

*MIRROR, MIRROR ON THE WALL...  
now you can have the most beautiful skin of all,  
with the Beurer*

# SoftLaser

## Beautiful Skin

As recommended by Fitness Magazine, August 2003, the safe and effective Beurer SOFTLASER for Beautiful Skin, Anti-Aging, Wrinkles and so much more!

## Anti-Aging

Learn the secrets of exclusive European Spas and Salons. The German-made Softlaser was designed for skin rejuvenation and improvement. It does not cut or burn, but penetrates into the skin to produce collagen and cell regeneration resulting in the youthful skin and look you crave. You feel no discomfort and will be amazed by the results.

## Non-Invasive Highly Effective

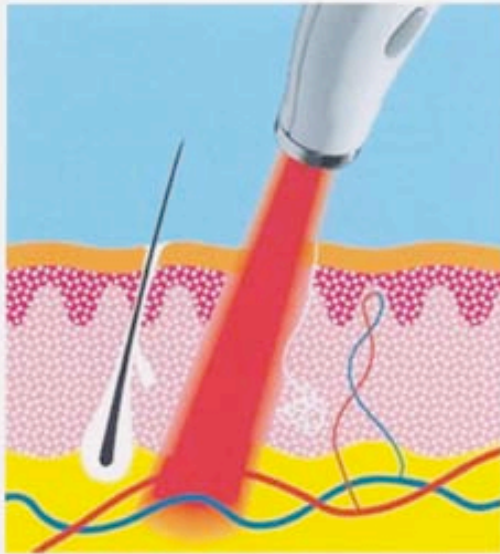
**Vitalmed**  
by beurer  
Made in Germany



Recommended  
by  
**fitness**  
Magazine  
August, 2003



## HOW TO USE THE SOFTLASER



### Using Your Softlaser

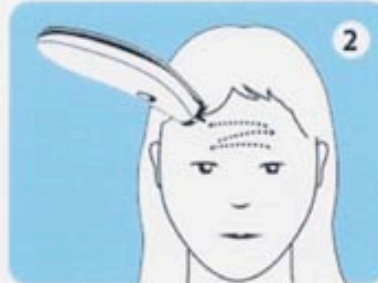
Softlaser therapy is based on the working principles of Low Level Laser Therapy (LLLT) in a process known as Bio-stimulation. LLLT employs a very low dosage of coherent laser light that has been proven to vitalize the cells by increasing the mitochondrial adenosine triphosphate (ATP) production in the cell.

This turn enhances the regenerative capacity of the cells making them act younger and promoting collagen production. In addition, LLLT has been shown to have positive effects on blood microcirculation, the immune response, and the modulation of pain of inflammation.

In Europe, the Beurer Softlaser has FDA equivalent approval for a number of conditions including acne, canker sores, small cuts, herpes, and other ailments alleviated by faster healing. In the United States, however, we make absolutely no medical claims and only recommend using the Softlaser for fine lines, wrinkles, and beautiful skin.

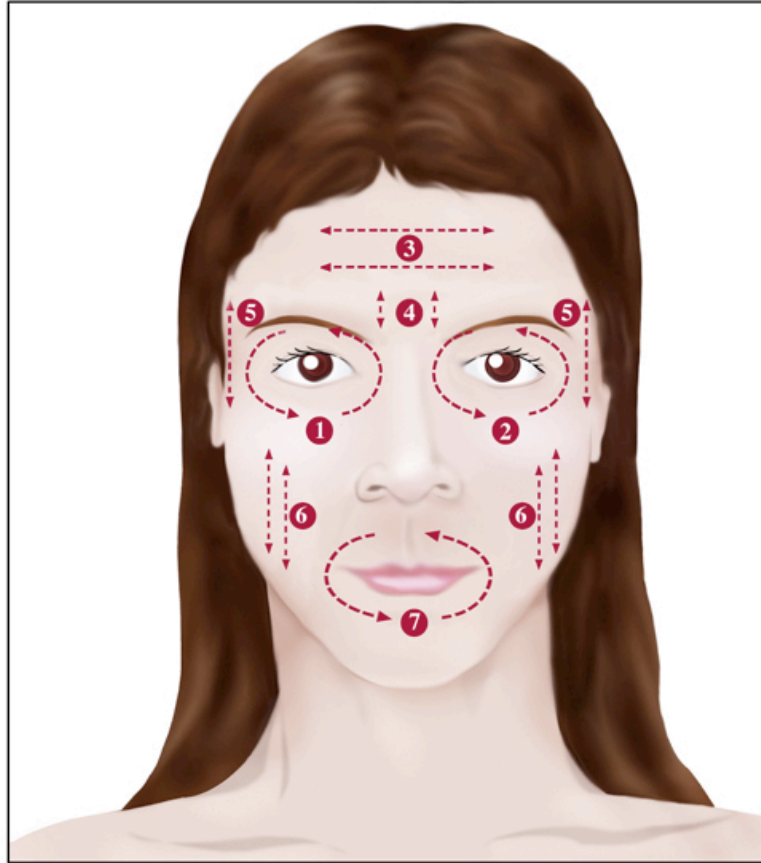
### Basic Techniques of Softlaser Treatment

The effects of LLLT begin at the new skin level. The biological response will be dependent on the individual's response. An improvement in the skin condition will usually be noticed within a few days. However, treatment should be carried out for a minimum of one week by applying the Softlaser directly to the clean skin between 6 to 18 minutes every day for each area you are treating. In the case of acne the laser should be held approximately 1 cm away from the skin, so as not spread bacteria. To achieve best results, try using the Softlaser twice a day, once in the morning and again in the evening.



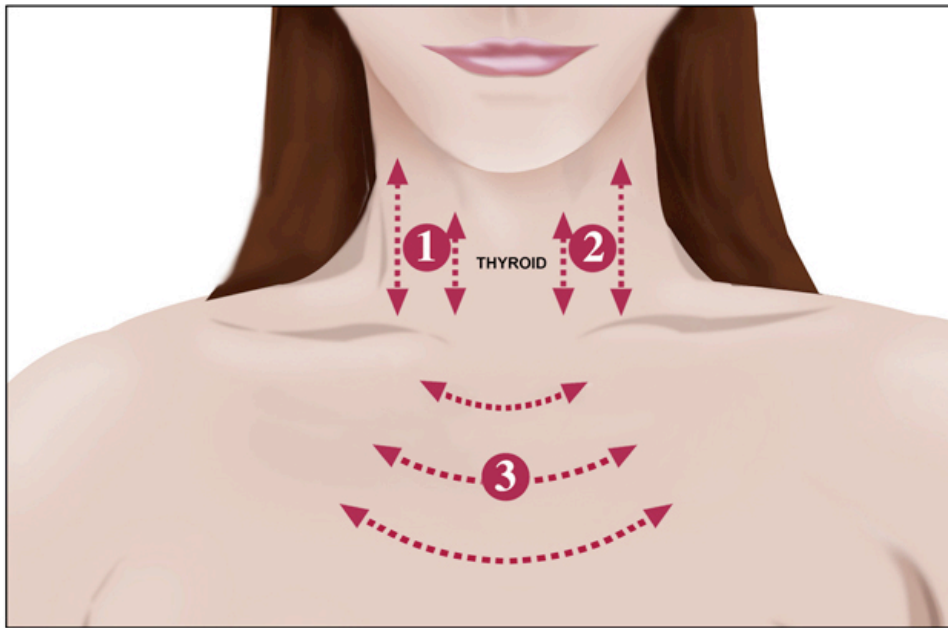
For beautiful skin and anti-aging, apply the Softlaser to clean skin. We recommend dividing the face into 3 areas: 1) the forehead; 2) the left side of your face; and 3) the right side of your face. Moving the laser in a zigzag motion, treat the left side of your face for 6 minutes. Remember, the idea is to have the laser light cover the entire area. Next, repeat for the forehead and finally the right side of the face, for a total treatment time of 18 minutes. For acne, insect bites or cuts, hold the softlaser stationary about 1 cm above the area for 6 minutes.

