The Intense Pulsed Light Systems

New treatment possibilities for vascular, pigmented lesions
and hair removal

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INTENSIEVE LICHTSYSTEMEN
Nieuwe behandelingsmogelijkheden voor vasculaire, gepigmenteerde lesies en haarverwijdering

PROEFSCHRIFT

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CHAPTER 1
Introduction

Lasers

A laser is a source of light in the visible or infrared region of the light spectrum that emits rays with a high spectral density on a very small area. The word laser is an acronym for "Light Amplification by Stimulated Emission of Radiation". Various lasers have been used for diverse medical purposes ranging from dermatological to ophtalmological indications. For example, Q-switched lasers, like the Ruby laser, deliver ultra short high intensity pulses, which are effective for removing tattoos, some benign pigmented lesions and hair removal. Vascular lasers, such as the flashlamp pumped dye laser, are effective for treating port wine stains, hemangiomas, telangiectasia, rosacea and spider naevi. CO_2 lasers are useful for treating disorders of the skin surface texture and topography such as wrinkles, scars, sun damage, benign skin appendages and rhinophyma (Table I and II).

Flashlamps

Although not a true laser, Intense Pulsed Light Sources (IPLS) is currently used for the same indications in dermatology as lasers. IPLS, also called flashlamp, is a device in which the full spectrum of non-coherent light and near infrared radiation are filtered to select a specified range of wavelengths. The cost of flashlamp devices and of the applying procedures is similar to that of comparable lasers. These devices are capable of effectively treating pigmented skin lesions, birthmarks, facial spider veins, leg veins, as well as performing hair removal. For example, the IPL EllipseFlex® DDD (Danish Dermatologic Development, Hoersholm, Denmark) has been used in the treatment of pigmented lesions like epidermal lentigo solaris, macular melanocytic nevi, Becker's nevi and nevus spilus. The PhotoDerm®VL (ESC Medical Systems Ltd., Yokneam, Israel) has been used in the treatment of vascular lesions (telangiectasia, spider nevi, erythrosis interfollicularis colli, senile angioma, port wine stains) and to remove hair. Recently a new technology combining IPLS with radio frequency was introduced. An example of this is the Aurora DS/SR® from Syneron. This new ELOS™ (electro-optical synergy) can be used to treat a broad range of skin, vascular and pigmented abnormalities, as well as to remove hair (Table III and IV).

Historical developments

Albert Einstein postulated the occurrence of stimulated emission of radiation in 1917. Four decades passed before his theory was applied in the construction of the first laser instrument. In 1958, Townes and Schawlow succeeded in developing maser technology incorporating microwaves of the electromagnetic spectrum that could be used for infrared and visible light. In 1960, Theodor Maiman of Hughes Aircraft excelled in constructing the first working laser that used a ruby crystal. Javan, Bennet and Harriot are considered to be pioneers in the area of helium neon lasers from which the CO_2 laser followed in 1966 and the Argon laser in 1968.

Components of a laser

There are three essential components of a laser system. The first is a lasing medium, which may be a gas, crystal, liquid, or semiconductor. The second is a source of excitation for the lasing medium, such as flashlamps or continuous light, radio frequency, high voltage discharge, diodes, and in some cases, another laser. The third component are mirrors used to reflect the excited photons back into the resonant cavity containing the lasing medium.

Generation of laser radiation

As the lasing medium is excited, molecules are elevated to a higher energy level. Some of the excited molecules spontaneously decay back to the original lower energy, or ground state, releasing a photon. If the photon is emitted in the right direction, then it will hit one of the mirrors at the end of the resonant cavity and be reflected back into the excited lasing medium. This excited photon can "stimulate" another excited molecule to decay back to the ground state, releasing another photon that travels in the same direction, and in turn is reflected back into the resonant cavity stimulating emission of even more photons. If most of the molecules in the lasing medium are in the excited state, termed a "population inversion", there is a net amplification of light energy.

The Q-switched laser is one in which a device introducing important losses in the resonant cavity and preventing lasing operation is suddenly switched to a state where the device introduces very low losses. This rapidly increases the quality factor (Q) of the cavity, thereby allowing the build-up of a short and very intense laser pulse. Typical pulse durations are in the nanosecond range.

Properties of laser light

Unlike ordinary light, laser light is coherent, collimated, and monochromatic. Coherent refers to the synchronized phase of the light waves, collimated refers to the parallel nature of the laser beam (laser light is emitted in a very narrow beam with all the light rays parallel) and monochromatic refers to the single color or wavelength of the laser beam.

Some important parameters of lasers

Absolute Energy: The total energy in a laser pulse or system, the unit is Joule (J), and a typical value for a single laser pulse is 100 mJ.

Fluence: The amount of energy per surface or fluence, also called dose, is usually stated in J/cm^2.

Laser Power: Refers to the laser optical power output. If the selected laser power is low, the processing time must be increased. However, if the selected laser has more power than necessary, the operation expense will be higher. So choosing the laser power properly is very important.

Intensity: The laser power per unit area, measured in W/cm^2. Intensity is closely related to the laser focus spot size and the pulse lasting time.

Wavelength (l): The wavelength of a laser is related to stimulated energy transition. The shorter the wavelength, the higher is the energy of the photon. The wavelength also affects the maximum resolution and focalization: the shorter the wavelength, the higher is the resolution and the better is the focal property.

Focal Spot Size: Focal spot size determines the maximum energy density that can be achieved when the laser beam power is set. This parameter is very important for materials processing.

Depth of Focus: The laser light is first converged at the lens focal plane, then it diverges to a wider beam diameter again. Depth of focus is the distance over which the focused beam has about the same intensity. It is defined as the distance over which the focal spot size changes from –5% to +5%. Usually the longer depth of focus is preferred.

Light-tissue interactions

Laser light's monochromaticity is responsible for its selective effect on biological tissue. Whenever light encounters tissue, it can be transmitted, scattered, reflected, or absorbed, depending on the type of tissue and the wavelength (color) of the light. However, light absorption must take place for there to be a biological effect. Any given wavelength of light may be strongly absorbed by one type of tissue, and be transmitted or scattered by another. Each type of tissue has its specific absorption characteristics depending on its specific components (i.e., skin is composed of cells, hair follicles, pigment, blood vessels, sweat glands, etc.). The main absorbing components, or chromophores, of tissue are:

- Hemoglobin in blood
- Melanin in skin, hair, moles, etc.
- Water (present in all biological tissues)

When light is absorbed, it delivers energy to the tissue, and the tissue's reaction depends upon the intensity and exposure time of the light. An extremely intense, but very short pulse of laser light will usually cause an explosive expansion of tissue, called a photomechanical (photodisruptive, photoacoustic) reaction. A less intense, longer pulse causes a rapid heating, or photothermal effect. Lower intensities applied for longer times will cause a photochemical change, either by a slow transfer of energy as heat, or by a specific chemical reaction as made use of in photodynamic therapy. In actual practice, all of these interactions coexist. By selecting the proper wavelength, intensity, and pulse duration, the desired effect can be maximized.

Selective Photothermolysis[1] is the process in which the transfer of laser energy is restricted to a particular site because of the selective absorption of a chromophore at that site. In other words, proper selection of the wavelength and of the exposure time results in specific damage of the desired target tissue. For selective photothermolysis to occur, the following must be chosen accordingly:

- The appropriate wavelength selectively absorbed by the target tissue
- The appropriate exposure time which should be less than the thermal relaxation time of the target tissue

- The appropriate energy density, or fluence to produce the desired effect, such as vaporization, coagulation, or photo disruption

Extended Theory of Selective Photothermolysis[2] is a relatively new theory that postulates the selective thermal damage of non-uniformly pigmented structures in biological tissues. The following conditions should be met:

- Just as is the case with the classical selective photothermolysis, here too the electromagnetic radiation (EMR) wavelength should be chosen to maximize contrast between the absorption coefficient of the pigmented area and that of the tissue surrounding the target
- The EMR power should be limited to prevent absorption loss in the pigmented area, but it must be sufficient to achieve a heating temperature higher than the target damage temperature
- The pulse width should be made shorter than or equal to the thermal damage time, which can be significantly longer than the thermal relaxation time

There are many medical laser systems available today, and most of them use the principal of selective photothermolysis, which means getting the right amount of the right wavelength of laser energy to the tissue to be treated in order to damage or destroy only that tissue and nothing else (for example chromophores).

Taking all these points into consideration it also is important to evaluate the skin type (Table V) before treatment. With increasing skin type, the risk of postinflammatory hyperpigmentation is greater.

The following lasers are widely used in medical practice:

Argon Laser

As one of the first lasers in clinical use, the Argon laser is a continuous wave gas laser that emits blue-green light at 488 and 514 nm which is strongly absorbed by hemoglobin and melanin. Although the beam may be mechanically pulsed, there is significant, non-selective heating in surrounding tissues, thus increasing the chance of scar formation. It uses include:

- Retinal and inner ear surgery
- Treatment of thick or nodular port wine birthmarks
- Treatment of facial spider veins, small dark moles, cherry hemangioma

Pulsed Dye Laser (PDL)

In this laser, a lasing medium of Rhodamine dye is excited by a flashlamp. The Pulsed Dye Laser is effective in treating vascular lesions such as cutaneous hemangiomas, port wine stains, cutaneous lupus erythematosus, oral granulation tissue and some vascular birthmarks.

Ruby Laser

The Ruby laser emits red light at a wavelength of 694 nm. The lasing medium is a synthetic ruby crystal of aluminum oxide and chromium atoms, which is excited by flashlamps. Ruby laser light is strongly absorbed by blue and black pigments, and by the melanin in skin and hair. Current uses include:

- Treatment of tattoos (Q-Switched mode)
- Treatment of pigmented lesions including freckles, liver spots, Nevus of Ota, cafe-au-lait spots (Q-Switched mode)
- (free-running mode)

YAG Lasers

YAG lasers use an Yttrium-Aluminum-Garnet crystal rod as their lasing medium. Dispersed in the YAG rod are atoms of rare earth elements, such as Neodymium (Nd), Erbium (Er) or Holmium (Ho), which are responsible for the different properties of each laser. All YAG lasers may be operated in continuous or pulsed mode, although a particular medical device is usually only capable of one or the other. The Q-Switched Nd:YAG is effective for black tattoo ink and has been used with fair results to remove hair. The millisecond-range Nd:YAG laser light is very effective for long-term hair removal.

CO_2 Laser

Often referred to as the "Surgical Laser", it is unlike any other medical laser, because its action on tissue is directly visible when used. Strongly absorbed by water, which constitutes more than 80% of soft tissue, the CO_2 laser emits continuous wave or pulsed far infrared light at 10,600 nm, which can be focused into a thin beam and used to cut like a scalpel, or defocused to vaporize, ablate, or shave soft tissue. Its uses include:
- Removal of benign skin lesions, such as moles, warts, keratoses
- As a "laser scalpel" in patients or body areas prone to bleeding
- "No-Touch" removal of tumors, especially of the brain and spinal cord
- Laser surgery for snoring
- Shaving, dermabrading, and resurfacing scars, rhinophyma, skin irregularities
- Cosmetic laser resurfacing to remove wrinkles

Table I: The use of lasers in treating different skin conditions

Type of laser	Indication	Reference
(Pigment lasers)	nevus of ota	Taylor CR[3]
Nd.YAG	tattoos	Alster TS[4]
	cafe-au-lait maculae	Kilmer SL[5]
	lentigines	
Ruby	drug-induced pigmentation	Collins P[6]
(Vascular lasers) PDL	granuloma faciale	Ammirati CT[7]
	pyogenic granuloma	Gonzalez S[8]
	keloid	Alster TS[9]
	verruca plantaris/vulgaris	Jain A,[10] Tan OT,[11] Kauvar AN[12]
	warts	
	striae distensae	Alster TS,[13] McDaniel DH[14]
	acne scars	Alster TS[15]
(Cutting lasers)	epidermal nevus	Hohenleutner U[16]
CO_2	vulvar intraepithelial neoplasia	Helmerhorst TJ[17]
	benign familial pemphigus	Touma DJ[18]
	lichen sclerosus et atrophicus	Windahl T[19]
	warts periungual	Lim JT[20]

Table II: New laser systems for hair removal and skin renewal

Sr no.	Name	Company	Indication	λ / ss nm/ mm	Reference
1)	CoolGlide® Vantage, CoolGlide® Excel, Laser Genesis.	Altus Medical, Burlingame, CA.	hair removal vascular lesions	λ = 1064 nm ss = 3,5,7 or 10	–
2)	Palomar SLP®1000 Diode Laser, Palomar Q-YAG 5TM Nd:YAG laser,	Palomar Medical Tech.	hair removal vascular lesions tattoos and pigmented lesions	λ = 810 nm 532 nm, 1064 nm ss = 4-12 ss = 2,4,6	Rogachefsky AS[21]
3)	Dornier Medilas D Skinpulse Medilas D Skinpulse S	Dornier Medizin-Laser.	vascular lesions hair removal	λ =940 nm ss = 0.5-5	–
4)	CoolTouch II laser CoolTouch VARIA	ICN Pharmaceutic Als, Inc. CA.	wrinkle treatment hair removal vascular treatment	1320 nm 1064 nm ss = 6-10	Chan HH[22] Pham RT[23]
5)	IRIDERM 810 Diolite 532	IRIDEX Corporation	hair removal vascular lesions	810 nm 532 nm	Cassuto DA[24]

λ - wavelength in nm; ss- spot size in mm.

Flashlamps

The flashlamp, also known as intense pulsed light source (IPLS) , is the perfect complement to lasers. Employing a broad spectrum of light energy in a range of wavelengths, IPL supplies high levels of light power in millisecond bursts. IPLS devices also offer sophisticated, computer-driven precision and tremendous versatility. Due to the nature of the treatment, Intense Pulsed Light energy can be applied to the sub-surface skin layers for gentle and gradual results with almost no side effects and patient downtime. For certain aesthetic challenges, IPLS technology provides a refining touch to laser procedures in general.

Developed in the 1930's by Harold E. Edgerton, a flashlamp is an arc lamp that operates in the pulsed mode and is capable of converting stored electrical energy into intense bursts of radiant energy covering the ultraviolet, visible and infrared regions of the spectrum.

As is the case with lasers, flash lamps began to be used for medical purposes in the 1960's. By the mid-1990's, researchers were exploring the use of flashlamps to treat vascular lesions such as port-wine birthmarks. Today the flashlamp pulsed dye laser is also designed to permanently remove or greatly reduce the appearance of blemishes.

Flashlamps are similar to all other arc lamps in that an electrical current gets passed through a gas, producing optical radiation. Xenon is used in most flashlamps, since it is the most efficient of the inert gases at converting electrical energy into optical energy. Krypton is sometimes used because of its high efficiency in the near-infrared region.

Although there are many shapes and sizes of flashlamps, there are only two distinct types - linear, or wall-stabilized; and bulb, or probe-stabilized. One such well-known type is the linear xenon flashlamp. It consists of a quartz tube with two sealed electrodes - cathode and anode, made from tungsten or from special low-sputtering materials. The device is usually filled with the xenon gas at ca. 200 to 400 Torr pressure. However, krypton or a mixture of noble gases at various pressures could also be used. A flashlamp can also have a spherical or a spiral envelope. The distance between the electrodes varies from a few milimeters (in photo cameras) to almost 100 cm for special high power lamps. A typical linear xenon flashlamp has a distance ranging form about 100-300 mm between electrodes and a bore diameter of about 4-9 mm.

Flashlamp operation

To operate a flashlamp, first the electrical energy is loaded into a capacitor. A high voltage switch provides the means to unload this stored energy quickly into a flashlamp tube and to generate a light emitting plasma. Its parameters are defined by lamp impedance and by electrical parameters of a driving circuit - the lamp's Pulse Forming Network.

The electrical scheme is far more complicated and costly if heat for a flashlamp cathode is required continuously between pulses. It can be accomplished with a so-called simmer - a steady DC discharge (or long-pulsed discharge) that keeps the cathode at a desired temperature (e.g. at 800°C). This is done to sustain a special porous matrix structure of a cathode that in turn dramatically reduces the cathode sputtering by trapping discharged ions. Failing to do so especially at high loads, causes an extensive sputtering that will darken a quartz envelope around the cathode area. As a result, respective parts of the quartz envelope will absorb more light and the quartz will overheat to the point of breaking.

A typical energy load onto a flashlamp ranges from a few Joules to hundreds of Joules or even thousands of Joules for high-power applications. The respective peak currents can be up to a few thousand amperes.

The temperature of the plasma and its light output strongly depend on the parameter called the Current Density J (A/cm^2) which is often defined as the ratio of the lamp peak current to the surface area of the lamp bore.

Current densities from hundreds to thousands A/cm^2 produce a discharge plasma with respective electron temperatures ranging from ca. 9.000 °K to ca. 25.000 °K. A flashlamp can be considered somewhat similar to the solar spectra because of its dense spectrum.

Any repeatedly pulsing device, including a flashlamp, has three powers:

- Average power, which is the total electrical power consumed by a lamp
- Pulse power which is a ratio of pulse energy to pulse duration
- Root-mean-square power, a function of pulse parameters and their repetition rate

A flashlamp bombards a media with UV photons at extreme densities a thousand times more often than a continuous wave lamp does. It eliminates toxic chemical substances, bacteria, etc. that are present in or on a treated medium.

It also provides unique conditions for pulsed curing and for cold vapour deposition; and it provides a lot of light for photographic devices, for pumping lasers, etc. Recent advances in high voltage/high current components and the improvement of the lifetime of flashlamps made it possible to design cost-effective pulsed UV systems for many applications.

Full spectrum (non-coherent) light and near infrared radiation are filtered to select a specific range of wavelengths. This filtered light is delivered from a handpiece into the

Table III: Use of flashlamps in treating different skin conditions

N.	Flashlamp	Indication	λ / ss	Reference
1)	IPL (Ellipse Flex; DDD) [Danish Dermatologic Development, Hoersholm, Denmark]. IPL (Ellipse Relax Light 1000; DDD)	naevi, lentigines solaris, macular melanocytic nevi venous-lake angioma nevus spilus facial rhytids hair removal	600 950 ss = 48 x 10	Bjerring P[25] Jay H[26] Gold MH[27] Goldberg DJ[28] Bjerring P[29]
2)	PhotoDerm®VL (ESC Medical Systems Ltd., Yokneam, Israel)	vasculair lesions port-wine stains cavernous hemangioma hair removal leg veins	λ = 500-1200 nm ss = 8 x 35 ss = 8 x 15	Schroeter CA[30] Raulin C[31] Cliff S[32] Foster TD[33] Schroeter CA[34-36] Weiss RA[37] Goldberg[38] Schroeter[39]
3)	SkinStation®, SpaTouchTM, SPRTM. Radiancy, Orangeburg, NY.	acne therapy hair removal skin rejuvenation hair removal skin rejuvenation	λ = 400-1200 ss = 22 x 55 ss = 12 x 35	
4)	Palomar EsteluxTM Pulsed- Light System (LuxY, LuxG, LuxR, LuxRs from Palomar Medical Technologies)	hair removal vascular lesions sun-induced pigmented lesions acne treatment	λ = 500-1400 ss =16 x 46 ss = 12 x 12 ss = 16 x 46 ss = 12 x 28	–
5)	Aurora DSTM, Aurora SR System (with radio frequency from Syneron Corporation)	hair removal treatment of pigmented & vascular lesions wrinkle reduction	λ = 680-980 I = 580-980 ss = 12 x 25	Sadick NS[40-42] –

λ - wavelength in nm, ss- spot size in mm

Table IV: Comparing the use of intense pulse light during hair removal

Advantages of using IPL	Disadvantages of using IPL
Some patients have experienced long-lasting hair removal or permanent hair reduction.	Long-term data on safety and effectiveness have not been established.
Light-skinned patients with dark hair have the best results.	It is not as effective on unpigmented hairs and red or blonde hair.
It is useful for large areas such as backs or legs.	It must be used very cautiously on darker skin tones or on consumers who like to tan themselves.
It is considered to be safe if performed properly.	Improper treatment can cause burns, skin discoloration lasting for several months, or patchy or grid-like regrowth.

skin, where it targets dark material such as the pigment in the hair. This is intended to cause thermal and/or mechanical damage to a hair follicle while sparing its surrounding tissues. The filters can be adjusted to match the patient's skin type and the target lesion.

Table V. Fitzpatrick classification for sun-reactive skin types

Skin type	Colour	Reaction to uva	Reaction to sun
Type I	Caucasian; blond or red hair, freckles, fair skin, blue eyes	Very Sensitive	Always burns easily, never tans; very fair skin tone
Type II	Caucasian; blond or red hair, freckles, fair skin, blue eyes or green eyes	Very Sensitive	Usually burns easily, tans with difficulty; fair skin tone
Type III	Darker Caucasian, light Asian	Sensitive	Burns moderately, tans gradually; fair to medium skin tone
Type IV	Mediterranean, Asian, Hispanic	Moderately Sensitive	Rarely burns, always tans well; medium skin tone
Type V	Middle Eastern, Latin, light-skinned black, Indian	Minimally Sensitive	Very rarely burns, tans very easily; olive or dark skin tone
Type VI	Dark-skinned black	Least Sensitive	Never burns, deeply pigmented; very dark skin tone

Differences between flashlamps and lasers

Type of light

As mentioned earlier, flash lamps do not use one wavelength of light the way a laser does. Flashlamps emit every wavelength of light in the visible spectrum, and emit partially into the band of infrared radiation (up to about 1200 nm). Practitioners select a cutoff filter to block out lower wavelengths. In addition flashlamp light is noncoherent while that of lasers is coherent.

Size and shape of the spot (beam)

Most flashlamps emit a beam that covers more area than a laser would, and most flashlamps also have a rectangular spot, rather than the round type usually standard for lasers.

Examples of IPL sources used for medical purposes (Table III and IV)

1) Plasmalite®: A light source that produces non-coherent broad band of pulsed light, with emitted wavelengths ranging from 600-920 nm with a spectral peak at 700 nm. It is used in the treatment of wrinkles and both vascular and pigmented skin lesions.
2) PhotoDerm®VL (vascular lesions): The light pulses are directed at the spider and varicose veins as well as at vascular birthmarks. The tissue targeted is the haemoglobin in the blood.
3) PhotoDerm®PL (pigmented lesions): The light pulses are directed at age spots, freckles, flat-pigmented birthmarks and other types of discoloration. The tissue targeted is the melanin in the epidermis.
4) PhotoDerm®HR and EpiLight® (hair removal): This appliance makes it possible to eliminate unwanted hair, supposedly permanently. The pulsed light is computer controlled and with the use of special filters *Selective Photothermolysis* damages the follicle permanently. The pulses of light target the melanin in the hair shaft and travel to the follicle, heating and destroying it.

5) Syneron has introduced a new ELOS™ (Electro-optical synergy) technology for the treatment of a wide range of skin, vascular and pigmented abnormalities, as well as for hair removal. ELOS technology utilises the synergy between electrical (conducted radio frequency) and optical (light or laser) energies. This promises to be a highly efficient, safe and cost-effective system for the future use.

Given all of the differences in between laser and IPLS devices and the need for additional information in IPLS treatment applications, the aim of this study was to evaluate new treatment possibilities using Intense Pulsed Light Sources and to address the following questions:

1. What are the treatment effects on the skin after using IPLS?
2. Efficiency of IPLS on hair removal ?
3. Is the hair removal achieved using IPLS long-lasting and can we conclude permanent?
4. Is there an advantage to using IPLS over needle epilation in hair removal in transsexual patients?
5. Can IPLS be effectively used in the treatment of facial and leg telangiectasia?
6. Regarding vascular lesions, is IPLS an effective alternative treatment to for Rosacea?
7. How effective is IPLS in the treatment of pigmented lesions?

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CHAPTER 2

Transforming growth factor-beta and extracellular matrix stimulation using Intense Pulsed Light Systems: an experimental study

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Submitted Lab Investment

Introduction

Transforming growth factor-beta (TGF-β) is a protein, which plays a principal role in the intracellular signalling.[1] The most important function is its ability to stimulate synthesis of extracellular matrix (ECM) that is responsible for wound formation and tissue reconstruction.[2] TGF-β acts via autocrine and paracrine mechanisms to regulate the interactions between cells and between cells and matrix in wound healing, involving inflammation, re-epithelialization, angiogenesis, and the production of extracellular matrix.[3,4] It stimulates the synthesis of multiple ECM components, including collagens, fibronectin, vitronectin, tenascin, and proteoglycans.[5,6] It suppresses matrix degradation by down regulating the expression of proteases, such as plasminogen activators[7,8] and stromelysin[9] and by inducing protease inhibitors, such as plasminogen activator inhibitor-1[8,10] and tissue inhibitor of metalloproteases-1.[7] The presence of extracellular matrix has been found to down regulate the expression of the TGF-β1 gene.[11] Thus, TGF-β may act as a feedback for extracellular matrix formation. TGF-β is also involved in scar formation as neutralisation of TGF-β1 and TGF-β2 in adult wounds reduces scarring in rat dermal wounds.[12] By contrast, exogenous addition of TGF-β3 to dermal rat wounds results in reduced scar formation.[13] Therefore it is clear that different isoforms of TGF-β can have completely opposite effects in wound repair although the mechanisms behind these differences are still under investigation.[14] Transforming growth factor-β is also found to be involved in lymphopoiesis and is required for the development of plasma cells secreting all secondary isotypes.[15]
It has been documented that TGF-β plays important roles in the induction of catagen phase of the human hair cycle.[16,17] An isoform of TGF-β acts as an inducer of hair follicle morphogenesis and is both required and sufficient to promote this process.[18]
During embryological development, specialized cells of developing multicellular organisms are surrounded by extracellular matrix, comprising largely of different collagens, proteoglycans, and glycoproteins. This ECM is a substrate for tissue morphogenesis, which lends support and flexibility to mature tissues and acts as an epigenetic informational unit in the sense that it transduces and integrates intracellular signals via distinct cell surface receptors. Consequently, ECM-receptor interactions have a profound influence on major cellular programs including growth, differentiation, migration, and survival. In contrast to many other ECM proteins, the tenascin (TN) family of glycoproteins (TN-C, TN-R, TN-W, and TN-Y) displays highly restricted and dynamic patterns of expression in the embryo, particularly during neural development, skeletogenesis, and vasculogenesis. These molecules are reexpressed in the adult during normal processes such as wound healing, nerve regeneration, and tissue involution, and in the pathological states including vascular disease, tumour genesis, and metastasis. Expression of tenascins is known to be regulated by a variety of growth factors, cytokines, vasoactive peptides, ECM proteins, and biomechanical factors.[19]
Different research studies have been undertaken to examine the role of tenascin and transforming growth factors in the diagnosis and prognosis of various diseases and pathological conditions. Kava et al in a series of ductal carcinomas of the breast observed that tenascin limits tumour spread.[20]
Immunohistochemical detection of molecules involved in inflammatory reaction can be useful for the diagnosis of vitality in skin wounds. Ortiz-Rey et al studied the ex-

pression of fibronectin (FN) and TN in 58 human skin wounds. Both vital and postmortem hemorrhages showed an enhanced positivity for FN and TN, thus impeding the diagnosis.[21] The presence and distribution of tenascin in the human intervertebral disc has been studied. It was found that in young, healthy disc, tenascin was abundant throughout the annulus, while degenerating discs in adults showed localization restricted to the pericellular, and rarely, more restricted intra territorial matrix.[20] These observations indicated that changes in the amount and distribution of tenascin might have a role in disc aging and degeneration.[22]

The role of transforming growth factor- β in the pathogenesis of liver diseases and its possible use as an indicator of disease progression has been suggested.[23] The effect of tropically applied TGF-β1 on the rat gingival wound healing process after flap surgery was evaluated by immuno-histochemistry for extracellular matrix molecules, such as tenascin, heparan sulfate proteoglycan and type IV collagen, and for proliferating cell nuclear antigen in fibroblasts. It was found that TGF-β1 application appeared to promote granulation tissue formation in periodontal wound healing.[24] A study on wound healing proposed that the frozen cultures of human keratinocytes promote faster reepitheliazation through the release of growth factors such as TGF-alpha and through the stimulation of murine sub epithelial cells, by TGF-β, to secrete basement membrane proteins such as collagen IV, laminin, and tenascin, which provide a provisional substrate that improves migration of the murine epidermal cells.[24]

There have been very few studies probing into the changes brought about by radiation on TN and TGF. An early response to radiation exposure was the induction of TGF-β, which mediated numerous events during tissue repair, growth, and extracellular matrix production.[25] Radiation induced activation of TGF-β may have profound implications for understanding tissue effects caused by radiation therapy.[26] Transforming growth factor-β was recently shown to be rapidly activated after in vivo radiation exposure, which also generates reactive oxygen species. It was postulated that oxidation of specific amino acids in the latency-conferring peptides leads to a conformation change in the latent complex that allows release of TGF-β.[27]

The aim of our study was to investigate the stimulation of growth factor e.g. TGF-β and release of ECM proteins such as tenascin after radiation with intense pulsed light sources.

Materials and methods

Animal Model

The protocol was approved by the Veterinary Ethical Commission (DEC), Maastricht, the Netherlands. Two male dark-haired pigs were chosen randomly from the Experimental Surgical Department of the University Hospital Maastricht, the Netherlands. An intra muscular injection of Azopyrone (0.5 mg/kg) was given to initiate anaesthesia in them. The anaesthesia was maintained with halothane (3-4%) and nitrous oxide. The back region of the pigs- between their forelegs and hind legs, and the abdomen was shaved to achieve a maximum penetration depth. The area was washed with hibiscub. Treatment sites were outlined by West Indian ink applied to the skin with hypodermic needles. Four marks outlined a $40x20cm^2$ treatment area. No ointment was applied pre- and postoperatively in the treatment area. No chemical or mechanical debridement was performed during follow up examinations. To be certain that the pigs did not experience any pain, Buprenorphine 0.05-0.1 mg/kg i.p. was given soon after the treatment. The animals were euthanized after 120-360 days after treatment using intravenous nembutal (100-150 mg/kg) (Table I).

