The use of lasers in dermatology

Žužul, Kristina

Master's thesis / Diplomski rad

2014

Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj: **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:380227

Rights / Prava: In copyright / Zaštićeno autorskim pravom.

Download date / Datum preuzimanja: **2025-01-13**

Repository / Repozitorij:

Dr Med - University of Zagreb School of Medicine Digital Repository

UNIVERSITY OF ZAGREB

SCHOOL OF MEDICINE

Kristina Žužul

The use of lasers in dermatology

GRADUATE THESIS

Zagreb, 2014

This graduate thesis was made at the Department of Dermatology and Venerology, mentored by prim. dr. sc. Krešimir Kostović and was submitted for evaluation in the academic year 2013/2014.

CONTENTS

1. SUMMARY

The use of lasers in dermatology

Kristina Žužul

This graduate thesis explains the basic laser principles and provides an overview of indications for laser treatment in dermatology. The term laser is an acronym for light amplification by the stimulated emission of radiation. Since the development of first laser by Maiman and the introduction of theory of selective photothermolysis in 1980 by Anderson and Parish, it gained widespread acceptance in dermatology and is now used for the treatment of numerous cutaneous conditions including pigmented and vascular lesions, tattoos, scars, unwanted hair, and aging skin. When a laser is used on the skin, the light can be absorbed, reflected, transmitted or scattered. Once laser energy is absorbed, the possible effects are photochemical, photothermal and photoacoustic. Due to different clinical applications of wavelengths and pulse durations, the choice of laser should be based upon the individual absorption characteristics of the target chromophore.

Pigment specific lasers target melanin and can successfully lighten or eradicate a variety of benign epidermal and dermal pigmented lesions and tattoos with minimal risk of unwanted effects. Nowadays, Q-switched lasers are the first choice for most pigmented lesions, but continuous wave and quasi-continuous wave lasers can also be effective if used properly by experienced operator. Laser systems for hair removal include alexandrite (755 nm), diode (800 and 810 nm) and Nd:YAG (1064nm). Vascular specific laser systems target intravascular oxyhemoglobin to destroy congenital and acquired vascular lesions. Lasers used for this purpose include PDL (585 nm), long pulsed-dye laser (595 nm), KTP (532 nm) and the Nd:YAG (1064 nm). CO_2 and Er:YAG lasers were traditionally used for laser skin resurfacing, but one of the newest trends in dermatology has been development of nonablative and fractional laser systems whose advantages are less side effects and decreased downtime.

Of outmost importance is the safety of both patient and the operating room personnel during laser irradiation. Key safety measures include education, eye, skin and teeth protection, as well as protection from plume, fire and electrical hazards.

Keywords: laser, dermatology, indications, safety measures

2. INTRODUCTION

Laser therapy is currently one of the most rapidly evolving areas of medical technology, and the developments of laser technology from the cradle of modern physics in 1900 by Planck to its latest medical boundaries is an exciting example of how basic physics finds its way into the clinical practice. Until 1900, the study of light was limited to examining its behavior. By the time scientists had identified light sources, but they didn't know how light was generated. In 1900, Planck defined a relation $E=hf$, but it took until Albert Einstein in 1917 postulated the phenomenon of extremely focused light beams in his publication on quantum theory.

During World War II, scientists became engaged with radar equipment and developed interest in the spectral part of microwaves. In 1954, Robert H. Dicke proposed the "optical bomb" in the US, in which a short excitation pulse would produce an inverted population, which would then generate an intense burst of spontaneous emission. In 1956, he filed a patent using a pair of parallel mirrors, forming Fabry-Perot interferometer, as a resonant optical cavity. At the end, this led to production of a "maser" in 1954 by Townes at the Columbia University. The acronym "maser" stands for Microwave Amplification by Stimulated Emission of Radiation. After all, it took 43 years after Einstein's first theories, until Maiman developed a laser in 1960. He introduced a ruby laser as a first commercially available laser, and consequently set Einstein's theory into practice. The acronym LASER was already created by Gould, and stands for Light Amplification by Stimulated Emission of Radiation (Gross AJ and Herrmann TRW 2007). In the first true laser, microwave energy was amplified by a ruby crystal to create a beam of red light travelling in a phase at a wavelength of 694 nm. The ruby laser was followed shortly by the development of other solid laser systems such as the Nd:YAG 1064 nm. Gaseous lasing mediums, including argon, helium-neon and CO_2 lasers, offered an alternative to solid glass rods (Houk LD and Humphreys T 2007).

The laser's first medical use was in ophthalmology to repair detached retinas by means of "spot welding". Their use in dermatology started by Goldman, who was the first physician to exploit the properties of the ruby laser to treat tattoos (Goldman et al. 1964). Early lasers, such as the argon and CO_2 systems, emitted an uninterrupted beam of light, which in addition to destroying the desired target, also exposed the surrounding healthy tissue to laser energy

for prolonged periods, causing collateral damage with unacceptably high rates of hypertrophic scarring and pigment alteration. In order to limit the amount of this nonselective thermal damage, the continuous wave lasers were later made “discontinuous” using a mechanical shutter to interrupt the beam of light (Houk LD and Humphreys T 2007).

Later, advances in laser technology have progressed rapidly, resulting in development of new laser systems with better therapeutic results and low risk of adverse effects (Tanzi El et al. 2003). In the 1960s, the emphasis was on the mode locking of flashlamp-pumped ruby, neodymium-glass and organic dye lasers; in the 1970s and 1980s there were major developments in the generation of sub-picosecond and femtosecond pulses from continuous wave organic dye lasers; whereas in 1980s and 1990s there were concerted efforts in the generation of femtosecond pulses in the near-infrared spectral region (Lipozenčić J and Bukvić Mokos Z 2010).

For many years following the initial studies of the effects of lasers on the skin, the use of lasers was limited to nonselective coagulation and vaporization of tissue. It was with the flashlamp-pumped pulsed dye laser (PDL) in the early 1980s that Anderson and Parrish developed the theory of selective photothermolysis that revolutionized the practice of cutaneous laser surgery (Anderson RR and Parrish JA 1983). They explained how site-specific, thermally mediated injury of microscopic targets can be achieved without thermal injury of surrounding tissue. The majority of subsequent developments in laser technology for cutaneous disorders have been based upon this theory.

Laser technology has been further refined to perfect selective delivery to a specific target and minimize unwanted adverse effects. Cooling technology limits inadvertent damage to tissues adjacent to targeted sites, allowing higher levels of light energy to be directed towards the target.