## Smoothing of wrinkles with Low Level Laser according to Prof. P.H. Peter Marti.



**Duration of Treatment:** Each region is treated in numerical order. Treat regions 1-7 for 6 minutes each.

## Smoothing of wrinkles with Low Level Laser according to Prof. P.H. Peter Marti.

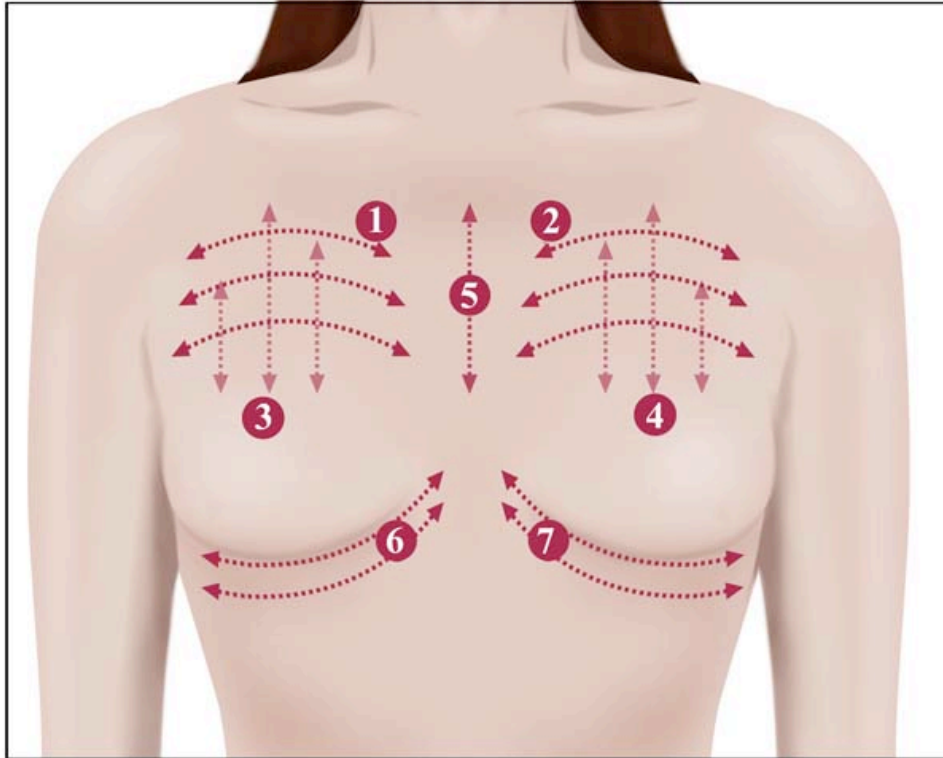


**Duration of Treatment:** Each region is treated numerical order. Treat regions 1 - 3 for 6 minutes each.

**WARNING:** Do not treat over the Thyroid gland.



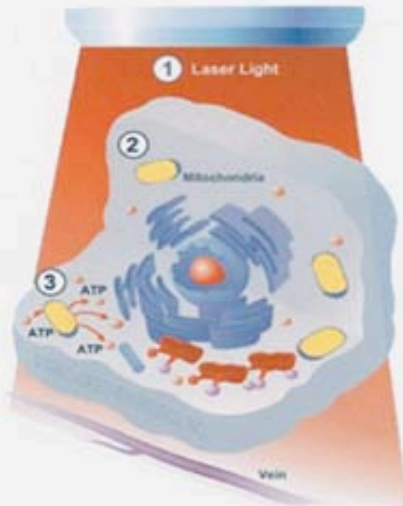
## Smoothing of wrinkles with Low Level Laser according to Prof. P.H. Peter Marti.



**Duration of Treatment:** Each region is treated in numerical order.  
Treat regions 1 - 7 for 6 minutes each.

## The Effect of Laser Light on Skin Cells

**1** Coherent laser light penetrates about 1 cm to endodermis skin (660nm)



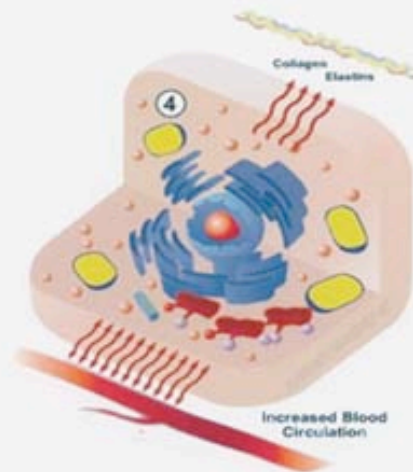
**2** The Mitochondria absorbs the photon light energy and is energized.

**3** The stimulated Mitochondria produces more ATP which in turn, makes the cell reproduce faster, making them act like younger cells.

**4** The coherent laser light also promotes cell wall exchange increasing blood micro circulation.

The effects of increased cell reproduction and

blood circulation is more collagen and elastin bundling between the cells, leading to reduced wrinkles and faster healing times. Skin will appear younger, plumper and healthier looking within 2-6 weeks.





## Testimonials for the Beurer hand held lasers

In an ongoing effort to demonstrate the power and effectiveness of the Softlaser, we regularly conduct clinical trials, using real-life clients. The following case studies are just a few examples of what the Softlaser can do:

### Case Study 1:



Before Photo taken October 2005 - After Photo taken November 2005.

Saiko (age 34) used the Softlaser twice a day for 4 weeks. According to Saiko, she used the laser once in the morning for 3-6 minutes while watching TV and again in the evening for about the same amount of time. After 4 weeks her skin was noticeably brighter which her husband described as a "beautiful glow." Saiko also said that her skin felt healthier and lighter and she experienced much less acne.

Note: These photographs present actual examples of Softlaser usage. Absolutely no photo manipulation or retouching has been done to any case study photographs. In some instances, the images have been cropped in order to maintain a uniform presentation.

### Case Study 2:



Before Photo taken October 2005 - After Photo taken November 2005

Yoshie (age 37) used the Softlaser for 4 weeks, 2 times a day. Each session was 6-15 minutes once in the morning and again at night. Yoshie had noticeable results within the first week. She said that the Rosacea (not visible in photo) under her eyes disappeared completely within a week, Before the Softlaser; she had tried many types of creams and ointments with no results. Within 4 weeks, Yoshie's skin was noticeably tighter, brighter and healthier looking.