Table I: Characteristics of the pigs

	Pig 1	Pig 2
Colour	Black	Black
0Weight	25 kg	60 kg
Gender	Male	Male

Technique

The pigs were treated according to the protocol (Table II). A stencil was placed on the back of the pigs, in order to treat the same surface every time. The pigs underwent general anaesthesia for 15-30 min (5 times for the treatment and 5 times for the biopsies). In total there were 40 flashes per pig per treatment. Using Vasculight® 590 and 695 nm and using Quantum®, 565 and 640 nm filters were used. The pulse times used were 6.5-21 ms and the fluence was 35-60 J/cm^2.
An entire surface of 40 x 2.8 cm^2 was treated per pig. The treatment took 4-5 min. There was an interval of 4 weeks between the treatments.
Biopsies were performed immediately following light treatment and then on the 2nd, 7th, 14th and 28th days postoperatively. In the second month, one week after the last biopsy, the pigs were reradiated and after 3 weeks biopsies were performed again. This was continued for four months. A total amount of 240 biopsies were thus taken. Full thickness 3-mm punch biopsies were obtained from each treated site. Tissue specimens were fixed in formalin, embedded in paraffin, sectioned and stained with hematoxylin and eosin for light microscopic examination.

Table II: Parameters used for the treatment of the pigs

Wavelength (nm)	Pulse time (ms)	Energy (J/cm^2)	Delay between pulses (ms)	Pulse mode
550	5-3	40	20	Double pulse
590	7-7	40	60	Double pulse
645	4-2.5	35	20	Double pulse
695	7-7-7	60	60	Triple pulse
565	4.2-5-4	40	20	Triple pulse
640	4.2-4.8	35	20	Double pulse

Follow-up

The pigs were followed daily during the first week. After that they were seen and evaluated after 1, 2, 3, 6, 12, and 30 weeks. They were examined for among other things; presence of crust formation, swelling, bleeding, erythema, wound healing, scar formation, depigmentation and loss of hair. Photographs were taken before and after the treatment.

Intense pulsed light

The Vasculight® (ESC Medical Systems Ltd., Yokneam, Israel) and Quantum® (ESC Sharplan) are based on the principal of selective photothermolysis. In contrast to laser systems, these flashlamps use non-coherent light of a broad band spectrum in the range of 500-1200nm. By applying different cut-off filters (550, 570, 590 nm), a specific part of the shorter wavelengths can be cut off.
The pulse duration ranges between 2-5 ms (Vasculight®) and 6-26 ms (Quantum®). The fluence ranges between 3-90 J/cm^2 (Vasculight®) and 5-45 J/cm^2 (Quantum®). The size of the treatment head (8X35mm and 8X34mm) plays an important role in improving light penetration into the tissue since a large spot size diminishes the scattering of the light beam.
A water-containing gel is used between the skin and the probe during treatment, which allows a good optical coupling of the light and also a better heat transfer from the epidermis to the gel.
By changing the different parameters of the flashlamps; namely energy, wavelength, pulse duration etc., one can achieve efficient treatment for a variety of lesions with a high degree of selectivity and safety.

Method

Tissue preparation for immunohistochemistry

Tissue blocks of pig skin biopsy were fixed in 4% neutral buffered paraformaldehyde at 4°C for 4-12 hours. The specimens were then routinely processed for paraffin embedding at 56°C as previously described. Paraffin sections measuring 4 μm were used for light microscopy and immunohistochemistry.

Immunohistochemistry

Paraffin sections were deparaffinized and rehydrated. Immunohistochemical demonstration of tenascin and TGF-β antigens was performed on these sections with the avidin-biotin peroxidase (ABC) method. Briefly, these sections were processed through the following incubation steps: 1) hydrogen peroxide 3% in methanol for 30 min to block endogenous peroxidase; 2) normal goat serum for TGF-β1 and normal horse serum for tenascin, diluted 1:75 v/v, for 30 min to 1h to reduce non-specific background staining; 3) incubation with primary antibody anti TGF-β1 (Santa Cruz Biotechnology, Inc., Santa Cruz, CA) and with primary antibody anti tenascin (Sigma, St Louis, MO) overnight at 4°C; 4) biotinylated secondary antibody: goat anti-rabbit IgG (for TGF-β1), and horse anti-mouse IgG (for tenascin), diluted 1:200 v/v, for 30 min to 1 h (Vector Labs, Burlingame, CA); 5) ABC complex for 1h (Vectastain ABC kit, Vector Labs), 6) histochemical visualisation of peroxidase using 3',3'diaminobenzidine hydrochloride as chromogen (Sigma) for 5 min in a dark room. Sections were then rinsed in tap water, counterstained with haematoxylin, dehydrated and mounted with Eukitt (Kindler GmbH & Co., Freiburg, Germany).

For the above immunohistochemical procedures controls were performed: a) by omitting the primary or secondary antibody; these controls showed negative results; b) by using human placenta as positive control for tenascin and TGF-β1 antibodies.

Statistical data

The statistical analysis of the data was descriptive. The data is presented as contingency tables in order to detect association between technical and clinical parameters. Exact Fisher tests were used to evaluate the homogeneity of the tables, p- values below 0.05 are considered significant.

Results

Clinical Observations

After every treatment erythema was observed. It was noted that after using the following parameters: wavelength 640 nm, pulse time between 4.2-4.8 ms and energy of 35 J/cm^2 the erythema seen was negligible. In some cases the upper epidermis was sealed off but it later recovered. Transient depigmentation was noticed, which disappeared after some time. Hair was burnt. There were no blisters seen.

Histological Findings

In the biopsy samples, after the first day, TGF-β immunohisto-reaction was localised in the epidermal layer, the hair follicle, endothelial vessels, fibroblasts and the plasma cells. After 1 week a subsistent increase was recorded. On the 14th day, there was a sharp decrease, similar to that on the first day of the treatment and at some places even lower to those levels. After one month, TGF-β rose to achieve a peak value and began to slowly fall to day 60 and continued to do so till the 90th day. After that its presence began to pick up and on day 120 we again saw a high occurrence.
Tenascin was visible below the epidermal germ layer and around the hair follicles immediately after treatment. After one week, its presence increased in the germinative epidermis, papillar dermis and the plasma cells, while in the endothelial vessels and the follicular bulb there was a sharp decrease. On day 14, tenascin continued to rise in the germinative epidermis, papillar dermis, in the endothelial vessels and follicular bulb a subsistent amount was recorded, while in the plasma cells a sharp fall was seen. After a month there was a sharp decrease, but this gradually recovered in the germinative epidermis, papillar dermis and the follicular bulb on day 60. In the endothelial vessels and plasma cells it was absent. After three months a gradual increase in its presence was seen (Figure 1-3).

Discussion

The results of this study indicate that there is an increase in the immunoreactivity of transforming growth factor-β (TGF-β) and tenascin (TN) in the cells when stimulated

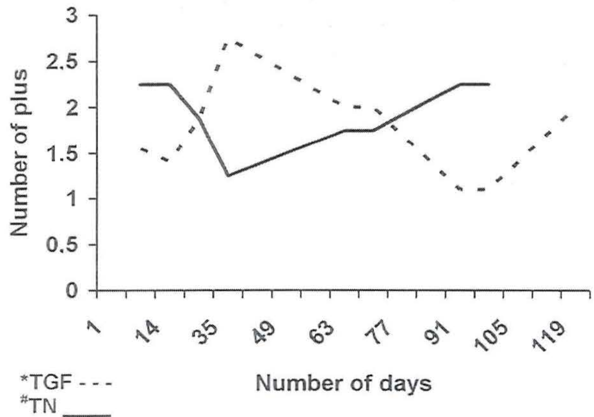

Figure 1. TN and TGF-β in follicular bulb.

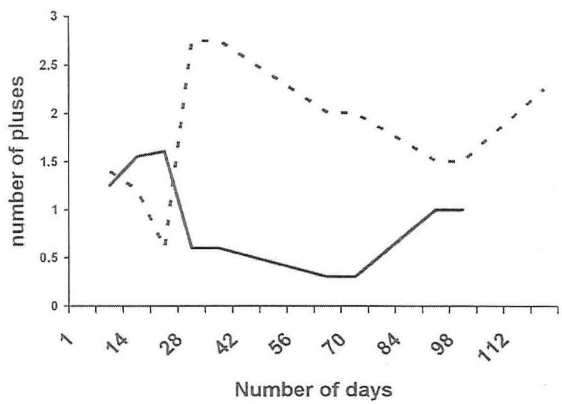

Figure 2. Tn and TGF-β in germinative epidermis.

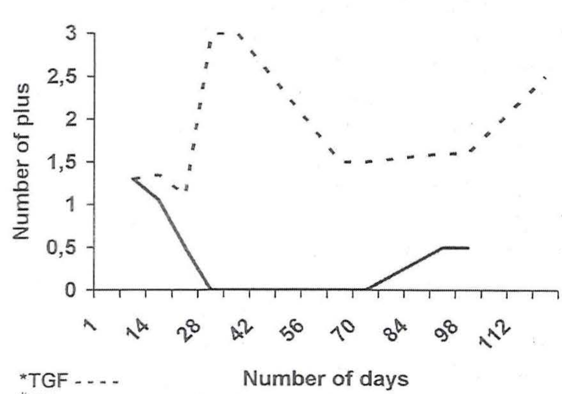

Figure 3. Tn and TFG-β in plasma cells.

by irradiation with an intense pulsed light source. Moreover we observed that TGF-β stimulates the increase in the concentration of fibroblasts and plasma cells.
One day after radiation, the appearance of TGF-β in the basal epidermal layer and the follicular bulb was detected. Fibroblasts and plasma cells were also strongly positive. After 1 week the outermost epidermis, endothelial vessels, follicular bulb, fibroblasts and plasma cells were intensely stained. TGF-β immunoreactivity decreased after 2 weeks, similar to that as on the first day of the treatment. After one month, the expression of TGF-β reached a peak value. This began to slowly fall to the second month and continued to do so till the third month. Subsequent to that its presence started to increase and on day 120 we again saw a high occurrence.
Tenascin was visible below the epidermal germ layer and around the hair follicles. At about 7-10 days after radiation, the biopsies showed a strong increase in tenascin expression. It was localised in the papillar dermis, the epidermal layer and also in the depths of the dermis, while in the endothelial vessels and the follicular bulb there was a sharp decrease. Biopsies showed a sharp decrease in tenascin immunoreactivity after one month, but this gradually recovered in the germinative epidermis, papillar dermis and the follicular bulb in the second month, but not in the endothelial vessels and plasma cells, where it was absent. In the third month a gradual increase in its presence was seen.
The results from the present clinical trial are consistent with the general clinical experience of the principal investigators in other trials. Radiation has already been discovered to be the first exogenous stimulus known to cause latent TGF-β activation in situ.[27] In animal models, the TGF-β1 and matrix metalloproteinase content of the medium of cultured cells was significantly elevated after near-infrared irradiation, and it was found that the rate of wound closure was significantly accelerated by repeated exposures.[28] Preliminary human studies have shown that exposure to short wave ultraviolet light significantly decreased the time to healing of superficial pressure ulcers.[29,30] Application of exogenous TGF-β either locally or systemically has been found to accelerate healing, particularly in chronic or impaired wounds.[31,32] In one study extracellular and intracellular TGF-β increased in the periepithelial stromal sheath at 1 h post radiation and it was also expressed in the previously negative adipose stroma.[26] This elevated expression persisted for 7 days after irradiation.[26] Immunoreactive tenascin was induced in the epithelium by day 1 after radiation, was manifested at the epithelial-stromal interface by day 5-9 and persisted as a condensed layer beneath the basement membrane through day 14.[33] Dissanayake and Mason detected increased TGF-β1 in the culture media of irradiated keratinocytes after 24 hours.[34]
In analysing radiation-induced connective tissue, TN expression was found to be increased in irradiated human skin, which was considered to be due to activation of cytokines as a result of irradiation.[35] In an animal study, within 24 hours after wounding, tenascin appeared in the basement membranes beneath epidermis and hair follicles adjacent to the wound edges and in the wounded edges of cutaneous muscle layer.[36] At about 5-7 days, all of the granulation tissue was intensely stained with anti-tenascin serum. Tenascin immunoreactivity decreased as granulation tissue was replaced with reconstructed dermal tissue at 7-14 days, after which it disappeared.[36]
Betz et al reported that tenascin appeared first in the wound area pericellularly around fibroblastic cells approximately 2 days after wounding. In all wounds with an age of 5 days or more, intensive reactivity for tenascin could be observed in the lesional area

(dermal-epidermal junction, wound edge, areas of bleeding). In wounds with an age of more than approximately 1.5 months no positive staining occurred in the scar tissue.[37] Inflammation is the normal acute reaction of the tissues after any wound or injury. Macrophages and neutrophils enter the wounded area and start to clean up foreign material, bacteria and dead cells.[38] When inflammation has subsided proliferation of fibroblasts begins, which also stimulates the synthesis of ECM.[39] Eventually fibroblast proliferation stops and ECM matures to provide a connective tissue structure.[39] Several growth factors including TGF-β are responsible for this wound healing process. The most common cause of laser-induced tissue damage is thermal in nature, where the tissue proteins are denatured due to the temperature rise following absorption of laser energy. The thermal effect of lasers on biological tissue is a complex process resulting from three distinct phenomena: conversion of light to heat, transfer of heat and the tissue reaction. The thermal injury is known to induce a pronounced activation of leukocytes in the connective tissue matrix of the burned skin along with migration and activation of white blood cells from the circulation.[40] This phase is followed by release of numerous vasoactive agents known to play an important part in the pathophysiological changes ensuing a burn injury and resulting in increased capillary permeability and impaired circulation.[41,42]

Resurfacing techniques such as dermabrasion, chemical peeling, and laser and flashlamp skin resurfacing have been established to attain their therapeutic effects by stimulating a wound-healing response that leads to an increase in dermal collagen.[43-48] For example: the nonablative laser is able to generate dermal temperature increase of 30-40 degrees C while limiting thermal injury to the epidermis.[49] The dermal heat may eventually result in activation of fibroblasts to produce a long term healing response and subsequent collagen remodeling.[49,50] Shorter wavelength technologies have been hypothesised to induce a heat-mediated cytokine activation.[51]

The biological activity of transforming growth factor β1 is controlled by its secretion as a latent complex in which it is non-covalently associated with latency-associated peptide (LAP).[52] Barcellos-Hoff et al postulated that oxidation of specific amino acids in the LAP leads to a conformation change in the latent complex that allows release of active TGF-β.[53]

Synthesis of TGF-β increase was registered 1-2 days after activation with BCG vaccine, lipopolysacharide and gamma radiation.[54] One study demonstrated activation of latent TGF-β after wounding and noticed that introduction of the latent TGF-β1 gene into keratinocytes markedly increased the release and activation of TGF-β after burn injury.[55]

From our findings too we demonstrate that the use of high-intensity flashlamp produces an artificial wound, which in turn stimulates the induction of transforming growth factor-β and tenascin, as shown by immunohistochemistry.

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CHAPTER 3

Hair removal in 40 hirsute women with an intense laser-like light source

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Abstract

Until recently, previously applied methods to remove hair have ultimately proven ineffective or resulted in the formation of scars and small wounds. Different methods for removing hair in a more or less permanent way have been used: electrolysis, thermolysis and the blend method. In this study we describe the removal of hair without side effects by means of non-laser incoherent emitted light, produced by the ILS flashlamp. In a multicentre study we treated 40 women with a median age of 38.6 years with hirsute hair growth of different hair colours on the upper lip and chin. In general 76.7% of the hair was removed within 6 treatments, with an average fluence of 38.7 J/cm^2 and a mean wavelength of 585 nm per patient.
A correlation was found between the percentage reduction of hairs and the number of treatments and between hair removal and needle epilation before treatment. Furthermore, a correlation was seen between hair reduction and wavelengths of 570 nm and 550 nm. No association was found between hair removal and clinical data of the patients, nor between hair reduction and technical data of the device. This study presents a new alternative for hair removal.
Key words: hair removal, hirsute, light-source, pulse mode, laser therapy.

Introduction

Women with unwanted hair growth on the face, neck and body have social and physical problems, which are encountered daily in dermatological and cosmetic practices. Female patients are devided into three groups: a group of hirsute patients, who show a male pattern of hair growth due to the increased influence of androgenes on hair follicles; a group of patients with hypertrichosis, which is in general a density of hair growth; and a group of patients with cosmetic concerns. The patient should be asked which type of hair removal she prefers. There are several physical methods of temporary hair removal: shaving, which does not change the quality, quantity or texture of the hair, but whichgives many side-effects such as skin irritation, crusts and beard stubbles;[1, 2] hair removing gloves, which can be used several times a day, which are made of dermabrative paper;[3] bleaching hair with 6% H_2O_2 which does not remove hairs but makes it invisible as there is no shadow of the beard on the upperlip and chin anymore; plucking, which is generally used for small areas and may give postinflammatory hyperpigmentation; and waxing, which lasts longer than shaving or depilatory agents.[4] Side-effects are among others, thermal burns, folliculitis and erythema of the skin. Chemical depilatory agents include thioglycol acid, barium, sulphur compounds and antimony, which hydrolise bonds through which hairshafts are broken down. [2,3,5]
Electrical epilation methods for hair removal are: electrolysis, thermolysis and the blend method.[6,7] Electrical epilation has several disadvantages, such as pain, even if local anaesthetics are applied. Furthermore, this method is more time consuming and side effects are seen, such as scars, irritation of the skin, hyper and hypopigmentation.
Surgical depilation was introduced by Bouwman in 1978, who performed a submental incision, where the subcutaneous fat is trimmed until the follicles were visible, and the hair roots were cut with serrated scissors.[8]

Different lasers are used for removing hair. The concept of using selective photothermolysis with laser light for hair removal was first described by Kuriloff in 1988 for pharyngo-oesophageal hair growth.[9] The Argon Laser was used for photo-epilation in the treatment of trachomatous trichiasis10,11 and the Neodynium Yag Laser for epilation of hair-bearing urethral grafts.[12] Dover was one of the first to succeed in showing that the Ruby laser caused selective injury to pigmented hair follicles.[13] Zaias proposed the concept of a pulsed laser for hair removal in 1991.[14] Grossman performed another study in which he showed that the normal mode Ruby laser pulses damage the hair follicles.[15]
The other mode methods are: Alexandrit laser: 755 nm wavelength; one pulse mode; 20 ms pulse duration, the Diodenlaser (LightSheer): 800 nm wavelength; 1 pulse mode; 5-30 ms pulse duration, the Lichtblitzgerat (Ellipse R): 600-950 nm wavelength; 1-5 pulse modes; 0.2-50 ms/pulse for pulse duration, the Nd: YAG-laser: 1,064 nm wavelength; 1 pulse mode; 20-40 ns (q-sw.) pulse duration, and lastly the Ruby laser: 694 nm wavelength; 1 pulse mode; 0.8-3.0 ms (frm) pulse duration.
It is necessary that the laser beam penetrates deep into the dermis in order to reach the hair follicles and to be selectively absorbed by melanine.
A new laser-like device, the PhotoDerm®VL was developed by Energy Systems Corporation (ESC), Israel, mainly for the treatment of vascular lesions located deep in the skin, such as therapy resistent portwine stains, essential telangiectasia, erythrosis interfollicularis, red keloids and small varicose veins.[16-23]
This treatment consists of an intense light source which emits non-coherent light with a constant spectrum between 515 and 590 nm, variable pulse times, energy ranges between 20 and 60 J/cm^2 and different operating modes.
Although the PhotoDerm®VL is not a coherent light source, the operation principle is the same as that of lasers. The energy produced works on a specific structure in the skin without inducing much heat in the surrounding tissues. This process is called selective photothermolysis.[24] The risks for side-effects such as scar formation or hyperpigmentation are negligible as long as the right parameter settings for each individual patient are respected. It was noticed that during the treatment of vascular lesions on the face permanent hair loss in the face occurred as side-effect of this treatment with the PhotoDerm®VL. Case reports have been described for definitive hair removal.[25]
A new device introduced after the PhotoDerm®VL flashlamp was the Epilight.® This device works with different wavelengths (e.g. 590, 615, 645, and 695 nm), is expected to penetrate deeper into the skin and works with higher energy and as many as five pulse modes.
This study was carried out due to our interest in treating patients with hypertrichosis and hirsutism, and because research into the use of selective photothermolysis for hair removal is nonexistent.

Materials and methods

Patients

Forty female patients were randomly chosen in the Medical Centre Maastricht, the Netherlands, the Karsruhe Lasercentre, Germany, and the Zürich Lasercentre, Switzerland.

A careful history of abnormal hair growth was taken for each patient. When necessary, patients were sent for further investigations by an endrocrinologist or gynaecologist. The median age of the patients was 38.1 years with a minimum of 20 and a maximum of 58 years. Patients were being divided into 4 different age-groups: group 1: < 30 years (8 patients); group 2: < 40 years (13 patients); group 3: < 50 years (16 patients) and group 4: > 50 years (3 patients). Patients were scored in relation to their skin types, according to Fitzpatrick's classification: there was one patient with skin type 1, 24 patients with skin type 2, 13 patients with skin type 3 and 2 patients with skin type 4. Out of 40 patients, 8 had black hair, 26 brown hair, 5 blond hair and 1 mixed hair. In the group of forty patients, 8 (20%) women had a positive family history of hirsutism, 34 (87.5%) patients had normal periods, 4 (10%) patients had irregular periods and 1 (2.5%) patient was menopauzal. Fourteen (35.1%) women were using contraceptive drugs, 3 (7.5%) were being hormonally treated, 2 (5%) patients were shaving daily, and 36 (90%) were plucking daily (of which 23 (63.8%) were plucking hair for up to 5 min and 13 (36.1%) for longer than 5 min). Patients were seen and scored by two different physicians. They were asked to shave 3-4 days before treatment. They were advised to shave rather than pluck the hair or dewax and to use a sunblocker during the time of treatment. The treated area was cooled with an icepack and, if necessary, Zilversulfadiazine creme, Flammazine®, (Solvay Pharma), Weesp, the Netherlands was applied. A test spot was marked beneath the left chin (with a right side as control). After one week, a month and three months, hair counts of the test spots beneath the chin were estimated in the same patients at the Medical Centre Maastricht. An estimation was used, without counting. The percentage of hair before treatment was compared to the percentage present at evaluation.

PhotoDerm®VL

The principle of the operation of the PhotoDerm®VL (ESC Medical Systems Ltd, Yokneam, Israel) is based on the principle of selective photothermolysis, where the light, absorbed by the specific lesion, leads to its heating to a temperature, high enough to cause thermal damage (T>80°C), sparing the epidermis and the surrounding healthy dermis. In contrast to laser systems, the PhotoDerm®VL uses incoherent light of a broad band spectrum in the range of 500-1,200 nm. By applying different cut-off filters (515, 550, 570, 590 nm), a specific part of the shorter wavelengths (below the indicated filter) can be filtered off.

The tissue penetration depth of visible light depends on the wavelength; longer wavelengths are less absorbed by the skin. Alteration of the spectral range used during PhotoDerm®VL treatment (which is done by selecting different cut-off filters) allows for modification of the light penetration depths to match the specific target structure, i.e. vessels of different sizes and depths, hair follicles etc.[19] The use of different cut-off filters also allows for adjustment of the treatment parameters to the patient's skin type. Using longer filters, which control the spectrum to higher wavelengths, results in less overlap with the higher absorption coefficient of melanin, the concentration of which depends on the skin type.

The pulse duration can be varied, ranging between 2 and 25 msec and should be lower than the thermal relaxation time of the target tissue, so as to avoid cooling of the lesion during application of light energy. In order to improve the selectivity of the light to the target tissue only, the PhotoDerm®VL also provides- besides a single pulse- se-

ries of two and three pulses, with controlled intervals between the pulses in the range of 10-500 msec. This delay allows for cooling of the epidermis.
Fluences applied by the PhotoDerm®VL range between 3 and 90 J/cm^2.
The size of the PhotoDerm®VL treatment head (8 x 35 mm) plays an important role in improving light penetration into the tissue, since the large spot size diminishes the scattering.
A cooling gel is used over the skin during PhotoDerm®VL treatment, which allows good optical coupling of the light to the patient's skin and also allows better heat transfer from the epidermis to the cold gel.

Statistical analysis

The statistical analysis of the data was performed in a descriptive way. The data are presented as contingency tables in order to detect association between technical and clinical parameters. Exact Fisher tests were used to evaluate the homogeneity of the tables; p-values below 0.05 are considered significant. The Pearson Coefficient interval tested the relation between hair removal and mean treatment intervals per patient.

Results

Histology

Hair shafts showed fragmentation. No focal ruptures of the follicles and no hemorrhage was found (Fig.1). No coagulation of the surrounding dermalcollagen was seen. The replace follicle showed new collagen formation without any sign of scarring, and capillaries were present in the new collagen formation (Fig. 2a and 2b). The control biopsies showed no changes in follicles of the surrounding area.

Clinical observations

In the beginning of the study there was a tendancy in all centres to use a single pulse as a pulse mode, a pulse duration of approx. 5-6 msec, a wavelength of 590 nm for dark hairs, 550 nm for blond hair, and a fluence between 35-40 J/m^2. Later on, the treatment was changed to double pulses as pulse modes, with 5 msec per pulse duration and fluences between 35-40 J/m^2.
At the Medical Centre Maastricht the treatment intervals were as follows:
6 weeks after the first treatment, 8 weeks after the second treatment, 3 months after the third treatment, and 3-4 months after the fourth treatment.
Depending on the skin type, delays were chosen to cool the epidermis in between the pulses, e.g. for skin type 1 and 2 a delay of 10-20 msec was chosen, with a double pulse as pulse mode, for skin type 3 a delay of 30 msec was chosen, and if treating skin type 4, a delay of > 50 msec was used.
The patients experienced the treatment as the stinging of a needle, but less painful than needle epilation. Observations made from the immediate results were subsidiary

Figure 1. The epithelial cells of the follicle have partially disappeared and are replaced by macrophages containing melanin pigment. HE, magnification 40x.

Figure 2a. Replacement of the hair follicle by new formation of fibrous tissue and collagen. The capillaries are enclosed. Trichome stain, magnification 10x.

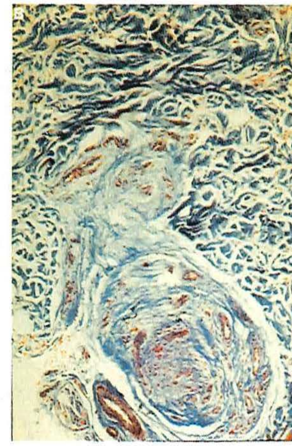

Figure 2b. The newly formed collagen bud, trichome stain, magnification 40x

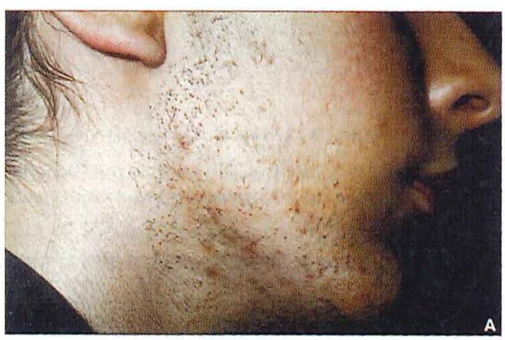

Figure 3a. Patient with hirsute hair growth on the chin.

Figure 3b. The same patient treated after one year.

to the fluences, pulse times and pulse modes. The shorter the pulse times (< 3 msec) were, the more edema and erythema was observed. Fitzpatrick skin types 1 and 2 with dark hairs showed less side- effects than skin type 3. Only two patients with skin type 4 were treated. As epidermal side- effects in skin type 3 and 4 we first noticed erythema. Imprints, which turned into crusts, were observed after 24 hrs and sealed off after 4-7 days. Hyperpigmentation was seen in 20% of patients; hypopigmentation was not seen at all. The skin of the neck and the upper lip was much more sensitive. Fluences were reduced about 2-3 J/cm^2 in the neck compared to the cheeks and chin. Most of the time about 20% of hair disappeared after the first treatment in dark- haired individuals. Depending on the hair cycles, growth of new hair was observed. Dark hair was removed in fewer treatment sessions, compared to blond hair (Fig. 3a and 3b). According to our experience, hair loss is proportional to wavelength (the higher the wavelength the more delayed the hair loss), and therefore it was mostly longer than one week.

In the Medical Centre Maastricht, treated hairs which were long enough were plucked out beneath the chin, as was untreated hair from the opposite side of the chin. These were subsequently compared under the microscope. The treated hair was shrunk and broken at the epidermal border and the follicle was partly damaged. The untreated hair showed normal outer and inner root cell sheet and a normal follicle.

Clinical data

The median age of the 40 hirsute women was 38.6 years with a minimum age of 20 years and a maximum of 58 years. The median percentage of hair loss was 76.6% with a minimum of 50% and a maximum of 95% with an average of 6 treatments. The treatment data of the patients, such as hair color, energy, wavelength, percentage of hair reduction and number of treatments, are found in Table I.

The treatment interval was 57.6 days per patient, but only data from 30 patients was available. The Pearson Coefficient interval tested the relation between the hair removal and mean treatment intervals per patient. The Pearson Coefficient interval was -0.55, which means the shorter the treatment interval, the greater the hair removal reduction.