Examination of recent trends in laser treatment modalities reveals that longer wavelengths are being paired with longer pulse durations to target deeper structures and minimize collateral damage. This has been particularly true in the case of vascular lasers designed to target larger vessels and produce less purpura. Also, there is a quest for photorejuvenation without “downtime”, which resulted in emergence of nonablative laser systems focused on dermal remodeling (Houk LD and Humphreys T 2007).

3. GENERAL PRINCIPLES AND PHYSICS OF LASER

3.1. Laser principles

Laser is a device based on the luminance stimulated by photons of characteristic frequency with unique features. Laser light is monochromatic (composed of single wavelength), parallel (even in long distance, and enables precise tissue destruction), coherent (all the waves travel in phase) and high energy (Brnjas Kraljević J 2001).

The first principle of Einstein's quantum theory comprehends that light travels in packets of energy known as photons. The second principle implies that most atoms or molecules exist in a ground or low energy state (E_0) relative to their energy levels. However, a small percentage of atoms naturally occur at any given time at a higher, discrete energy level (E^1, E^2, E^n). It is possible by adding thermal, electric, or optical energy to atoms in the ground state to convert the majority of E_0 atoms to higher energy levels. The energy is then released spontaneously in the form of photons or electromagnetic waves to return to the ground state. Einstein also discovered that, when a photon of light energy of the same wavelength strikes an excited atom (E^n), that photon and the photon of light that is released are discharged simultaneously and therefore will be identical in frequency and phase. This is the concept of simulated emission used in the creation of a laser (Gross AJ and Herrmann TRW 2007). Simultaneous emission is possible in systems with inversed population. It is crucial for the laser systems to possess metastable state, because that will assure simultaneous excitation of system with inversed population and continuous simultaneous emission.

Each laser system is composed of the following primary components: the laser medium which can be solid, liquid or gas, the optical cavity which surrounds the laser medium, the power supply or pump which excites the atoms of laser medium, and a delivery system which delivers light to target with precision.

One laser pulse of 1μs duration emits the beam of energy 10 mJ. With the beam diameter of 10 μm, the density is 10^{14} Wm^{-2}, which is 10^{11} times higher power density than the density of the Sun radiation on the Earth surface. It is also important to emphasize that all the photons are of the same energy, which means that the same effects are achieved when interacting with tissues (Brnjas Kraljević J 2001).

3.2. Interaction with tissue

Photon – tissue interactions include photochemical, photothermal or photoacoustic effect (Watanabe S et al. 1988). Photochemical events are more likely to occur with wavelengths less than 500 nm and can be seen with either short or long exposures of up to several hours. Thermal events are more likely to occur from visible or infrared radiation, and exposures may last from fractions of milliseconds to many seconds. Damage mechanisms dependent upon electric field strength, may occur after very short exposures of very high intensity (Watanabe S 2008).

When the light of any wavelength or intensity hits the skin, four possible results ensue. The light can be directly reflected (usually in stratum corneum, which is the reason for wearing protective eyewear), scattered by collagen in the dermis, or transmitted through the dermis to the subcutaneous tissues. The light that results in actual work being done on the tissues is the light that is absorbed (Baumann L 2009).

As compared to other treatment options, the use of lasers aims at a selective removal of diseased target structures with maximum sparing of uninvolved adjacent skin. Several features are unique and responsible in order to achieve this goal. Laser light is both coherent and monochromatic. Thus, light of a given wavelength can be focused, enabling the delivery of extremely high power densities to a given treatment spot. Depending on the absorption of the irradiated light energy in tissue and on the delivered power density, different effects can be obtained. Lasers can be used to coagulate, vaporize, cut or ablate the skin surface. They also can be employed for photostimulation (Kaufmann R 2006). Moreover, a given chromophore target can be destroyed by selective photothermolysis, a theory introduced by Anderson and Parish in 1983 (Anderson RR and Parrish JA 1983). This theory states that the selectivity of a laser for its target relies on the fact that different wavelengths of light will be absorbed by different chromophores in the skin. Since the three main chromophores in the skin – water, hemoglobin and melanin, have different wavelengths, it is possible to select a specific laser with a wavelength that will be absorbed by the chromophore which allows treating the target without damaging surrounding tissues. In order to achieve this, the pulse width should be sufficiently long to heat the tissue to the level of destruction, but not long enough for that heat to transfer out of the target to surrounding normal skin.

The duration of active lasing is termed “pulse width” or “pulse duration”. The ideal pulse duration for selective destruction of a target is determined by the size of the target. The time it takes for the target to dissipate two-thirds of its heat to surrounding tissue is directly proportional to its size. This is termed the thermal relaxation time. The pulse width should be equal or shorter than this thermal relaxation time in order to selectively destroy the target and not the normal surrounding tissue. Since lasers can emit light in a continuous fashion, in spurts, or in pulses, it is important to emphasize that the theory of selective photothermolysis only applies to pulsed laser systems, as continuous lasing results in bulk heating of tissue and hence little “selectivity” (Baumann L 2009). Two important laser parameters are irradiance and energy fluence. Energy is expressed in joules, while the power of laser is expressed in watts. Fluence is defined as energy per area and calculates the amount of laser energy delivered in a single pulse (J/cm^2), and irradiance, also known as power density, determines the capacity of laser to incise, coagulate and vaporize tissue, with units in $watts/cm^2$.

By selecting a wavelength specific for the desired target chromophore and delivering that energy fast enough so that the chromophore’s relaxation time is not exceeded, thermal damage to nearby structures would be avoided. If the energy density (fluence) is sufficient to destroy the chromophore in this short window of time, therapeutic destruction could be maximized while minimizing thermal damage to the surrounding tissue (Houk LD and Humphreys T 2007). On the basis of these principles, laser parameters can be tailored to effect destruction of the tissue confined to microscopic sites of selective light absorption in the skin, such as blood cells and pigmented cells, with minimal collateral thermal damage (Anderson RR and Parrish JA 1983). Absorption and the amount of energy transfer per tissue volume mainly depend on the exposure spot size and wavelength of the laser used while the achievable power densities depend on the time in which a certain amount of energy is delivered to the tissue. That means that selectivity of laser light treatment can at least to some degree be achieved by choosing an appropriate laser light wavelength and spot size responsible for penetration depth (Anderson RR and Ross E 2000), and appropriate pulse duration responsible for the amount of heat diffusion.