Note: These photographs present actual examples of Softlaser usage. Absolutely no photo manipulation or retouching has been done to any case study photographs. In some instances, the images have been cropped in order to maintain a uniform presentation.

## Clients Testimonials:


My name is Linda B, I purchased a Softlaser about three months ago from you. During the month of August 05, we had a hurricane in South Louisiana. This little machine has been a wonder and has been used to death. I used it on myself for cuts and scrapes and insect bites, sticker wounds from brush and trees that had to be moved. I even used it on the dog when she cut her paw pad, and used it on my horse when she had a cut on her eye and leg from tin on the barn. I felt that every emergency operator should carry one of the health lasers to immediately treat wound and bug bites. I really appreciate this little machine. My only regret is that I can not get a more powerful one.

-Linda B. (October 2005)



I had been using the Beurer Softlaser for 6 weeks and while my skin felt smoother I didn't think any one could tell, until my boss said to me that I look younger and healthier. She thought I had started exercising but I only used Softlaser. They were both so impressed that both she and her friend bought one too. I use it everyday.

Sincerely  
Hanae O. (June 2006)



You've made me a believer in lasers. I first used it for my acne and saw results in 1 day! I now use it everyday not only for my skin, but also for cuts and bruises.

-Andrea L. (February, 2006)



The Softlaser is terrific! I used for a boil that had appeared over my eye 2 days before a job interview. I could not believe how fast it helped reduce the boil on my skin. My skin looked so much better after 2 weeks of use that I got one for my mom and my sister. I keep it in car and use it while I commute to my new job.


-Lana F. (November, 2005)





I am a message therapist and saw your Softlaser at the spa where I work. .After reading the brochure I decided to give it a try. I started using the Softlaser to relieve the swelling on my knuckles and was surprised by the great results. It is the only thing that has worked so far. I recommend it to all my clients.

-Monique T. (August, 2005)



Dear Softlaser: It has been a true confidence booster helping minimize recent scarring that left me very self conscious. I am now more confident that ever thanks to 5-10 m inutes a day with my Softlaser.

With Gratitude,

-Dan G. (August 2006)




The Softlaser has had an effect on my eczema on the back of my arm, where no cream or ointment had effect. The Softlaser reduced and thinned the areas in several weeks. I am really happy with my Softlaser.

-Valerie B (August, 2006)




DDX tennis elbow: After 2 days of treatments (3 per day), patient reported significant decrease in pain levels. After 1 week, symptoms abated.

-44 yoa male c/o pain upon use in the right cubital joint that radiates into the forearm, lateral aspect.



Patient history of broken ulna and fractured radius d/ t skiing accident 2 1/2 years prior to laser use. After reduction of feelings of heaviness in limb. After 3 weeks, patient reported an increase in the range of motion and a further decrease in sensations of heaviness. At 4 weeks, the patient reported an increase to full range of motion and little to no pain with extreme exertion.

-1 yoa female c/o fatigue, restricted movement, feelings of heaviness, and pain upon extreme exertion in the left forearm and elbow



Swelling, an increase in temperature, as well as other signs of infection were noted. After 24 hours of use (3 times) visible signs of infection reduction a pain control were noted. After 2 days of use the wound was closed with only slight indications that the wound existed. Patient states that she has a tendency to produce moderate amounts of scar tissue upon injury. At the time of the last visit, no scarring was visible

-43 yoa female c/o open wound in the ring finger of the right hand.

Canker sores were present in the inside of the upper lip and also upper gums. After 2 treatments, patient reports abatement of all signs and symptoms of infection.

-43 yoa female has history of cold/canker sore infections that usually take 5 to 7 days to resolve.

After 8 treatments visible results were noted by herself and her husband. Patient presented in my office and the patient asked me to find the area of complaint. I was unable to find area.

-53 yoa female c/o spider veins present from injury on right fore-leg/ shin area.

10 treatments in three days were given, with a subsequent 5 in three weeks. Patient reports significant decrease of lines that were most visible and elimination of those lines that were smaller.

- 27 yoa female c/o sun damage in the form of micro-wrinkles of "crow's feet" around eyes bilaterally.

Injury sight noted of right calf area sustained 15 years ago from barbed wire fence. Original size of scar was approximately 6 to 6 1/2 inches in length, 2/4 inch wide and was raised from skin surface. 27 treatments were given over 1 month, scar now measures 3 inches in length, 1/8 inch in width and cannot be detected by touch from skin surface. Surgical sights were noted beneath breasts bilaterally that measured 2 1/2 inches in length and 1/4 inch in width. After 17 treatments scars are greatly diminished.

-28 yoa female c/o keyloid scarring after injury and surgical incision sights.



Within two weeks I noticed I needed to moisturize much less, my eyes were less dry. My Rosacea is going away and now three months into my love affair with your product my wrinkles are reduced by 30 percent and I have begun using it on my neck. The only problem is, make the aperture and the lens bigger so a larger area of the body can be covered! Whenever I am in front of the TV my Softlaser is in my hand keeping me young and beautiful at 41 and far into the future.

Best Regards,  
~Melinda Miller (May 2007)



## **FREQUENTLY ASKED QUESTIONS**

### **Will the Softlaser burn my skin? Does it hurt to use it?**

No. The Softlasers are non-invasive and do not burn or cut your skin in any way. They are completely painless and safe to use.

### **How long does it take to work? How soon will I see results?**

For anti-aging, results of using the Softlaser everyday can be visible in a little as a week. However, everyone is different, so results will vary. Most everyone sees the rejuvenating effects within 3-4 weeks. For pimples or small cuts and bruises, increased healing times are noticeable in as little as a day. We are always interested in how well the Softlaser has worked for you. Please tell us about your Softlaser experience by emailing [allergyantidotes@verizon.net](mailto:allergyantidotes@verizon.net)

### **How often should I use it?**

We recommend using your Softlaser everyday between 6 and 18 minutes, depending on the type of condition you are treating and the size of treatment area. A guide is provided with your Softlaser. In general, the larger the area, the longer the treatment times, but we usually recommend treating a 3-5 inch radius area for 6 minutes. For best results, use your Softlaser twice a day, once in the morning and again in the evening. We find that treating the skin twice a day is more effective than one long treatment because the cells can only absorb so much coherent laser energy light. After you have energized your skin cells in the morning, they slowly give off their energy during the day and therefore able to absorb more energy during an evening treatment.

### **Does the Softlaser work for acne?**

While we make absolutely no claims for Acne in the U.S., yes, Softlasers have been proved to be extremely effective for acne and pimples. Not only does Bio-Stimulation decrease acne healing times but the new, more energized cells are more sterile and less susceptible to infection. When using the Softlaser for acne it is important that your skin is clean and that you do not rub the laser against the skin while treating, as it will spread the bacteria around the treatment area. It is best to hold the laser about 1 cm above the skin. Some people find treatment easier when they hold laser directly to the skin, if this is the case; please put a piece of clean cellophane over the aperture of the laser during every treatment. The cellophane can be secured around the laser body with a rubber band.



