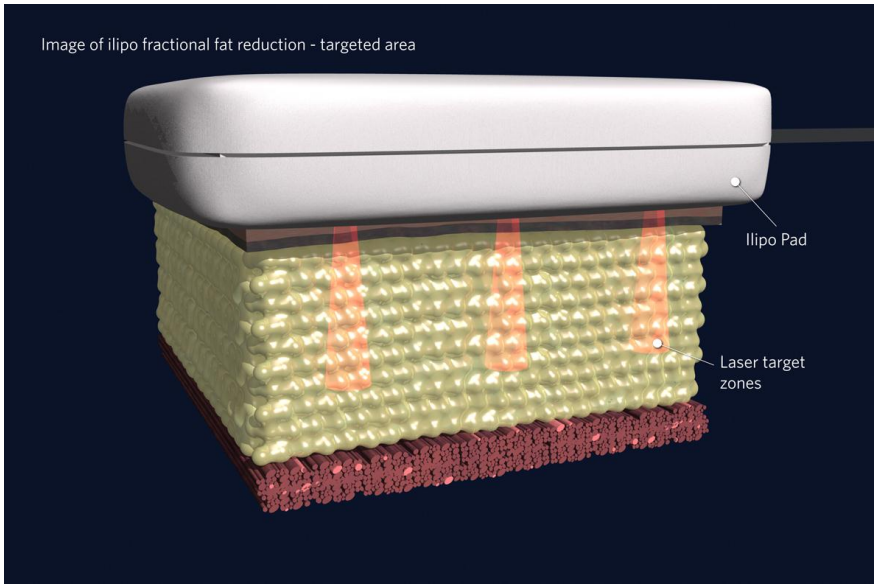


Fig 5. ilipo LLLT treatment pad on the skin targeting fractional columns of laser area

Only the fat cells within the laser beams would be stimulated to release their contents creating channels which will essentially be voids of empty fat cells. Other untreated 'full' fat cells can then relocate and space-fill into these empty channels (see Fig 6. below).

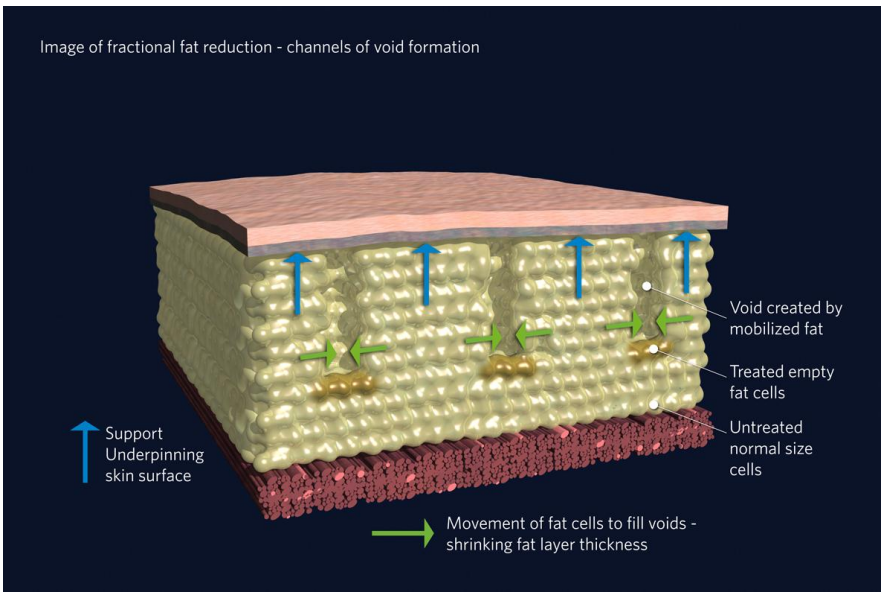


Fig 6. Image of fractional channels of void formation from ilipo, creating sponge effect with underpinning support to epidermis/dermis and gradual migration of untreated fat cells to fill voids

Over-all fat volume is reduced, causing immediate and measureable circumference reduction, but this sponge structure would maintain the support for the skin surface, providing 'scaffolding' support of untreated fat cells to underpin the epidermis/dermis immediately after the treatment and gradually allow the natural skin elasticity to contract at its own pace as the remaining fat cells relocated into the voids. This would prevent the possible formation of excess puckered skin and also allows a more even treatment. Many patients can actually feel this effect, where the texture of their treatment area is described as 'doughy' or more 'spongy' after treatment (See Fig 7. below).