When the target tissue is beneath the epidermis, protection of the epidermis is achieved by cooling systems which are critical in several laser procedures including vessel destruction and laser hair removal. There are several modes of cooling used in lasers today, including cryogen cooling, contact, ice and direct cold air (Baumann L 2009)

4. PIGMENT SPECIFIC LASERS

The main advantage of laser therapy compared to conventional methods of treatment of pigmented lesions is in selective photothermolysis, which results in excellent cosmetic result with minimal risk of scarring. It is also necessary to select the proper laser according to the location of the pigment within the lesion. Before treating pigmented lesions, it is extremely important to make a correct diagnosis. In cases of initially misdiagnosed melanomas, laser therapy not only prevents appropriate and timely therapy but may also worsen the prognosis. In most cases prior the treatment, dermoscopy is indicated, and if there is any doubt whether the lesion is benign, biopsy for histologic evaluation is mandatory (Bukvić Mokos Z et al. 2010).

The first invented laser was also the first one to be used for pigment removal. The ruby laser is excellent for the removal of any pigment, but unfortunately due to inability to differentiate unwanted from normal pigment, it has been replaced by the longer-wavelength lasers. Taking into account that melanin absorbs light from 500 to 1100 nm, there are several lasers that can be used to treat pigmented lesions of the skin, divided in the two main groups: 1) pulsed and quality switched (QS) lasers, 2) continuous wave (CW) and quasi-continuous wave lasers (Alster TS and Lupton JR 2001).

Since melanosomes are very small and have very short thermal relaxation time (around 1 millisecond), in order to selectively target melanin without harming the surrounding tissue, relaxation times equal or shorter than the thermal relaxation time of melanin should be used. Q-switched lasers have a mechanism that stores the generated energy and releases it as very short, intense pulses with the pulse width in the nanosecond range. This extremely short pulse duration makes Q-switched lasers ideal for selective destruction of melanin, without dissipation of heat from the target to the surrounding tissues. The most common Q-switched lasers used today are the Q-switched ruby (694 nm), Q-switched alexandrite (755 nm), Q-switched Nd:YAG (1064 nm) and the frequency-doubled Nd:YAG (532 nm). Choosing which Q-switched laser to use largely depends on the color and depth of the lesion to be treated. Longer wavelengths are better for deeper pigment and pigment in dark-skinned patients, whereas shorter wavelengths are used in fair-skinned patients with superficial lesions (Baumann L 2009).

Continuous wave (CW) and quasi-continuous wave lasers emit a constant beam of light with pulse duration longer than thermal relaxation of melanosomes, which results in surrounding tissue injury. Since they are unable to deeply penetrate the skin due to their shorter wavelengths, they are mainly used for treatment of epidermal lesions (Wheeland 2005). They remove the epidermal pigment by denuding the epidermis and destroying dermo-epidermal junction. Argon laser (488/514 nm) is a continuous wave laser, while potassium titanyl phosphate KTP (532 nm), copper vapor (511 nm) and krypton (520 nm) are quasi-continuous wave lasers which shutter the continuous wave beam into short segments producing interrupted emissions of constant beam. Nowadays, Q-switched lasers are the first choice for most pigmented lesions, but continuous wave and quasi-continuous wave lasers can also be effective if used properly by experienced operator (Wheeland RG 2005).

Adverse effects of laser therapy include hyperpigmentation or hypopigmentation, more often present in dark-skinned patients. Due to possibility of developing post-inflammatory hyperpigmentation when a higher epidermal melanin content is present, it is strongly recommended to avoid treating tanned patients or pre-treat with bleaching agents acting on pre-melanin synthesis (tretionin), melanin synthesis (hydroquinone, arbutin, vitamin C), or post-melanin synthesis (alpha hydroxy acid) (Baumann L 2009 & Bernstein EF 2007).

Pigmented lesions are categorized by location of pigment in three groups. Epidermal pigmented lesions include solar lentigines, ephelides, café au lait macules and seborrheic keratoses. Dermal lesions include melanocytic nevi, blue nevi, drug induced hyperpigmentation, and nevus of Ota and Ito. Some lesions exhibit both an epidermal and dermal component: Becker's nevus, postinflammatory hyperpigmentations, melasma and nevus spilus (Stratigos AJ et al. 2000).

4.1. Epidermal pigmented lesions

4.1.1. Solar lentigines

Solar lentigines are benign, brownish lesions that occur on light exposed skin surfaces from age 30 onwards, as a sign of photoaging. The size varies from 0,2 to 2 cm, there is no bleaching during winter, and the number increases with advancing age. Although not

premalignant, they present a significant cosmetic problem, and show the best results to laser therapy among all pigmented lesions (Bukvić Mokos Z et al. 2006).

Lasers used for treatment include Nd:Yag (532nm) laser, associated with purpura due to slight absorption by superficial melanin and dermal hemoglobin (Fitzpatrick RE et al. 1993 & Tan OT et al. 1992), Q-switched alexandrite (755 nm) laser, and QSRL (694 nm) which can cause hypopigmentation. Using QSRL laser, lentigines usually become 50% lighter after only one treatment, with lesions on the face being more responsive to treatment than those on the trunk or the extremities. Excellent results are accomplished after usually two to three laser sessions repeated in six to eight weeks interval (Bukvić Mokos Z et al. 2006).

4.1.2. Ephelides

Ephelides (freckles) are flat, round and tan spots that appear on a person's skin, most commonly on the cheeks and nose, as well as the arms and upper shoulders. They are seen most often in the red-haired or blond person as sharply demarcated, light brown-ginger macules, usually less than 5 mm in diameter. They multiply and become darker with sun exposure. Increased melanin is seen in the basal layer of the epidermis without any increase in the number of melanocytes, and without elongation of the rete ridges. No treatment is necessary (Weller R et al. 2011). In some cases, the appearance of ephelides is a genetic trait.

They are usually removed for cosmetic reasons using different methods, but good results are accomplished using QSRL laser with prior local anesthesia in a form of cream (EMLA, lidocain 2,5% and prilocain 2,5% in oil in water emulsion) during approximately one hour with occlusion. There are sometimes transitory hypopigmentations present, and photo protection is mandatory after the treatment (Bukvić Mokos Z 2006). The absence of purpura after the treatment with QSRL (694 nm) and alexandrite (755 nm) laser makes their use preferable when compared with green light lasers (Gravelink JM et al. 1993 & Nehal KS et al. 1996).

4.1.3. Café au lait spots

Café au lait spots are benign pigmented skin lesions that develop due to an increase in melanin content. The color varies from light to dark brown, and borders are either smooth or irregular. They are characterized histologically by an augmentation of pigmentation in the basal layer of epidermis. They can be seen in 20% of healthy people, or are associated with neurofibromatosis (in 95% of people with neurofibromatosis type 1), McCune-Albright syndrome, tuberous sclerosis and Fanconi anemia.