### **What else can I use my Softlaser for?**

While we make absolutely no medical claims in the U.S., clinical trials in Europe have proven the Softlaser to be highly effective as part of an overall treatment regime for conditions such as:

- Acne
- Bruising
- Ulcers
- Eczema Dermatitis
- Psoriasis
- Herpes/Cold Sores
- Pressure, Sores,
- Blisters
- Chapped Skin
- Plantar Fasciitis
- Sprains
- Burns
- Wrinkles
- Spider Veins
- Tennis Elbow,
- Tendinitis
- Arthritis
- Gingivitis
- Dental Ulcer
- Sinusitis Rhinitis
- Stimulation of Acupuncture / Meridian Points (See the Meridian Laser Techniques manual)

### **Can I use skin creams with your Softlaser?**

Yes but it is best to use any cream or-moisturizer after the laser treatment, as creams applied to the skin before using the laser can block the laser light penetration making the treatment less effective. Also, cream and jells can get trapped behind the laser lens making it impossible to clean. It is best always use the laser with clean skin, guaranteeing the most effective treatments.

### **Does it work on darker African American skin?**

Yes. All skin colors receive the same rejuvenating effects of the Softlaser, However, in some cases longer periods of treatment time may be required for darker skin types.

### **Is the laser dangerous to use around my eyes?**

No. Just use caution not to look directly into the laser's aperture or shine it directly into your eye. If you accidentally glance into the laser light no harm will occur. Always follow the directions and read all warning labels.

## **Are there any side effects to using the Laser?**

After 30 years of ongoing clinical tests, trials and studies, there have been no reported short or long-term side effects from low level laser treatments of any kind. However, be sure to follow all precautions included with your laser.



# **Low Level Laser Therapy**

Mary Dyson PhD, FCSP

**Emeritus Reader in the Biology of Tissue Repair, Kings College London, UK;  
Former Professor, Department of Physical Therapy & Rehabilitation Sciences, University  
of Kansas Medical Center, Kansas City, USA.**

## **INTRODUCTION**

Low level laser therapy (LLLT) is widely used to accelerate tissue repair including wound healing. It is also used to alleviate skin conditions such as acne (Hirsch and Shalita, 2003) and scarring (Patel and Clement 2002). These conditions involve tissue injury, sometimes acquired many years ago. Their improvement is achieved by tissue repair, which can be initiated and stimulated by exposure to low intensities of red light and to some other forms of electromagnetic radiation such as infrared (IR) electromagnetic radiation. Exposure to red light increases blood flow to the skin thus improving its metabolism and stimulates the manufacture of collagen, the protein that gives strength to the skin (Bjerring et al 2002). Other uses of red light and infrared irradiation include accelerating the resolution of inflammation (Dyson 2004) and the reduction of pain (Moore et al 1988; Chow and Barnsley 2005).

The laser technique used to deliver this light is usually termed *low level laser therapy* (LLLT), also referred to as *low intensity laser therapy* (LILT), *low energy photon therapy* (LEPT) and *phototherapy*. Unlike the high intensity medical lasers used to cut and coagulate tissues, LLLT involves the use of medical lasers such as the Beurer SoftLaser<sup>TM</sup> and Laser Therapeutics SL50 Cluster Laser that operate at intensities too low to damage living tissues. Unlike most LLLT devices that are relatively large and designed for clinical use, the Beurer SoftLaser<sup>TM</sup> is a small, single-diode, hand held device emitting red light and designed for home use. The Laser Therapeutics SL50 Cluster Laser consists of twelve laser diodes combined in a treatment head but smaller than the devices designed for clinical use. These devices are now available for home use; the Laser Therapeutics Inc. SL50 Cluster Laser is an example of a cluster probe suitable for home use. It contains 8 laser diodes that emit red light at 640-660 nm and 4 laser diodes that emit infrared (IR) electromagnetic radiation at 775-795 nm.



The Beurer SL30 Softlaser



The Laser Therapeutics SL50  
Cluster Laser

Wound healing can be stimulated by photons from the visible and infrared parts of the electromagnetic spectrum when applied to the skin and mucous membranes by low level lasers and light-emitting diodes (LEDs) at appropriate wavelengths, powers and durations. When absorbed these photons induce cellular changes which accelerate tissue repair (Fulop et al 2009) and relieve pain (Chow, Barnsley 2005). Changes induced by photons in immune cells and stem cells assist in the acceleration of wound healing (Dyson 2008); changes induced in nerve conduction assist in the short term relief of pain (Baxter 1994)

## LIGHT

Light consists of photons transmitted at wavelengths of the electromagnetic spectrum that are visible to the human eye. This part of the spectrum extends from violet to red. Infrared (IR) is just beyond the visible range. The perceived colour depends on the wavelength. White light is a mixture of all the visible wavelengths. For photons to reach the skin, all that is required is that it be either exposed to air or to be covered by a transparent dressing. Exposure to red light and/or infrared radiation can stimulate the healing of both chronic injuries of the skin (Mester et al 1985) and acute injuries (Dyson & Young 1986).

**Photons** are quanta of electromagnetic radiation that originate in the burning gases of the sun. They have zero mass, are electrically neutral, behave both as particles and as waves and are pure energy. When they are absorbed this energy is transferred to the chemicals that absorb them, for example cytochromes (coloured materials present in all cells). Absorption of photons by cytochrome C oxidase in mitochondria increases the amount of energy-rich ATP the mitochondria produce, (Karu 1988) and also temporarily increases cell membrane permeability to calcium ions, the latter acting as a stimulus for cell activity (Young et al 1990). Depending on their type and metabolic status, the cells are induced to proliferate, manufacture proteins, secrete mediators, contract, conduct, phagocytose pathogens or kill cancer cells. Following absorption, photons trigger metabolic activities that stimulate wound healing and relieve pain. They can be delivered in effective wavelengths and doses by low level laser therapy (LLLT) devices (Tuner, Hode 2002).



## LASER

This is an acronym for **L**ight **A**mplification by the **S**timulated **E**mission of **R**adiation. The stimulated emission of radiation occurs when a photon interacts with an energized atom. When an atom is energized, for example by electricity, one of its electrons is excited, i.e. raised to a higher energy orbit than its orbit when in the resting state. If the energy of the incident photon is equal to the energy difference between the electron's excited and resting states, then stimulated emission of a photon occurs and the excited electron returns to its resting state. This photon has the same properties as the incident photon, which is also emitted. This process is repeated in the adjacent energized atoms, producing a laser beam. Unlike light from non-laser sources, this light is:

- Monochromatic, i.e. of a single wavelength
- Collimated, i.e. its light rays are non-divergent
- Coherent, i.e. in phase, the troughs and peaks of the waves coincide in time and space.

With regard to the biomedical effects of LLLT, wavelength is particularly important. To produce an effect, the light must be absorbed, and absorption is wavelength-specific. Different substances absorb light of different wavelengths. Mitochondria, present in all mammalian cells except erythrocytes, contain cytochromes that absorb red light. Light emitting diodes emitting effective wavelengths are now often used instead of the more expensive lasers, making phototherapy more economical. Light could now be substituted for **L**aser in the LLLT acronym.