In this study we found a significant correlation between the percentage of hair loss and the number of treatments ($p = 0.04$) (Table II). Two out of 39 patients showed a reduction of 50% within two treatments. Five out of 39 women had lost 89% of hair after 7 treatments (Table II).

Furthermore a correlation was found between hair removal and needle epilation before treatment ($p = 0.002$) (Table IIIA). Twenty- six out of 40 (65%) patients had undergone no previous needle epilation. This group reacted much better to hair removal than the group which had experienced prior needle epilation. Moreover, a correlation was seen between the reduction of hair and the wavelength of 570 nm ($p = 0.0001$) and a trend was observed with wavelength of 550 nm ($p = 0.08$). Further association was observed between hair removal and the different energy groups. Energies were separated into 5 groups (Table IIIB). A correlation was seen between hair removal and energy groups 1 (< 30 J/cm^2) and 5 (46-50 J/cm^2) ($p = 0.04$), as well as between hair removal and energy groups 2 (31-35 J/cm^2) and 5 (46-50 J/cm^2) ($p = 0.008$). This indicates that a fluence below 30 J/cm^2 and the fluence between 31-35 J/cm^2 had more

Table I. Clinical and technical data of patients

No. of Patients	Hair colour	Energy J/cm^2	Wave length nm	Haire Reduction	No. of Treatment
I	fair	35.0	560.0	90	4
2	fair	31.6	558.0	90	7
3	dark	41.0	560.0	50	2
4	dark	33.5	590.0	90	6
5	dark	38.3	590.0	80	4
6	fair	28.8	572.0	95	5
7	dark	44.6	570.0	90	7
8	dark	34.3	567.5	90	13
9	dark	28.0	560.0	95	7
10	dark	30.0	570.0	90	7
11	dark	34.3	587.0	90	6
12	dark	28.0	580.0	90	6
13	dark	30.0	570.0	90	6
14	dark	29.4	586.0	80	8
15	dark	29.5	585.0	60	5
16	dark	32.3	590.0	60	5
17	dark	37.3	580.0	80	5
18	fair	36.0	617.5	80	4
19	dark	38.5	602.5	75	11
20	fair	35.0	586.3	75	8
21	dark	40.0	602.5	50	4
22	dark	44.0	585.0	95	11
23	dark	ND	615.0	75	6
24	dark	44.4	586.0	90	5
25	dark	50.0	590.0	80	9
26	dark	46.0	590.0	50	4
27	dark	45.0	590.0	70	5
28	dark	40.5	590.0	80	11
29	dark	48.0	590.0	66	4
30	dark	51.0	590.0	85	9
31	dark	43.5	590.0	90	9
32	dark	37.4	590.0	60	5
33	dark	49.0	590.0	50	4
34	dark	43.7	590.0	90	12
35	dark	47.3	590.0	66	6
36	fair	41.0	565.0	50	3
37	dark	43.8	590.0	80	7
38	dark	39.3	590.0	50	3
39	dark	50.0	615.0	50	2

ND : not done.

Table II. Specification of number of treatments

No.of treatments	N	Mean reduction	Std Dev	Min	Max
2	2	50.0	0.0	50	50
3	2	50.0	0.0	50	50
4	7	66.6	17.0	50	90
5	7	73.6	14.9	60	95
6	6	83.5	10.5	66	90
7	5	89.0	5.5	80	95
8	2	77.5	3.5	75	80
9	3	85.0	5.0	80	90
10	3	83.3	10.4	75	95
11	1	90.0		90	90
12	1	90.0		90	90
					$p = 0.04$

Table IIIa. Clinical data of the patients

Variable		N	Mean	St Dev	P
Needle epilation	No	26	81.3	13.1	
	Yes	15	68.8	16.7	0.02
Age group	1	8	68.3	17.0	
	2	13	73.2	16.1	0.52
	1	8	68.3	17	
	3	16	80.3	13.6	0.10
	2	13	73.2	16.1	
	3	16	80.3	13.6	0.2
Skin type	2	24	77.7	16.4	
	3	13	78.2	13.7	0.93
Family history	No	32	78.5	14.4	
	Yes	8	68.3	18.9	0.18
Pil	No	26	77.1	15.4	
	Yes	14	75.1	16.7	0.71
Medication	No	37	76.9	15.3	
	Yes	3	70.3	22.8	0.66
Hair colour	Blond	6	80.0	16.4	
	Brown	34	75.8	15.7	0.57
No plucking	0	4	81.5	11.4	
Daily 5 min	I	23	74.6	16.9	0.34
No plucking	0	4	81.5	11.4	
Daily 15 min	II	13	78	14.9	0.64
Daily 5 min	I	23	74.6	16.9	
Daily 15 min	II	13	78	14.9	0.52

Table IIIb. Technical data

Variable Wave lengths		N	Mean	St Dev	P
	550	7	83.6	16.3	
	590	23	70.5	14.3	0.08
	570	8	90.6	1.7	
	590	23	70.5	14.3	0.0001
Energy groups					
1	< 30 J/cm^2	5	84	14.7	
5	46-50 J/cm^2	7	63.8	14.6	0.04
2	31-35 J/cm^2	9	85	10.6	
5	46-50 J/cm^2	7	63.8	14.6	0.005

effect on hair loss than higher energies, but the number of patients (three) was too small to formulate a conclusion.

There was no statistically significant correlation found between the percentage of hair reduction and the different hair colours (black, brown, blond or mixed). Furthermore no correlation was seen between hair removal and the four age groups, nor among patients with a positive family history, contraception use or hormonal treatment (Table IIIA). No relationship was found in hair removal between skintype 2 and 3, nor was there an association between hair removal and the different times of plucking (Table IIIA) and technical data, such as pulse modes and pulse times (Table IIIB).

Discussion

In our multicentre study, in which we investigated the use of the ILS flashlamp, for hair removal in hirsute women, we found a correlation between hair removal and number

of treatments and needle epilation prior to treatment. Moreover a relationship was observed between hair loss and wavelength, of 570 nm and 550 nm. Further association was seen in hair removal and two different energy groups. There was no statistically significant correlation found between the percentage of hair reduction, the number of treatments and the different hair colours (black, brown, blond or mixed). There was no relation between hair removal and the four age groups, nor among patients with a positive family history, contraception use or hormonal treatment. No correlation was found in hair removal between skintypes 2 and 3, neither was there any association between haie removal and the different times of plucking and technical data, such as pulse modes and pulse times.
Previous methods such as epilation (using a needle inserted into the follicle to destroy the germinative bulb), can cause many side- effects, such as superficial crusting, erythema and scar formation with pitholes in the skin resulting in an irregular surface, especially on the upper lip and chin. If left untreated, these side-effects persist throughout the years, but they can be avoided by reducing the current.[26] In patients who experienced prior needle epilation, scar tissue is regularly found around the follicles. This would explain our finding that patients who did not have needle epilation before treatment with the flashlamp show much better results. Scar tissue limits the scattering of light, therefore less absorption of melanin in hair shafts and follicles is observed. This effect explains our finding that patient who had undergone needle epilation previously need more treatment sessions.
New methods which cause less side effects and which are at least as efficient need to be developed. The ILS removal of hair fulfills these requirements. As shown in the study, this device causes no scars or skin infections.
Using the ILS, the pigment of the hair is absorbed from the light beam, transformed into energy, then into heat. As the hair shaft is 1-2 mm long coming out of the epidermis, it may enhance the absorption of melanine and scattering throughout the dermis up to the follicle. The heat coagulates the hair follicle in the deep dermal tissue. In the early post-treatment period partial or complete coagulation necrosis takes place. This necrosis does not extend into the surrounding dermal fibrous tissue. In our study the feeding vessels and the hair erector muscles remained intact. If the dermal papil cells are completely destroyed, this will result in a complete loss of hair. Hair can come out of the same follicle if the dermal papil cells are not completely destroyed. Hair can regrow from the bulging area which is not destroyed by light and which is localised in the opposite side of the sebaceous glands.
Depending on the structure of the hair and the content of pigment, a choice of variable energy has to be made to destroy the follicle. The different pulse modes of ILS make it possible to apply higher energies, cooling the skin between each pulse, yet still generating enough heat to destroy the hair follicle. The setting has to be changed in relation to the thickness and the colour of the hair.
One of the advantages of the treatment with ILS flashlamp is the extremely selective thermolysis leading to an intact epidermis, in contrast to the Blend method. Only in rare cases, about 15%, were lesions of the epidermis imprints observed at a treatment protocol of short-pulse times. Most of the times the epidermis remained intact. Folliculitis, which is sometimes seen with the Blend method or home epilating devices,[26-28] can be avoided by using the flashlamp. No cases of folliculitis were observed in this study. One advantage of this treatment is reduced pain, as compared to needle epilation. Most patients experienced this treatment as a mild sunburn sensation last-

ing for several hours. Having the choice of different fluences makes it possible to treat skin appendages without damaging the epidermis. Our group of patients, divided into different energy groups, was too small to allow for the formulation of any conclusions.
Another advantage of the ILS flashlamp is its broad spectrum of wavelengths. Depending on the skin type and hair colour, a choice can be made between the range of 515 nm and 590 nm.
In our study, a correlation was found between hair reduction and the wavelengths of 570 nm. With this device, there are many technical factors which have an effect on hair removal, such as pulse times and pulse modes. The number of patients was too small in our study to conclude that the wavelengths of 570 nm may be the best wavelength. All other technical data have to be taken into consideration as well. Depending on the colour and the thickness of the hair, different energy ranges can be used. Compared with the Blend method, the ILS flashlamp has a spot size of 1 mm and can treat skin-surfaces of 2.8 cm^2 per impulse. ILS is much more time - efficient and financially beneficial than the former methods, because this device offers many varieties of possible settings.
With a choice of using individual parameters for each type of hair and skin, hair can be removed in an easier manner in the near future. The ILS therapy will be more successful than the classical methods described above. A larger area can be treated and due to a good application of energy to the hair, scar formation as a result of overheating can be avoided. To adjust the exact parameters for each type of hair and skin, more investigation, including pathological examination of the skin up to 5 years, has to be carried out. One such follow-up study is currently being carried out in our clinic.
Our multicentre study was the first of its kind in Europe, carried out on a long-time basis. The number of forty patients is too small to confirm our clinical observations. To confirm long-term results, further studies should be performed, including patients of skin type 6.

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CHAPTER 4

Ninety percent permanent hair reduction in transsexual patients

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Summary

Transsexualism as a condition requires hair removal. Twenty-five male-to-female transsexual patients were included in this study on epilation using the Intense Pulsed Light Source (IPLS). Patients received a varying number of treatments, depending on their response. A mean hair clearance rate of 90% was achieved in the studied patients. The average number of treatments per patient was nine. A negative correlation was found between hair removal and the age of the patient. Hair removal was also found to be more effective when the patients had not used any needle epilation. No difference in hair removal was found between transsexual patients, who were hormonal, and these who were not. Follow-up lasted an average of 44 months. This study proved that the IPLS has the potential to be effective, permanent, and painless especially in younger patients who have not used any mechanical methods for epilation before photoepilation.

Transsexualism can be defined as a syndrome characterized by an incongruency of gender identity and biological sex.[1] According to the American Psychiatrists Association's Diagnostic and Statistical Manual of Mental Disorders, 4th edition, transsexualism is classified as a gender identity disorder and can be diagnosed in the presence of the following criteria[2]: a strong, persisting cross-gender identification; persisting discomfort with one's assigned natal sex and its associated gender role; and absence of any physical intersexual condition.

Although it is not the aim of this article to refer to the essentials of diagnosis for transsexualism, it is important to know that there are more than one set of criteria for the same in use. This depends on the geographical region.[2-4] In general transsexuals are put on hormonal therapy to accomplish some degree of feminization.[5] Feminizing hormones given together with antiandrogenic hormones inhibit the effects of endogenous male hormones. This has a varying consequence on the distribution of body hair in these individuals. Some of the effects of feminizing hormones include reduction of the growth of body hair and lightening of the hair texture and the color. These effects are, however, slow in onset and have unpredictable results.[2] Furthermore, a reduction in facial hair is seldom achieved. An effective, permanent method of hair removal is therefore ideal for transsexuals as part of the supportive management in gender reassignment. Several methods, including the different types of electrolysis and laser epilation, are used with varying effectiveness.[6,7] These are the more permanent methods of hair removal available in contrast to shaving, plucking, and waxing, which are temporary. [8-10] During electrolysis, patients regularly require repeated treatments over several years. Many patients find this procedure very painful, and anesthesia as well as sedation is aften required preoperatively.

It is believed that lasers and other light sources effect hair removal selectively by acting on melanosomes. These tend to be concentrated around the hair bulb, precisely the area responsible for hair growth. Laser light and intense pulsed light, at a wavelength that is absorbed preferentially by the melanin in the hair follicle, heat the hair and its root selectively, causing destruction of the hair follicle yet sparing the surrounding tissue. This is the principle of selective photothermolysis first described by Anderson and Parrish.[11]

Photoepilation has the advantage that many hairs can be treated at the same time and, unlike electrolysis, there is no need to use a needie or anesthesia. Clinical experiments will have to prove its permanency.
When light energy interacts with tissue (in this case, skin) it is converted into other forms of energy, including heat energy. As a result there are three major methods[12] by which lasers in particular bring about the removal of hair: mechanical destruction, thermal destruction, and photochemical destruction of hair follicles. It is easier to treat light-skinned individuals with dark hair than dark-skinned individuals, because in dark-skinned individuals melanin-absorbing laser light causes dangerous heating of the skin itself. However, there are reports on the effectiveness and safety of the Intense Pulsed Light Source (IPLS) in removing hair in individuals with Fitzpatrick types V and VI skin.[13] This study, though, did not encounter skin types V and VI.
In the past, studies were carried out on hair removal in hirsute women using the IPLS.[14] To our knowledge this is the first study dealing with hair removal exclusively in male-to-female transsexual patients. This population, with unique characteristics, lends itself well to our study. To assess further the technique of selective photothermolysis, this study was carried out in a group of individuals in whom an effective, permanent method of hair removal is of great importance.

Patients and methods

Twenty-five patients between the age of 22 and 67 years (average, 36.5 years) were selected in the Medical Center Maastricht, the Netherlands; the Lasercentre Karlsruhe, Germany; and the Lasercentre Zürich, Switzerland.
These were patients diagnosed by a psychiatrist to be candidates of transsexualism who were undergoing the Real Life Test to confirm the diagnosis before allowing gender reassignment surgery. A careful history of hair growth was ascertained from each patient. If necessary the patients were sent for further investigations to an endocrinologist or gynecologist.
Skin types II, III, and IV were encountered in the study. Seventeen patients (68%) had skin type II, 6 patients (24%) had skin type III, and the remaining 2 patients (8%) had skin type IV. The 244 majority of the patients (N = 22, 88%) had dark hair; the rest were blond.
Patients were advised to shave 1 to 2 days before the treatment (instead of plucking and waxing) and to use a sunblock during the time of treatment.
An IPLS (Photoderm®VL; ESC Medical Systems Ltd., Yokneam, Israel) was used. Gel was applied to the skin to act as a coupling agent between the treatment head and the skin. The settings on the machine were adjusted according to the patient characteristics of skin type and hair color. Irradiation with intense light was first carried out on a test spot. This was viewed 10 minutes later to assess the surrounding skin for adverse side effects such as perifollicular ederna. If there were no side effects then the therapy with IPLS was continued over a larger surface area. Twenty of the 25 patients had hair removed from the face and the neck, and the remaining 5 patients had hair removed from the face only. The area of treatment was a spot 2.8 cm^2. Depending on whether the hair was removed from the face and neck (approximately 80 spots) or only from the face (approximately 60 spots), time taken for the treatment sessions varied. It ranged from 30 to 90 minutes.

The condition of the hair under the test spot was also assessed. Two parameters in particular were examined: breakage of the hair and retraction of the hair into the sheath.
The face and neck were cooled with an ice pack afterward, and Flammazine cream (silver sulfadiazine from Solvay Pharma, Netherlands) was applied.
After the first treatment the patients were again examined at intervals of 4 to 6 weeks. Thereafter, patients were seen at varying intervals depending on their response to therapy with the IPLS.

Treatment modalities

The IPLS Photoderm®VL uses incoherent light of a broadband spectrum in the range of 500 to 1,200 nm. The wavelength is filtered by cutoff filters (515, 550, 570, 590, 615, 645, 695, and 755 nm). The longer the wavelength, the deeper the penetration of the light into the epidermal tissue.
The pulse duration, varying between 2 to 25 msec, has to be lower than the thermal relaxation time of the target tissue, so that the tissue does not cool down during the application of the light energy. By providing trains of two and three pulses, the Photoderm®VL improves the selectivity of the light only to the target tissue and enables the surrounding tissue to cool down by causing delay in between the pulses, using intervals of 10 to 500 msec. A cooling gel is applied during treatment to allow good optical coupling of the light to the patient's skin for better heat transfer from the epidermis to the cold gel.
Fluences applied by the IPLS range between 3 and 90 J per square centimeter. The size of the IPLS treatment head (8 X 35 mm) plays an important role in improving light penetration into the tissue because the large spot size diminishes the scattering.

Statistical analysis

A descriptive study was carried out to collect data on patient characteristics and technical data related to treatments. Hair removal results were then examined for possible correlations with various technical variables and the age of the patients using Pearson's correlation coefficient. Other patient characteristics were compared with the hair removal for possible association using Wilcoxan's two-sample test. These patient characteristics included skin type, mechanical pretreatments, and hormonal pretreatments.

Results

In this study, 25 male-to-female transsexual patients were treated for a mean duration of 691 days (range, 57-1,485 days). During this time an average of nine treatments per patient (range, 2-18 treatments) were performed. The mean success rate in hair clearance was 90% (range, 70-100%). Patients were observed for an average of 44 months.
Table 1 shows that 16 of 25 patients (64%) had used mechanical methods of epilation before photoepilation. Of these patients, only one had used a combination of mechanical methods to achieve hair removal (shaving and needle epilation). Twelve of the 25

Table 1: Mechanical pre-treatments

Mode of Treatment	Yes	Percent	No	Percentage
Needle epilation	12/25	48%	13/25	52%
Shaving	5/25	20%	20/25	80%
Plucking	0/25	0	25/25	100%
Other methods	0/25	0	25/25	100%

Table 2: Technical data

Variable	Mean	Std. Deviation	Minimum	Maximum
Duration of treatment (days)	691.8	426.7	57	1485
Number of treatments	9.1	4.4	2	18
Mean energy used (J/cm^2)	37.2	4.1	28.1	46.5
Mean pulse duration (msec)	4.1	1.1	2.5	7.3

patients (48%) had used needle epilation, and 5 of the 25 patients (20%) had used shaving. None of the patients in the study had used plucking or waxing as a method of hair removal. Twenty of the 25 patients (80%) were on hormonal treatment before starting photoepilation treatments using the IPLS. Of the remaining patients, 4 (16%) were not treated hormonally and in 1 patient this status was unknown at the time of treatment. Of the patients who were on hormonal pretreatment, 6 patients were on combination therapy (24% of the total study population).

During the treatment, the mean energy (fluence) to which each patient was exposed per treatment was 37.2 J per square centimeter, as shown in Table 2. The most commonly used filter was 590 nm, accounting for 35% of the treatments.

A significantly better result was obtained in patients who did not use any mode of mechanical epilation before hair removal with the IPLS system ($p = 0.047$). Hormonal pretreatment did not make any significant difference in. terms of hair removal. A negative correlation was found between hair removal and the age of the patients, indicating a more favorable outcome in younger patients ($p = 0.052$). Finally, no correlations were found between hair removal and any of the technical variables such as fluence, pulse time, number of treatments, or total duration of treatment.

Discussion

Using the IPLS, it is possible to achieve long-term hair reduction. Long-term hair reduction is defined as a substantial decrease in the number of terminal hairs at any given body site that is stable for a period of time longer than the follicle's complete growth cycle.[15] Both lasers and the IPLS system use the principle of selective photothermolysis for epilation. The ideal method of epilation would be the one that achieves longterm/ permanent hair removal in a single treatment without having any adverse effects. This would be especially desirable for the current study group of male-to-female transsexual patients.

In our study approximately 90% hair removal was attained in 25 patients over a mean total treatment duration of 691 days. These patients were observed for an average of 44 months after the last treatment. At the end of this follow-up period, all patients were still satisfied by the results obtained, and the level of depilation was generally maintained.

Markedly better results of hair removal in the transsexual patients were found if they had not used any mechanical method to remove hair before the treatment with the IPLS (the mechanical methods used in this study were needle epilation/electrolysis and shaving). These findings are in agreement with former studies showing that electrolysis before photoepilation worsened the results of hair removal. This is believed to be the result of scarring produced by electrolysis. The epidermal tissues are destroyed by the nonselectivity of the electrolysis methods including needle epilation.
A significant negative correlation was found in this study between hair removal and the age of the patients ($p = 0.052$), indicating that hair removal was more effective in younger transsexual patients. This is the first time that age has been found to influence depilation. It is not known whether this is the result of local factors, such as changing skin structure with age, or whether hair removal is influenced by the hormonal constitution of transsexual patients. Because previous studies on hair removal did not find age to be a factor affecting the effectiveness, it is reasonable to assume that this is a factor peculiar to hair removal in transsexual patients. Previous research already demonstrated that gender reassignment is more successful if the individual starts treatment at an earlier age. In studies carried out in male-to-female transsexual inmates, loss of androgenization was most dramatic in those who had started estrogen and progesterone therapy early in life, whereas feminization was a function of the duration of the treatment with the same hormones.[6] The age of the initial diagnosis of transsexualism and the age at which hormonal therapy started was not taken info account in our patients. These could also be confounding factors influencing our results. It is an area to be investigated in future studies.
Considering that hair is most susceptible to laser light during the late anagen phase and that the hair in different parts of the body is in various stages of the hair cycle (mosaic pattern of human hair growth), it is necessary to give several treatments before achieving satisfactory epilation. This explains the need for multiple treatments used in this study (also dependent on the individual response to photoepilation). Several studies have been undertaken, recounting hair removal using the IPLS system. Some of them described the effectiveness of hair removal after a fixed number of treatments.[16,17] This study bas been carried out in the setting of daily practice and the course of treatment was tailored to individual needs, which accounts for the rather high number of treatments. Clinically, the photothermolytic effect occurs in stages of immediate and delayed effects. After a treatment session, depilation (seen as breakage of hair) takes place but this is usually not complete. The heat coagulates the hair follicle in the deep dermal tissue. During the early posttreatment period, partial or complete coagulation necrosis takes place. This necrosis does not extend into the surrounding dermal fibrous tissue. Macrophages phagocytose the necrotic hair cells, which are limited to the hair follicle. These are replaced gradually by fibrous tissue, leaving behind only some scattered groups of pigment containing macrophages. These disappear after several weeks.[18] The epilatory effect therefore continues over a period of a few weeks as the local physiological processes adapt to the selective damage. If the dermal papillary cells are destroyed completely, complete hair loss results. Hair can regrow from the bulging area that is not destroyed by light and that is localized on the opposite side of the hair follicle from the sebaceous glands. This is an area actively under research by molecular geneticists, particularly to elucidate the nature of molecules responsible for the coding of messages between epidermal and dermal (mesenchymal) cells. Studies performed in mice show that these messages occur

at particular points in the hair cycle and that they could be responsible for the activation of hair “germ” cells in the bulge area.[19] This variation in the hair growth cycle and the bulge area as a source of hair growth could account for the failure of lasers to produce “permanent” hair removal after only one treatment.[20,21] Furthermore, some lasers failed to remove hair even for the length of one complete hair growth cycle.[21] There are many technical factors that affect hair removal, such as wavelength, pulse duration, and pulse mode. All these technical factors have to be considered while managing patients. Depending on the color of the hair, the thickness, and the skin type (Fitzpatrick), different settings can be used. In this study, no correlations were found between hair removal and any of the technical data. Different cutoff filters, pulse durations, and fluences were used for patients with different characteristics to achieve optimal epilation while minimizing side effects. Prospective studies with a large number of standardized patients (e.g. only patients with skin type II) are lacking. The IPLS has already been shown to be an effective method in the removal of hair in various groups of patients including hirsute women.[22] Within the scope of management for transsexual patients, the IPLS will certainly create its own niche. For these patients (male-to-female transsexuals), IPLS is added to the list of options for epilation. This technique has demonstrated clear advantages in comparison with other methods designed specifically to remove hair. Most of the patients had been exposed to needle epilation (electrolysis), a method that has disadvantages over IPLS in that it frequently causes scarring and pain.[22] In the case of male-to-female transsexual patients, not only male facial hair has to be removed but frequently hair from the much more sensitive genital area must be removed as well. This hair removal is necessary because of the nature of gender reassignment surgery, which often entails hair-bearing genital skin in inaccessible and inconvenient areas (e.g. inside the vagina). The use of the IPLS device (used in this study) saves time because it can treat surfaces of 2.8 to 5.6 cm^2 per pulse. This cuts costs and saves time. With a choice of using individual parameters for each type of hair and skin, hair can be removed in an easier manner in the near future. We conclude that the IPLS system is effective in hair removal in transsexual patients because it saves time, cast, and inflicts less pain.

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CHAPTER 5

Hair reduction using Intense Pulsed Light Source

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Abstract

Background. Long-term hair removal in hirsute women remains a challenging issue. Various laser and laser-like devices are currently in use for hair removal, but little is known about the permanence of their results. This study deals with the permanence of hair removal using the Intense Pulsed Light Source (IPLS).
Objectives. To test the effectiveness in long- term hair reduction.
Methods. Seventy female hirsute patients were selected in the department of Laser Therapy at the Medical Centre, Maastricht, the Netherlands. The average age of the mostly dark haired patients of various skin types (Fitzpatrick I to V) was 41 years. They were subjected to a mean of 8.0 treatments (range of 2 to 23) followed for a mean period of 27.3 months.
Results. Using the IPLS, 87% hair removal was achieved, whereby the number of treatments correlated with the amount of hair lost. No correlation was found between hair removal and patient- related or technical data. Minimal side effects occurred in 10% of the patients.
Conclusion. The IPLS system with its broad range of technical variables is effective in achieving long-term hair removal.

The management of hirsutism remains a challenge to dermatologists and cosmetic surgeons. Women with unwanted hair in the face, neck, or any part of the body have physical and social problems. There are four distinct groups with this problem: a group of hirsute patients that show a male pattern of hair growth caused by increased influence of androgens on hair follicles, patients with hypertrichosis with a general increase in density of hair growth, male-to-female transsexual patients, and patients presenting for cosmetic reasons. Previous studies raised the question as to which method of hair removal was preferable for hirsute patients.[1] A distinction was made between temporary and permanent/long-term methods of hair removal. Temporary methods include shaving,[2] plucking, mechanical and chemical dermabrasion.[3-5] Long-term methods include needle, surgical, and laser epilation as well as more recently epilation using an incoherent, intense-pulsed light source (IPLS). Each method has a distinct set of advantages and disadvantages. The question raised is about the method that will give enduring satisfactory results with a minimum of side effects.
Electrolysis consists of a direct current being passed between two electrodes to form hydrogen gas and hydroxide ions that chemically destroy the hair bulb and the papilla.[6] Thermolysis was first used by Bordier, a French physician in 1924.[7] This technique uses high frequency electro-coagulation and destroys the hair bulb by the heat generated. It is much faster than electrolysis (galvanic) but is more likely to produce pain and scarring.[8] Surgical epilation was introduced by Bouwman in 1978. He performed a submental incision; the subcutaneous fat was trimmed until the follicles were visible, and the hair roots were then cut with serrated scissors.[9]
Laser assisted epilation uses the principle of selective photothermolysis.[10] The laser energy is selectively absorbed by a target chromophore. In the case of hair removal, this chromophore is melanin, which is concentrated around the hair bulb. Performed by experienced hands, the use of laser leaves no damage to the surrounding tissues. Different lasers are used for removing hair. The concept of using laser light for hair removal was first described by Kuriloff et al.[11] in 1988 for pharyngo-oesophageal hair growth. The Argon laser was used for photo-epilation in the treatment of tracho-

matous trichiasis[12,13] and the Neodynium:YAG laser for epilation of hair- bearing urethral grafts.[14] Dover et al.[15] was one of the first groups who succeeded in showing that the Ruby laser caused selective injury to pigmented hair follicles. Grossman et al.[16] performed another study in which she showed that the normal -mode Ruby laser pulses damage the hair follicles. Zaias[17] proposed the concept of a pulsed laser for hair removal in 1991.
It is necessary that the laser beam penetrates deep into the dermis in order to reach the hair follicles and be selectively absorbed by melanin. This is important if there is to be selective destruction of the hair follicle.
Our study is concerned with the permanence of the results obtained after application of an incoherent IPLS for epilation in hirsute patients. This device has also been called Flashlamp,[8] Epilight,[18] and PhotoDerm®VL.[19] Just like lasers, it uses the principle of selective photothermolysis. The IPLS was mainly developed as a means to treat vascular lesions located deeper in the skin and it has been used for the treatment of portwine stains,[20,21] leg telangectasias,[22-24] essential telangiectasias,[25,26] venous malformations,[27] and pigmented lesions.[28,29] Various studies have reported on the efficacy of the IPLS system in removing hair.[1,18,19,30] The IPLS is also known to be effective in long-term hair removal.
Recently, second-generation IPLS devices have been marketed.[30] These are also effective in hair removal, and the side- effect profiles are documented in one study relating particularly to pain development after treatment.[30]
The IPLS has several distinct advantages over lasers, mainly arising from its flexibility in allowing a wide range of settings relating to individual patient characteristics. For the same reasons, it is an effective tool in the hands of an experienced specialist. This research aims to study the permanence of hair removal using IPLS system.