Café au lait spots respond variably to laser therapy and recur in as many as 50% of patients. Repeated treatments over a long period (several months or even years) are needed to achieve maximal clearing of the lesion. Repigmentation occurs from adjacent untreated melanocytes; therefore, the entire lesion should be treated at each session (Bukvić Mokos Z et al. 2010 & Stratiagos AJ et al. 2000 & Alster TS Lupton JR 2001).

4.1.4. Seborrheic keratoses

Seborrheic keratoses are common benign epidermal tumors, unrelated to sebaceous glands. They usually arise after the age of 50 on the face and trunk, often are multiple, but may be single. The appearance varies as flat, raised, filliform or pedunculated, color from yellow to black. In most cases the cause is unknown, but multiple lesions may be inherited in autosomal dominant manner, may follow an inflammatory dermatosis, or rarely may be associated with internal neoplasm (Leser-Trélat sign). Lesions may multiply with age, but remain benign (Weller R 2011). They can be removed for cosmetic reasons with curette under the local anesthetic, criotherapy or laser therapy. Treatment with QRSL or QS Nd:YAG laser systems is effective in removing the lesions, although after the treatment, transitory pigmentary alterations are common (Grekin RC 1993).

4.2. Dermal pigmented lesions

4.2.1. Melanocytic nevi

Melanocytic nevi (moles) are localized benign tumors of melanocytes. The cause is unknown, but genetic factor is likely in many families, working together with excessive sun exposure during childhood. With the exception of congenital melanocytic nevi, most appear in early childhood, with a sharp increase in numbers during adolescence and after severe burns. Further crops may appear during pregnancy, estrogen therapy, flare-ups of lupus erythematosus, or rarely after cytotoxic therapy and immunosuppression (Weller R 2011).

The use of pigment-specific lasers to remove congenital and acquired melanocytic nevi remains controversial. Around five percent of people with a large congenital nevus are at risk of developing a melanoma. Even though a laser could destroy all the melanocytic cells, it may enhance the likelihood of neoplastic change in the remaining nevus cells. This hypothesis is also explained by the fact that laser destroys the protective pigment, making the remaining cells an easier target for the UV light radiation (Rosenbach A et al. 1997). It is necessary to emphasize that the primary treatment of choice for nevus removal is surgical excision followed by histopathologic examination. Laser therapy has been reserved for the lesions located at cosmetically or functionally sensitive areas where surgical excision might leave a disfiguring scar (Bukvić Mokos Z et al. 2010).

Acquired melanocytic nevi should always be carefully evaluated clinically before laser treatment. Benign junctional melanocytic nevi show good therapeutic response to relatively short wavelengths, while deeper compound or dermal types of melanocytic nevi require longer wavelengths, higher fluencies and longer pulsewidths, and still tend to recur (Stratigos AJ et al. 2000 & Alster TS Lupton JR 2001 & Hague JS Lanigan SW 2008 and Suzuki H Anderson RR 2005). Still, laser treatment is associated with several problems: variable response, permanent hypopigmentation, local scarring and rarely achieved complete clinical response. Additionally, incomplete nevus removal may be followed by pseudomelanoma development, and early melanoma lesions can be easily mistaken for benign spots (Bukvić Mokos Z et al. 2010).

4.2.2. Blue nevi

Blue nevi, so-called because of their striking gray-blue color; usually appear in childhood and adolescence as solitary lesions on the limbs, buttocks and lower back (Weller R 2011). They can be successfully removed by longer wavelength red-light lasers. However, since the differential diagnosis includes melanoma, surgical excision is the safest method in this indication (Milgraum SS et al. 1995).

4.2.3. Drug induced hyperpigmentation

Drug induced hyperpigmentation should be in a differential diagnosis in a patient presenting with unexplained pigmented lesion, especially when on multidrug regimen. It can be induced by various drugs, most commonly amiodarone and minocycline (Alster TS Lupton JR 2001).

Patients taking amiodarone may develop a phototoxic exanthema limited to sun exposed areas, or a blue-gray dermal melanosis – ceruloderma, which develops due to deposition of melanin and lipofuscin contained in the macrophages and the endothelial cells in the dermis. This pigmentation is reversible within a year when the drug is stopped (Wolff K Johnson RA 2009). The treatment is successful using QRSL with disappearance of lesions after one session (Karrer S et al. 1999).

The skin hyperpigmentation seen with minocycline doesn't occur due to melanin deposits, but an iron containing brown pigment located in dermal macrophages usually on extensor surfaces of the legs, dorsa of the feet and around the eyes. After stopping of the drug, the discoloration will disappear within a year (Wolff K Johnson RA 2009). Both the QSRL and 1064nm QS Nd:YAG lasers have been reported to be very effective in cases where pigmentary reaction is profoundly disfiguring (Zollner et al. 1996 & Knoell KA et al. 1996).

4.2.4. Nevi of Ota and Ito

Nevi of Ota and Ito are colored skin markings of slate-brown or blue/grey coloring. They are unusual birthmarks in which the melanocytes are found to be in the dermis instead

of the epidermis. They are most commonly found in Asian populations with estimation that 0.2-0.6% of Japanese people have nevi of Ota which are much more common than nevi of Ito. They are present at birth in 50% of cases but may appear during adolescence or adult life. The difference between the two is in a location. Naevus of Ota is on the forehead and face around the eye area, while naevus of Ito is on the shoulder and upper arm area. Laser treatment by 1064 nm Q switched Nd:YAG or QS ruby laser is more effective in light skinned individuals than in those with dark skin. Multiple treatments are necessary, often with a combination of devices. Unfortunately, recurrence is common after laser clearance, sometimes resulting in a darker hue. Q-switched Alexandrite was found to be effective in the treatment of nevus of Ota but limited results were accomplished for the nevus of Ito (Wang HW et al. 2006).

4.3. Mixed epidermal/dermal pigmented lesions

4.3.1. Becker's nevus

Becker's nevus usually appears in boys in puberty, unilaterally on the shoulder, pectoral region or back, in a form of sharply demarcated hyperpigmentation with hypertrichosis. Sometimes, these changes may be accompanied with hamartoma of the smooth muscle (Bukvić Mokos Z 2006). Patients should be evaluated for soft tissue and bone abnormalities, as those can occasionally be associated with this condition. Treatment is usually done by a combination of QSRL, which damages superficial pigmented cells of the nevus, although a significant amount of pigment persists in the adnexal structures, and longer pulse pigment specific laser, which removes the hairs of Becker's nevus (Alster TS 2000 & Kilmer SL et al. 1994). Complete removal is difficult with a high rate of recurrence associated with hypopigmentation and incomplete removal.