Only low powers (5-500 milliwatts) are required for effectiveness. The duration for which the photons are applied is clinically important because there is a temporal window of effectiveness. Within this window longer treatments are more effective than shorter treatments in accelerating healing, probably because they allow more of the circulating immune cells and stem cells of the body to be exposed to photons. Energy (power x duration) doses of 4-20 Joules/cm<sup>2</sup> are usually effective in stimulating wound healing and relieving pain (Tuner, Hode 2002).

Generally red or infrared electromagnetic radiation is employed using either single-diode probes to irradiate small areas such as acupuncture points and trigger points or cluster probes to irradiate larger areas such as wounds or joints.

## LLLTH EQUIPMENT

This has three essential components:

1. *Lasing medium*, which is capable of being energized sufficiently for light amplification by the stimulated emission of radiation to occur
2. *Resonating cavity* containing the lasing medium
3. *Power source* that transmits energy into the lasing medium.

The type of lasing medium used determines the wavelength, and therefore the colour, of the laser beam. For example, a HeNe laser, in which the lasing medium is a mixture of helium and neon gases, produces red light with a wavelength of 632.8 nm. Gallium, aluminium and arsenide, the lasing medium of GaAlAs semiconductor diodes, also produces monochromatic radiation, the wavelength of which depends on the ratio of these three materials and is in the red-infrared range of the electromagnetic spectrum, typically 630-950 nm.

The resonating cavity containing the lasing medium has two parallel surfaces, one being totally reflecting, the other being partially reflecting. Photons emitted from the lasing medium are reflected between these surfaces, some of them leaving through the partially reflecting surface as the laser beam. The cavity of a HeNe laser is many cms long, whereas that of a GaAlAs semiconductor diode is tiny, the diode being the lasing medium and its polished ends the reflecting surfaces.

Modern low intensity laser therapy devices are generally of the GaAlAs type. Their treatment heads may contain either one or many diodes. Those with one diode resemble laser pointers and are designed to treat acupuncture and trigger points; they can also be used to treat points in and around skin injuries. Those with many diodes are generally called cluster probes and allow large areas to be treated rapidly. The diodes may be housed in a rigid head or in a flexible material. The latter can be applied around curved surfaces such as the shoulder. Each diode emits either red or IR radiation. Red light is absorbed by all cells, whereas different wavelengths in the infrared range appear to target specific cell types.

The power source for a LLLT device may be either a battery or mains electricity. Many LLLT devices are portable. The main function of the power source is to energize the lasing medium.

## HOW LLLT PRODUCES ITS EFFECTS

For LLLT to be effective, the tissue targeted must absorb photons. Absorption is wavelength dependent. Red light is absorbed by cytochromes in the mitochondria; all human cells, other than mature red blood cells (erythrocytes) contain mitochondria. Provided that appropriate wavelengths and energy densities are used, cell activity can be stimulated if it is suboptimal. Cells in which this has been investigated include mammalian keratinocytes, lymphocytes, macrophages, mast cells, fibroblasts and endothelial cells, all cells of significance in tissue repair. Much of the research on this has been reviewed by Baxter (1994) and by Tuner and Hode (2002). Cells affected by LLLT show a temporary increase in permeability of their cell membranes to calcium ions (Young et al 1990). This may be an important component of the mechanism by which LLLT modulates cell activity; other electrotherapeutic modalities, such as ultrasound, may act in a similar fashion (Dyson 2004).

The triggering of cell activity by reversible changes in membrane permeability when photons are absorbed could be responsible for the stimulation of tissue repair (Young & Dyson 1993). Increase in calcium uptake by macrophages exposed to red light and IR *in vitro* has been shown to be wavelength and energy density dependent. Of the wavelengths tested, 660, 820 and 870 nm were effective; 880 nm was ineffective. These same wavelengths also affected growth factor production by the macrophages, 660, 820 and 870 nm being stimulatory, whereas 880 nm was not. Energy densities of 4 and 8 J/cm<sup>2</sup> were found to be effective; 2 and 19 J/cm<sup>2</sup> were not (Young et al 1990). Red light of 660 nm wavelength is absorbed by the cytochromes of mitochondria, where it stimulates ATP production and increases cytoplasmic H<sup>+</sup> concentration, which can affect cell membrane permeability (Karu 1988). IR radiation of 820 and 870 nm may be absorbed by components of the cell membrane. Some of these components vary in different cell types, which may be why the IR wavelengths absorbed by cells differ according to the cell type. For example, 870 nm affects macrophages (Young et al 1990) but not mast cells (El Sayed & Dyson 1990). It may be possible to selectively stimulate macrophages but not mast cells *in vivo* by exposure to an 870 nm probe.

Following a reversible change in membrane permeability to calcium ions, the cells respond by doing

what they are programmed to do. In the case of macrophages, this is to produce soluble protein mediators such as growth factors and to phagocytose debris, whereas fibroblasts manufacture collagen and other extracellular components of the dermis.

The molecular mechanisms by which LLLT affects cell activity begin with photoreception, when the photons are absorbed. This is followed by signal transduction, amplification and a photoresponse, e.g. cell proliferation, protein synthesis and growth factor production, all of which assist in tissue repair. Membrane structure differs according to the cell type, which, if IR is absorbed by parts of the membrane, may explain why different cell types absorb different wavelengths of IR. Theoretically, it should be possible, by the judicious selection of IR wavelengths, to affect some cell types while leaving others unaffected. In contrast red light, since it is absorbed by the mitochondrial cytochromes present in all mammalian cells other than erythrocytes, and also by the haemoglobin contained in erythrocytes, affects all mammalian cells.

## **WOUND HEALING**

Wound healing consists of a closely regulated cascade of events that follow injury and in skin normally result in the regeneration of the epidermis and the replacement of the damaged dermis with scar tissue. The events can be grouped into the sequential and overlapping phases of *inflammation*, *proliferation*, and *remodeling*. If the dermis is damaged, haemostasis is the initial major component of inflammation, following which debris and damaged tissue are removed from the wound site by neutrophils and macrophages. Antigens are also detected and presented to T-lymphocytes by macrophages such as Langerhans cells. All these cells are components of the immune system. During proliferation, angiogenesis and the formation of matrix rich in type III collagen results in the production of granulation tissue over which the epidermis migrates and regenerates. Myofibroblasts which develop in the granulation tissue produce wound contraction, reducing the size of the wound. During remodeling, the granulation tissue is gradually transformed into less vascular, less cellular and more collagenous scar tissue which replaces the injured dermis. Much of the type III collagen is replaced by stronger type I collagen arranged in wider fibre bundles, increasing the tensile strength of the scar tissue although this remains weaker than uninjured dermis (Ovington, Schultz 2004).