Method

Patients

Seventy female patients, aged 18-67 years (mean of 41.7 years), were chosen at random in the Medical Centre Maastricht, Maastricht, the Netherlands.
A detailed history of abnormal hair growth was taken from each patient, and when necessary, the patients were sent to see an endocrinologist or gynaecologist for further investigation.
Patients were scored according to their skin types (Fitzpatrick). Three patients (4.3%) had skin type I. Thirty-nine patients (55.7%) had skin type II. Twenty-one patients (30%) had skin type III. Four patients (5.7%) had skin type IV, and three patients (4.3%) had skin type V. Patients were asked to shave 1–2 days before the treatment (advised to shave instead of plucking and waxing) and to use a sun blocker during the time of treatment.

Treatment protocol

Test spots were first performed on each patient and reviewed 10 minutes later to observe hair breakage and perifollicular oedema. After this evaluation and after ensuring that there were no adverse reactions, the treatment was continued. Settings were made taking patient characteristics into account (discussed later here). The treated area was cooled with an ice pack afterwards, and when necessary, flammazine (silver sulphadiazine from Solvay Pharma) cream was applied.

Follow-up

Follow-up was performed 4–6 weeks after the first treatment. Thereafter, it was performed regularly at intervals based on the individual hair-growth characteristics of each patient.

IPLS

The IPLS uses incoherent light of a broadband spectrum in the range of 500-1200nm. By applying different cut-off filters (515, 550, 570, 590, 615, 695, and 755 nm), a specific part of the shorter wavelengths (below the indicated filter) can be filtered. The tissue penetration depths of visible light depends on its wavelength; longer wavelengths penetrate deeper into the skin. Alteration of the spectral range used during IPLS treatment (which is done by selecting different cut-off filters) allows modifying the penetration depth of the light to match the specific target structure, i.e., vessels of different sizes and depths and hair follicles. The use of different cut-off filters also allows adjusting the treatment parameters to the patient's skin type; using longer filters to control the spectrum of higher wavelengths results in reduced overlap with a higher absorption coefficient of melanin, the concentration of which depends on the skin type.
The pulse duration can be varied, ranging between 2 and 25 ms, and should be lower than the thermal relaxation time of the target tissue in order to avoid cooling of the lesion during the application of light energy. To improve the selectivity of the light to the target tissue only, the IPLS system provides, besides a single pulse, trains of two and three pulses with controlled intervals between the pulses in the range of 10-500 ms. This delay allows the cooling of the epidermis. Furthermore, a cooling gel is used on the skin during the IPLS treatment, which permits good optical coupling of the light to the patient's skin and also results in better heat transfer from the epidermis to the cold gel.
Fluence applied by the IPLS system ranges between 3 and 90 J/cm^2. The size of the IPLS treatment head (8x35 mm) plays an important role in improving light penetration into the tissue because the large spot size diminishes the scattering.

Statistical analysis

The statistical analysis of the data consists of frequency tables for all categorical variables and a standard description (by mean, SD, and range) for all quantitative parameters. Results are presented for all treatment-related variables as well as for all patient-specific data. Treatment parameters were averaged for each patient in order to analyse the effect of treatment- specific variables on the outcome for the patient. The association between the outcome (reduction) and quantitative variables was analysed using correlation and linear regression analysis. The possible effect of categorical variables on the outcome was tested with a Kruskal-Wallis test or a Wilcoxon rank-sum test (for binary variables), respectively. Because of the observational nature of the study, all p values are to be interpreted in an exploratory sense.

Results

In this study, a mean of 87% (range of 50% to 100%), hair reduction was achieved after a mean of 8.0 (range of 2 to 23) treatments. This was maintained after a mean of 27.4 months (range of 9 to 74 months) of follow-up. Hirsutism in these patients had been present for an average of 18 years (range of 2 to 60 years) before treatment with the IPLS.

Of the 70 patients enrolled in the study only 3 had not used other methods for hair removal before presenting to our department. Of the remaining 67 patients, 19 (27%) had shaved, 53 (76%) had plucked and 26 (36%) had used needle epilation to remove hair. Furthermore 19 (27%) patients were on hormonal medication (including the use of the oral contraceptive pill). All patients expressed dissatisfaction with the previously used methods.

The most common skin types encountered were type II (39 patients – 56%) and type III (21 patients – 30%). The majority of patients had black or dark hair (55–78%). In 34 patients (49%) there was a positive family history of hirsutism (Table 1). Fifty-one patients (73%) had normal menstrual cycles. Six patients (9%) reported irregular cycles. In 4 patients polycystic ovaries (Stein-Leventhal syndrome) had been diagnosed by the gynaecologist (Table 2).

The most common body sites treated were the chin (50 patients) and the upper lip (32 patients) (Table 3).

A correlation was found between hair removal and the number of treatments received ($p = 0.0042$). No correlations were found between hair removal and any of the clinical (patient-related) variables including age ($p = 0.8864$), skin type ($p = 0.8583$), hair colour ($p = 0.1613$), family history of hirsutism ($p = 0.3580$) and previous treatments used (Table 1). Furthermore hair removal did not correlate with any of the technical vari-

Table 1: Clinical data of the patients

Variable		N	Mean	St Dev	P
Skin type	I	3	93.3	5.7	0.8583
	II	39	86.4	11.6	
	III	21	84.5	13.3	
	IV	4	91.7	2.9	
	V	3	91.7	2.9	
Hair colour	black or dark	55	87.5	11.3	0.1613
	blond/fair/mixed	15	83.7	12.5	
Family history	positive	34	88.0	10.7	0.3580
	negative	36	85.4	12.3	
Pill (OC)	yes	20	86.1	13.0	0.9829
	no	50	86.8	11.1	
Needle epilation	yes	26	86.2	10.2	0.4636
	no	44	87.0	12.4	
Shaving	yes	19	86.6	13.6	0.5770
	no	51	86.6	10.8	
Plucking	yes	53	88.0	9.9	0.1806
	yo	17	82.2	15.3	

Yes - used treatment; No - did not use treatment; Missing frequency = 0

Table 2: Gynaecological status

	Number of patients	Percentage
Increased androgens	4	5.7%
Polycystic ovaries	4	5.7%
Menopause	8	7.7%
Hysterectomy	4	5.7%
Surgical Sterilization	4	5.7%
In-vitro Fertilization	3	4.3%
Other*	7	10%
No significant gynaecological history	36	51.4%
TOTAL	70	100%

Frequency missing = 0; * includes menstrual abnormalities, diabetes gravidarum, endometriosis and history of operative delivery

Table 3: Sites treated

Site	Number of Sites	Percentage
Chin	50	48.1%
Upper Lip	40	38.5%
Neck	4	3.8%
Cheeks	2	1.9%
TOTAL	104	100%

Frequency missing = 0

Table 4: Hair removal in relation to clinical and technical data

Variable	Pearson correlation (p-value)
Number of treatments	0.0042
Age	0.8864
Pulse time	0.6688
Wavelength	0.6730
Energy	0.7162

ables including the wavelength ($p = 0.6370$), the pulse time ($p = 0.6688$) and the energy ($p= 0.7162$) (Table 4).

Discussion

The IPLS is being studied as a method of long-term hair removal. In our study, after a mean of 8 (range of 2 to 23) treatments, an average of 87% hair reduction was achieved. To our knowledge, no study with IPLS with such a high percentage of hair reduction has been published so far.[18,30,31]

It was observed that hair reduction depended on the hair color, skin type, and the number of treatment sessions given (i.e., the more treatment sessions, the greater the hair reduction). It was also found that blond- and grey- haired patients required a larger number of treatments then dark- haired patients. Blond hair contains less melanin compared with darker hair. Consequently, the light source can target less chromophore, and hence, the response is less reliable. It was easier to treat fine hair compared with coarse hair because coarse hair often has a thick layer of keratin and requires a higher energy level for removal. We did not use higher energy levels, as they would have resulted in more side-effects, such as scar formation, hyoppigmentation, etc. In some patients, we observed paradoxical growth of hair. This was particularly seen in patients whose treatment intervals were more than 8 weeks apart. Our hypothesis is that light helps to stimulate the hair follicles to enter the anagen growth phase more readily (has yet to be scientifically proved). Therefore, we suggest that the interval between two treatments should be between 4 and 6 weeks in order to avoid any paradoxical growth of hair.

At first we used short pulse times, such as a pulse of 5 ms; the optimal parameters of the new light source were not confirmed. Time taken for the hair follicles to be destroyed was longer, and subsequently, hair reduction was less. Thus, more sessions were necessary to satisfy the patients. The conclusion based on our histological study later was that pulse times longer than 12 ms were more effective (data not published yet). Consequently, longer pulse times were used in this study, which gave better results, ensuring hair reduction with fewer treatment sessions to satisfy the patients.

Previously, quite a few studies have been done using first- generation flashlamps for hair removal. In one such study, 37 subjects received a single treatment using one of four cut-off filters consisting of two to five pulses with energies of 34 to 55 J/cm^2.[18] Approximately 60% hair removal was noted at 12 weeks. Long-term epilation of 75% hair removal was found in this group of patients after one year with a single treatment.[31] Weiss et al.[32] enrolled 23 patients with Fitzpatrick types I-III for a single- treatment IPLS and 48 patients with Fitzpatrick skin types I-V randomly for two treatments. Their results showed that for the double- treatment protocol, hair clearance of 64% was achieved immediately after the second treatment. By week 8, reduction of hair counts was 42%, whereas at 6 months, hair counts were reduced by 33%.

Intense pulsed light has been shown to be more effective when multiple treatments are given.[30,33] Some studies showed that 3 treatments were optimal, beyond which no significantly better result could be obtained.[30,34] Sadick et al. [34] demonstrated long-term results of photo epilation with Epilight (IPLS) in 34 hirsute patients. The mean hair removal efficiency achieved was 76% after a mean of 3.7 treatments in patients followed up for a mean of 21.1 months. The parameters used in this study were wavelength spectrum of 615 to 695 nm, pulse duration of 2.6 to 3.3 ms, fluence of 34 to 42 J/cm^2, and a 10x45-mm exposure field. In our study, we treated each of the 70 patients with individual parameters and with lower mean energy. Moreover our mean follow-up period was longer, i.e., 27.3 months. These could be some of the reasons why more treatment sessions were required for hair removal in our study.

Bjerring et al.[29] compared the effectiveness of a second generation IPL (Ellipse) with a normal mode Ruby laser for hair removal in 31 patients. Another study with a second-generation IPLS was conducted by Troilius and Troilius.[33] They observed a hair reduction of 74.7% ± 18.3% (mean ± SD) 4 months after the treatments and 80.2% ± 20.3% 8 months after the last treatment.

Because our study was conducted using the first- generation flashlamps and the mean follow-up period was more than 2 years (i.e., longer than the follicles' complete growth cycle), we had to carry out an average of 8 sessions to be able to demonstrate permanence rather than long-term reduction in hair. Future studies using the new generation of flashlamps will reveal whether a lesser number of treatments will be sufficient for a substantial number of hair reduction.

It was emphasised that both the hair follicle and the bulge area were important in hair regrowth.[35,36] At first it was assumed that only the hair follicle was involved in this function. This is now known to be inaccurate. Animal experiments showed that hair could be regenerated from totally follicle- free skin.[37] The bulge area of the pilosebaceous unit in the mouse skin model is capable of such a function.[36] Liew et al.[35] demonstrated that the mere destruction of the bulge area, however, resulted in only temporary hair reduction. In conclusion, from these studies, it can be said that both the hair bulb and the bulge area have to be destroyed before long-term hair removal is achieved. This could be an explanation for the need for multiple treatments in order to destroy both structures in the hair follicles. Theoretically, this should be possible in one treatment. However, complete selective destruction depends on how much energy can be delivered to the hair follicle without causing side effects. Furthermore, it is known that hair follicles are most sensitive to laser light in the mid- to late anagen phase.[38] This plus the fact that human hair follows a mosaic pattern of growth means that only a certain proportion of important structures in hair follicles can be destroyed in one treatment.

As pointed out by some authors, the term "permanent hair removal'' means different things to different people. Dierickx et al.[39] defined permanent hair loss as a significant reduction in the number of terminal hairs after a given treatment stable enough for a period longer than the complete growth cycle of the hair follicle at the given body site. Patients, on the other hand, understand ''permanent'' to mean lifelong. The clinician is then responsible for explaining to the patient the capabilities of the method, as already elucidated by scientific methods.

No correlations were found between hair removal and any of the technical variables. These variables include pulse time, interval, wavelengths used, and pulse mode used. For each patient, a different combination of technical settings is required. The aim is to apply selectively as high an amount of energy to the hair follicles while avoiding any side effects. Given the many different combinations of possible settings, a very large number of patients would be required to find any correlations with technical variables.

As seen, the amount of energy is important in having an impact on hair removal. It was found in a study carried out by Sadick et al.[40] that hair removal by the IPLS is a direct result of the amount of energy delivered to the follicle. The possibility that the treatment with the IPLS interfered with the hair growth cycle in any way was excluded. Side effects were encountered in the study. These were mostly limited to a burning sensation experienced by many patients after the treatment. In our study, only 4 out of the 70 patients experienced pain and erythema after the treatment. This was followed days later by postinflammatory pigmental changes such as hyperpigmentation appearing in the form of a "footprint". The small amount of side effects could be explained by the tailoring of various technical settings to the requirements of each patient.

We conclude that the IPLS offers an effective method of long-term hair reduction free of side effects when applied by an experienced and trained clinician. Multiple treatments are necessary for long-term hair removal. Because of the many different technical settings, studies with larger numbers of patients are required to understand further which effects each of these variable factors might have during hair removal with IPLS.

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CHAPTER 6

An Intense Light Source The PhotoDerm®VL-Flashlamp as a New Treatment Possibility for Vascular Skin Lesions

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Abstract

Background. Up to now, vascular diseases were treated with various lasers, such as Argon, Pulsed Dye, and Copper Vapour lasers, which can lead to side-effects like hypopigmentations, hyperpigmentations, and scarring. We treated patients with vascular lesions with an incoherent intense light source the PhotoDerm®VL- flashlamp.
Objective. The aim of the study was to test the effectiveness and safety of the PhotoDerm®VL for vascular skin lesions.
Methods. One hundred and twenty patients with facial or leg telangiectasias, spider nevi, erythrosis interfollicularis and senile angiomas were treated with the PhotoDerm®VL.
Results. In 73.6% of patients there was an immediate clearing, and in 84.3% of the patients a clearing after 1 month was found of leg telangiectasias up to 1 mm in diameter. Facial telangiectasias and erythrosis interfollicularis colli showed clearance up to 90%. Spider nevi and senile angiomas often only needed to be treated once.
Conclusion. From our experience we conclude that the PhotoDerm®VL is an excellent device to treat vascular lesions as there were hardly any side-effects seen, however, the user needs a sufficient experience to get good results.
Keywords: Erythrosis interfollicularis, facial- and leg-telangiectasias, PhotoDerm®VL, spider nevi, senile angiomas

Vascular skin lesions such as facial- and leg telangiectasias, spider nevi, erythrosis interfollicularis, and senile angiomas are very common. Most patients with those kinds of skin lesions will visit their dermatologist for cosmetic reasons. For most of the concerned patients telangiectasias in the face are a big cosmetic problem, which they try to hide with a thick layer of make-up. Telangiectasias are superficial vessels, which may represent expanded venules, capillaries and arterioles and may have a diameter of 0.1-3.0 mm. They are classified as: linear, aborizing, spiders, and punctiform. Spiders have a central vessel of arteriolar origin, compared to linear and aborizing telangiectasias which are of venular origin. Up to now, a good, safe, and easy treatment did not always provide an effective solution for their problem. Reasons for developing facial telangiectasias are excessive sun radiation, topical steroids, and hormonal replacement therapy. Fine wire diathermy was used for a long time. This a non-selective process that is painful and destroys excessive normal tissue surrounding the vessels. Electric stinging bears the risk of hypopigmented, depressed scar formation, and mostly turns out to be inefficient.[1] The Argon laser was one of the first lasers being used for port-wine stains and telangiectasias of the face. The green light of the Argon 514 nm was used for treatment but the penetration was not deep enough.[2,3] The light of Argon lasers absorb melanin and oxyhemaglobin because of their wavelength, and due to this they destroy epidermis and vessels.[4-6] Pulse lasers for yellow light followed the Argon. Lasers such as Pulsed Dye (PDL) and Copper Vapour (CVL) lasers absorb oxyhemoglobin around 577-585 nm. Glasberg et al demonstrated a direct destructive effect upon endothelial cell structures with the 577nm pulsed dye laser.[7] The penetration is only up to 0.5 mm in depth from the epidermal-dermal junction.[8] Tan showed that by increasing the wavelength from 577 to 585 nm the depths of penetration for destroying microvessels (50-100 μm in diameter) could be increased from 0.5 to 1.2 mm.[9] Unfortunately, this cannot be achieved with

larger vessels. To damage specific vessels, laser energy delivery time has to be shorter than the delivery time required for the cooling of the veins. In superficial, very small (less than 100 μm) cutaneous blood vessels, the thermal relaxation time ranges from 2 to 10 msec. Several studies were performed with different pulse-widths starting from 1 to 450 nsec with intravascular damage and destruction of endothelial cells.[10,11] The PDL is used for treating port-wine stains with good results. One of its side-effects is an intra-cutaneous hemorrhagia.[5,12-14]
The CVL is supposed to produce less edema and pain. With the emission peek of 578 nm the CVL corresponds well to the absorption peek of oxyhemoglobin. The absorption of melanin is less, at 488-515 nm. Histological studies have shown that the thermal damage of the CVL is more selective than that of the Argon.[15-18]
A combined therapy of pulsed dye and sclerotherapy was proposed, e.g. for telangiectasias on the nasolabial folds, where telangiectasias were difficult to remove. As for these facial vessels higher energy is necessary, which again can lead to scarring. Generally sclerotherapy of vessels in the face is not performed because of deep anastamoses with cerebral vessels.[5]
In the last decade laser therapy has also been used for treating leg telangiectasias. At first this treatment unfortunately turned out to be less promising. The carbon dioxide (CO_2) laser obliterates telangiectasias, but the overlying skin is destroyed with hypopigmented scars.[19-21] Due to its non-selective action this type of laser cannot be used as a treatment for telangiectasias. With Neodymium (Nd): YAG laser (1060 nm) telangiectasias can be coagulated, but like the CO_2 laser the treatment is non-specific, resulting in scar formation. Apfelberg et al. reported linear depressed hypopigmented scars after Nd:YAG treatment.[20] The Argon laser is commonly used for vascular skin lesions, but only in 16% of skin lesions were excellent or good results obtained.[22]
Recently, the PhotoDerm®VL was introduced as an intense light source, which is, in use, comparable with lasers, for the treatment of telangiectasias.[23,24] In this article we will describe the possibilities and limitations of the PhotoDerm®VL flashlamp for the treatment of vascular skin lesions.

Patients and methods

Patients

In total, 120 patients with vascular skin diseases were randomly chosen from the department of dermatology: 30 patients (5 male and 25 female) with facial telangiectasias; 40 patients (40 female) with leg telangiectasias; 15 patients (15 female) with spider nevi with a diameter of 0.5-2.0 mm; 15 patients (15 female) with erythrosis interfollicularis; and 20 patients (12 male and 8 female) with senile angiomas. There was no history of coagulopathy or use of anti-coagulants.
In all 40 female patients with leg telangiectasias, venous hypertension was ruled out using photoplethysmography and Doppler Ultrasound as described before.[25] Varicose veins were first treated with selective surgery if necessary and/or sclerotherapy. Patients were evaluated for immediate response and followed-up after 1 week, 2 weeks, 4 weeks, and 3 months. Patients were divided into three groups, according to the diameter of the vessel treated: group 1, < 0.2 mm, group 2, 0.2-0.5 mm; and group 3, 0.5 -1.0 mm.

PhotoDerm®VL

The principle of operation of the PhotoDerm®VL (ESC Medical Systems Ltd. Yokneam, Israel) is based on the principle of selective photothermolysis, where the light, absorbed by the specific lesion, leads to its heating to a temperature high enough to cause thermal damage (T>80°C), sparing the epidermis and the surrounding healthy dermis. In contrast to laser systems, the PhotoDerm®VL uses non-coherent light of a broad band spectrum in the range of 500-1200 nm. By applying different cut-off filters (515, 550, 570, 590 nm), a specific part of the shorter wavelengths (below the indicated filter) can be filtered off.

The tissue penetration depths of visible light depends on the wavelength, with longer wavelengths being less absorbed by the skin. Alteration of the spectral range used during PhotoDerm®VL treatment (which is done by selecting different cut-off filters) allows modification of the penetration depth of the light to match the specific target structure, i.e., vessels of different sizes and depths, hair follicles, etc. The use of different cut-off filters also allows adjustment of the treatment parameters to the patient's skin type; using longer filters, which control the spectrum to higher wavelengths, results in less overlap with the higher absorption coefficient of melanin, the concentration of which depends on the skin type.

The pulse duration can be varied ranging between 2 and 25 msec, and should be lower than the thermal relaxation time of the target tissue, in order to avoid cooling of the lesion during application of light energy. In order to improve the selectivity of the light to target tissue only, the PhotoDerm®VL provides, besides a single pulse, also trains of two and three pulses, with controlled intervals between the pulses in the range of 10-500 msec. This delay allows the epidermis and the microvessels to cool (typical thermal relaxation time 10 msec) between consecutive pulses without significant cooling of the bigger, deeper localised vessels. This is in accordance with the thermal relaxation time of different objects, which is proportional to their size ($T \propto r^2$), where r is the radius of a cylindrical object such as a blood vessel. Fluences applied by the PhotoDerm®VL range between 3 and 90 J/cm^2. The size of the PhotoDerm®VL treatment head (8 x 35 mm) plays an important role in improving light penetration into the tissue since the large spot size diminishes the scattering. The large spot size is advantageous also in terms of the ability to treat a relatively large area with a single pulse, which speeds up the treatment time and causes less pain to the patients.

A cooling gel is used over the skin during PhotoDerm®VL treatment, which allows good optical coupling of the light to the patient's skin and also allows better heat transfer from the epidermis to the cold gel.

By changing the different parameters of the PhotoDerm®VL, namely wavelength, number of pulses, pulse duration, and delay between pulses, one can achieve efficient treatment for a variety of lesions with a high degree of selectivity and safety.

Results

The settings of the different parameters of the PhotoDerm®VL and the percentage of clearance of the different types of leg telangiectasias are given in table I. Clearance is based on the estimations of two physicians.

Blue facial telangiectasias on the nose were treated most of the time with a cut-off filter of 590 nm and triple pulses, with pulse times of 3.8, 3.1, and 2.6 msec, using energy rates of 38 and 50 J/cm^2. Seven nasal blue vessels, which hardly reacted to laser therapy, showed good response to the PhotoDerm®VL. Clearing was seen in up to 90%. Red telangiectasias were treated with 550 nm, 30-34 J/cm^2, 4-5 msec, and single pulse. Clearing was found in up to 95% (Figure 1).

Spider nevi, if they had not been treated before with electro- coagulation, showed a good result, with parameters of 550 and 570 nm, with pulse times of 4-5 msec and energy rates of 32-36 J/cm^2 using a single pulse, and triple pulses with 550 and 570 nm with pulse times of 3.8, 3.1, and 2.6 msec, with a pulse delay of 10 msec for skin type 1 and 2, and a pulse delay of 20 msec for sun- tanned skin, using 38 and 50 J/cm^2. For senile angiomas the same parameters were used as for spider nevi. Almost all spider nevi and senile hemangiomas cleared (95%).

Erythrosis interfollicularis colli, which has 2 components, a vascular and a pigmental one, was treated with cut-off filters of 515 and 550 nm, depending on the color of the skin and of the skin lesions and pulse times of 2.5 and 3 msec, and energy rates of 22-26 J/cm^2. This skin lesion showed 90% clearance in the vascular part.

Patients with leg telangiectasias were divided into 3 groups, according to the diameter of vessel treated: group 1, < 0.2 mm; group 2, 0.2-0.5 mm; and group 3, 0.5-1 mm. Only leg telangiectasias above the knee were treated. In the group of up to 0.2 mm vessel diameter, we observed an immediate clearing in 82.0% of this patient group, with a clearing of 92.1% after 4 weeks. In the second group of patients, with a vessel diameter of 0.2-0.5 mm, 78.9% of those treated had an immediate clearing, and 80.0% of patients after 1 month. In the group of patients with a vessel diameter from 0.5-1 mm, 42.3% showed an immediate clearing and 81.0% after 1 month.

In general we saw hardly any side- effects in our expanded study. In 2 patients with facial telangiectasias, who were pre-treated with cortisone cream due to psoriasis, small bullae were found, which did not leave any scarring. We did not see any hyperpigmentation, but temporary hypopigmentations were seen five times, and improved after a few weeks. Spider nevi and senile angiomas only showed in dark skin types from sealing of the horny layer of the epidermis, which also improved.

Table 1. Parameters used in the Maastricht experiment for vascular lesions

Vascular lesions	W.L.nm	E/Jcm^2	P.M.msec	P.T.msec	PD.msec	Cl.(%)
Blue facial telangiectasias	590	38	T.P.	3.8/3.1/2.6	10.20	90
	590	50	T.P.	3.8/3.1/2.6	10.20	
Red facial telangiectasias	550	30-34	S.P.	4-5	0	95
Spider nevi	550	28-34	S.P.	4-5	0	95
	570	30-35	D.P.	3/2	10.20	
Erythrosis interfollicularis	515	22-26	S.P.	2.5-3	0	90
	550	22-28	S.P.	2.5-3	0	
Senile angiomas	550	30-36	S.P.	4-5	0	95
Leg tel. <0.2mm	550	22-28	S.P.	3-4	0	92
Leg tel. 0.2-0.5mm	570	24-30	D.P.	2.4/2.4	10.20	80
Leg tel. 0.5-1mm	570	38-40	T.P.	3.8/3.1/2.6	10.20	81
	590	50	T.P.	3.8/3.1/2.6	20.30	

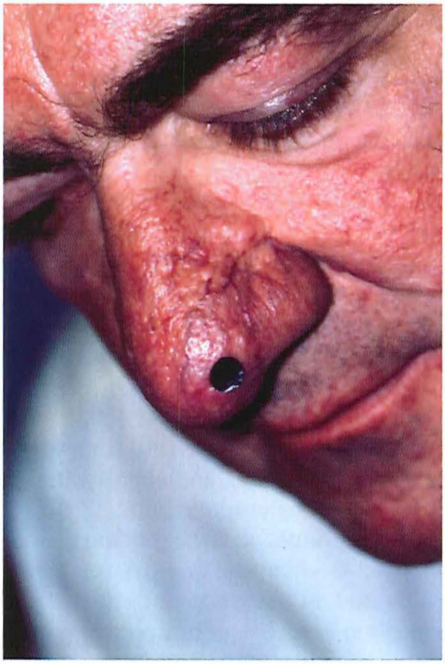

Figure 1a. Blue and red teleangiectasias an the back and an the ala of the nase before treatment.

Figure 1b. Ten weeks after the first treatment.

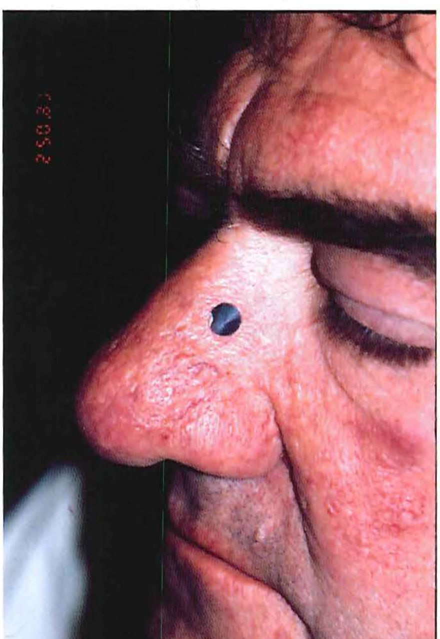

Figure 1c. Immediately after the second treatment with triple pulses, 590 nm, and different energies.

Concerning side effects in leg veins, in 20 patients hyperpigmentation was seen, 9 patients showed erythema with hyperpigmentation, 2 patients showed hyperpigmentation and a blister, and in 3 patients erythema was visible followed by hypopigmentation. One patient experienced only hypopigmentation and 5 patients only erythema.

Discussion

In this study we showed that there is a good clearance of leg telangiectasias up to 1 mm (84.3%), a good clearing of facial telangiectasias (95%), erythrosis interfollicularis colli (80%), and spider nevi and senile angiomas in general cleared in one treatment. Age did not play a role concerning our reported results. Single treatments gave content results; repeated treatments after 10-12 weeks diminished residual telangiectatic lesions.