4.3.2. Postinflammatory hyperpigmentations

Postinflammatory hyperpigmentations present after numerous inflammatory dermatoses, especially in patients with darker skin. In these changes, there is a rupture of epidermal-dermal border, with the location of melanin in the dermal macrophages. Postinflammatory

hyperpigmentations are especially resistant to therapy, with only slight improvement after multiple sessions with QSRL (Bukvić Mokos Z 2006).

4.3.3. Melasma

Melasma is an acquired, symmetrical hypermelanoses occurring on the sun-exposed skin, especially the face. The areas of increased pigmentation are well defined and their edges may be scalloped. The condition is much more common in women, affects all races, but is more prevalent among dark-skinned individuals. The hypermelanoses becomes darker after exposure to the sun. There are many causes, including sunlight, pregnancy, estrogens, oral contraceptives, scented cosmetics, thyroid dysfunction and photosensitizing drugs. Treatment is unsatisfactory. Some find treatment with bleaching agents that contain hydroquinone helpful (Weller R 2011). Laser treatment produces variable results, with sometimes even worsening of the condition (Stratigos AJ 2000 & Alster TS and Lupton JR 2001 & Taylor CR Anderson RR 1994).

4.3.4. Nevus spilus

Nevus spilus is a typical café au lait macule with multiple darkly pigmented speckles within it. These often represent either compound or junctional nevi. There are several reports of dysplastic nevi developing within nevus spilus and of melanoma arising within these lesions, which is the reason why it is recommended to make biopsy in case of any atypical appearing lesion within nevus spilus (Bukvić Mokos Z et al. 2010). Several session with 510 nm PLDL, 532 nm QS Nd:YAG, QRSL or QS alexandrite laser are needed in six to eight weeks intervals to progressively remove the unwanted pigment (Goldberg DJ 1999 & Kilmer SL and Alster TS 1996).

4.4. TATOOS

With the increase of prevalence of tattoos in the past years, there is also an increased need for their removal. In the past, laser tattoo removal involved the non-specific ablation of the skin overlying the tattoo, resulting in removal, but also pigment alteration and scarring. Currently, tattoo removal is performed primarily via selective photothermolysis, using the tattoo ink as a chromophore for the laser. Each color of the ink is absorbed by a different wavelength of light, and hence the more ink colors in the tattoo, the more difficult it is to remove. Cosmetic tattoos are usually a blend of several different inks, rendering them extremely challenging to remove with laser. Professional tattoos typically place ink in the mid-dermis, requiring a device that can penetrate to this depth in order to achieve adequate treatment. Amateur tattoos typically use less ink and placement is more superficial, making them easier to remove (Baumann L 2009).

The removal of tattoo ink must be achieved with a very short pulse-width system in the nanosecond range, just as in removal of melanosomes from the skin. These systems are Q-switched laser devices – ruby, alexandrite, and Nd:YAG. The ruby (694 nm) was the first one available and is good for the removal of blue and black pigments (Taylor CR et al. 1990). The alexandrite (755 nm) is also effective at removing blue and black pigments, but in addition, has the unique ability to remove green, which is historically one of the most difficult colors to eliminate (Fitzpatrick RE Goldman MP 1994). The ND:YAG (1064 nm) is used for the basic black ink, especially in professional tattoos due to its capacity for deep penetration. The frequency doubled Nd:YAG (532 nm) can be used for red pigments.

The mechanism of removing tattoo is photoacoustic effect which leads to rupture of the pigment containing cells – perivascular fibroblasts, macrophages and mastocytes. As a result, there is accumulation of neutrophiles, and re-deposition of ink into fibroblasts, macrophages and mastocytes, with the part of the ink being removed by the lymph. Adittionally, part of the pigment is removed by transepidermal migration. Older tattoos are more easily removed than the new ones, and distally placed tattoos are less responsive to treatment, probably due to the effect of lymphatic system (Bukvić Mokos Z 2006).

Generally, a combination of lasers is needed for successful removal of a tattoo, although residual ink or shadow may persist despite numerous treatment sessions. For the removal of professional tattoos, eight to twelve treatments spaced at least 6 weeks apart are required, while for amateur tattoos, three to five treatments are generally effective (Bernstein EF 2006).

In patients with darker skin types, tattoo removal may result in scarring or dyspigmentation. Moist wound healing via topical emollient creams and a dressing are recommended for all patients for 1 to 2 weeks after laser treatment. Straying from this regimen will increase the risk of postinflammatory changes and scarring, and delay additional treatments (Baumann L 2009).

5. LASER HAIR REMOVAL

Mechanism of laser or light-assisted hair removal is based on the principle of selective photothermolysis with wavelengths of light well absorbed by follicular melanin and pulse durations that selectively thermally damage the target without damaging surrounding tissue (Dierickx C et al.1998).

The stem cells responsible for the hair growth cycle are located at the outermost cell layer of the hair follicle and do not contain melanin pigment. Thermal injury to the follicular stem cells causes permanent hair loss. Therefore, thermal diffusion from the hair absorbing laser light must reach the follicular stem cells. Nanosecond or microsecond pulsed light cannot be used for permanent hair removal, because it can destroy melanin-containing hair, but cannot destroy follicular stem cells which have no melanin. Therefore, pulse-width of lasers available for hair removal must be longer than pigment-specific lasers, and millisecond pulse-width lasers are chosen for hair removal (Watanabe S 2008).

The choice of laser depends on the hair color and texture, as well as the patient's skin color. The strongest absorption of light by melanin is at the shorter wavelengths, which penetrate less deeply, so some do not effectively reach the hair bulb. For this reason, the ruby laser (694 nm) is no longer used. Darker and coarser hair absorbs more light energy from the laser device, and hence can be removed at even longer wavelengths. However, melanin in the skin competes with the melanin in the hair for laser absorption. The darker the skin color, the more difficulty laser has in distinguishing the hair melanin from skin melanin and the more difficult the treatment.

Cooling is critical for protection of epidermis in hair removal. Without cooling, the melanin in the skin would first absorb the laser light and burn the skin as opposed to removing hair. When used without cooling, many of the wavelengths used for hair removal, can be actually used for epidermal pigment removal.

In the book Cosmetic Dermatology (Baumann L 2009), the author presents three most important lasers used nowadays used for hair removal.