### **Regulation of wound healing**

For wound healing to be successful, the multitude of events comprising it must be spatially and temporally regulated. This regulation is dependent on intercellular communication. Soluble protein mediators (SPMs), produced initially by immune cells and consisting of chemokines, cytokines and growth factors, together with hormones, neurotransmitters and their receptors are involved in this communication; protease and protease inhibitors modify the wound bed and affect the ease with which cells can migrate within it. (Ovington and Schultz 2004). SPMs are produced mainly by immune cells, eg neutrophils, macrophages and lymphocytes, but also by peripheral nerve fibres, fibroblasts, endothelial cells and other non-immune cells. Following SPM synthesis and secretion, the SPMs diffuse to target cells involved in the healing process or are transported to them in blood and lymph vessels. They bind to specific receptor sites on the target cell surface. Binding triggers cell activation, the activity depending on the target cell type. For example, myofibroblasts will contract, fibroblasts will (depending on their stage of differentiation) either proliferate or secrete matrix materials, endothelial cells will produce new blood capillaries.

SPM actions during wound healing include the following:

1. Initiation of inflammation, by Il-1, TNF, etc.
2. Cell recruitment to wound bed, by PAF, Il-1, Il-3, Il-6, TNF, etc.
3. Debris removal, by Il-1, Il-2, Il-4, Il-5, Il-6, TNF, etc.
4. Promotion of proliferative phase of healing, by FGF, PDGF, TGF- $\beta$ , Il-1, Il-6, TNF etc

Key: Il = Interleukin; TNF = Tumor necrosis factor, PAF = Platelet activating factor, FGF = Fibroblast growth factor, PDGF = Platelet derived growth factor, TGF- $\beta$  = Transforming growth factor-beta.

Acute inflammation is a vital stage in healing, setting the stage for the proliferative phase by the removal of debris and pathogens, and by the secretion of regulatory SPMs. In contrast, chronic inflammation inhibits healing. For chronic wounds to heal, acute inflammation must be induced in them by, for example, debridement.

## **LLLT ACCELERATES WOUND HEALING**

Many publications during the last 30 years report the acceleration of delayed healing by LLLT and other forms of phototherapy when used appropriately. To quote from a recent meta-analysis ‘...our findings leave no doubt whatsoever that phototherapy promotes tissue repair’ (Fulop et al 2009). In addition to treating the wound bed, it is recommended that the intact tissue around the wound also be treated (Baxter 1994). This will induce the peripheral nerve fibres and immune cells present in epidermis and dermis to secrete SPMs. Acute inflammation is a vital part of wound healing. Its resolution should be accelerated so that the proliferative phase of repair begins earlier, thus accelerating the healing process. Cells that have absorbed sufficient quantities of photons of effective wavelengths will secrete these SPMs earlier and thus accelerate healing. In contrast, chronic inflammation inhibits repair; it has to be converted to acute inflammation for healing to progress. This may require debridement and should be followed as soon as possible by phototherapy so that the immune cells are stimulated to secrete SPMs. It is recommended that this be continued, ideally on a daily basis or at every dressing change, throughout the acute inflammatory phase of repair. Continuing the treatment into the proliferative phase may also be of value since phototherapy can stimulate the proliferation of endothelial cells (Ghali, Dyson 1992) and fibroblasts (Hawkins, Abrahamse 2006), accelerating the development of the granulation tissue over which epidermal cells migrate.

### **The Beurer SoftLaser™**

This hand-held LLLT device is a low power Class 2M laser manufactured by Beurer GmbH. It contains a single 5 mW GaAlAs diode producing red light of 635-670 nm wavelength. It is powered by 2 AAA batteries.

#### **Application of SoftLaser™ to Skin**

The probe is placed in contact with clean skin or over a transparent dressing at right angles to the skin's surface and moved slowly over the region to be treated for a few minutes, typically 3-6 minutes for a region of about 1 cm diameter. A convenient way to use it is twice daily, shortly after cleansing the skin in the morning and evening, and before the application of a moisturizing cream and/or cosmetics.

### **Laser Therapeutics Inc. SL50**

The Laser Therapeutics Inc. SL50 is an example of a cluster probe suitable for home use. It has 8 laser diodes that emit red light at 640-660 nm and 4 laser diodes that emit infrared electromagnetic radiation at 775-795 nm.

#### **Application of Laser Therapeutics Inc. SL50 to Skin**

The cluster probe is placed in contact with clean skin, or, if the skin has an open wound, over a transparent wound dressing. The cluster probe does not operate if contact is broken and there is no need to move the cluster during the treatment period, typically 5 minutes per point.

## **LLLT EFFECTS ON DAMAGED SKIN**

### **Effects of the Laser Therapeutics SL50 Cluster Laser and Beurer SoftLaser™ on Skin**

The Laser Therapeutics SL50 Cluster Laser and Beurer SoftLaser™ have been reported by its users to:

- Reduce wrinkles
- Make scars less visible
- Tighten large pores
- Elevate pock marks
- Improve skin tone
- Give a temporary radiance to the skin
- Soften chapped lips
- Accelerate wound healing

Treatment of damaged skin with red light accelerates the resolution of acute inflammation, leading to faster repair (Dyson 2004). The stimulated secretion of collagen by fibroblasts at the site of a wrinkle or of a pock mark will increase the thickness of the dermis locally, helping to fill in the tissue deficit. The gradual removal of excessive scar tissue may be due to the activation of fibroblasts, fibrocytes and other cells in and around the scar.

As with any other technique, tissue repair can only be stimulated by LLLT if it is absent or delayed. In these circumstances, epithelialisation and granulation tissue production can be stimulated by LLLT as can wound contraction (Dyson & Young 1986) which reduces the area in which scar tissue is produced resulting in less obvious scarring.



## THE IMMUNE SYSTEM

The immune system plays a vital role in the response of the body to pathogens, cancer and injury. The main cellular components of the immune system are lymphocytes and macrophages, including the Langerhans cells of the epidermis. These are located either in peripheral tissues such as the epidermis and dermis of the skin, the epithelium and lamina propria of mucous membranes and superficial lymph nodes or in deeper organs such as the deep lymph nodes. The key molecular components of the immune system are antibodies and SPMs such as cytokines and growth factors.

All the components of the immune system are linked by blood vessels and lymphatic vessels, via which immune cells and the molecules they secrete are carried around the body. SPMs released from peripheral immune cells such as Langerhans cells in response to the *direct* action of absorbed photons can be transported to and affect cells that have not been exposed to photons. Injuries other than those directly exposed to photons can therefore be affected by them *indirectly*.

Peripheral immune cells are located mainly located in the skin associated lymphoid tissue (SALT) and mucous membrane associated lymphoid tissue (MALT). Their superficial location renders them accessible to photons during phototherapy. Other immune cells, the natural killer (NK) cells, patrol the body in the blood and lymph, lysing cancer cells and virus-infected cells. The initial response of the immune system is non-specific and immediate. It is enhanced by cytotoxins secreted by the NK cells. During it neutrophils, macrophages, NK cells, T lymphocytes and antimicrobial proteins inhibit the spread of the invading substances. SPMs released locally recruit immune cells to the infected region and promote tissue repair. SPMs consist of 3 groups:

1. CHEMOKINES, for example fractalkine, are chemotactic molecules that attract and activate inflammatory cells
2. CYTOKINES, for example interleukins, are molecules that regulate division and differentiation of immune (inflammatory) cells
3. GROWTH FACTORS, for example platelet derived growth factor (PDGF), are molecules that stimulate division of both immune and non-immune (non-inflammatory) cells.