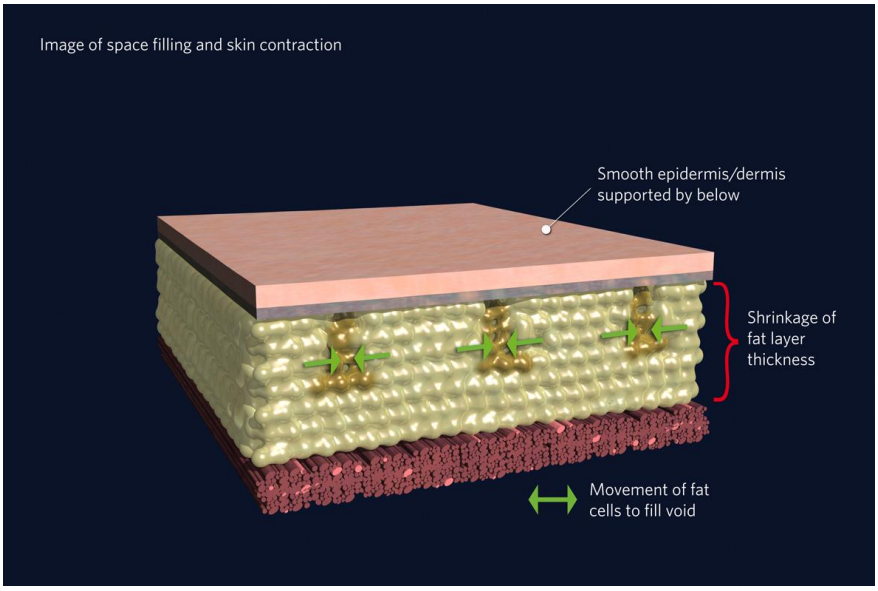


Fig 7. Gradual skin tightening allowed as fat layer shrinks with relocation of untreated cells into fractional channels

The other important factor of fractional fat reduction is the amount of calories this method mobilises with each treatment, ensuring fat reduction at a much more sustainable rate for each treatment, and for each patient, than treatment of the entire cosmetic area as described by other devices.

For example, another LLLT device that markets the homogenous treatment of the entire area covered by the laser pads during treatment would treat an area of 78.0cm^2 per pad per treatment. Their suggested protocol is the placement of 4 pads in 2-3 locations on a treatment zone, i.e. 8-12 pads worth of surface area covered. This equates to 624-936cm^2 of skin surface and thus, subcutaneous fat exposed to the lasers during a typical treatment. From their clinical results published, the manufacturers indicate an average reduction of 0.55cm per treatment from any single circumference measurement of the treatment zone.

To calculate amounts of calories involved we do have to make some assumptions to make the mathematics a little easier to manage, so the following results are

approximations of the real life situations. The basic assumptions made are that the patient torso is cylindrical with a starting circumference of 80cm.

Data presented at the 30th ASLMS annual conference in April 2010[6] demonstrated from a retrospective study of 311 patients, an average measured loss from a single treatment session of 0.55cm.

To calculate the volume of fat reduced from the treatment we need to calculate the radius of the cylindrical torso before treatment and then again after treatment using the circumference data measurements.

Circumference $c = 2\pi r$
and the reduction in fat layer thickness
$r_{loss} = r_{before} - r_{after}$

Before we begin the calculations we have to take into account the fact that the calculated reduction in radius of the cylindrical torso, will only actually be from one half of the torso being treated since a typical treatment of pads placed around the torso, 8 in number, laid side by side on a patient of circumference 80cm will only actually cover half of the circumference of the torso. This means we have to consider the torso as two separate semicircles, with the front half or semicircle being treatment and the back semicircle untreated.

Therefore the measured average reduction of 0.55cm is only caused by volume reduction effect on the front semicircle; the half of the circumference at the back would be constant in before and after measurements.

Thus c before treatment = 80cm = $2\pi r$
And radius before treatment r_{before} = 12.74cm

Measured c after treatment = 79.45cm (measured reduction of 0.55cm)

But this reduction is all accountable to the front half of the torso, meaning the radius of the front of the torso after treatment has to be calculated as the radius of a circle with circumference reduction of twice the measured value

C required to calculate r_{after} =78.9cm

And radius after treatment r_{after} = 12.55cm

r_{loss} = 0.19cm
= the calculated reduction in fat layer thickness under the treatment pads

So, from the surface area calculations previously, we would expect to see a volume of fat reduced after treatment to equal 118.6cm^3, where volume = area x thickness.

Since 1cm^3 of fat equals 1.09g and 1g of fat is equivalent to 9.072kcals, then each treatment is averaging 1172 kcals of fat mobilised in a single treatment.

This is equivalent to over half a day worth of calories for the average woman (who would be trying to maintain current weight) and would require significant hours of cardiovascular exercise to ensure complete metabolism.

This device also has one of the smallest actual treatment pad areas compared to others on the market suggesting that other devices, if they are treating the entire surface area evenly, may be mobilising even more calories.

The conclusion we can derive from this is that either:

1. the other devices are moving so much fat that much of it, perhaps as much as 50-60% is likely to be restored again in the hours/days after treatment even with a significant post treatment exercise period or
2. these devices professing homogenous surface treatment are not actually achieving this.

The ilipo has been specifically designed to perform fractional fat reduction to reduce the risk of skin folds or laxity after treatment and also to maintain the actual rate of fat reduction at a sustainable level for patients to be able to manage complete elimination from the body through a reasonable exercise regimen.