The alexandrite laser (755 nm) is the shortest wavelength removal system used. Due to high absorption of light by melanin at this wavelength, the alexandrite is able to remove lightly pigmented hairs from light skin. It should be used with extreme caution in darker skin types

due to possible hypopigmentation and postinflammatory hyperpigmentation. There are also reports of paradoxical hypertrichosis after laser hair removal with alexandrite (Alajlan A et al. 2005).

The diode (800 and 810 nm) laser can be used on all skin types, while the best results are achieved on darker hair. This is the most commonly used laser for hair removal nowadays.

The Nd:YAG (1064nm) operates at wavelength minimally absorbed by melanin, which makes this laser effective for removal of dark, coarse hairs. It is the safest system for hair removal in darker skin types, although in comparison to other lasers, in one study it was found to be more painful and less efficacious (Rao J and Goldman MP 2005).

Prior the treatment, skin should not be tanned, damaged, or show any signs of infection. Test spots are performed 2 weeks before the full treatment. Immediately after the treatment, the area should exhibit follicular edema and erythema which is the normal response to laser heating of the follicle. To avoid postinflammatory changes in darker skin types, topical steroid is often used for 5 days. Complete removal can take from three to ten sessions spaced 1 month apart, depending on the hair, treatment area and the patient's skin type. Sun protection is critical both before and after laser hair removal (Baumann L 2009).

6. VASCULAR LASERS

In the treatment of vascular lesions, the targets of laser treatment are not red blood cells, but endothelium and vessel walls. The laser treatment of vascular lesions is based on selective absorption by blood with thermal injury to the vessel wall. Therefore, the pulse-width of the vascular-specific lasers must be longer (microsecond-domain) than that of pigment specific lasers. In general, a pulse-width of 450 μs is chosen for the treatment of port wine stain. Longer pulse-width lasers are better for the treatment of vascular lesions with thicker vessels, but shorter pulse-width ones are better for those with thinner vessels. Since lasers with microsecond-domain pulse-width have a higher possibility to cause scarring than those with nanosecond domain pulse-width, cooling devices are needed for protection of the skin surface from thermal injury by laser irradiation (Watanabe S 2008).

The chromophore for vascular lesions is oxyhemoglobin. The peak absorption by oxyhemoglobin lies somewhere between 500 and 600 nm. Most of the lasers used for vascular lesions emit light with wavelengths in this range, but longer wavelengths can also be used because they penetrate deeper, owing to less scattering by collagen. The oxyhemoglobin target must absorb the light, generate heat, and coagulate the vessel, all without damaging the surrounding tissue. The most popular systems used today for vascular lesions are the pulsed dye laser PDL (585 nm), long pulsed-dye laser (595 nm), the potassiumtitanylphosphate KTP (532 nm) and Nd:YAG (1064 nm) neodymiumdoped yttrium aluminium garnet.

PDL devices are effective for telangiectasias on the face, neck, and chest, but perform less well on the body, which is related to the short wavelength and superficial penetration of the laser. They are used for vascular malformations in both adults and children, including hemangiomas, port wine stains and lymphangiomas. PDLs available today come equipped with cryogen cooling, various spot sizes, and adjustable pulse durations that should be adjusted to the vessel diameter and its thermal relaxation time. The larger the diameter of the vessel, the longer the optimal pulse width should be, because very short pulse widths lead to rupture of the vessel and resultant purpura. Side effects in addition to purpura include blistering, postinflammatory pigment alteration (PIPA) caused by the cryogen spray, as well as scarring from overly aggressive fluences. Lesions on the chest and neck should always be treated with lower energies than those on the face (Baumann L 2009).

In less than 1% there are side effects of PDL treatment such as ulceration with scarring and hypopigmentation. After the treatment, local ecchymoses, swelling and discomfort can occur, but the application of cooling gel or ice packs will minimize discomfort. Local erythema or purpura may persist for 7 to 14 days, sometimes followed by hypopigmentation or hyperpigmentation and atrophic scarring. High SPF creams and emollients should be used until clearing of the purpura. PDL therapy can be repeated at 8-12 week intervals, and several treatments are frequently required (Barčot Z and Župančić B 2010).

The KTP laser (532 nm) is highly absorbed by oxyhemoglobin, and has proven to be at least as effective for facial telangiectasias as the PDLs (Uebelhoer NS et al. 2007). It can operate in a range of longer pulse widths, resulting in no purpura, but its shortcomings are related to its shorter wavelength and lack of penetration. KTP is the most effective for treatment of very superficial vessels, but the treatment of darker skin should be performed with caution because 532 nm wavelength is as well absorbed by melanin.

Longer wavelength lasers allow for deeper penetration and are excellent choice for lower extremities. They are also particularly useful for high flow vessels on the face (Baumann L 2009).

Lesions amenable to laser treatment with a vascular wavelength include hemangiomas, nevus flammeus (port wine stains), lymphangiomas, venous lakes, cherry angiomas, telangiectasias, spider veins, poikiloderma of Civatte, and erythema from rosacea (Baumann L 2009). These lesions are removed after several treatments, usually 4 to 5 weeks apart (Railan D et al. 2006). In most cases, treatments are very efficient and well tolerated, without the need for anesthesia (Dover JS Arndt KA 2000). The exceptions are treatments of nevus flammeus and hemangiomas in children, which frequently require general anesthesia (Tanzi EI et al. 2003).

Taking into account a great number of vascular changes and a limited frame of this paper, in the following section the analysis will be focused on the most frequently treated vascular changes by lasers.

6.1. Congenital vascular changes

Almost all congenital vascular abnormalities affect the skin and are evident from birth or become so during the first few weeks of life. The two most common types of vascular birthmarks, hemangiomas and vascular malformations, may appear to be very similar but their course and treatment are different (Barčot Z and Župančić B 2010).

Prior to formal laser therapy, a test treatment should be considered with evaluation of patients in 2-3 months. During each application, overlapping of pulses (25-30%) is done with PDL. At least transiently immediate purpura is desired, and indicates appropriate laser energy settings (Eifert S 2000).

6.1.1. Hemangiomas of infancy

Hemangiomas of infancy are the most common benign tumors of childhood, composed of proliferating endothelial tumor cells. They usually manifest as cutaneous birthmarks, characterized by early, rapid proliferation and regression in the majority of cases (Lin RL Schwartz RA 2006). They present in 3% of newborns, as a result of abnormal changes in angiogenesis, which leads to over-proliferation of vascular entities (Geronemus RG 1995). Most of them develop sporadically, but may also be a part of larger syndromes associated with high rates of life-changing morbidity and mortality. Their frequency tends to be higher in infants who are preterm, weighing less than 1500 g, with females being more affected than males (No D et al. 2003). The most common location is head and neck (59%), followed by the trunk (24%), lower extremities (10%), and upper extremities (7%) (Chiller KG et al.2002). Although majority of hemangiomas begin to slowly involute by 1 year of age, complete resolution often takes 5 to 12 years. Regression typically occurs in 50% of patients by age 5, in 70% by age 7, and in 90% by age 9 (Kapur N et al. 2002).