Immune or inflammatory cells include Langerhans cells, neutrophils, natural killer cells, monocytes, macrophages, T & B lymphocytes, plasma cells and mast cells. All play significant roles during the inflammatory and proliferative phases of wound healing (Martin, Leibovich 2005). Non-immune or non-inflammatory cells that are of importance during wound healing include epidermal cells, endothelial cells, fibroblasts and myofibroblasts.

Photons can be absorbed not only by the superficially-located immune cells of the SALT and MALT and but also by immune cells and stem cells in transit through the superficially-located blood and lymph capillaries of the skin and mucous membranes. Phototherapy can have a direct effect on the secretion of SPMs by these cells. By doing so it can accelerate the resolution of inflammation and thereby accelerate repair if this is delayed. The deeper cells of the immune system and also non-immune cells of injured tissues can be affected indirectly by SPMs released from peripherally-located cells that have absorbed photons. Phototherapy thus has both local and systemic effects. Cells

of injured tissues are more sensitive to phototherapy than cells of intact tissues, so lower power and energy levels can affect them while leaving less susceptible cells unaffected.

The secretion of different SPMs may assist chronic wounds to heal by allowing them to progress from inflammation to the proliferative phase of wound healing when granulation tissue is formed and re-epithelialization occurs. Because of the indirect, systemic, effects of photons, the treatment of one wound of a patient may lead to improvements not only in this wound but in the patient's other wounds.

### **Link between cutaneous nerves and SALT**

Cutaneous contact hypersensitivity (CH) reactions are closely correlated with Langerhans cells (LC), macrophages that arise from stem cells in the bone marrow and migrate into the epidermis (Streilen et al 1999). Also known as epidermal dendritic cells they help to activate the immune system by presenting antigens to lymphocytes. LCs may be linked synaptically to cutaneous nerve termini containing calcitonin gene-related peptide (CGRP), suggesting that there is a link between innervation and immune responses in the skin. It has been proposed that 'cutaneous nerves dictate whether antigen applied to the skin will lead to sensitivity or tolerance' (Streilen et al 1999), linking the nervous system to the immune system. There is evidence that phototherapy can affect mast cell degranulation (El Sayed and Dyson 1990) resulting in activation of pain fibres. Nerve conduction (Vinck et al 2005) is also affected by phototherapy, supporting the hypothesis that it may affect the immune system via the nervous system.

### **CLINICAL RELEVANCE OF EFFECTS OF LLLT ON IMMUNE SYSTEM TO WOUND HEALING**

Phototherapy has been used for many decades to treat the chronic wounds of patients (Mester et al 1985). It is suggested that treatment of the intact skin around chronic wounds may, provided that the correct parameters are used, activate immune cells of the SALT. This will increase the efficiency with which pathogens and debris are removed and stimulate the release of cytokines of value in the inflammatory and proliferative phases of repair. Furthermore latent SPMs such as transforming growth factor-beta 1 (TGF- $\beta$ 1), of crucial importance in wound healing, can be activated by phototherapy. In addition to exposing SALT to phototherapy, irradiation of peripheral lymph nodes could also be of value in that more immune cells will be exposed to the beneficial effects of phototherapy. Immune cells from these nodes will enter the lymphatics and be transported to the wounds where they and the cytokines they secrete can assist in the healing process (Dyson 2008).

It is possible that variation in the treatment parameters used may determine which SPMs are secreted. Different mediators are necessary for different activities during wound healing, including the initiation of inflammation, the recruitment of inflammatory and non-inflammatory cells to the wound bed, debris removal by neutrophils and macrophages, and the

induction of granulation tissue formation. Chronic wounds may be trapped in the inflammatory phase of healing; compared with healing wounds, they have more inflammatory cytokines, higher protease activity, lower mitogenic activity and contain fewer mitotically competent cells (Dyson 2008). Selection of appropriate treatment parameters may move them on to the proliferative phase of healing. What these parameters are remains to be determined. Antibody array screening allows the rapid monitoring of the induction of different SPMs (Chang et al 2009). Selection of the best parameters could optimize the treatment of chronic wounds with phototherapy, helping improve the quality of life of millions of people world wide.

### **Cellular effects relevant to skin repair**

The cellular effects of LLLT relevant to skin repair include the stimulation of

- adenosine triphosphate (ATP) production
- growth factor release by macrophages
- keratinocyte proliferation
- collagen synthesis
- angiogenesis.

All of the above are required for skin to renew itself and repair the damage done to it by, for example, environmental factors such as excessive exposure to the elements, damage that accumulates with age.

Temporary vasodilatation following the exposure to red light improves the transport of essential nutrients and oxygen to the skin and the removal of toxic waste materials from it. It also gives sallow skin a radiant glow.

### **PAIN RELIEF BY LLLT**

Although many of the reports of pain relief following exposure to LLLT are anecdotal, there have been a number of reports based on trials aimed at assessing LLLT as an antinociceptive or analgesic modality, one of the earliest being that of Walker 1983 who implicated alteration in serotonin metabolism as one mechanism of LLLT-mediated analgesia.

### **Rheumatoid pain**

Walker et al (1987) reported a highly significant reduction ( $p < 0.001$ ) in the levels of pain and analgesic medication intake reported by rheumatic patients either treated with low intensity red laser or sham-irradiated, pain relief being greater in those given laser treatment. Palmgren et al (1989) found that treatment of the small joints of the hand in rheumatic patients with low intensity infrared laser was followed by reduced pain and swelling, reduced early morning stiffness and increased grip strength and range of movement. In contrast Basford et al (1987) found that red laser irradiation of the osteoarthritic thumbs of patients was not followed by significant reduction in pain; however, the power and energy levels used (0.9 mW and 0.081J) are well below those recommended for clinical application (Baxter 1994) and may have been sub threshold.

### **Chronic neurogenic pain**

Moore et al (1988a) have investigated the effect of red laser in the treatment of patients with chronic neurogenic pain including that of post-herpetic neuralgia. It was found that there was a significant reduction in reported pain following treatment in comparison to that in sham-irradiated patients. Similar effects have been reported by Hong et al (1990) using the same equipment.

### **Mechanisms**

It has been suggested by Obata et al (1990) that laser-mediated relief of rheumatic pain may be linked to autonomic changes that produce vasodilatation and slight increases in local temperature. It is also possible that laser treatment affects the synthesis, release and metabolism of a range of neurochemicals involved in nerve transmission and pain relief (Walker 1983). Relief following the stimulation of acupuncture points with LILT has been ascribed to the production of endogenous opiate-like peptides and serotonin (Zhong et al 1989).

## **CONCLUSIONS**

Cells of the immune system initiate acute inflammation, an essential part of the healing process. The peripheral components of the immune system such as the Langerhans cells of the epidermis are readily accessible to photons and can be affected by them directly, triggering the release of a variety of SPMs which orchestrate the sequential events of the inflammatory, proliferative and remodeling phases of wound healing. These SPMs can either diffuse or be transported by blood and lymph vessels to the other parts of the immune system and to distant injured tissue where they can initiate reparative changes, thus amplifying the direct effects of the superficially absorbed photons. Cells can therefore be affected indirectly by photons without the need to absorb them. Photon-induced changes in peripherally located nerve fibers and in the endocrine system can also modulate wound healing and relieve pain either directly or indirectly. There is some evidence that exposure of immune cells to different parameters of phototherapy can alter the types of SPMs produced. Further research on the effects of different parameters on SPM production by immune cells is indicated. It may therefore be possible to select the most effective parameters to use to accelerate healing where it is either delayed or chronic.