Telangiectasias develop out of dilatations within arterioles, venoles, or capillaries. Telangiectasias in the face are seen as punctures of branched lesions or as spider nevi.[4] One of the main important factors for developing facial telangiectasias is chronic exposure to the sun. The Argon Laser was another alternative, as it gave sufficient results and cheaper treatments.[26] Side-effects of the Argon Laser were risk of scars and permanent pigmentation problems.[5,12,14] The penetration depths of the PDL and Argon laser (1 and 1.2 mm, respectively), limit their indications, as vessels that are localised deeper in the skin cannot be treated.[5] For years the PDL was one of the main laser sources for treating vascular lesions, using the principle of selective photo -thermolysis, where the energy works on special targets, in this case, the effecting erythrocytes and avoiding scars in the surrounding tissue.[5,14,27,28] One of the main side-effects of PDL is haemorrhage, which remains for up to 2 weeks. These haemorrhages are difficult to cover with cosmetics.[26,29]

The PhotoDerm®VL as a light source, shows, compared with older laser types, several advantages. First, with one application of the PhotoDerm®VL, a surface of 2.8 cm^2 can be treated, while with the PDL this is considerably less (for a diameter of 5 mm a surface of 19.6 mm^2 and for a diameter of 10 mm a surface of 78 mm^2), and with the Argon Laser this is only 3 mm^2. Less haemorrhage is seen when treating patients with the PhotoDerm® VL, and even if it appears, it only remains for up to 2 - 5 days. With the PhotoDerm®VL we hardly ever saw hypo- or hyperpigmentations treating facial telangiectasias and erythrosis interfollicularis. Furthermore the PhotoDerm®VL even offers new treatment possibilities, e.g., erythrosis interfollicularis, as these vessels have a very small diameter and are very superficially localised.

Bullae formation was seen in two cases of facial telangiectasias. These patients were pre-treated with topical cortison creams due to psoriasis.

As a conclusion the PhotoDerm®VL has several advantages compared with previously used lasers such as the PDL and the Argon laser.[30,31] Even though we are able to show good results with the PhotoDerm®VL, in different vascular skin lesions, we have to limit our enthusiasm. The PhotoDerm®VL turns out to be very difficult to handle. Too little energy will not occlude the vessels, too much energy develops too much heat, leading to bullae and finally to scar formation and depigmentation. Also, the pigmentation rate of the skin will influence the final result. More pigmentation will increase the risk of absorption of light, and thus damage the skin. The difficulties in handling this machine are at the same time also the key for good results in this treatment. Since not all parameters of the skin lesions can be put in a mathematical formula, the operator has to be extremely experienced. For setting the parameters of the device, one has to remember all the different alternatives.

First are the several treatment modalities, which means different energy types, pulse modes, and pulse time, which can be chosen according to the disease of the patient. The larger surface of 2.8 cm^2 using the PhotoDerm®VL offers a more time-efficient treatment, and the side-effects you generally see with other laser types can be neglected, which means that patients have less pain, there is less edema formation and there are fewer haemorrhages. The very large spot size enables much deeper light penetration into the skin. For years it has been known that port-wine stains are treated much better with a pulse duration from 1 to 10 msec, although there was no possibility to implement this fact practically in therapy until the PhotoDerm®VL was developed. By splitting the energy into 2 or 3 pulses with different pulse delays, the skin can be cooled in between. This results in fewer side effects in the surrounding tissue. Using these pulse sequences purpura, which is common with the PDL, does not appear even when high frequencies are used. The intense pulsed light source has the following other advantages. The wavelength can be produced with cut-off filters ranging from 515 to 590 nm. In general vessels require different wavelengths for optimal treatment. Deeper penetration into the skin can be performed with longer wavelengths. The pulse duration can be varied between 0.5 and 25 msec so that the energy can be applied to the vessel with a controlled power. The advantage of the PhotoDerm®VL is found in its flexibility. This makes an individual treatment for every patient possible. We can conclude out of our experience with the PhotoDerm®VL up to now that the user needs a lot of experience with this device to become familiar with all the possible settings. These depend on the individual requirements of the patient's condition. It seems the relative low energy settings will avoid extravazation of erythrocytes. This lack of purpura, which increases acceptance for the patients, is one of the important reasons that hypopigmentation can be avoided, what is seen in other therapeutical modalities. In conclusion, the PhotoDerm VL- flashlamp is an excellent device for treating vascular lesions in the hands of experienced users.

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Commentary

The development of the pulsed dye laser in the mid 1980s revolutionized the treatment of cutaneous vascular lesions. Based on the theory of selective photothermolysis, spatial confinement of thermal injury in blood vessels was achieved by selective absorption by hemoglobin of 577-585 nm light with pulse durations in the millisecond domain. While effective in the treatment of a variety of vascular lesions and a revolutionary development in the treatment of port-wine stains, the pulsed dye laser has limitations. Treatments are not without pain, mutiple treatments are required for port-wine stain lightening, treatment of dark-skinned patients is limited by increased pain, there is a high risk of side effects including pigmentary changes, and purpura develops after all treatments, lasting from 5 to 14 days.

In the past few years a broad band pulsed light source (PhotoDerm) has been developed in an effort to optimize results in the treatment of vascular lesions without some of the limitations of the pulsed dye laser. The PhotoDerm is a flashlamp-pumped broad band light source with wavelength ranging from 515 to 1200 nm, and pulse durations varying from 1 to 10 msec. While not a laser, this pulsed broad band light source has the ability to achieve selective vascular injury, a tissue effect that we associate with pulsed lasers. The ability to choose wavelength from the visible to the near infrared range, to adjust the pulse duration between 1 and 10 msec (the thermal relaxation time of vessels most commonly found in port-wine stains and telangiectasia), and the ability to produce from one to three successive pulses per treatment sites lends the PhotoDerm substantial versatility. It facilitates treatment without purpura, treatment of darker skin types, and the ability to target nonvascular sites such as pigment and hair.

Early results with the PhotoDerm have been encouraging. Schroeter and Neumann demonstrate the versatility of the PhotoDerm with effective clearing of a wider range of vascular lesions. While the ability to alter wavelength, pulse duration, fluence, and the number of pulses offers users tremendous choice, this choice is also one of the PhotoDerm's limitations. Unlike pulsed lasers used in cutaneous surgery where only the spot size and fluence can be varied, the PhotoDerm offers users a wide array of choices and, as a result, ideal treatment parameters have been slow to be established. The tremendous variation in parameters used by these experienced authors is shown in Table 1. Six different types of vascular lesions were treated with four different wavelengths, 12 different fluences, single, double, or triple pulses, with different pulse durations and different pulse delays. These numbers reflect the wide choice available to PhotoDerm users and explain, at least in part, the difficulty in maximizing the PhotoDerm's capability.

Drs. Schroeter and Neumann's long experience with the PhotoDerm is evidenced by the excellent results they have reported in 120 patients treated with a variety of vascular anomalies. As our experience grows with the PhotoDerm, ideal parameters will become known and the device will, no doubt, find its niche as a tool in our therapeutic armamentarium, not only for the treatment of vascular lesions but also for pigmented lesions and hair removal.

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CHAPTER 7

Effective treatment of rosacea using Intense Pulsed Light Systems

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Abstract

Background: To date, a variety of lasers have been used for treating vascular skin lesions. Intense pulsed light source (IPLS) is a new and promising technology for vascular lesion management such as rosacea.
Objectives: The aim of this study was to test the effectiveness of IPLS in treating vascular facial lesions in rosacea patients.
Methods: Sixty patients presenting with telangiectasia due to facial rosacea were selected randomly from the patient population in the Department of Laser Therapy at the Medical Centre Maastricht, The Netherlands. Patients of various skin types (Fitzpatrick I to IV) were selected with an average age was 44.2 years. A total of 508 sites were treated with a mean of 4.1 site and an IPLS spectrum ranging from 515 to 1200 nm with different pulse durations between 4.3 to 6.5 ms. The energy density varied from 25 to 35 J/cm^2.
Results: Patients were assessed clinically and photographically. A mean clearance of 77.8% was achieved and was maintained for a follow-up period averaging 51.6 months (range: 12 to 99 months). No correlation was found between the clearance of rosacea and patient-related or technical data. For approximately three years post-treatment, lesion recurrence was noted at 4 out of the 508 treated facial sites.
Discussion: This study demonstrated that IPLS treatment of facial rosacea is effective in obtaining clearance of 77.8%, with minimal side effects and that treatment effects are maintained.
Conclusion: The IPLS system with its broad range of technical variables is an effective tool in achieving meaningful and lasting rosacea clearance.
Key words: facial telangiectasia, incoherent light, IPLS, erythema, rosacea.

Introduction

Rosacea is a common but often overlooked skin condition that can lead to significant facial disfigurement and ocular complications. The progression of rosacea includes typical stages: facial flushing, erythema and/or oedema as well as ocular symptoms, papules and pustules, and rhinophyma.[1] The exact etiology of rosacea is unclear but it is likely due to a combination of factors. Exposure to certain climatic conditions and/or radiation resulting in vessel wall abnormalities may play a role in the developing of the disease.[2,3] The Demodex folliculorum mite could also be involved.[4,5] Other causes of facial telangiectasias are thought to be excessive exposure to sun, topical steroids, and hormonal replacement therapy. The acne rosacea syndrome can cause telangiectasia on the nose. Although the papulo-pustular elements respond well to medium or long-term antibiotic therapy, the vascular elements are frequently persistent. Usually the patients try to hide the blemishes with a thick layer of cosmetic foundation. Many treatment modalities have been attempted to eradicate these lesions including excision, razor blades,[6] electro surgery [7] and laser therapy.
Telangiectasias develop out of dilatations within arterioles, venules or capillaries. The superficial lesions of the telangiectasia are a suitable aim for photocoagulation using yellow light lasers. Yellow light of the wavelength 575 to 585 nm is absorbed well by oxyhaemoglobin with only minimal damage to the overlying skin.[8]

Selective laser treatment of vascular skin lesions is based on the principle that laser light of certain wave lengths can be preferentially absorbed by hemoglobin, and this generates thermal energy which diffuses in the immediate perivascular tissue, damaging the vessel wall. Thermal diffusion, not confined to the epidermis can produce unwanted epidermal and dermal damage. Clinically this can result in pigment and textural changes, hypertrophic scarring, depending on the site and the degree of non-vascular damage. In addition to wave length, laser-skin interactions depend on other laser variables such as energy density, duration of exposure and laser beam diameter, as well as lesion-variables such as the vascular structure and the epidermal melanin content.

Lasers used for the treatment of micro vascular lesions include among others: Argon, Pulsed Dye, Neodymium YAG, Carbon Dioxide and Krypton lasers.[9-14] Frequent hypopigmentation, scar, blister formation and pain was reported using these lasers.[9,10,15] In particular, laser studies[16-20] for rosacea and facial telangiectasias propose clearance of the vascular elements of rosacea but they are uncontrolled and lack actual measures of improvement.

An effective technology in the treatment of telangiectasia is intense pulsed light source (IPLS). PhotoDerm®VL and Vasculight® are IPLS systems developed to treat a variety of vascular lesions of the skin, including deeper ones. These devices use a wide band of an incoherent intense pulsed light source, which emits a continuously adjustable spectrum in the range of 515 to 1200 nm.

One of the earlier studies using Photoderm®VL for different skin lesions including vascular lesions was carried out by Hellwig et al.[21] A number of studies have reported the successful use of the IPLS for the treatment of port wine stains,[22,23] leg telangiectasias,[24,25] essential telangiectasias,[26,27] venous malformations[28] and poikiloderma of Civatte.[29,30] Findings from one of our earlier studies described a clearance of up to 90% of facial telangiectasias and erythrosis interfollicularis colli.[31] Spider naevi and senile angiomas cleared following one treatment session only.[31] Using appropriate parameters 70 to 100% clearance could be achieved in venous malformations smaller than 100 cm^2.[28] In one study 75 to 100% clearance was achieved in 174/188 patients with facial veins (primarily telangiectasia), facial hemangiomas, rosacea and port wine stains.[32] Another study reported more than 50% reduction in the number of vessels in 79.2% and a 75%-100% reduction in 37.5% patients of facial telangiectasia.[33] Taub AF reported that after treatment 83% of the patients had reduced redness, 75% reduced flushing and improved skin texture, and 64% noted fewer acneiform breakouts.[34]

The aim of the current study was to demonstrate the treatment of erythema and the vascular components associated with rosacea using the IPL source, and to compare the results with those of the existing lasers.

Patients

Sixty patients (55 women and 5 men), with skin types I – IV and a mean age of 44.2 years (range: 32 to 67 years) diagnosed to have telangiectasia associated with rosacea were chosen at random in the Medical Centre Maastricht, the Netherlands. Thirty-eight of the 60 patients had not received any previous treatment before presenting at Maastricht Medical Centre. Nine had been on an antibiotic therapy, 7 had been treated with laser, 2 with coagulation therapy, and the rest had received other medication (Table I).

The telangiectasias were located on the forehead, nose, cheeks and chin (Table II). The most commonly used filter was 550nm accounting for 93% of the treatments. In 436/508 treatments a pulse of equal to 5 ms or less was used and in the rest (72/508) a pulse greater than 5ms. The mean pulse duration used was 4.8 ms. Fluence applied by the PhotoDerm®VL ranged between 25 and 35 J/cm^2. In our study a mean fluence of 30.4 J/cm^2 was used. In 87.5% patients treatment was with a single pulse.

A detailed personal history of each patient was taken. Photographs were taken before and after each session. Some of the patients were also treated topically with a metronidazole cream. Patients were evaluated for an immediate response and followed by controls after 1 week, 2 weeks, 4 weeks and 3 months. The patients were followed for an average of 51.6 months (range: 2 to 99 months) until June 2004.

Table I. Prior treatment received by patients

Previous treatment	Patients
Antibiotics	9
Coagulation	2
Laser	7
Other medication	10
No therapy	38

Table II. Correlation between the sites treated and the clearance obtained

Site/localization	Number of sites	Mean number of treatments	Result/Clearance
Forehead	17	3.12	87%
Left cheek	191	4.19	77%
Right cheek	190	3.87	78%
Nose	77	5.11	75%
Chin	31	2.97	75%
Cheekbone	2	4.00	75%
Total	508		

Intense Pulsed Light System (IPLS)

In this study the IPL system, PhotoDerm®VL (ESC Medical Systems Ltd., Yokneam, Israel) and the Vasculight® (Lumenis, Yokneam, Israel) were used. Their effectiveness is based on the principle of selective photothermolysis. The PhotoDerm®VL uses incoherent light of a broadband spectrum in the range of 500 - 1200 nm by applying different cut-off filters (515, 550, 570 and 590 nm). An alteration of the spectral range during the PhotoDerm®VL treatment, allows to modify the penetration depth of the light to match the specific target structure, i.e. vessels of different sizes and depths, etc. Fluence applied by the PhotoDerm®VL ranges between 15 and 90 J/cm^2.

The size of the PhotoDerm®VL treatment head (8 x 35 mm) plays an important role in improving light penetration into the tissue since the large spot size diminishes the scattering. A cooling gel was applied to the skin during the treatment, which allows good optical coupling of the light to the patient's skin and also better heat transfer.

Statistical analysis

The statistical analysis of the data consists of frequency tables (absolute and relative) for all categorical variables. For all continuous variables, mean, standard deviation, median, minimum, maximum, and lower and upper quartiles are calculated.
The Kruskal-Wallis-test, and if appropriate, the Mann-Whitney-U-test are used to compare continuous variables between categories.
The correlations between continuous variables are measured by the Pearson correlation coefficient. All tests are strictly exploratory. The type I error for all tests is set to $p = 0.05$.

Results

In this study, 60 patients (55 women and 5 men) with a mean age of 44.2 years (range: 32 to 67 years) were treated for rosacea for a mean duration of 1.93 years. During this time 508 sites were treated with an average of 4.1 treatments per site. The mean success rate in clearance was 77.8% (figure 1a,1b, 2a). Patients were followed up for an average of 51.64 months (range: 12-99 months).
The majority of the rosacea lesions were present in the left (191/508) and the right (190/508) cheeks of the patients. In other cases they were located on the chin (31/508), forehead (17/508), nose (77/508), and cheekbone (2/508). It was observed that the lesions on the forehead showed the best clearance, that of 87% (Table II).
During the treatment, the mean energy that each patient was exposed to was 30.52 J/cm^2 (Table III). Two hundred and twenty five treatments out of 508 were carried out using fluence greater than 30 J/cm^2 and 283/508 with lesser or equal to 30 J/cm^2.
Table IV shows the immediate reaction after treatment. One hundred and nine out of 508 treatments showed erythema, 67/508 purpura, and 5/508 complained of pain. Three patients showed oedema, one had blisters, five showed footprints, and one transient hyperpigmentation. After 3 years in 4/508, there was a recurrence of the lesion. There was no reaction observed in 315/508 treatments (62%).
No correlation was found between any of the clinical (patient-related) variables including, lesion duration ($p = 0.0515$), previous treatments ($p = 0.3410$) and age ($p = 0.7192$) when the lesions cleared. The clearance also did not correlate with any of the technical variables including the pulse time ($p = 0.1179$), the number of treatments ($p = 0.2486$), the wavelength ($p = 0.8710$), or the fluence ($p = 0.9636$) (Table V).

Table III. Mean values of clinical and technical data

Variable	Mean
Duration of treatment (years)	1.9
Number of treatments	4.1
Filter used (nm)	549.4
Energy used (J/cm^2)	30.5
Pulse duration (msec)	4.9
Follow up (months)	2-99

Figure 1a, Patient with rosacea both cheeks and chin prior to treatment.

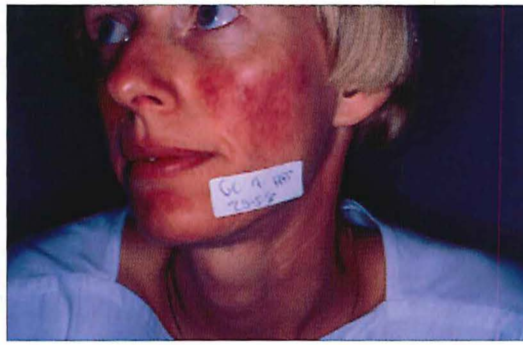

Figure 1b. Left Cheek.

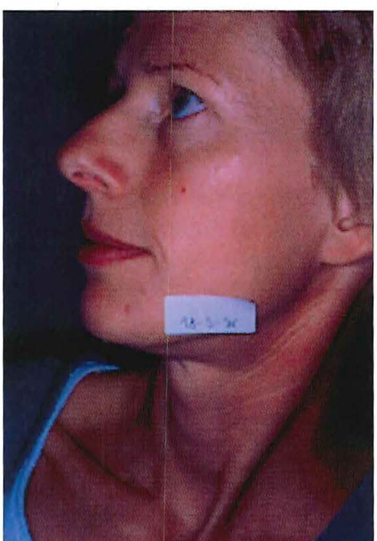

Figure 2. After 4 treatments with IPLS one year later.

Table IV. Immediate and late reactions after treatment

Reactions	No. of treatments
None	315
Erythema	109
Purpura	67
Pain	5
Oedema	3
Recurrence in 2002	2
Footprints	5
Hyperpigmentation	1
Blister	1
Total	508

Table V. Clearance in relation to clinical and technical data

Variable	Pearson correlation (p-value)
Number of treatments	0.249
Localization	0.004
Duration of lesion	0.066
Previous treatments	0.341
Age	0.719
Pulse time	0.118
Wavelength	0.87
Energy	0.96

Discussion

We observed a 77.8% clearance of facial telangiectasias associated with rosacea after an average of four treatments. Age did not play a role in the reported results, although the location of the lesion influenced the degree of their clearance. It was observed that the lesions on the forehead showed the best clearance (87%). Of the different sites treated the nose needed the maximum number of treatments (5) for the lesions to vanish. Furthermore there was no correlation found between the clearance of rosacea lesions and clinical or technical data of the patients.
The IPLS we used has several advantages in treating facial telangiectasia compared to other lasers. Firstly, the Pulsed Dye, Copper Vapor, Argon and CO_2 lasers are coherent and monochromatic lights in contrast to the IPLS, which is an incoherent, wide band light source with a spectrum in the range of 515 to 1000 nm. Deeper penetration into the skin can be achieved using longer wavelengths. Shorter pulse-time of micro seconds obtained with the Pulsed Dye laser is not enough to close the vessels so the deeper penetration depth and longer pulse time is indicated. Furthermore the different filter settings of IPLS enable a higher selection of a broad range of vessel colour of the vascular system. Second, with one shot of the IPLS a surface of 2.8 cm^2 can be treated, while with the PDL this is considerably less (for a diameter of 5 mm a surface of 19.6 mm^2 and for a diameter of 10 mm a surface of 78 mm^2) and with the Argon Laser this is only 3 mm^2. The large surface of 2.8 cm^2 offers a more time-efficient treatment and less patient discomfort. The large spot size enables much deeper light penetration into the skin. Third, by splitting the energy into 2 or 3 pulses with different pulse delays, the skin can be cooled between pulses. This results in fewer and negligible side effects.

Since treatment is relatively painless, it was carried out without anesthesia. No serious local or systemic adverse effects occurred in any of the patients treated. The immediate response was a slight erythema and purpura, which disappeared within 24 to 96 hours.
Although treating different vascular skin lesions with Photoderm®VL, yields positive results, there are some difficulties. The Photoderm®VL must be used by highly trained individuals. Too little energy will not occlude the vessels; too much energy develops too much heat, leading to bulla, scar formation and depigmentation. Also, the pigmentation rate of the skin will influence the final result. More pigmentation increases the risk of light absorption and thus increases the risk of skin damage. The specificity in using this technology also contributes to the treatment success. Not all parameters of the skin lesions can be translated into a mathematical formula. Successful parameter selection includes all of the following: pulse type, pulse duration, pulse delays, colour and depth of the vessels and the type of skin. It should be noted that due to sample size and a large variation in the technical parameters, there was no correlation found between the technical data and lesion character. Future studies using a larger sample size need to be carried out in order to compare the results of flashlamps with those of other existing lasers.
In conclusion the results from this study suggest that the Photoderm®VL is an excellent device for treating vascular skin lesions associated with rosacea, when used by an experienced physician.

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CHAPTER 8

Clinical significance of an Intense Pulsed Light Source on leg telangiectasias of up to 1 mm diameter

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Abstract

Telangiectasias on the legs are difficult to treat in contrast to those on the face. Sclerotherapy is widely used but often results in hyperpigmentation. Procedures such as argon, pulsed dye and copper vapour laser treatment may lead to scarring.
Forty female patients with blue and red telangiectasias on the legs were treated with a new, intense light source, the PhotoDerm®VL, developed by Energy Systems Corporation Inc (ESC), Boston, U.S.A. The diameter of the vessels was between 0.2 mm and 1 mm. The average age of the patients was 41.7 years, the youngest was 24 years and the oldest 72 years. Patients were treated within the spectrum of 515 nm to 590 nm with varying pulse duration. Energy varied from 20 to 70 J/cm^2. Reticular and feeding veins were treated first.
Immediate clearing was achieved in 73.6% of the patients and in 84.3% of the patients after four weeks. Concerning the immediate response, 82.0% clearing was seen in the group with veins of up to 0.2 mm diameter, 78.9% was seen in the group from 0.2 up to 0.5 mm and 59.7% was seen in the group, from 0.5 to 1 mm. After one month, clearing was seen in 92.1% in the first group, 80.0% in the second group and 81.0% in the third group of patients.
Cosmetic results were excellent, neither telangiectatic matting nor scarring was seen. There was no recurrence in the follow-up period of 1 year. Our results show that treatment of telangiectatic veins of the leg with the PhotoDerm®VL is an effective treatment with minimal damage to the skin.
Keywords: intense light source, laser, leg telangiectasias, PhotoDerm®VL.

Introduction

Leg telangiectasias are very common, but have been difficult to treat. The term telangiectasias refers to superficial, cutaneous vessels which can be seen macroscopically,[1] although this term provides no information about their origin. Telangiectasias can be dilated arterioles, venules or capillaries. In general, the small red ones are regarded as being arteriolar and venular vessels are those which turn blue or purple as a result of venous backflow and increased pressure.[2] Although a wide variety of cases of cutaneous telangiectasias is known, the majority of leg telangiectasias are related to chronic venous insufficiency. The incidence of leg telangiectasias is high: 29 to 41% for women and 6-15% for men.[3] Although up to 53% of the patients have symptoms of telangiectasias on the leg, the majority of patients consult the dermatologist for cosmetic reasons. The ideal treatment has not yet been developed; sclerocompression therapy is the most common. However, post-treatment hyperpigmentation occurs in up to 30% of patients with or without telangiectatic matting.[4] In the last decade, laser therapy has also been used for the treatment of leg telangiectasias. Unfortunately, this treatment has turned out to be somewhat disappointing. The carbon dioxide laser obliterates telangiectasias, but the overlying skin is destroyed with hypopigmented scarring.[5-7] Because of its non-selective action, this type of laser cannot be used as a treatment for leg telangiectasias. With the neodymium: YAG laser (1,060 nm), leg telangiectasias can be coagulated, but as with the CO_2 laser, the treatment is non-specific, resulting in scar formation. Apfelberg reported depressed, linear, hypopigmented scars after neodymium: YAG treatment.[6] The argon laser is commonly used for vascular skin lesions, but only in 16% of skin lesions were excellent or good results obtained.[8] Glassberg et al,[9] demonstrated a direct destructive effect upon endothelial cell structures with the 577 nm pulsed dye laser; penetration is only up to 0.5 mm depth from the dermal-epidermal junction.[10] Tan et al[11] showed that by increasing the wavelength from 577 nm to 585 nm the depth of penetration for destroying microvessels (50 up to 100 microns in diameter) could be increased from 0.5 mm to 1.2 mm. Unfortunately, this cannot be achieved with larger vessels. In very small (less than 100 microns), superficial cutaneous blood vessels the thermal relaxation time ranges from 2 ms to 10 ms. Several studies have been performed with different pulse widths starting from 1 ns to 450 ns with intravascular damage and destruction of endothelial cells.[12,13] Until now, the best results have been seen with the 585 nm flash lamp pulsed dye laser (PDL).[13] The PhotoDerm®VL was developed to treat a variety of vascular lesions of the skin including deeper skin lesions.[14] This device is a high intensity, pulsed light source with a spectrum that can be selected for optimal treatment of a variety of vascular lesions using incoherent light. The PhotoDerm®VL can be used for the treatment of veins under the skin up to a depth and a diameter of 5 mm. With this device it is possible to use, not only a broad spectrum of energy and a wide range of pulse duration, but also different wavelength ranges. The device turned out to be very effective for the treatment of leg telangiectasias. In this study we report our first results for leg telangiectasias up to 1 mm in diameter.

Materials and methods

Patients

Patients were randomly selected and treated in 4 centres for dermatological laser therapy. Two centres are located in Germany (Oberndorf and Karlsruhe), one in Switzerland (Zurich) and one in the Netherlands (Maastricht).
Forty women with leg telangiectasias, aged 24 to 72 years, with an average age of 41.7 years were selected for treatment. A personal medical history was taken, as well standard clinical investigations. The patients were examined before treatment with Doppler-ultrasound and photoplethysmography (LRR) to exclude functional reflux in the venous system of the legs.[14] Photographs and measurements were taken before treatment. Patients were evaluated for immediate response and followed-up after 1 week, 2 weeks, 4 weeks and 3 months. Major sources of venous problems such as saphenofemoral or popliteal junctions and/or incompetent perforators or feeder veins were dealt with first. Patients were divided into three groups according to the diameter of vessel treated: group 1 < 0.2 mm, group 2 between 0.2 and 0.5 mm and group 3 between 0.5 and 1 mm. The vessel diameter was recorded with a transparent ruler. Only leg telangiectasias above the knee were treated. It was safer to treat them first, as at the beginning of our study we had had very little experience with the PhotoDerm®VL and leg telangiectasias below knee are more difficult to treat. Three to up to 12 telangiectasias were treated in each patient, the average diameter and clearing were calculated.

Methods

The PhotoDerm®VL is an intense, pulsed light source with a continuous light spectrum with most of its energy at wavelengths between 515 and 1,000 mm.[15] The pulse duration of the PhotoDerm®VL range varies between 2 ms and 25 ms per pulse. The energy fluence varies between 3 J/cm^2 to 90 J/cm^2 in one pulse sequence. Operating modes are single, double or triple pulses in each pulse sequence. In contrast to lasers, the intense pulsed light source produces incoherent light, The spot size is larger than that of other lasers with an illuminated area of 8 mm x 35 mm. The optical energy is directly coupled through a light guide. All settings are computer controlled. Treatments with the PhotoDerm®VL were performed within energy ranges of 20 to 70 J/cm^2, lower cut-off filters of 515, 550, 570 and 590 nm, pulse duration between 3 and 6 ms and single or double pulses. The treatment parameters were chosen according to the diameter of the vessels, the colour of the vessels and the skin type. For vessels up to 0.2 mm in diameter, a single pulse of 3 ms and energy of 22 J/cm^2 was used. For veins with a diameter greater than 0.5 mm, a double pulse mode was used with pulse duration of 2.4 ms each, a pulse delay of 20 ms and 35 J/cm^2 for the larger ones between 0.5 mm, and up to 1 mm a triple pulse of 3.5 ms, 3.1 ms and 2.6 ms was used with pulse delay of 20 ms and 50 J/cm^2. The choice of filter depended upon the colour of the skin and the vessel and the depth of the telangiectasia, ranging between 515 nm and 590 nm. Purpura and extravasions were avoided by careful adjustment of fluence, pulse duration and pulse mode.

Statistical analysis

For comparison of improvement of the immediate response and the response after 1 month for all the patients and in each age group, the signed Rank Wilcoxon test was carried out. The two sample Wilcoxon test was performed to compare the groups of patients with different vessels diameters.
The Kruskal Wallis test was carried out to compare in general, the immediate clearing and the clearing after one month for each group.