The goals of management are to prevent or avoid life or function threatening complications, to prevent permanent disfigurement, to minimize the psychological impact on the patient and parents, to avoid aggressive or scarring treatments, and to avoid/treat ulceration to minimize pain or scarring (Iyer S Fitzpatrick RE 2005). The selection of optimal laser therapy for hemangiomas depends strongly on the evolutionary stage of the lesion, because early lesions or those in the late evolutionary phase tend to respond better.

Treatment parameters of PDL are generally 585 nm, 0,5-1,5 ms, 5 to 7 J/cm^2 with epidermal cooling. For proliferative lesions, treatments are spaced at 2-3 weeks intervals and at 4-6 weeks for nonproliferative lesions. However, PDL is limited by its depth of penetration, and is ineffective for deep hemangiomas (Barčot Z and Župančić B 2010). Lesions up to 3 mm in depth can usually be completely removed, while lesions deeper than 3 mm are more resistant to PDL treatment.

For the deeper situated lesions, lasers of choice are continuous wave Nd:YAG, newer long-pulsed dye lasers (595 nm, 1,5 ms) or pulsed Nd:YAG that have more vascular selective tissue reaction (Čeović R 2006).

6.1.2. Vascular malformations

Vascular malformations are always present from birth even though they might not be apparent, never disappear, and often grow during person's lifetime (Chiller KG et al. 2002). Two thirds are venous, and unlike hemangiomas don't have a growth cycle and spontaneous regression, but persist throughout lifetime, grow slowly, sometimes in response to injury or changes in blood and lymph pressure. They progressively produce ectasia of vascular structures, increasing the diameter of vessels without increasing their number. While expansion of hemangiomas is due to hyperplasia, in vascular malformations it is hypertrophy (Barčot Z and Župančić B 2010). The diagnosis of vascular tumor is based on history and physical examination alone in about 95% of cases (Frieden IJ et al. 1997), but ultrasound with Doppler is the most cost-effective imaging technique. Venular malformations can be divided into midline malformations and traditional venular malformations known as port wine stains, telangiectatic nevus, or nevus flammeus (Barčot Z and Župančić B 2010).

6.2. Acquired vascular changes

6.2.1. Telangiectases

Telangiectases are permanently dilated and visible small vessels in the skin. They appear as linear, punctuate, or stellate crimson-purple markings anywhere on the body, but

most frequently on cheeks, beard, nose or legs. They are usually just a cosmetic defect as a consequence of chronic sun exposure, radiation, or corticosteroid therapy, but can also be a part of clinical picture of different diseases (Ataxia telangiectasia, Rendu-Osler-Weber, CREST syndrome, Xeroderma pigmentosum, Lupus erythematosus) (Tan OT et al. 1989). Treatment of telangiectases on the face is one of the most frequently performed laser procedures using PDL, KTP laser, or pulse Nd:YAG laser. With newer PDL, it is possible to avoid post treatment purpura, often seen in the past. KTP lasers do not cause purpura, but the degree of removal is lower than with PDL (Čeović R 2006).

6.2.2. Venous lake

A venous lake is a solitary, compressible, violaceous, 0.2 to 1 cm papule commonly found on sun-exposed surfaces of the vermilion border of the lip, face and ears in elderly. Treatment may be requested for cosmetic reasons using argon and KTP laser when blood vessels have diameter of less than 1,2 mm (Dehkor PS 2006). Nd:YAG laser is shown to be highly effective, with a clearance rate of 94% following a single treatment (Bekhor P 2006).

6.2.3. Cherry angiomas

Cherry angiomas are benign small bright red papules, usually multiple most frequently seen on the trunks of middle aged and elderly. Treatment is by flashlamp PDL or KTP laser (Landthaler M and Hohenleutner U 2006).

6.2.4. Pyogenic granulomas

Pyogenic granulomas are common benign acquired hemangiomas often seen in children and young adults. They develop at sites of trauma, over the course of a few weeks, as bright red raised, sometimes pedunculated and rapsberry-like lesions which bleed easily (Weller R et al. 2011). Smaller pyogenic granulomas are treated by argon or KTP laser, and bigger ones by CO2 laser (Landthaler M Hohenleutner U 2006).

7. RESURFACING LASERS

Over the last 20 years there have been major advances in the field of nonsurgical skin rejuvenation. With advances in laser technology it is now possible to reduce, and in some cases remove, facial wrinkles, acne scars and other facial scars, and a variety of skin growths and blemishes with minimal disruption and downtime for the patient.

However, laser „resurfacing“ is considered to be the most complicated corrective laser operation, which demands elaborate preoperative and postoperative procedure (Kostović K 2006). One of the crucial parts of treatment is patient selection. An ideal candidate is patient of any age in good health, with fair skin type, who has photodamaged skin and moderate postoperative expectations (Alister TS 1999). It is important to take detailed anamnesis in order to establish the capacity of wound healing, as well as possible conditions that could have an impact on it: diet, anemia, immunodeficiency, connective tissue disorders, and isotretinoin therapy (Kostović K 2006).

Absolute contraindications to the procedure include a history of keloids and connective tissue disease, and history of radiation therapy or scleroderma due to reduction in adnexal structures that serve as a pool of stem cells for reepithelialization. Other contraindications are recent (within one year) isotretinoin therapy that can result in atypical scarring, unrealistic expectations, and epilepsy. Resurfacing performed soon after a face-lift procedure or blepharoplasty increases the risk of skin necrosis, ectropion and scarring due to undermined vascularization. In order to improve the outcome of laser resurfacing preoperative regimens, local hydroquinone and topical tretinoin are used. In all patients, prophylactic oral antiviral therapy and antibiotics should be prescribed (Štulhofer Buzina D et al. 2010).

Anesthesia can be achieved by local anesthetics, regional nerves block, or IV anesthesia. After the procedure, wound care can be performed using the opened or closed technique. Possible early complications are infection, contact dermatitis, acne and milia. Late complications include postinflammatory hyperpigmentation - especially in darker skin, relative hypopigmentation, permanent hypopigmentation which appears in 5-12 months after laser resurfacing and is more common in light skin individuals, erythema that lasts longer than 3 months, and scarring (Kostović K 2006).