Using specialist specification laser diodes with minimal divergence as opposed to more competitively priced diodes found in some devices that are much more divergent, the ilipo is able to maintain a collimated focus into the subcutaneous fatty tissue to empty the fat cells in fractionated columns within the treatment area as described previously.

Traditional laser theory suggests that the visible red wavelengths used in the ilipo have a depth of penetration of several mm into the tissue, although those calculations and measurements have been based on depth of penetration to provide suitable power densities capable of creating a photo thermal reaction in the target chromophore. Since the ilipo relies on a mechanism of photochemical stimulation the amount of photons of light required to do this are considerable lower.

The human retinal cell can respond to photon densities of as few as 30 photons per second to create a chemical signal via the nerve cells.

If we take a laser probe of 40mW and direct this over a 3mm diameter surface area (typical diode size), the power density is 440mW/cm^2. At 2cm into the tissue (assuming transmission value of 0.01% which is the most conservative estimate in human tissue) the laser power is as low as 4.4x10-5/cm^2, the rest of the light has been absorbed, been transmitted or after scattering, has been reflected away. At this power the amount of photons passing through the 2cm depth barrier is equal to

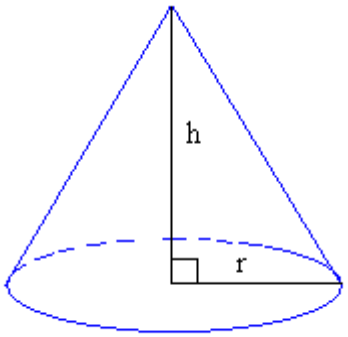
150,000,000,000,000 photons per second ($6.6x10^{-5}/3x10^{-19}$J = $1.5x10^{14}$ photons per second)

At 4cm deep the power would be 0.004microwatts, corresponding to 15,000,000,000 photons per second – still about 500 million times more than the 30 photons per second it takes to stimulate the retinal nerve signal.

At 6cm deep we get 15,000,000 photons per second, 50000 times more than the required amount to stimulate a nerve signal in the human eye.

Clinical studies using laser light to activate PDT therapies for cancer treatments also report effective results at depths of 1.5cm or more[(7)(8)].

Each diode has a small angle of divergence, meaning that the area of the beam does increase as we pass deeper into the tissue. The volume of fat cells exposed to the laser effect is in effect a cone with the diode source at the tip.



Calculated volume of fat cells exposed with each single diode during treatment

$$V = 1/3\pi r^2 h$$

Where r is the radius of the cone and h is the penetration depth into the tissue

Thus assuming 1cm penetration into the tissue

$$V = 1/3\pi(0.3728)^2 \times 1.3$$

Were r is calculated from the angle of divergence and the adjacent measurement (1.3cm) and Height h = 1.3cm allowing for the 1cm penetration depth and the additional factor for the length of distance from the diode surface within the treatment pad to the skin surface.

Thus

V = $0.19cm^3$ per diode
V = $1.71cm^3$ per pad
V = $13.6cm^3$ per treatment of 8 pads

$13.6cm^3$ of fat equates to approximately 15g of fat or 135kcals of fat.

If we then assume a 1.5cm penetration depth into the tissue

V = $0.5cm^3$ per diode
V = $36cm^3$ per treatment

= 39g of fat or 356kcals

Based on previous experiences with PDT activation it is not unreasonable to assume effective fat cell stimulation to depths of 1.5cm, which with this fractional method of reduction would mobilise approximately 356kcal of energy, a reasonable amount to metabolise off with a suitable exercise session post treatment.

Patients with very thick layers of fat within the target zone could conceivably have stimulation at depths deeper than 1.5cm, although the amount of calories mobilised in this may be too much for them to successfully manage elimination of. In reality for sustained long term results, we suggest fat reduction at a controlled pace of around 300-400 kcals per session.

Conclusion

The mechanism of action of the ilipo uses existing natural reactions and processes used by the body on a day to day basis. The ilipo simply gives the patient the control of which fat to target for metabolism rather than let the body make the decision. Because of this, the ilipo poses no increased risk to a patient's medical well being at the time of treatment or in the future.

The limits of speed at which a patient can reduce fat is limited by the body, only so much fat can be transported at a time and only so much exercise can realistically be achieved effectively in one session. Long term maintenance of the results are limited by how committed the patient is to achieving and maintaining their goal. If they over indulge in calories surplus to the body's requirements, these calories will be stored as fat.

Fractional fat reduction techniques to treat an anatomical target area will:

1. provide additional support to the epidermis/dermis after treatment by targeting columns of fat cells for evacuation while leaving other columns of untreated cells to act as underpinning support to the epidermis/dermis and to allow time for the natural skin elasticity to tighten and reduce the risk of excess skin puckering and
2. manage the rate of fat release per treatment to sustainable levels for the patient to support treatment success, calculations suggesting approximately 360kcals per treatment session as opposed to nearly 4 times that if more diffuse diodes are used to cover the entire surface area.

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