Results

Clearing of the vessels was assessed by finding a vascular depression in the skin immediately after treatment and a cordlike structure in the dermis after a month. Forty women with a median age of 41.7 years, the youngest patient being 24 and the oldest 72 years old, were treated for leg telangiectasias. Four patients needed treatment for reflux before laser treatment. Out of these, 3 patients showed up with an insufficient sphenofemoral junction and one patient with a leak at the saphenopopliteal junction. Two patients initially received sclerotherapy, with 0.5% and 1% polidocanol depending on the type veins. In the group of up to 0.2 mm vessel diameter, we observed an immediate clearing in 82.0% of this patient group, with a clearing of 92.1% after four weeks. There was an improvement in clearing after 1 month in the first group, which was significant ($p = 0.0003$). This was shown with the signed rank Wilcoxon test. In the second group of patients, with a vessel diameter from 0.2 mm up to 0.5 mm, 78.9% of those treated had an immediate clearing and 80.0% of patients after 1 month. In the

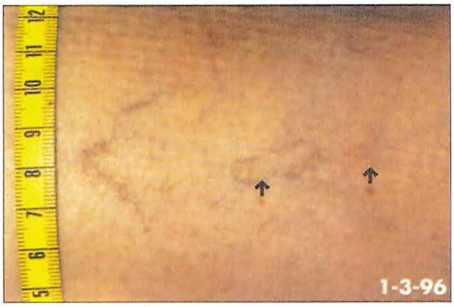

Figure 1. Before treatment, Right arrow- legs telangiectasias 0.2-0.5 mm diameter. Left arrow-leg telangiectasias 0.5-1 mm diameter

Figure 2. After treatment. Right arrow-leg telangiectasias 0.2-05 mm diameter. Left arrow-leg telangiectasias 0.5-1 mm diameter. 0.5-1 mm diameter

second group there was no difference (p = 0.63), as 17 patients already showed immediate clearing in what remained in the follow-up time. Of those patients in the 0.5 mm to 1 mm diameter group 42.3% experienced immediate clearing. After 1 month, 81.0% of the treated vessels had cleared (Table I) (Figs. 1 and 2). This difference between 42.3% and 81.0% was again statistically significant (p = 0.0001). The Kruskal Wallis test was used to compare the results of all three groups. This test showed that in the immediate response there were difference in clearing between the three groups (p = 0.0001). After one month, a difference in clearing was seen with the same test (p = 0.039). The Wilcoxon two sample test was carried out to compare two groups of patients with different vessel diameters. Between the first group, up to 0.2 mm, and the second group, 0.2-0.5 mm, no difference in clearing has seen in the immediate response (p = 0.636), compared to the difference in clearing after one month which was statistically significant (p = 0.0177). The difference in clearing between group 1 and group 3 was significant for the immediate reaction (p = 0.0003), there was almost no difference in clearing after one month between the first and the third group (p = 0.0449). There was a difference seen in the immediate clearing between groups 2 and 3, which was significant (p = 0.0003). After four weeks there was no difference between the two groups (p = 0.670). Within the age group 20-49 years, there was a drop in the immediate clearing and in the clearing after one month. In the age group 20-29 years, there was an immediate clearing of 86% and 100% clearing after one month; in the age group 30-39 years, there was an immediate clearing of 80% and 90.5% clearing after one month; in the age group 40-49 years, there was an immediate clearing of 70.1% and 80% clearing after one month. In the older age groups there were not enough patients participating, so the result had to be discounted. The signed rank Wilcoxon test showed an improvement in the immediate clearing compared to the clearing after one month only in age group 30-39 years (p = 0.0005) and in the age group 40-49 years (p = 0.0002) (Table II). Concerning the side-effects, in 20 patients, only hyperpigmentation was seen, 9 patients showed erythema combined with hyperpigmentation, 2 patients showed hyperpigmentation and a blister, and in 3 patients erythema was visible followed by hypopigmentation. One patient just experienced hypopigmentation and 5 patients just erythema (Table III). There was none of the telangiectatic matting seen with sclerotherapy, which is a common problem. During the treatment period no thombophlebitis was seen. In the follow-up period, brown-red spots were seen in 12 patients with erythema. None of our patients devel-

Table I. Differences in immediate and after one month clearing

Group 1: size < 0.2 mm				Group 2: size 0.2-0.5 mm				Group 3: size 0.5-1 mm			
Patient	Age	Imm. (%)	4W (%)	Patient	Age	Imm. (%)	4W (%)	Patient	Age	Imm. (%)	4W (%)
1	47	100	80	1	47	80	60	1	47	70	40
2	45	90	90	2	45	70	60	2	45	70	60
3	54	80	60	3	54	50	30	3	54	40	20
4	30	100	100	4	30	90	60	4	30	70	60
5	48	80	80	5	48	60	50	5	48	50	60
6	61	80	90	6	61	80	60	6	61	50	70
7	40	70	80	7	40	60	50	7	40	60	60
8	31	100	100	8	31	100	60	8	31	80	70
9	49	100	80	9	49	90	40	9	49	60	60
10	38	90	90	10	38	90	50	10	38	50	60
11	39	70	90	11	39	70	90	11	39	40	80
12	41	60	80	12	41	50	80	12	47	20	80
13	44	70	80	13	44	50	80	13	57	20	70
14	47	50	80	14	47	50	80	14	51	10	30
15	40	80	100	15	32	70	80	15	32	60	90
16	40	50	70	16	40	40	60	16	40	40	70
17	43	70	100	17	43	70	80	17	43	40	60
18	46	60		18	43	50	70	18	44	50	70
19	33	40	80	19	33	30	60	19	44	60	100
20	44	40	70	20	44	40	60	20	46	60	70
21	44	100	100	21	44	100	100	21	48	60	100
22	46	100	100	22	46	100	100	22	30	60	100
23	30	100	100	23	30	100	100	23	30	100	100
24	30	100	100	24	30	100	100	24	72	70	100
25	72	100	100	25	72	100	100	25	49	70	100
26	49	70	100	26	49	100	100	26	37	60	100
27	37	70	100	27	37	100	100	27	28	60	100
28	28	100	100	28	28	100	100	28	49	60	100
29	49	100	100	29	46	100	100	29	46	60	100
30	46	100	100	30	36	80	100	30	36	70	100
31	36	100	100	31	55	80	100	31	55	60	100
32	55	70	100	32	31	100	100	32	31	70	100
33	31	70	100	33	24	80	100	33	24	100	100
34	24	80	100	34	31	100	100	34	31	70	100
35	31	80	100	35	33	100	100	35	33	70	100
36	33	80	100	36	41	100	100	36	41	60	100
37	41	100	100	37	39	100	100	37	39	70	100
38	39	100	100	38	43	70	80	38	43	100	100
39	43	100	100								
mean		82.0	92.1	mean		78.9	80.0	mean		59.7	81.1
standard deviation		18.5	11.2	standard deviation		21.9	21.4	standard deviation		19.4	22.5

Imm. - immediate clearing; 4W - clearing after 4 weeks.

Table III. Side-effects

	No side effects	Erythema	Blister	Total
No side-effects	75	0	0	75
Hypopigmentation	1	3	0	4
Hyperpigmentation	20	9	2	31
Erythema	5	0	0	5
Total	101	12	2	115
	(87.33%)	(10.43%)	(1.74%)	(100.00%)

oped scarring. In those patients who were dark in colour or sun-tanned, temporary depigmentation in the total probe area was seen. No compression therapy was given for the leg telangiectasias. The same lesions were treated on each occasion. Generally 2-3 treatment sessions were necessary.

Table II. Difference in response according to each age group

	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	> 70 years
n	6	40	55	8	3	3
Mean age	26	33	44	54	61	72
Immediate response	86%	80%	70%	51%	70%	90%
Four week response	100%	90%	80%	63%	73%	100%
p-value	0.25	0.005	0.0002	0.26	1.0	1.0

Discussion

In our combined study at four international laser centres, we have shown that the PhotoDerm®VL is an excellent device for treating leg telangiectasias. Other studies have shown that the PDL is effective for treating leg telangiectasias up to 0.2 mm in diameter.[2] The PhotoDerm®VL was successful for the treatment of leg telangiectasias up to 1 mm diameter. The treatment showed fewer complications such as telangiectatic matting and hyperpigmentation, which are usually seen with sclerotherapy and other laser device. Red blood cells are the targets, which undergo morphologic changes during treatment with the PhotoDerm®VL. Pulse duration and delay between pulses and double pulse sequences depend on the diameter of the vessels and the thermal relaxation time.[16] The very large spot size enables much deeper light penetration into the skin. For years it has been known that port wine stains are much better treated with a pulse duration from 1 ms to 10 ms, although there had been no possibility of implementing this practically in therapy until the PhotoDerm®VL was developed. By splitting the energy into 2 or 3 pulses with different pulse delays, the skin can cool in between. This results in fewer side effects in the surrounding tissue. Using these pulse sequences, purpura, which is common with the PDL, does not appear even when high frequencies are used. The intense, pulsed light source has the following additional advantages.

The wavelength can be produced with cut-off-filters ranging from 515 to 590 nm. Vessels require different wavelengths for optimal treatment. Deeper penetration into the skin can be performed with longer wavelengths. The pulse duration can be varied between 2 ms and 25 ms so that the energy can be applied to the vessel with a degree of control. Flexibility is the great advantage of the PhotoDerm®VL. This makes an individual treatment for every patient possible. We can conclude from our experience with the PhotoDerm®VL that the user needs a lot of experience with this device to become familiar with all the possible settings. The choice of settings depends on the individual requirements of the patient's condition. Using the PhotoDerm®VL, the pulse type, pulse durations, pulse delays and fluence depend on the diameter, the colour, the depth of the vessel and on the skin type. These parameters have to be investigated before treatment. It seems that particularly the relatively low energy settings will avoid extravasation of erythrocytes. The lack of purpura is one of the important reasons that hypopigmentation is avoided, a side- effect that is often seen with sclerotherapy and PDL.

Leg telangiectasias related to chronic venous insufficiency demand proper investigation of reflux in the venous system. The combination of LRR and ultrasound-Doppler is very useful to exclude serious hemodynamic venous problems. Major reflux always has to be treated first. Long-lasting results will only be obtained in patients if reflux and feeder veins are treated first[17].

As our own experience shows, patients with perforators need more treatments and also higher energy treatments to damage feeder veins effectively. Because of the wavelengths, some melanin will be absorbed in the epidermis, therefore sun-tanned patients should be informed about the possibility of temporary hypopigmentation. In our study, hypopigmentation in each of the 4 patients affected disappeared within 3 to 6 months, Furthermore, we conclude that the PhotoDerm®VL seems to be the treatment modality of choice for leg telangiectasias up to 1 mm in diameter. Our own research (unpublished result) shows that veins larger than 1 mm in diameter, typical of reticular and feeder veins, will be able to be treated in the not-to-distant future with the PhotoDerm®VL. More research in needed to optimise the treatment parameters.

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CHAPTER 9

Effective treatment of nevus of Ota with Intense Pulsed Light Source after incomplete clearance with Q-switched Ruby laser

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Abstract

Introduction: The nevus of Ota is a pigmented lesion occurring normally along the distribution of the fifth cranial nerve. Earlier dermabrasion, freezing and laser irradiation have been used for its treatment. There are no reports of its handling using the Intense Pulsed Light Source (IPLS).
Patients and methods: Three case reports of patients with a diagnosis of nevus of Ota are presented. All of them had been treated with Q-switched ruby laser prior to treatment with IPLS. Initially an evaluation of the skin reaction to IPLS was conducted, which was later followed by a complete treatment.
Results: Treatment intervals tended to be longer than those with the Q-switched ruby laser. Oedema occurred and lasted for up to 24 hours. No erythema was noted after treatments. There were no permanent pigmented changes.
Discussion/Conclusion: Treatment of nevi of Ota using IPLS is effective, however, many treatment sessions are necessary; even after partial treatment with Q-switched ruby laser. On the other hand there are no permanent side effects and the cosmetic result is better in comparison to the lasers.

Keywords: IPLS, laser, nevus of Ota.

Introduction

The management of pigmented lesions by lasers is a relatively new field in dermatology. However, within a short period of time, a wide range of applications for different types of lasers has been found. Nevus of Ota was first described by Ota and Tanino in 1939.[1] Usually nevus is unilaterally located and found situated on the sclera as well as somewhere along the course or distribution of the trigeminal nerve, in the skin and tissues innervated by the first or second branches.[2] Studies done on ocular findings in Japanese women with nevus of Ota showed some changes in the optic disc.[3] This, however, did not interfere with visual acuity.
Nevus of Ota is thought to occur mainly in the people of Asian descent but it also occurs in people of African and European descent. The consequences of the lesion are mainly cosmetic although other more adverse effects may occur for instance chronic glaucoma.[4,5]
More recently another classification has been offered based on therapeutic response of the nevus specifically to laser therapy.[6] This classification can be used to predict clinical outcome unlike other classifications employed before. In designing this classification the peri-orbital under-response was used (panda's sign), defined as the degree of peri-orbital laser clearing significantly less than clearing in other areas. Ueda *et al* also noted variation in response to Q-switched ruby laser therapy based on the colour of the lesion. The best results were obtained with brown lesions while blue-green lesions were the most difficult to treat.[7] Other researchers using the Q-switched Alexandrite laser have found that the depth of the lesion was more important than the colour in determining outcome of the treatment, lesions < 1mm in depth give good to excellent results. Blue-black nevi tended to show deeper infiltration of melanocytes into the dermis than the dark brown nevus. However, it was concluded that colour itself was not a reliable indicator for predicting therapeutic outcome.[8]

Several modes of therapy have been used in the treatment of nevus of Ota including dermabrasion (nevus of Ota-like maculae),[9] freezing,[2,10] and skin grafting. Patients may also use cosmetic foundation or obtain cosmetic tattoos. Different types of lasers have now been added to the choice of therapies for the nevus.

Lasers have already been shown to be effective in the management of pigmented lesions. These include the Q-switched Ruby,[2,7,11] Alexandrite,[12,13] and Nd:YAG[14,15] lasers which have been successfully used. The quality-switched lasers produce very short pulses of very high energy. This increases the photo selectivity. The pulse duration is shorter than the tissue relaxation time of the target chromophore.[14] This means that high energies can be delivered with enough time for cooling so that surrounding tissues are not adversely affected. Histological studies have shown that Q-switched Alexandrite laser irradiation fragments the melanosomes present in dermal melanocytes leaving behind empty spaces in the form of vacuoles. This occurs secondary to a photo-acoustic event, the high energy delivered in a short pulse creates a high-energy gradient, which then acts as a mechanical wave causing shattering of the target. No damage is seen in surrounding tissues.[12]

Ono et al ranked therapeutic effectiveness of Q-switched ruby laser in 14 patients: 6 were judged excellent, 5 good, and 3 fair.[11] Taylor et al reported treating nine nevi with 65 treatments using Q-switched ruby laser with significant cosmetic improvement.[2] In another study 151 patients were treated, depending upon the predominant colour of the lesion.[7]

Kunachak et al in a follow-up study of treatment of bilateral nevus of Ota-like maculae after irradiation with a Q-switched Nd:YAG laser found that clearance of 100% after a mean of 2.8 treatments (range: 2-5) was maintained over a mean of 42 months of follow-up in 68 patients.[15]

Up to now no published literature has reported on the use of the Intense Pulsed Light Source in the treatment of nevus of Ota. The Intense Pulsed Light Source has already been applied in the treatment of other benign pigmented lesions, based on the same principle of selective photothermolysis.[16,17] It is a versatile system capable of delivering high energies by trains of short pulses. It is therefore likely that this is an ideal system for the management of nevus of Ota lesions. Presented are case reports of patients with nevus of Ota, which did not improve after several Q-switched ruby laser sessions and were successfully managed by IPLS.

Patients and methods

Three cases of nevus of Ota are presented here for discussion. All were initially treated using a Q-switched ruby laser (694nm, 40ns) followed by treatment using the Intense Pulsed Light Source (IPLS). The first patient had 4 Q-switched ruby laser sessions and 14 IPLS, the second patient had 6 treatment sessions with Q-switched ruby laser and 12 with IPLS. And the third patient had 2 Q-switched ruby laser sessions and 3 IPLS treatments, which are still continued.

Intense Pulsed Light Source

PhotoDerm®VL was used. This IPLS uses incoherent light of a broad band spectrum in the range of 500-1200nm. By applying different cut-off filters (515, 550, 570, 590, 615,

Figure 1. After 5 times with ruby laser .

Figure 2. After 8 times with IPL whole face.

Figure 3. After 8 times treatment with IPL.

695, 755 nm), a specific part of the shorter wavelengths (below the indicated filter) can be filtered off. The use of different cut-off filters allows adjusting the treatment parameters to the patient's skin type; using longer filters, which control the spectrum at higher wavelengths, results in reduced overlap with the higher absorption coefficient of melanin, the concentration of which depends on the skin type.

For skin types IV-V, pulse times >4 ms and energy of 22J/cm^2 and above were used. For skin type V double pulses with a delay of 30ms were used. For all the three patients the wavelength of 590 nm was used.

A cooling gel is used on the skin during the IPLS treatment that allows good optical coupling of the light to the patient's skin and also better heat transfer from the epidermis to the cold gel.

The intervals between different sessions varied from 3 to 6 months.

The size of the IPLS treatment head (8x35 mm) plays an important role in improving light penetration into the tissue since the large spot size diminishes the scattering.

Case Reports

Case 1

An 18-year old woman was referred to the department with a congenital lesion on her forehead and left cheek for which a diagnosis of nevus of Ota had been made by the dermatologist. There was no family history of a similar lesion. She had not been treated elsewhere for the same problem. Local examination of the frontal area showed a dark blue lesion 10 x 4 cm in size on the left side. In the left buccal area a similarly coloured lesion of 5 x 6 cm was seen which extended medially onto the nose. In the department she was initially treated using a Q-switched ruby laser. A test spot in the frontal area was first made using 8 J/cm^2. There were no side effects noted. She was treated a year later at irregular intervals using energies ranging between 8.5-20J. Based on dissatisfying results she was then treated with IPLS. She received 11 treatments at intervals of 6 to 8 weeks. A cut-off filter of 590nm was used throughout the treatments. After these treatments the lesion on the cheek cleared about 95% and there was significant lightening of the frontal lesion. This was maintained over 6 months of follow-up. Photographs were taken before and after the treatment. (Figures 1,2,3)

Case 2
A 25-year old man was referred by his General Practitioner with a history of a dark pigmented patch around the right eye extending into the temporal region on the same side. It had appeared when the patient was 7 years old. There was progressive worsening of the lesion and at 13 years of age his dermatologist diagnosed it as nevus of Ota. There was no family history of a similar lesion. He denied that the lesion had caused him any psychological problems. He was initially treated with a Q-switched ruby laser. He received 11 treatments over a period of 22 months at irregular intervals using energies ranging between 7–20 Joules. The inter-treatment interval was based on the extent of the lesion covered during the treatment and individual response to the treatment. The Q-switched ruby laser did not give uniform results – spotting occurred within the lesion. He was then treated using the IPLS. After 7 treatments with the IPLS there was significant lightening of the lesion. A cut-off filter of 590nm was used for all treatments with a pulse of 5 ms and low energy. A clearance of about 90% was achieved.

Case 3
A 26-year-old woman was referred to the Medical Centre with a dark coloured patch under her left eye, measuring 2X5X0.8 cm, which had been present since birth. She had another hyperpigmented patch on the right shoulder and on the upper arm present since puberty. A diagnosis of nevus of Ota was made by the dermatologist. The patient was initially treated using the Q-switched ruby laser. But due to side effects leading to discoloration, she was switched over to IPLS. After three treatments she showed an improvement of about 80%. The patient is still being followed up to receive further treatment with IPLS as this paper is written (Figure 1, 2 and 3).

Discussion

The purpose of treating nevus of Ota lesion is by and large a cosmetic one. People with these lesions are known to be stigmatised by societies in which they live and this has adverse psychological consequences for each of them. Unlike concerning the treatment of congenital and dysplastic nevi, there is less controversy in the literature surrounding the treatment of nevi of Ota using lasers and other light sources.[18] This is because nevi of Ota are not associated with increased risk of malignant transformation. Therefore treating these lesions would not interfere with the monitoring of a possible malignant transformation.

We began treating the three patients with a Q-switched ruby laser initially. But the results obtained were not uniform, there was a spotty appearance and the presence of discoloration and hyperpigmentation was seen; therefore we switched to IPLS. Although the treatment using IPLS takes many sessions, the advantage is that an optical homogenous fading of the pigment was achieved.

The possibility of occurrence of side effects such as pigmental changes is virtually eliminated because of the versatility of the IPLS in catering to individual patient characteristics. A treatment session consists of an initial assessment of the skin reaction by a test spot. This reaction determines the parameters to be used in treating the lesion of the patient. In all three cases presented here significant improvement (lightening) of the lesions was demonstrated after treatment with IPLS. A distinct advantage of IPLS was the larger treatment head (2.8 cm^2), which allowed the entire treatment area to be covered in a single session in comparison to the Q-switched ruby laser with a limited spot size of 5mm. In addition a more uniform result could be obtained for the same reason. With the ruby laser an entire area was covered over a number of days and this also created variation in the intervals between treatments. The intervals between treatment sessions became more definite with the IPLS. In the cases presented here the intervals tended to be longer than those between the ruby laser treatments. The intervals are important as the maximum effect of a single treatment becomes fully apparent in about three months. This has been shown histologically following treatments using the Q-switched Alexandrite laser.[12] This is the duration of time in which particles from destroyed melanosomes are phagocytosed and mobilised by macrophages in the dermal tissue. Kunachak *et al* used shorter intervals between treatments while treating nevus-of-Ota-like macules with a Q-switched ruby laser.[15] Their objective was to retreat lesions before epidermal repigmentation had occurred, thus eliminating the barrier effect to laser light of epidermal melanin. This approach remains controversial and probably causes more permanent pigmental changes.

The wavelength of 590nm was used in all the patients presented. This wavelength has been reported to be effective in the treatment of Nevus Spilus using the IPLS.[19]

During treatments using IPLS on our patients, oedema occurred and lasted for up to 24 hours before resolving. There was no occurrence of erythema. Brown-grey crusts formed after the treatment, which fell off later. The odd case of hyperpigmentation was transient and was dependent on the dose of energy used. This may occur as a post-inflammatory phenomenon, but has also been thought to be a reactive process occurring in (deeper localized) partially damaged melanocytes.[20]

We conclude that the IPLS offers a new possibility for the treatment of nevus of Ota and it can also be used to improve the skin structure after previous treatment with other lasers for pigmented lesions. Summing up it can be noted that using IPLS to treat nevi of Ota takes more sessions than using lasers, but there are no permanent side effects and the cosmetic results are better.

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CHAPTER 10
DISCUSSION

This thesis is the result of several studies in which flash lamps, also known as Intense Pulsed Light Sources (IPLS) are used to treat various dermatological conditions. Seven major questions were raised as summarised in Chapter 1, and each was answered in the cumulative research project.

Before the introduction of IPLS, lasers were a widely used device for major dermatological indications. The major progressions of laser are summarized in Table 1.[1-13] Lasers are a perfect complement to IPLS, and for certain aesthetic challenges, IPLS technology provides a refining touch to laser procedures. IPLS technology employs full spectrum, non-coherent light and low-range infrared radiations that are filtered to allow a specified range of wavelengths. This filtered light is delivered from a hand piece into the skin, where it targets different chromophores such as melanin in the hair sheath and haemoglobin in the capillaries. Thermal and/or mechanical damage to the hair follicle results while sparing surrounding tissues in a process known as selective photo-thermolysis. The filters can be adjusted to match the patient's skin type and the target lesion. As the light energy is target specific, adjacent tissue is spared, and the possibility of scar formation is decreased. Due to the nature of the treatment, intense pulsed light (IPLS) energy can be applied to the surface skin layers for gentle and gradual results with reduced side effects and patient downtime.

Flashlamps started to be used for medical purposes in the 1960's with published data on treating eye and skin disorders emerging in the latter half of the decade.[14,15] By the mid-1990's, researchers were exploring the use of flashlamps for treating vascular lesions, and in the year 1995, the FDA cleared the first flashlamp for the treatment of vascular lesions.[16]

Little information is available about the mechanisms of flash lamp action into the skin, and one of our questions was to elucidate the post-treatment effects of IPLS. To solve this question we started an experimental study on 2 pigs with a given protocol. We investigated the histology of the epidermis, dermis and subcutaneous fat immediately after treatment, one and two day's post-treatment and, after 1 week, 2 weeks, 1 month, and 3 months post-treatment. Our study showed that IPLS targets several components including pigment, vessels and hair.

Another histological study aiming to understand the effects of IPLS on transforming growth factor beta (TGF-b), and extracellular matrix proteins in the skin was also carried out in our clinic. This showed that TGF-b in the epidermis increases to the outermost layers one week post IPLS treatment while tenascin expression increase begins one day after treatment at the epidermal/dermal layer and remains for about two weeks. These findings support the hypothesis of growth factor stimulation following IPLS treatment. Additional investigations regarding this point are currently ongoing in

our clinic (data unpublished). These findings also suggest that due to targeted heat in the skin post treatment, vessel dilatation occurs and this increased blood flow transports growth factors and/or their receptors to the wound healing area. These stimulate collagen and elastin production leading to a better skin texture.
Skin rejuvenation and skin improvement are in demand by patients worldwide. Today the flash-lamp is increasingly used to permanently remove or greatly reduce the appearance of blemishes and for skin rejuvenation. All aspects of photo-damage including wrinkling, skin coarseness, irregular pigmentation, pore size, and telangiectasias showed visible improvement.[17-21] The results for superficial skin problems such as skin pores, acne scars, and superficial wrinkles are encouraging; however, there is much more going on in the skin compared to what we macroscopically see. In one study by Negishi et al., forty-eight full-face photo-rejuvenations for Asian patients was carried out in Japan.[22] After the fifth treatment, a combined rating of greater than 60% improvement was given to more than 80% of patients for pigmentation improvement, telangiectasia reduction or removal, smoother skin texture, and overall improvement. Histological evaluations showed strong staining of Type I and Type III collagen in the upper dermis indicating new formation of collagen. There is an increasing demand for a safe, effective, and long-term hair removal method. One study noted hair loss as a side effect of treatment with IPLS.[13] This side effect promoted research into the area of hair removal. An ever-increasing number of published studies have confirmed the long-term efficacy of flash lamp treatment in removing hair. Some of our studies support this claim including a study with 40 hirsute women completed in 1999 that showed effective hair removal in these 40 patients with a 76% of clearance.[23]
Perhaps Tse gives the best overview regarding the clinical data in hair removal,[24] however, most of the studies published on hair removal have a follow-up of a few months, therefore no conclusion is possible on long lasting hair removal.[25-34] According to the FDA, a one-year follow-up is sufficient to claim permanent hair removal. From our experience we conclude that long-lasting hair removal can be demonstrated after a two-year hair free period in the treated area. One of our studies published in 2004 in the J Derm Surg showed a clearance of 87% after 27.3 months in 70 hirsute women, which confirms our findings on long lasting hair removal with IPLS.[35]
The possibility of permanent hair removal is important for transsexual patients as well. In another study by our group, we have shown "satisfactory" results of 90% clearance of hair removal in a group of 25 transsexual patients.[36] This study proved that hair removal with IPLS is cheaper, shorter in duration, has less side-effect and is more suitable for the patients than hair removal with needle epilation.
The challenge still remains to eliminate light-coloured hair as well as the capability to safely treat individuals with darker skin. The rapid movement of technological advancement as well as continued studies of hair follicle biology promise to improve this field over the years to come. Recent observations are made that IPLS offers the option for hair removal of blonde hair when double treatment in one session is carried out (own observation). A very recent new development - the combination of light (IPLS) and radio frequency (RF) - provides good results and gives an added benefit of fewer required treatment sessions in comparison to any devices used previously. Whether this device is superior to the former systems has to be proven in further studies.
Since IPLS is approved to clear vessels, our next question was to determine whether IPLS can be effectively used for vascular lesions. Indeed, the wide range of treatment parameters, have been used in the treatment of cavernous hemangiomas, venous

Table I: Laser and flashlamp treatment studies

First author	Machine used	No. of pat.	Treatment	Result	Follow-up	Skin type
Laser treatment studies						
Brunnberg[1]	Alexandrite laser	20	Leg vein telangiectasia	In 15/20 a clearance of 26-75%	3 months	I-III
Omura[2]	Nd:YAG laser	20	Reticular veins	2/3[rd] of (1-3mm diameter) vessels- >75% clearance	3 months	
Spendel[3]	KTP laser	70	Spider leg veins	Variable clearance	7,5 months	
Kaudewitz[4]	diode laser	20	Leg vein telangiectasia	50-75% clearance	12 months	
Sarradet[5]	Nd:YAG laser	15	facial telangiectasia	Moderate to significant improvement	3 months	
Clark[6]	KTP laser	204	Facial telangiectasia, spider angioma	90-98% improvement	24 months	I-III
Kelly[7]	Pulsed dye laser	20	Port wine stains	Variable from <25 to >75% blanching	—	
Westerhof[8]	Ruby laser	12	Melanocytic nevi	100% removal of all flat lesions, others partial response	12 months	
Levy[9]	Nd:YAG laser	29	Unwanted facial hair	46% hair reduction	9 months	
Sadick[10]	Diode laser	24	Unwanted hair	79% hair removal	6 months	II-IV
Keller[11]	KTP laser	62	Glabellar frown lines and forehead creases	Effective skin rejuvenation	18 months	
Lee[12]	KTP and Nd:YAG lasers	150	Mild rhytides and skin toning	Mild to moderate degree of improvements	18 months	I-V
Hellwig[13]	Ruby laser, pulsed dye laser and Photoderm®VL	100	Vascular malformations and benign pigmented lesions	Excellent results		
Flashlamp treatment studies						
Bitter[17]	IPLS	49	Photo rejuvenation	Visible improvement		
Goldberg[18]	IPLS	30	Rhytides	Some improvement	6 months	I-II
Hernandez-Perez[19]	IPLS	15	Striae distensae	Clinical improvement		
Weiss[20]	IPLS	80	Photoaged skin	Long lasting improvement	48 months	I-IV
Ho[21]	IPLS	19	postburn hyperpigmentation	50-75% clearance	32 months	
Negishi[22]	IPLS	73	Full face photorejuvenation	60% improvement		Asian pat.
Schroeter[23]	IPLS	40	Unwanted hair	76.7% hair reduction		
Gold[25]	Epilight	37	Unwanted hair	60% hair removal	3 months	
Gold[26]	IPLS	24	Unwanted hair	75% hair reduction	12 months	
Weiss[28]	IPL	23	Unwanted hair	33% hair reduction	6 months	I-III
Raulin[32]	Photoderm®VL	14	Essential telangiectasia poikiloderma of Civatte	Excellent results		
Schroeter[35]	IPLS	70	Unwanted hair	87% hair removal	27.3 months	I-V
Schroeter[36]	IPLS	25	Unwanted hair in transsexuals	90% hair reduction	44 months	
Schroeter[38]	Photoderm®VL	120	Vascular skin lesions	90% clearance		
Angermeier[39]	Photoderm®VL	200	Facial vascular lesions	75-100% clearance	2 months	
Raulin[41]	IPLS	37	Port wine stains	70-100% clearance		
Weiss[42]	IPLS	135	Poikiloderma of Civatte	75% clearance		
Goldman[43]	IPLS	66	Poikiloderma of Civatte	50-75% clearance		
Goldman[44]	IPLS	159	Leg veins	50-100% clearance		
Schroeter[45]	IPLS	40	Leg veins	74-92% clearance	12 months	I-III

malformations, facial telangiectasias, spider nevi, the vascular part of poikiloderma of Civatte, and leg telangiectasias with great success. Facial veins were found to clear up to 100%.[37-39] The fading of port wine stains depends on the thickness, colour, localization of the lesion, age of the patient and the pre-treatment conditions [40,41] and excellent results have been achieved worldwide using IPLS for port wine stains (PWS) and facial telangiectasias. Poikiloderma of Civatte on the face and neck are a challenge to treat with flashlamps.[42,43] If both a pigmented and vascular component are present, the pigment has to be treated first due to its localization in the skin. If only a vascular component is present, a clearance can be gained of up to 90% (personal observation).
Leg telangiectasias remain a difficult problem to treat due to different factors such as variations in anatomic microcirculation, thickness and pigmentation of the skin. A light source such as IPLS that produces a non-coherent light as a continuous spectrum longer than 550 nm has certainly more advantages over a single wavelength laser system. First, both oxygenated and deoxygenated haemoglobin will absorb at a combination of wavelengths. Second, blood vessels located deeper in the dermis will be affected. Third, thermal absorption by the exposed blood vessels occurs with less overlying epidermal absorption since the longer wavelengths penetrate deeper and are absorbed less by the epidermis. Leg vein results range between 50 -100% clearance are a potential new indication for flash lamps if the user is experienced with the technology,[44,45] Table I. [17-45]
Following the excellent results we obtained in treating facial lesions, we pioneered the treatment of rosacea with IPLS in 1998 which was not previously treated with lasers or such similar devices. Rosacea patients are traditionally treated with local systemic and antibiotics for a few months. Rosacea is a good example of an indication that can be successfully treated (even when treatment resistant) using a combination of IPLS with locally applied medicines.
The final question we addressed was whether IPLS is also a new treatment possibility for pigmented lesions, and indeed it is when treatment is given by a highly trained individual. Nevi respond better to lasers than flash lamps. In the author's opinion, Becker's nevi do not respond well to treatment with either lasers or flash lamps. Lentigines, ephilides etc. do however respond well. Melasma, if epidermal, requires a lot of care to treat effectively and avoid unwanted treatment-related side effects. Pigmented lesions should be treated with long intervals of up to 3-4 months. Nevus of Ota is a potential new indication for IPLS treatment, but it might require more treatments using flashlamps compared to lasers; however, the lesion will be much more equal and less spotty after the IPLS treatment. In erythrosis interfollicularis colli one should first treat the more superficial pigmented part if present, and then the vascular part (personal observations).