Scarring associated with acne and skin deterioration due to ageing and sun damage can be alleviated by LLLT. These skin conditions involve tissue injury, the repair of which is improved by exposure to LLLT in the form of red and IR radiation. LLLT can reduce the duration of inflammation, improving tissue repair where this is delayed or defective. It can also reduce both acute and chronic pain. By assisting in the resolution of inflammation, the proliferative phase of tissue repair begins earlier and the reparative process is completed earlier. Cell activity is jump-started by changes in membrane permeability. This occurs when the cells absorb red and/or infrared radiation. The cells are also energized when red light is absorbed by their mitochondria, stimulating the synthesis of ATP and thus providing readily available energy for cell activity. The improvement in the skin produced by LLLT has been described as skin rejuvenation (Lee 2002). The portable Beurer SoftLaser<sup>TM</sup> and the Laser Therapeutics Inc. SL50 take LLLT from the clinic into the home where it can be used regularly for skin care and pain relief.

## REFERENCES

- Basford JR, Sheffield CG, Mair SD et al 1987 Low-energy helium-neon laser treatment of thumb osteoarthritis. *Arch Phys Med Rehab* 68:794-797 et al 1987
- Baxter D 1994 *Therapeutic lasers: theory and practice*. Churchill Livingstone, Edinburgh.
- Bjerring P, Clement M, Heickendorff L, Lybecker H, Kiernan M 2002 Dermal collagen production following irradiation by dye laser broadband light source. *J Cosmet Laser Ther* 4:39-43
- Chang DT, Jones JA, Meyerson H et al 2009 Lymphocyte/macrophage interactions: Biomedical surface dependent cytokine, chemokine and matrix protein production. *J Biomed Mater Res A* (Epublished ahead of print, accessed via PubMed).
- Chow RT, Barnsley L 2005 Systematic review of the literature of low-level laser therapy (LLLT) in the management of neck pain. *Lasers Surg Med* 37:46-52
- Dyson M 2004 Adjuvant therapies: ultrasound, laser therapy, electrical stimulation, hyperbaric oxygen and negative pressure therapy. In: *Chronic wound care: a problem-based learning approach*. Eds: Morison MJ, Ovington LG, Wilkie K Mosby: Edinburgh, pp.129-159
- Dyson M 2008 "How phototherapy affects the immune system". In "Mechanisms for Low-Light Therapy", edited by Hamblin MR, Waynant RW, Anders J. *Proc. SPIE* 6846: 68605-1 – 68605-10
- Dyson M, Young SR 1986 The effects of laser therapy on wound contraction and cellularity. *Lasers Med Sci* 1:125-130
- El Sayed S, Dyson M 1990 Effect of laser pulse repetition rate and pulse duration on mast cell number and degranulation. *Lasers Surg Med* 19:433-437
- Fulop MA, Dhimmer S, Deluca JR, Johanson DD, Lenz RV, Patel KB, Douris PC, Enwemeka CS 2009 A meta-analysis of the efficacy of phototherapy in tissue repair. *Photomed Laser Surg* (in press)
- Ghali L, Dyson M 1992 The direct effect of light therapy on endothelial cell proliferation. In *Angiogenesis. Key principles- Science-Technology-Medicine*. Edited by R Steiner, PB Weisz, R Langer. Birkhauser Verlag, Basel, pp.411-414
- Hawkins D, Abrahamse H 2006 Effect of multiple exposures of low-level laser therapy on the cellular responses of human skin fibroblasts. *Photomed Laser Surg* 24:705-714
- Hirsch RJ, Shalita AR 2003 Lasers, light, and acne. *Cutis* 71:353-354
- Hong JN, Kim TH, Lim SD 1990 Clinical trial of low-reactive laser therapy in 20 patients with post herpetic neuralgia. *Laser Ther* 2:167-170



- Karu TI 1988 Molecular mechanisms of the therapeutic effect of low-intensity laser irradiation. *Lasers Life Sci* 2:53-74
- Lee MW 2002 Combination visible and infrared lasers for skin rejuvenation. *Semin Cutan Med Surg* 21:288-300
- Martin P, Leibovich S (2005) “Inflammatory cells during wound repair: the good, the bad and the ugly”. *Trends Cell Biol* 15(11):599-606.
- Mester E, Mester AF, Mester A 1985 The biomedical effects of laser application. *Lasers Surg Med* 5:31-39
- Moore KC, Hira N, Kumar PS et al 1988 A double blind crossover trial of low level laser therapy in the treatment of post herpetic neuralgia. *Lasers Med Sci, Abstracts Issue*, July 1988:301
- Obata J, Yanase M, Honmura A, 1990 Evaluation of acute pain relief effects of serotonin in laser acupuncture analgesia. *Am J Acupuncture* 17:39-43
- Ovington LG, Schultz GS 2004 The physiology of wound healing. *Chronic Wound Care: a problem-based learning approach*. Edited by Morison MJ, Ovington LG, Wilkie K, 83-100. Mosby Elsevier, Edinburgh.
- Palmgren N, Jensen GF, Kaae K et al 1989 Low-power laser in rheumatoid arthritis. *Lasers Med Sci* 4:193-196
- Patel N, Clement M 2002 Selective nonablative treatment of acne scarring with 585 nm flashlamp pulsed dye laser. *Dermatol Surg* 28:942-945
- Streilen JW, Alard P, Niizeki H 1999 A new concept of skin-associated lymphoid tissue (SALT): UVB light impaired cutaneous immunity reveals a prominent role for cutaneous nerves”. *Keio J. Med.* PMID:10206015
- Tuner J, Hode L 2002 *Laser Therapy: Clinical Practice and Scientific Background*. Prima Books, Grangesberg, Sweden.
- Vinck E, Coorevits P, Cagnie B, De Muynck M, Vanderstraeten G, Cambier D 2005 Evidence of changes in sural nerve conduction mediated by light emitting diode irradiation. *Lasers Med Sci* 20(1):35-40.
- Walker JB 1983 Relief from chronic pain by low-power laser irradiation. *Neurosci Lett* 43:339-344
- Walker JB, Akhanjee LK, Cooney MM et al 1987 Laser therapy for pain of rheumatoid arthritis. *Clin J Pain* 3:54-59

Young SR, Dyson M, Bolton P 1990 Effect of light on calcium uptake by macrophages. *Laser Therapy* 2:53-57

Young SR, Dyson M 1993 The effect of ultrasound and light therapy on tissue repair. In: Macleod DAD, Maughan C, Williams CR, Sharo JCM, Nutton R (eds) *Intermittent high intensity exercise*. Chapman and Hall, London, pp.321-328

Zhong X et al 1989 Correlation between endogenous opiate-like peptides and low-power laser therapy in rheumatoid arthritis by thermography. *Laser Ther* 2:28