Guide lines

Technical data

IPLS is currently used to treat a variety of skin indications as well as for hair removal, and has several distinct advantages over lasers arising from its flexibility in allowing a wide range of settings relating to individual patient characteristics. Modification of various parameters that include (but are not limited to) wavelength, fluence, pulse du-

ration, pulse delay, pulse sequence and temperature control of the skin, gives a lot of flexibility. The use of the IPLS device saves time and costs because it can treat surfaces of 2.8 cm^2 to 5.6 cm^2 per pulse. Another cost benefit of IPLS over lasers is the fact that one IPLS device can treat a multitude of indications where as several different laser devices would be required to treat the same set of indications.
Another desirable property of flash lamp technology is the possibility to split an individual pulse into a maximum of 5 partial pulses. Each pulse can be adjusted to its own fluence level and the 2 to 4 in-between delays can be of varying duration. Multiple pulses can be effectively used in darker skin types as the epidermis can be cooled down during the delays. Despite this cooling, there is still enough available heat in the target area so that the next pulse delivered has an additive effect in increasing the heat more rapidly and extending the heat from the absorber, such as haemoglobin, to the target which is the vessel wall.
The initial cost of the devices and of the procedures is cheaper to that of comparable lasers.

How to use a flash-lamp

Flash lamps offer extensive treatment flexibility but care must be taken to select the proper wavelength which is determined by the colour and depth of the target. For example, if a red oxygenated facial vessel, 0.5 mm diameter is to be treated, a "cut-off" filter of 550 nm is used, due to the colour absorption of HBO_2 at 540 nm. Furthermore, pulse durations of 5 ms and greater are applied. If the target vessel is a thick blue vessel on the wings of the nose, multiple pulses are used in combination with a "cut-off" filter of 590 nm and pulse durations of 5 ms depending on the size of the vessels. Thus, various vessels can be effectively treated with the same flash-lamp due to the flexible parameter settings.
Multiple pulses are also useful in the treatment for deeper located leg telangiectasia. Triple pulses can be applied, referring to the diameter and the depth of the vessel, and pulse delays of 20-50 ms between the pulses can be defined according to the skin type bypassing the epidermis (due to the delay the epidermis is cooled down). Using multiple pulses, less fluence is needed for a partial pulse time to damage the endothelium of the target vessel wall. Biochemical and coagulation mechanisms then follow. In smaller leg veins with a diameter of 0.5 mm, oedema around the vessel is found immediately after treatment, which helps to occlude the vessel (personal observation). After a few weeks the treated vein is replaced by fibrous tissue which is a palpable cord-like structure.
The question remains as to whether all the various settings are necessary for effective treatment by any such flashlamp device. From a therapeutic and scientific point the answer is yes. Due to their great flexibility, multiple medical indications can be treated with a single flash-lamp device, which is a clear benefit over lasers, which must be matched with a specific indication to be effective. It is important that the physician makes the correct decision on the parameters such as wavelength, fluence, pulse type and duration including spot size for each patient treatment session (Table II). It is necessary to select specific parameters every time before treatment of an individual patient, independent on the previously applied parameters. Such is not the case with the use of lasers due to their limited flexibility.
Using the combination of all the flash-lamp settings results in:

a) Flexibility in a broad range of treatment possibilities
b) Faster results and a higher success rate in the clearance of the targets
Indeed IPLS is a revolutionary new mini-procedure, which is able to diminish or fully rid one of age/liver spots, fine wrinkles (rhytides), facial flushing, redness, broken capillaries, telangiectasias, hemangiomas, freckles, minor sun damage, port wine stains, tattoos, varicose veins, spider veins, flat birth marks, hyper-pigmentation and even hair removal. When combined with the relatively low cost of flash-lamps in comparison to lasers, the ease of maintenance, and the flexibility of treatment parameters, this makes IPLS an ideal tool for dermatological therapy.

Table II: Parameters used for skin lesions treated by flashlamps

Indication	Skin type	Wavelength (nm)	Pulse time (s)	Difference	Energy (J/m^2)
Vascular Lesions					
Facial telangiectasia	I-III	550/570	4-5		26-32
Rosacea	I-II	550	5	20	28-36
PWS: light	I-II	590	= 6		35
Dark	I-II	590	= 6		
Papula	I-II	550/570	4		30-36
Spider veins	I-II	550	> 8		30-40
Leg veins: red	I-II	590	4	20	30-40
Blue	I-II	550	4	20	30-40
Pigmented Lesions					
Lentigines	III	570	4	20	30-40
Hair removal:	I-II	655	7-7	60	26-36
	III	655	7-7	80	26-36
	IV	655	7-7	80-100	26-36
	V	750	7-7	100-120	26-36
	VI	750	7-7	> 150	26-36

The standardized evaluation of IPLS treatment results

Currently, there is no objective system or scale that is validated for the evaluation of laser or flash-lamps treatment results. Both patient- satisfaction and the judgement of a physician are used in evaluation of therapies, but an objective scoring of the results following treatment with flash-lamps or lasers is urgently needed. In our studies, standard photographs were taken in patients with vascular lesions, using a Minolta camera outfitted with a 200mm objective, before the treatment as an overview of the face, joined by the sides of the skin lesion after the 3rd, 5th and last treatment. These photographs are scored by 2 independent physicians and the patient as well.
Leg veins were assessed before treatment with Doppler-Ultrasound and photoplethysmography to exclude functional reflux. Photographs and measurements were taken before treatment, and the diameter of the vessel was determined with a transparent ruler.
For hair removal, photographs were taken before treatment, after the 3rd, and last treatment. The photographs were evaluated by two independent physicians. Additionally, hair counts were performed as an objective scoring system for successful epilation. Since the cosmetic satisfaction of a patient is an important aspect in most

laser and flash-lamp treatments, the patients' satisfaction of the treatment is also evaluated.

Limitations

Additional limitations that remain to be addressed in the effective use of flash-lamps include:

- Manufacturing companies should be aware to sell machines only to qualified and trained medical staff
- Depending on the variability of the treatment settings, limitations and protocols of the applied parameters are necessary and should be carefully defined
- Laser and flash-lamp systems users do need a high standard of qualification
- Technical data including wear of "cut-off" filters, head filters, fibres should be known
- Long learning curve is necessary

Taken together these facts dictate the involvement of a treating physician who is highly qualified including a training of at least one year, involving basic physics, histology, research and clinical application in the academic field. The Photoderm®VL is a commercially available flash-lamp device which offers all the aspects described above and can be effectively used by the trained physician.

Future aspects

An area of future research includes:

- The development of a device which analyses the clinical parameters of the patient's skin before and after each treatment. This data can be used to provide technical control and settings for flashlamp systems
- End filters
- The development of the combination of a low and high cut off filter
- The development of longer pulse times
- Better cooling systems
- Double or Triple pulse over layer treatments
- PDT
- Equal energy delivery by the condensator of the IPLS to obtain a full equal pulse in the wavelength spectrum and in energy

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CHAPTER 11

Summary

Introduction

This article deals with Lasers and laser-like devices such as flashlamps.
The word laser is an acronym for "Light Amplification by Stimulated Emission of Radiation". A laser is a source of light in the visible or infrared region of the light spectrum that emits rays with a high spectral density on a very small area. Various lasers have been used for a wide range of medical purposes. For example: CO_2 lasers are useful for treating disorders of skin surface texture and topography (wrinkles, scars, sun damage, benign skin appendages and rhinophyma). Vascular lasers such as the flashlamp pumped dye laser are effective for treating port wine stains, hemangiomas, telangiectasia, rosacea and spider naevi. Q-switched lasers, which allow ultra short high intensity pulses, are effective for removing tattoos and some benign pigmented lesions.
There are 3 essential components to a laser system. First is a Lasing medium, which may be a gas, crystal, liquid or a semiconductor. Second is a Source of Excitation for the lasing medium, for example, flashlamps or continuous light, radio frequency, high voltage discharge, diodes and in some cases another laser. Finally, Mirrors are needed to reflect the excited photons back into the resonant cavity containing the lasing medium.
As the lasing medium is excited, molecules are "pumped" to a higher energy level. Some of the excited molecules spontaneously decay back to the original lower energy, or ground state, releasing a photon, and if the photon is emitted in the right direction, it will hit one of the mirrors at the ends of the resonant cavity and be reflected back into the excited lasing medium. This excited photon can "stimulate" another excited molecule to decay back to the ground state, releasing another photon that travels in the same direction, which in turn is reflected back into the resonant cavity stimulating emission of even more photons. If most of the molecules in the lasing medium are in the excited state, termed as "population inversion", there is a net amplification of light energy.
The Q-switched laser is a laser in which the state of the device introducing important losses in the resonant cavity and preventing lasing operation is suddenly switched to a state where the device introduces very low losses. This increases the quality factor of the cavity rapidly, allowing the build-up of a short and very intense laser pulse. Typical pulse durations are in the nano second (ns) range.
Unlike ordinary light, laser light is coherent, collimated, and monochromatic. Coherent refers to the synchronized phase of the light waves, collimated refers to the parallel nature of the laser beam (laser light is emitted in a very thin beam with all the light rays parallel) and monochromatic refers to the single (wavelength) color of the laser beam.
Joule (J) is the total energy in a laser pulse or system, fluence is the dose stated in

J/cm^2, energy intensity is laser power per unit area, measured in W/cm^2, the wavelength is related to stimulated energy transition, the shorter the wavelength, the higher the energy of the photon, focal spot size determines the maximum energy density that can be achieved when the laser beam power is set, the depth of focus is the distance over which the focused beam has about the same intensity. Laser light is monochromatic, therefore it has a selective effect on biologic tissue, either being transmitted, scattered, reflected or absorbed. Light absorption must take place for there to be any biologic effect, and a given wavelength of light may be strongly absorbed by one type of tissue, and be transmitted or scattered by another. The components of the tissue are responsible for its specific absorption characteristics. The main absorbing components, or chromophores, of tissue are: hemoglobin in blood. melanin in skin, hair, moles, etc., water (present in all biologic tissues).

When light is absorbed, it delivers energy to tissue. An intense, but short pulse of laser light will usually cause an explosive expansion of tissue, or photomechanical reaction. A less intense, longer pulse will cause a rapid heating, or photo thermal effect. Selective photothermolysis is the process in which transfer of laser energy is restricted to a particular site because of the selective absorption of a chromophore.

One of the first lasers to be used clinically is the Argon laser whose light is strongly absorbed by hemoglobin and melanin but it shows significant non-selective heating in surrounding tissues, thus increasing the chance of scar formation.

YAG lasers use a Yttrium-Aluminum-Garnet crystal rod as the lasing medium. The Q-Switched Nd:YAG is effective in removing black tattoo ink. The Ruby laser emits red light with a wavelength of 694 nm. The lasing medium is a synthetic ruby crystal of aluminum oxide and chromium atoms, which is excited by flashlamps. Ruby laser light is strongly absorbed by blue and black pigments, and by melanin in skin and hair.

The pulsed dye laser (PDL) uses a lasing medium of Rhodamine dye which is excited by flash lamp. The Pulsed Dye Laser is useful to treat vascular lesions such as: cutaneous hemangiomas, port wine stains, cutaneous lupus erythematosus, oral granulation tissue and some vascular birthmarks.

A flashlamp is an arc lamp that operates in the pulsed mode and is capable of converting stored electrical energy into intense bursts of radiant energy covering the ultraviolet, visible and infrared regions of the spectrum. Xenon is used in most flashlamps, since it is the most efficient of the inert gases at converting electrical energy to optical energy.

There are two types - linear, or wall-stabilized; and bulb, or probe-stabilized.

One such well-known type is the linear xenon flashlamp. It consists of a quartz tube with two sealed electrodes - cathode and anode, made from tungsten or from special low-sputtering materials. A flashlamp is usually filled with the xenon gas at ca. 200 to 400 Torr pressure.

A typical energy load on a flashlamp is from a few Joules to hundreds of Joules. A flashlamp is, due to its dense spectra, somewhat similar to the sun spectra.

A flashlamp bombards a media with UV photons at extreme densities, thousands times as much as a continuous wave lamp does, it wipes out toxic chemical substances, bacteria etc. that are present in (or on) a treated media.

Flashlamp also known as intense pulsed light source (IPLS) is the perfect complement to lasers. Employing a broad spectrum of light energy in a range of wavelengths, IPLS supplies high levels of light power in millisecond bursts. IPLS devices also offer sophisticated, computer-driven precision and tremendous versatility. Due to the nature

of treatment, Intense Pulsed Light energy can be applied to the sub-surface skin layers for gentle and gradual results with reduced side effects and patient recovering time.
As mentioned earlier, flashlamps do not use one wavelength of light the way a laser does. Flashlamps emit every wavelength of light in the visible spectrum, and a little into the band of infrared radiation (up to about 1200 nm). Practitioners select a cut-off filter to block out lower wavelengths. Most flashlamps emit a beam that covers more area than a laser.
Flashlamp are currently used for the same field of indications in dermatology as lasers. These devices are capable of effectively treating pigmented skin lesions, birthmarks, facial spider veins, and leg veins, as well as for hair removal applications.

Transforming growth factor-beta and extracellular matrix stimulation using intense pulsed light systems: an experimental study

The skin's normal reaction to tissue damage is inflammation. Macrophages and neutrophils enter the wounded area and start to clean up foreign material and dead cells. Afters this, proliferation of fibroblasts begins, which also stimulates the synthesis of extracellular matrix (ECM) proteins. Several growth factors play an important role in this reconstruction process, including Transforming Growth Factor (TGF). One of the functions of TGF is the stimulation of the production of ECM proteins. Among the proteins TGF effects is the tenascin (TN) family of glycoproteins. These proteins are expressed in the adult during processes such as wound healing, vascular disease and tumour genesis.
Tenascin and TGF also play a role in the protection against various diseases such as cancer.
The aim of our study was to investigate the stimulation of TGF and the release of ECM proteins such as tenascin after radiation with intense pulsed light sources.
We treated two pigs on the back with the Vasculight® and the Quantum® light sources five times each according to the protocols. . At various intervals after each treatment punch biopsies were performed on the radiated back of the pig. A total of 240 biopsies were taken. The biopsies were examined microscopically and by immunohistochemistry.
Variations in the TGF levels corresponded to the time after treatment. Notably, one week and 60 days after treatment high levels of TGF-beta were observed.
Variations in the level of tenascin were also observed, two weeks post-treatment. A rise of the tenascin level in the epidermis and dermis and a fall of the tenascin level in the plama cells was found.
Thus it seems that radiation with a high-intensity flashlight provides Please double check if you mean flashlamp an exogenous stimulus to produce an artificial wound, which causes latent TGF-β and tenascin activation.

Hair removal in 40 hirsute women using an intense laser-like source

In this study the effective removal of hair was achieved without significant side-effects using an ILPS flashlamp emmitting non-laser incoherent light. The study involving 5 centres in Germany, The Netherlands and Switzerland was carried out on 40 women with a median age of 38.6 years with hirsute hair growth of different hair colours on the

upper lip and chin. In general the unwanted hair was removed within 6 treatments and a success rate of 76.7% was achieved. There were virtually no side effects and hardly any pain was reported.
The absence of side-effects and the high clearance rate led us to the conclusion, that the ILS is ideal for removing unwanted hair but that further research is needed in order to demonstrate that the hair loss is long term.

Ninety percent permanent hair removal in transsexual patients

Transsexualism is classified as a gender identity disorder and promotes the need to remove unwanted body hair in order to accomplish some degree of feminization. An effective, permanent method of hair removal is desired by transsexuals as part of the supportive management in gender reassignment. Several methods including the different types of electrolysis and laser epilation are used with varying effectiveness. The following study describes patients who received treatments with Intense Pulsed Light Source (IPLS) and achieved effective hair removal.
Twenty-five transsexual patients between the age of 22 and 67 were treated with IPLS at three centres in The Netherlands, Germany and Switzerland. The PhotoDerm®VL system was used. A mean hair clearance rate of 90% was achieved in an average of 9 treatments, and patients were followed up for an average of 44 months.
We found that IPLS is not only effective in permanently removing hair without painful side effects in transsexual patients, but it also saves time and operation costs.

Long-term hair reduction achieved in 87%of hirsute women treated with IPLS

The management of hirsutism remains a challenge to dermatologists and cosmetic surgeons. Women with unwanted hair on the face, neck or any part of the body have psychological and social problems. Various laser and laser-like devices are currently in use for hair removal, but little is known about the permanence of their results.
Our study examined the long-lasting of hair removal using IPLS on seventy female patients, aged 18-67 years who were treated in the Medical Centre Maastricht, the Netherlands for unwanted hair on the chin and upper lip. The average age of the mostly dark haired patients of various skin types was 41 years. They were subjected to a mean of 8.0 treatments followed up for a mean period of 27.4 months. This period of time was selected to demonstrate the permanence of the treatment since it is longer than the follicles' complete growth cycle. Long-term hair removal was achieved after several sessions.
Using the IPLS 87% hair removal was attained with virtually no side effects
Because of the high success rate we conclude that the IPLS offers an effective and safe method of long-term hair removal.

The PhotoDerm®VL flashlamp as a new treatment possibility for vascular skin lesions

This study examined the IPLS treatment of vascular skin abnormalities such as facial and leg telangiectasias, spider nevi, erythrosis interfollicularis and senile angiomas. The reason for treating these expanded linear, aborizing, spiders and punctiform venules, capillaries and arterioles is mostly a cosmetic one, and several lasers have been

used for skin lesions with differing results. In this study the treatment of vascular skin lesions and the limitations of such treatments with the PhotoDerm®VL flashlamp was examined.
A total of 120 patients were chosen randomly at the Department of Laser Therapy at the Medical Centre, Maastricht, the Netherlands and treated with the PhotoDerm®VL. A clearance rate of 84.3% was achieved for leg telangiectasis up to 1 mm. Additionally, 95% of facial telangiectasias and 80% of erythrosis interfollicularis colli were cleared. Spider nevi and senile angiomals cleared after a single treatment. While previous studies on treatment with other lasers showed side effects such as scars, permanent pigmentation, hemorrhage, hypo- or hyperpigmentation, the treatment with the PhotoDerm®VL produced only minimal side effects which resolved in a brief period of time.
The choice of setting variables is an important factor and makes a knowledgeable technician an asset. The range of settings determines the clearing rate. The challenges of operating the machine are at the same time also the key for good results. In conclusion, the PhotoDerm®VL flashlamp is an excellent device for treating vascular lesions if in the hands of an experienced operator.

Treatment of rosacea using PhotoDerm®VL

Rosacea is a common, but often overlooked skin condition that can lead to significant facial disfigurement, ocular complications and severe emotional distress. The progression of rosacea includes typical stages: facial flushing, erythema and/or oedema as well as ocular symptoms, papules and pustules, and rhinophyma. It is an idiopathic, widespread, chronic skin disorder commonly observed between the ages of 40 and 50. The exact reasons for developing of rosacea are unclear but it is likely to be due to a combination of factors.
Different lasers have been used for treating vascular skin lesions. Lasers used for the treatment of microvascular lesions are among others the Argon, Pulsed Dye lasers (PDL), Neodymium YAG, and Carbon Dioxide lasers. Frequent hypopigmentation, scar and blister formation have been reported using CO_2, Nd:YAG and Argon laser, which paved the way to use the PDL, which was also painful and caused bruises and hyperpigmentation. For years the PDL was one of the main laser sources for treating vascular lesions, using the principle of selective photothermolysis, whereby the energy works on special targets, (haemoglobine). The surrounding tissue is left free of scarring.
In this study we used the intense pulse light source and compared the results with those of lasers from literature review used to treat rosacea. We demonstrated a virtually side-effect free and successful treatment of the vascular abnormalities associated with rosacea using the intense pulse light source. In our department of Laser Therapy at the Medical Centre, Maastricht, the Netherlands sixty patients and a total of 508 sites of telangiectasia due to rosacea in the face (chin, nose, forehead) were treated with a mean of 4.1 treatments per location with a spectrum ranging from 515–590 nm with different pulse durations between 4.3- 6.5 ms. The energy varied from 24 to 32 J/cm^2. About half of the patients had no previous treatment before presenting at Maastricht Medical Centre. Some had been on an antibiotic therapy or other medication and/or had been treated with laser or coagulation therapy.

A mean clearance of 72 percent was achieved and maintained for a follow up period of about 4 years. Only in four treated sites, a recurrence of lesions was observed. Immediate side-effects such as erythema, purpura and pain were observed in 62% of the patients. But they were slight and disappeared 24-96 hours after the treatment.
In conclusion we infer that the PhotoDerm®VL is an excellent device for treating vascular skin lesions if applied by experienced technicians.

Clinical significance of an Intense Pulsed Light Source on leg telangiectasias of up to 1 mm diameter

Leg telangiectasias are common, but difficult to treat. They can be dilated arterioles, venules or capillaries, usually related to chronic, venous insufficiency, and are much more common in women than in men. Cosmetic reasons are usually the motivation for seeing a dermatologist. With time the classical sclerocompression therapy was replaced by laser therapy for treating telangiectasias. Although some of the lasers showed good result, the side effects turned out to be severe enough to attempt treatment with yet another device, relatively new at the time of the publication or this paper, the intense light source (ILS), provided by way of the PhotoDerm®VL. The PhotoDerm®VL was used on 40 women of an average age of 41.7 years with telangiectasias of up to 1 mm on the upper leg. Since neither scarring, nor telangiectatic matting was seen nor did other side effects worth mentioning occur, the treatment with this flashlamp turned out to be very successful. The younger patients (under 30 years of age) and those above 70 showed the best results after this treatment. In general three sessions were sufficient for a clearance of up to 100% in those above mentioned age groups, being around 75% for the age groups in between 30 and 70. There were no recurrences seen during the follow up of one year.
The outstanding results in the four research centres in the Netherlands, Germany and Switzerland in combination with the absence of side-effect lead us to the conclusion that the PhotoDerm®VL is an excellent tool for leg telangiectasias up to 1mm, but possibly also larger.

Effective treatment of nevus of Ota with Intense Pulsed Light Source after incomplete clearance with q-switched Ruby laser

Nevus of Ota, a pigmented lesion occurring normally along the distribution of the fifth cranial nerve has been treated more or less successfully in the past with dermabrasion, freezing and laser irradiation. The treatment of nevi of Ota using IPLS is relatively new, but so is the treatment attempt for pigmented lesions by lasers in general. It proves to be effective with no permanent side effects and gives excellent cosmetic result. Nevus of Ota is thought to occur mainly in the people of Asian descent but not exclusively. These lesions can be brown or blue-green, which are harder to treat.
Lasers that are effective in the management of pigmented lesions include: the Q-switched ruby, Alexandrite, and Nd:YAG lasers.
The purpose of treating nevus of Ota lesion is primarily a cosmetic one because it is not associated with increased risk of malignant transformation. We began treating the 3 patients with a Q-switched ruby laser initially, but the results obtained were not uniform, there was a spotty appearance and the presence of discoloration and

hyperpigmentation was seen. We therefore switched to IPLS. Altogether success was recorded between 3 and 9 treatment sessions in intervals of 3 to 6 months. Although the treatment with IPLS takes a few more sessions than using a laser, the advantage of an optical homogenous fading of the pigment outweighs the time needed for treatment.
The possibility of occurrence of side effects such as pigmental changes is virtually eliminated because of the versatility of the IPLS in catering to individual patient characteristics.
We conclude that IPLS offers a new possibility for the treatment of Nevus of Ota and it can also be used to improve the skin structure after previous treatment with other lasers for pigmented lesions has left its traces. There are no permanent side effects and the cosmetic results are superior to those attempted with other lasers, although more treatment sessions are needed.

Discussion

For a long time now, light energy has been successfully used in medicine, especially in surgery and dermatology. New devices are continuously being developed which have extended and improved treatment possibilities for many cutaneous and congenital defects, (including vasular, pigmented lesions) and for hair removal. Improvements in laser and flashlamp technology and methods have provided more therapeutic options and better clinical results. The devices have become non-selective, non-ablative from having been selective, ablative, and longer pulse times instead of a short pulses has been developed.
Originally it was speculated that melanin selectively absorbed laser light. Later is was established that the Q-Switched Ruby Laser (QSRL) targeted individual melanosomes, as well as the Alexandrite and Nd:YAG lasers with short pulses are effective in the management of pigmented lesions. The QSRL was reported to be very succesfull in completely removing flat acquired junctional melanocytic naevi. With IPLS longer pulse times were used and a clearance of 76-100% was obtained for superficial lesions such as ephelides, epidermal melasma, and cafe au lait macule. Further research led to the development of the pulsed dye laser, which was the first laser, where the principles of selective photothermolysis were applied to eliminate marks without damaging surrounding skin. Lasers were used in the treatment of vascular birthmarks (port-wine stains and hemangiomas) as well as for rosacea and facial telangiectasias. The treatment of vascular lesions is efficiently carried out with the IPLS where longer pulses are used in contrast to lasers and a good and complete clearance in 70% of the portwine stains was obtained.
In the treatment of leg veins mixed results of success were obtained using lasers and IPLS with 75-100% clearance using the IPLS.
In some instances, hair loss was observed that occurred accidentally in the treated areas, which led to experiments in epilation on animal models and later humans.[39]
Since then, there have been several studies on hair-removal using different lasers and flashlamps with long-lasting hair reduction of 80% achieved after 8 months with a second-generation IPLS.
Today lasers and flashlamps are extensively being used in skin rejuvenaton and in the permanent removal or reduction of blemishes. However, the side effects associated

with lasers, such as exudation and crusting followed by long-lasting erythema and a downtime of at least two weeks and redness in the treated areas that can occur up to a few months, makes IPLS the better choice in treatment.
IPLS devices offer sophisticated, computer-driven precision and tremendous versatility. Due to the nature of the treatment, IPLS energy can be applied to the subsurface skin layers for gentle and gradual results with recuded side effects and patient downtime. For certain aesthetic prodecures, IPLS technology provides a refining touch over lasers. All aspects of photo-damage including wrinkling, skin coarseness, irregular pigmentation, pore size, and telangiectasias showed visible improvement in more than 90% of subjects. The IPLS has several distinct advantages over lasers mainly arising from its flexibility in allowing a wide range of settings relating to individual patient characteristics, such as the modification of various parameters that include wavelength, fluence, pulse duration, pulse delay, pulse sequence, and temperature control of the skin. It saves time as surfaces of 2.8 cm^2 to 5.6 cm^2 per pulse can be treated, which also reduces operational cost.

Conclusion

We can conclude from our experiences that flashlamps give excellent results in permanent hair removal and vascular skin lesions. Compared to lasers a lesser number of treatments is needed tot get a clearance of up to 95%.
Skin rejuvenation and skin improvement are issues of great interest these days. This gives us the major impetus for continuing investigation in this field.
Indeed the IPLS is an outstanding, revolutionary new mini-procedure, which is effective in the treament of aging skin or liver spots, fine wrinkles, facial flushing, redness, broken capillaries, telangiectasia, hemangiomas, freckles, minor sun damage, port wine stains, tattoos, varicose veins, spider veins, flat birth marks, hypo-pigmentation and even hair growth.

Samenvatting

Inleiding

Dit artikel bespreekt lasers en laser-achtige apparaten, zoals flitslampen.
Het woord 'laser' is een acroniem voor 'Light Amplification by Stimulated Emission of Radiation'. De laser produceert licht uit het zichtbare en infrarode spectrum in een lichtbundel met een hoge spectral density op een zeer klein oppervlak. Er zijn diverse soorten lasers gebruikt voor vele medische doeleinden. Zo worden bijvoorbeeld CO_2-lasers succesvol gebruikt bij de behandeling van afwijkingen aan het huidoppervlak, zoals rimpels, littekens, schade t.g.v. zonlicht, benigne huidafwijkingen en rhinopyeem. Ook vaatafwijkingen, zoals wijnvlekken, heamangiomen, teleangiectasieën, rosacea en spider naevi, worden succesvol behandeld met flashlamp pumped dye lasers. Q-switched lasers produceren ultra korte pulsen met een hoge intensiteit en zijn effectief voor het verwijderen van tatoeages en enkele benigne gepigmenteerde leasies.
Een lasersysteem is opgebouwd uit drie essentiële componenten. Ten eerste is er het *Lasing medium*: een gas, kristal, vloeistof of semiconductor. Ten tweede is er de *Source of excitation* voor het lasing medium, bijvoorbeeld flitslampen of continu licht, diodes, high voltage discharge, radiogolven en in sommige gevallen een andere laser. Het laatste component bestaat uit de *spiegels*, die de geëxciteerde fotonen reflecteren naar de resonant cavity waar het lasing medium zich in bevindt.
Als het lasing medium wordt geëxciteerd worden de moleculen aangeslagen. Enkele van deze geëxciteerde moleculen vallen spontaan terug in hun oude energieniveau (ground state), waardoor er een foton vrij komt. Als dit foton in de juiste richting wordt uitgestraald, zal het een van de spiegels aan het uiteinde van de resonant cavity raken, waardoor deze weer terug gestuurd wordt. Dit geëxciteerde foton kan andere geëxciteerde moleculen door middel van een botsing er toe aanzetten ook een foton uit te zenden door terug te vallen naar de ground state. Het vrijgekomen foton beweegt in dezelfde richting als de eerste en zo wordt er een cascade op gang gebracht. Er is sprake van een netto amplificatie van lichtenergie als het gros van de moleculen in het lasing medium zich in de aangeslagen toestand bevindt (population inversion).
De Q-switched laser is een laser waarbij de stand van het apparaat, dat de grote losses in de resonant cavity veroorzaakt en de lasing operation voorkomt, plotseling omgeschakeld kan worden naar een stand waarbij het apparaat slechts kleine losses introduceert. Hierdoor neemt de quality factor in de lasing cavity snel toe, waardoor er een build-up ontstaat van een korte en zeer sterke laser pulse. De duur van zo een pulse is niet langer dan enkele nanoseconden (ns).
In tegenstelling tot gewoon licht is laserlicht coherent, monochroom met een parallelle eigenschap. Coherent betekent dat de lichtgolven zijn gesynchroniseerd, van de laserstraal en monochroom betekent dat de laserstraal bestaat uit een enkele golflengte/kleur licht. De eenheid die men gebruikt om de totale energie van de laserpulse of –systeem uit te drukken is Joule (J). Fluence is de dosis ‚stated' in J/cm^2. De energy intensity van de laser per oppervlak wordt gemeten in W/cm^2. De golflengte (?) is gerelateerd aan stimulated energy transition: hoe korter de golflengte, hoe hoger

de energie van het foton. De oppervlakte van de focal spot bepaalt de maximale energy density die bereikt kan worden als de kracht van de laserstraal wordt ingesteld. De diepte van de focus is de afstand waarover de gefocuste straal ongeveer dezelfde intensiteit behoudt. Zoals gezegd is laserlicht monochroom en hierdoor heeft het een niet selectief effect op biologisch weefsel als het wordt (door)geleid, verspreid, gereflecteerd of geabsorbeerd. Het licht moet geabsorbeerd worden om enig biologisch effect te veroorzaken en een bepaalde golflengte kan sterk worden geabsorbeerd door een bepaald type weefsel, terwijl het door een ander type juist wordt doorgelaten. De componenten van het weefsel zijn bepalend voor deze eigenschappen. De belangrijkste absorberende componenten (chromophores) van het lichaam zijn: hemoglobine in bloed, melanine in de huid, haar, 'moles' en water (deze laatste is aanwezig in alle biologische weefsels)
Als het laserlicht wordt geabsorbeerd, levert deze energie aan het weefsel. Een intense, maar korte puls laserlicht veroorzaakt meestal een explosieve uitzetting van weefsel (fotomechanische reactie). Een minder intense, langere puls veroorzaakt een snelle verhitting (fotothermale reactie). Selectieve fotothermolyse is het proces waarbij het vrijkomen van laserenergie wordt beperkt tot een bepaalde plek door de selectieve absorptie van een chromophore.

Intense Pulsed Light Source (IPLS), ook wel de flitslamp genoemd, wordt tegenwoordig gebruikt voor de behandeling van dermatologische aandoeningen in hetzelfde spectrum als de laser. De IPLS is een apparaat dat non-coherent licht en low-range infrarode straling filtert, waardoor er specifieke golflengtes geselecteerd kunnen worden. Deze kunnen succesvol worden gebruikt bij de behandeling van gepigmenteerde laesies, zoals moedervlekken, spider naevi in het gezicht, varices, maar ook voor de verwijdering van ongewenste haargroei. De aanschafkosten van de apparatuur en kosten per behandeling zijn gelijk aan die van vergelijkbare lasers.
Een flitslamp is een booglamp die, in de pulse mode, in staat is om opgeslagen elektrische energie om te zetten in sterke uitbarstingen van radiant energy opgebouwd uit licht van het ultraviolette, zichtbare en infrarode lichtspectrum. Xenon wordt het meest gebruikt in flitslampen, aangezien het het meest efficiënte edelgas is in het omzetten van elektrische energie in optische energie.
Een bekend type Xenon-flitslamp in de lineaire Xenon-flitslamp. Het is opgebouwd uit een buis van quartz met twee gesealde electrodes: de kathode en anode. Deze zijn gemaakt van tungsten of van speciale low-sputtering materialen. Gebruikelijk is een flitslamp gevuld met Xenon-gas onder een druk van 200 tot 400 Torr. De energy load van een flitslamp is over het algemeen tussen een paar tot enkele honderden Joules. Het lichtspectrum van een flitslamp is ongeveer gelijk aan dat van de zon.
Flitslampen, ofwel IPLS, zijn een perfecte aanvulling op de laser lichtbronnen. Ze hebben een breed spectrum van lichtenergie in vele golflengtes. IPLS voorziet veel lichtenergie in pulsen van slechts enkele milliseconden. IPLS-apparaten zijn zeer nauwkeurig en hebben een grote versatiliteit. De IPLS kan worden gebruikt voor de sub-surface lagen van de huid, met graduele resultaten, minder bijwerkingen en een kortere herstelperiode voor de patiënt door de aard van de behandeling.
Zoals eerder genoemd, gebruiken flitslampen niet een golflengte zoals men dat bij de laser ziet. Flitslampen stralen iedere golflengte van het zichtbare lichtspectrum uit en een kleine band van het infrarode lichtspectrum (tot en met 1200 nm). Artsen kunnen

een cut-off filter selecteren om lagere golflengtes weg te filteren. De meeste flitslampen kunnen ook met hun straal een groter oppervlak behandelen dan de laser.

Transforming growth factor-beta en extracellulaire matrix stimulatie door Intense Pulsed Licht Sources: een experimentele studie

De normale reactie op weefselbeschadiging is inflammatie. Macrofagen en neutrofielen komen naar het gewonde gebied en beginnen met het opruimen van vreemd materiaal en dode cellen. Hierna begint de proliferatie van fibroblasten, die de synthese van extracellulaire matrix (ECM) stimuleren. Verschillende groeifactoren spelen een belangrijke rol in dit reconstructieproces. Transforming growth factor (TGF) is een van deze belangrijke eiwitten. Een van zijn functies is de stimulatie van de productie van ECM. Onder de eiwitten waar TGF effect op heeft is de tenascine familie van glycoproteïnen (TN). Zij komen tot uiting in volwassen bij processen zoals wondheling, vasculaire pathologie en tumorgenese.
Tenascine en TGF lijken een belangrijke rol te hebben bij de bescherming voor verschillende ziektes zoals kanker en tussenwervelschijf degeneratie.
Het doel van onze studie was het onderzoeken van de stimulatie van TGF en het vrijkomen van ECM proteïnen zoals tenascine na bestraling met intense pulserende licht bronnen.
We behandelen twee varkens met de Vasculight® en de Quantum® licht bronnen vijf keer. Op verschillende momenten na elke behandeling werden er biopten afgenomen. Een totaal aantal van 240 biopten werd verzameld. De biopten werden microscopisch onderzocht met immunohistochemie.
We zagen variaties in het niveau van de TGF concentraties die afhankelijk waren van de tijd na de behandeling. Vooral na een week en na 60 dagen werden er hoge concentraties van TGF-beta geobserveerd.
We zagen ook variaties in de concentratie van tenascine. Vooral na twee weken zagen we een stijging van de tenascine concentratie in de epidermis en dermis en een daling van de tenascine concentratie in de plasmacellen.
Dus het lijkt erop dat radiatie met een intense pulserende flitslamp een exogene stimulus is om een kunstmatige wond te veroorzaken, die weer zorgt voor een activatie van latent TGF-beta en tenascine.

Haarverwijdering bij 40 overbehaarde vrouwen met een Intense Pulsed Light Source

In deze studie wordt haarverwijdering beschreven met een IPLS flitslamp waarbij geen bijwerkingen optreden zoals littekens of kleine wondjes. In deze studie zijn 5 centra betrokken in Duitsland, Nederland en Zwitserland. De studie had betrekking op 40 vrouwen met een gemiddelde leeftijd van 38.6 jaar met overbeharing op de bovenlip en kin; de haarkleur was verschillend. Over het algemeen was het ongewenste haar verdwenen binnen 6 behandelingen met een succes ratio van 76.7%. Er waren vrijwel geen bijwerkingen en er werd bijna geen pijn ervaren.
De PhotoDerm®VL is een flexibeler instrument dan een laser doordat het een breder gamma aan settings aanbiedt, deze kunnen aangepast worden aan de individuele karakteristieken van de patiënt door een ervaren technicus. Net als lasers is de werking gebaseerd op het principe van selectieve thermolyse.

De afwezigheid van bijwerkingen en de hoge clearance rate laat ons concluderen dat de IPLS een ideale manier is voor de verwijdering van ongewenst haar. Maar er is verder onderzoek nodig om aan te tonen dat de haarverwijdering ook op lange termijn een succes blijft.

Negentig procent permanente haarverwijdering bij transseksuele patienten

Transseksualiteit, een syndroom dat geclassificeerd is als een geslachtsidentiteitsstoornis met de wil om ongewenst haar op het lichaam te verwijderen om er vrouwelijker uit te zien. Deze studie gaat over patiënten die zijn behandeld met een Intense Pulsed Light Source (IPLS) daar dit een ideale methode is voor haarverwijdering.
Een effectieve, permanente haarverwijderingsmethode is ideaal voor transseksuelen als onderdeel van hun aanpak bij geslachtsverandering. Verscheidene methodes zoals verschillende types elektrolyse en laser epilatie worden gebruikt met uiteenlopende effectiviteit. Deze studie betreft vijfentwintig transseksuele patiënten bij wie een permanente methode van haarverwijdering van psychologisch belang is tijdens hun proces. De patiënten zijn tussen 22 en 67 jaar en zijn behandeld in drie centra in Nederland, Duitsland en Zwitserland. Een Intense Pulsed Light Source, PhotoDerm®VL werd gebruikt. Gemiddeld verdween 90% van de haren bij een gemiddelde van 9 behandelingen, met een gemiddelde follow-up van 44 maanden. Wij concluderen dat het Intense Pulsed Light System een effectieve methode is voor permanente haarverwijdering bij transseksuele patiënten daar het tijd en geld spaart en pijnloos is.

Haar reductie door gebruik van een Intense Pulsed Light Source

De aanpak van hirsutisme blijft een uitdaging voor dermatologen en plastisch chirurgen. Verschillende lasers en laserachtige apparaten worden tegenwoordig gebruikt om haar te verwijderen maar er is maar weinig bekend over de resultaten op lange termijn. Vrouwen met ongewenst haar in het gezicht, hals of een ander deel van het lichaam hebben fysische en sociale problemen.
Alle laserbehandelingen hebben gemeen dat de laserstraal diep in de dermis penetreert met als doel de haarfollikels te raken en selectief geabsorbeerd te worden door het melanine. Ook de intense pulserende lichtbronnen, PhotoDerm®VL en Epilight werken volgens dit principe. Het is flexibeler dan lasers omdat het door een ervaren specialist aangepast kan worden aan de eigenschappen van de individuele patiënt.
Deze studie gaat over de permanentie van haarverwijdering met behulp van de IPLS bij 70 vrouwelijke patiënten tussen 18-67 jaar die behandeld werden in het Medisch Centrum Maastricht, Nederland voor ongewenst haar op kin en bovenlip. De gemiddelde leeftijd van de meestal donkerharige patiënten met verschillende huidtypes was 41 jaar. Zij werden gemiddeld 8 keer behandeld en gemiddeld opgevolgd gedurende 27,4 maanden. Dit is langer dan de complete groeicyclus van de follikels en toont zo de permanentie aan. Bij het gebruik van de IPLS bereikte men een haarvermindering van 87% zonder bijwerkingen. We concluderen dat IPLS ons een effectieve methode biedt voor lange termijn haarverwijdering zonder bijwerkingen.

De PhotoDerm®VI flitslamp als een nieuwe behandelingsmogelijkheid voor vasculaire huidlaesies

Dit artikel gaat over de behandeling van vasculaire huidafwijkingen zoals teleangiectasiën in het gezicht of op het been, spider naevi, erythrosis interfollicularis en seniele angiomas. De reden om deze uitgebreide lineaire, aborizing, spiders en punctiforme venules, capillairen en arteriolen te behandelen is meestal een cosmetische. Met wisselend resultaat worden er vershcillende lasers gebruikt bij de behandeling van deze afwijkingen. In dit artikel wordt de behandeling van vasculaire laesies besproken met de PhotoDerm®VL flitslamp. De mogelijkheden en de beperkingen van dit apparaat worden besproken.
Op de afdeling lasertherapie van het Medisch Centrum Maastricht werden in totaal 120 patiënten at random gekozen en behandeld met de PhotoDerm®VL. De clearance rate van 84,3% werd behaald bij telangiectasiën op het been met een grootte tot 1mm. 95% van de faciale telangiectasiën en 80% van de erythrosis interfollicularis verdween. Spider naevi en seniele angioma's verdwenen na één enkele behandeling. Terwijl vorige studies over de behandeling met andere lasers bijwerkingen toonden, zoals: littekens, permanente pigmentatie, hemorrhage, hypo- of hyperpigmentatie, toont de behandeling met de PhotoDerm®VL bijna geen van deze bijwerkingen. Wanneer deze wel optraden dan verdwenen ze weer snel.
Een belangrijke factor is de keuze van setting variabelen en dit maakt een deskundige technicus een must. De range van settings bepaalt de clearance rate. Te weinig energie zal de vaten niet occluderen; te veel energie daarentegen veroorzaakt te veel warmte, hetgeen leidt tot blaar- en littekenvorming en depigmentatie.
De nadelen van het apparaat zijn op hetzelfde moment de sleutel naar een goede behandeling. Concluderend is de PhotoDerm®VL flitslamp een excellente methode bij de behandeling van vasculaire laesies indien toegepast door een ervaren arts.

Behandeling van rosacea met de PhotoDerm®VL

Rosacea is een veelvoorkomende maar ook vaak over het hoofd geziene huidaandoening die kan leiden tot significante gezichtsmisvormingen, oogcomplicaties en ernstige emotionele ellende. Het ziektebeloop van rosacea bestaat uit typische fases: blozend gezicht, erytheem en/of oedeem als ook oculaire symptomen, papels en pustels, en rhinophyma. Het is een idiopatische, wijdverspreide chronische huidaandoening die meestal zichtbaar wordt tussen 40 en 50 jaar. De exacte oorzaken van rosacea zijn onbekend maar het blijkt een combinatie van factoren te zijn.
Verschillende lasers worden gebruikt om vasculaire huidlaesies te behandelen. Er waren vaak bijwerkingen als hypopigmentatie, littekens, blaarvorming en pijn. Bij de behandeling met een intense pulserende lichtbron wordt gebruik gemaakt van het principe van selectieve fototthermolyse. Hierbij werkt de energie in op een specifiek doel (hier erythrocyten) waardoor men de vorming van littekens van het omliggende weefsel tegengaat.
Het doel van deze studie is de behandeling te tonen van vasculaire aandoeningen geassocieerd met rosacea gebruik makend van de Intense Pulse Light bron en de resultaten te vergelijken met die van de reeds langer bestaande lasers. Binnen onze afdeling Lasertherapie van het Medisch Centrum Maastricht, Nederland werden 60

patiënten (508 locaties) met teleangiectasiën te wijten aan rosacea in het gezicht gemiddeld aantal van 4,1 keer behandeld per locatie.
Gemiddeld verdween 72% van de laesies en dit resultaat werd behouden gedurende een follow-up van ongeveer 4 jaar. In slechts 4 behandelde gebieden werd er een terugkomst van de laesie gezien.
Wij concluderen dat de PhotoDerm®VL een uitstekend middel is voor de behandeling van vasculaire huidlaesies indien toegepast door een ervaren deskundige.

Klinische significantie van een Intense Pulsed Light Source op teleangiectasiën tot 1 mm diameter op het been .

Been teleangiectasiën komen veel voor maar zijn moeilijk te behandelen. Ze kunnen bestaan uit gedilateerde arteriolen, venulen of capillairen, meestal zijn ze gerelateerd aan chronische veneuze insufficiëntie, wat veel meer bij vrouwen dan bij mannen voorkomt. Cosmetische redenen zijn meestal de aanleiding om naar een dermatoloog te gaan. Gedurende de tijd is de klassieke sclerocompressie therapie vervangen door lasertherapie om teleangiectasiën te behandelen. Ook al lieten sommige lasers goede resultaten zien, de bijwerkingen bleken echter ook ernstig genoeg om een andere behandelingsmethode te proberen, relatief nieuw ten tijde van de publicatie van dit artikel, is de intense licht bron in de vorm van de PhotoDerm®VL. Net als andere lasers gebruikt de PhotoDerm®VL het principe van selectieve fotothermolyse. Het is echter meer flexibel dan andere lasers omdat het een grote variatie aanbiedt in instellingen die aangepast kunnen worden door een ervaren specialist aan de karakteristieken van de individuele patiënt.
Als behandelingsmethode werd bij 40 vrouwen met teleangiectasiën tot 1 mm op het bovenbeen met een gemiddelde leeftijd van 41,7 jaar de PhotoDerm®VL gebruikt. Er waren geen verschijnselen van bijwerkingen zoals littekens of matvorming dus de behandeling met de flitslamp bleek erg succesvol. De jongere patiënten (onder de 30 jaar) en degenen boven de 70 jaar lieten de beste resultaten zien na deze behandeling. Over het algemeen waren drie behandelingen voldoende om een clearance te bereiken tot 100% in de hierboven genoemde groepen, in de groep tussen de 30 en de 70 jaar werd een clearance tot 75% bereikt. Er werden geen recidieven gezien gedurende een follow-up periode van een jaar.
De uitstekende resultaten die werden behaald in de vier onderzoekscentra in Nederland, Duitsland en Zwitserland in combinatie met het gebrek aan bijwerkingen leidde tot de conclusie dat de PhotoDerm®VL een excellente methode is voor de behandeling van been teleangiectasiën tot 1 mm, maar mogelijk ook groter.

Effectieve behandeling bij naevus van Ota met Intense Pulsed Light Source na onvolledige verdwijning met q-switched Ruby laser.

Een naevus van Ota is een gepigmenteerde laesie die normaal uittreedt rond de distributie van de 5de hoofdzenuw. Het komt vooral voor bij personen van Aziatische afkomst maar niet uitsluitend. De laesies kunnen bruin of blauwgroen zijn, welke moeilijker zijn om te behandelen.
Het doel van de behandeling van de naevus van Ota is eerder cosmetisch want deze laesie is niet geassocieerd met een verhoogde kans op maligniteit. In het verleden werden de naevi behandeld met dermabrasion, bevriezen en laserbestraling. De

behandeling met laserbestraling geaf geen uniforme resultaten. De laesie werd vlekkerig en er werd verkleuring en hyperpigmentatie gezien. Daardoor zijn we overgeschakeld op de intense pulserende lichtbron (IPLS).
De behandeling van naevi van Ota met behulp van een intense pulserende lichtbron bewijst effectief te zijn zonder permanente bijwerkingen en geeft een uitstekend cosmetisch resultaat. Ook al duurt deze methode enkele sessies langer, de voordelen van een optisch gelijkmatig webebbende vlek overtreffen de behandelingstijd.
Drie patiënten zijn behandeld met een verbetering na 3 tot 9 behandelingen met een interval van 3 tot 6 maanden.
De kans op de bijwerkingen zoals pigment veranderingen is minimaal door de veelzijdigheid van de IPLS in catering to individual patient characteristics.
Samengevat, kunnen we besluiten dat IPLS een nieuwe methode aanbiedt ter behandeling van de naevus van Ota. Er zijn geen permanente bijwerkingen en de cosmetische resultaten zijn beter dan bij andere behandelingen.

Discussie

Lichtenergie wordt al vele jaren succesvol gebruikt in de geneeskunde, met name binnen de vakgebieden chirurgie en dermatologie. Nieuwe apparaten zijn voortdurend in ontwikkeling, waardoor de behandelingsmogelijkheden voor vele congenitale en huidafwijkingen (vasculaire malformaties, pigmentlaesies) en haarverwijdering verruimd worden. Verbeteringen in de laser- en flitslamptechnologie en –methodes zorgen voor betere klinische resultaten en meer behandelingsmogelijkheden. De apparaten zijn dus ontwikkeld van zeer selectief tot non-selectief, van ablatief tot non-ablatief en van een korte tot een langere pulse.
Oorspronkelijk werd gedacht dat melanine het laserlicht specifiek absorbeert. Later werd vastgesteld dat de Q-switched ruby laser (QSRL) individuele melanosomen target en dat dit soort lasers, evenals de Alexandrite en Nd:YAG laser met korte pulse, effectief zijn in de behandeling van van pigmentlaesies. De QSRL bleek erg effectief in het verwijderen van flat aqcuired juctional melanocytic nevi. Dit was de eerste laser waarbij selectieve fotothermolyse werden toegepast, welke aandoeningen verwijdert, zonder de omliggende huid te beschadigen. Verder onderzoek leidde tot de ontwikkeling van de pulsed dye laser. Lasers werden gebruikt voor de behandeling van aangeboren vasculaire malformaties, zoals wijnvlekken en hemangiomen en ook voor de behandeling van rosacea en faciale telangiectasieën. De IPLS is een goede behandelingsmethode voor vasculaire laesies. Deze werkt met langere pulsen, dit in tegenstelling tot lasers, waardoor een goede en volledige clearance wordt bereikt bij 70% van de laesies. Gemengd succes was er bij de behandeling van varices met lasers en IPLS. Met de IPLS werd een clearance van 75-100% bereikt. Een langere pulseduur kon worden gebruikt bij de IPLS en een clearance van 76-100% werd bereikt bij het behandelen van ephilides, epidermale melasma en café-au-lait vlekken.
In enkele gevallen werd er haarverlies in de behandelde huidoppervlakken geconstateerd. Dit leidde tot experimenten met laser en haarverwijdering, eerst op diermodellen, later op mensen. Sindsdien zijn er diverse studies gedaan naar haarverwijdering met verschillende types lase en flitslampen. Na 8 maanden werd er met een tweede generatie flitslamp een 80,2% langdurige reductie in haargroei bereikt.

Tegenwoordig worden lasers en flitslampen extensief gebruikt op het gebied van huidverjonging en permanente verwijdering of reductie van huidvlekken. De bijwerkingen van lasers, zoals exudatie en korstvorming gevolgd door langdurig erytheem en een downtime van tenminste twee weken en roodheid in het behandeld oppervlak maakt echter de IPLS een betere behandelingsmogelijkheid.
IPLS apparaten bieden een grote veelzijdigheid en enorme nauwkeurigheid. Door de aard van de behandeling kan IPLS-energie worden toegepast in de dermis met een geleidelijk resultaat en minder bijwerkingen en een kortere downtime. IPLS-technologie voorziet in bepaalde esthetische behandelingen een 'refining touch'. Een zichtbare verbetering werd gezien in 90% van de gevallen bij de behandeling. Dit geldt voor alle aspecten van photo damage, zoals rimpeling, irregulaire pigmentatie, poriegrootte, telangectasieën en een grove huid. De IPLS heeft diverse significante voordelen in vergelijking met lasers, met name op het gebied van flexibiliteit: een wijde range van settings waardoor de behandeling kan worden afgesteld op de karakteristieken van de patient. De IPLS bespaart tijd en kosten door het grote behandelingsoppervlak per pulse van 2,8 to 5,6 cm^2.

Conclusie

Uit onze ervaringen kunnen we concluderen dat de flitslamp uitstekende resultaten laat zien in de permanente verwijdering van haar en de behandeling van vasculaire huidlaesies. In vergelijking met lasers zijn er minder behandelingen nodig om een clearance van 95% te bereiken. Huidverjonging en huidverbetering zijn issues die steeds meer aandacht krijgen. Deze ontwikkeling is onze drijfveer om onderzoek op dit gebied voort te zetten.
De IPLS is inderdaad een uitstekende, revolutionaire nieuwe mini-procedure in de behandeling van ouderdoms- of levervlekken, kleine rimpels, roodheid, gebarsten capillairen, telangiectasien, hemangiomen, freckles, kleine zonbeschadigingen, wijnvlekken, tatoeages, varices, spider veins, platte moedervlekken, hypopigmentatie en zelfs ongewenste haargroei.

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Tenslotte wil ik ook mijn moeder bedanken.

Curriculum vitae

Afgestudeerd in januari 1984 aan de Universiteit Limburg, Maastricht in Nederland. Daarna 5 jaar algemene heelkunde gevolgd in Nederland en Ierland, tussendoor één jaar in het Fatima College, Medical School, Lahore, Pakistan in de oncologische chirurgie gewerkt te zijner tijd ook onderzoek op borstkanker en placenta vooral op het C-erbB-2 oncogen en aanvullende publicaties gedaan.
Een laserbasisopleiding gevolgd in Berlijn in het Laser Medizinisches Zentrum (LMZ) bij prof. Berlien, diverse stages in lasers gevolgd.
Ze leidt sinds november 1994 de afdeling lasertherapie.
Auteur en co-auteur van internationale publicaties over flitslampen en lasers. Sinds 1998 op nationaal en internationaal niveau opleidingen in flitslampen en bijbehorende therapieën.
In november 2003 de laser award van ILLAS (International Laser Light Association) Trier, Duitsland voor wetenschappelijk onderzoek in flitslampen en lasers ontvangen.

Biography

C. Schroeter graduated from the University of Limburg, Maastricht, the Netherlands in 1984 with a degree in general medicine. From 1985 to 1992 she followed a training in general surgery in the Netherlands, followed by a one-year oncologic surgery at Fatima Hospital Medical School, Lahore Pakistan and joined by two years general surgery residency in Ireland. In 1992 she completed a scientific year where she investigated oncogenes such as C-erbB-2 in breast cancer and placenta morphogenesis resulting in several publications. A basic training in laser physics and laser therapy was performed at the Laser Medizinisches Zentrum (LMZ) of prof Berlien, Berlin, Germany. From 1994 to the present, she serves as the Head of the Department of Lasertherapy in Maastricht, the Netherlands and is an active speaker and author in the area of Laser and flashlamp therapy. In November 2003 she was awarded the International Laserlight award (ILLAS) for her scientific research in Trier, Germany.

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