7.1. Ablative resurfacing

Ablative resurfacing involves wounding the skin to the dermal level, thereby removing photodamaged areas of the epidermis. Dermal wound healing stimulates collagen production. Ultimately, ultrastructural remodeling results in rejuvenated skin. Resurfacing occurs at the 3 levels: superficial (wounds from the stratum corneum through the papillary dermis), medium (wounds of the upper reticular dermis) and deep (wounds of the midreticular dermis). Options for ablative resurfacing include dermabrasion, chemical peeling, and laser surgery (Tanna N 2014). The popularity of dermabrasion has diminished because of an increased prevalence and awareness of blood-borne pathogens, as well as technical difficulties in maintaining the proper depth. While superficial peeling agents such as glycolic acid remain popular, they do not penetrate the dermis. A medium-to-deep chemical peel must be used to perform ablative resurfacing.

Laser skin resurfacing (LSR) has become an important component of rejuvenation surgery. Although this technology is relatively new, its benefits are clear. The laser allows for precise control of ablation depth, and it permits the surgeon to vary these depths as needed. In addition to such precision, LSR causes favorable heating of the dermis, which tightens collagen fibers and stimulates neocollagen secretion by fibroblasts (Tanna N 2014).

Resurfacing using Er:YAG laser is an optimal method for removal of mild to moderate superficial wrinkles and scars, while pulsed CO_2 laser is used for removal of deeper scars and wrinkles (Štulhofer Buzina D 2006).

With the rapid vaporization of tissue with any ablative laser comes tissue tightening and smoothening of the skin, which is not achieved with most other nonablative laser systems (Baumann L 2009).

7.1.1. CO_2 laser

Ablative resurfacing has historically been performed using the CO_2 laser. Since its introduction in 1968, it's been used for the treatment of acne scars, rhytides, actinic chelitis and other symptoms of photoaging (Baumann L 2009). At a wavelength of 10,600 nm, in far infrared spectrum, energy is preferentially absorbed by intracellular and extracellular water creating rapid heating and vaporization of tissue. New high energy short pulsed CO_2 lasers and scanned cwCO_2 produce relatively superficial tissue vaporization and minimize deeper

thermal injury that is associated with undesirable side effects like scarring and hypopigmentations (Štulhofer Buzina D et al. 2010).

The laser penetrates approximately 30 μm within the skin. Thermal injury is prevented when the laser pulse width is less than the thermal relaxation time of the tissue. The critical pulse width is less than 1 millisecond. The first pass of the CO_2 laser causes approximately 50-70 μm of ablation. Since the resulting layer of thermal necrosis has less tissue water than the uninjured skin, successive passes result in less tissue vaporization. With each pass, however, the total depth of thermal necrosis increases slightly, but does not exceed a depth of 100 μm if the pulse width is kept at less than 1 millisecond (Tanna N 2014).

The pulsed CO_2 resurfacing allows for precise depth of ablation and controlled thermal damage. It appears that thermal injury below the vaporization zone induces desiccation and collagen shrinkage, which serves as a scaffold for the formation and deposition of new collagen. Immunohistochemistry evaluations demonstrated up-regulation of procollagens I and II, interleukin 1-β, TNF-α, TGF-β1 and matrix. The CO_2 laser resurfacing is a painful method due to tissue heating, so topical anesthetic agents should be used for treatment of individual cosmetic units, with adding of systemic agents for larger areas such as the whole face (Štulhofer Buzina D et al. 2010).

After the treatment, edema and exudation occur, most severely during second and third postoperative days. The application of bio-occlusive dressings will minimize pain and speed up reepithelization which is usually completed in 10-14 days. Marked erythema can persist up to 1 year, and sun avoidance is mandatory. The most common adverse effects are dyspigmentations in the form of post-inflammatory hyperpigmentations in dark-skinned patients, and more serious late hypopigmentations which occur 6-12 months after the treatment. Other possible complications include eczema, scarring and skin infections (Štulhofer Buzina D et al. 2010).

7.1.2. Er:YAG laser

The erbium:yttrium-aluminum-garnet (Er:YAG) offers precise tissue ablation with minimal thermal damage. It emits a wavelength of 2940 nm and is even more highly absorbed by water (peak water absorption is at 3000 nm), which results in a more superficial depth when compared to the CO_2 laser and less collateral thermal damage (Baumann L 2009).

Pulsewidths of 200-350 microseconds result in thermal necrosis of less than 10 μm in depth. Unlike the CO_2 laser, with successive passes of the Er:YAG laser, the thermal injury depth remains stable. Additionally, stacking Er:YAG pulses slightly reduces the ablative efficiency. With the CO_2 laser, the ablative efficiency decreases with successive passes (Tanna N 2014).

During Er:YAG laser ablation, delivered energy is absorbed into heat, but escapes as steam decreasing thermal injury to the surrounding tissue. Hence, no visible contraction of dermal collagen fibers is observed (Tanzi EL et al. 2003). This may be a reason for moderate results after Er:YAG resurfacing in comparison with CO_2 treatment, but also makes it a safer method especially suitable for mild to moderate rhytids and photodamaged skin (Tenzel EL and Alister TS 2003).

Patient selection, preoperative and postoperative regimens are similar to the CO_2, but with the safer profile of Er:YAG in darker skin types and reduced risk of pigmentary changes. Post-treatment swelling may persist for 10-14 days, but post-inflammatory erythema resolves in 6 weeks to 6 months, depending on the depth of resurfacing. Major benefits of Er:YAG are lower morbidity, rapid reepithelization, faster resolution of post-treatment erythema and less serious complications when compared to CO_2 treatment (Štulhofer Buzina D et al. 2010).

7.2. Nonablative resurfacing

Nonablative lasers developed as an alternative to traditional ablative resurfacing. Nonablative methods induce careful heating of deep dermal layers while protecting the epidermis by cooling (Kelly KM et al. 1999). Nonablative nonfractionated lasers produce a gentler effect on the skin, inducing controlled tissue injury in the dermis and stimulating dermal remodeling and collagen production (Preissig J, et al. 2012).

Although these devices do not produce the same degree of improvement as traditional CO_2 or Er:YAG resurfacing techniques, they are an excellent alternative for people seeking gradual aesthetic improvement with minimal downtime and side-effects. The potential damaging risks associated with nonablative lasers are significantly lower compared to ablative lasers (Ciocon D et al. 2011), and patients experience as little as a few hours of erythema with no scaling or peeling of the skin. Patients with darker skin tones are also candidates for nonablative lasers

as they do not induce the abnormal pigmentation that often arises with ablative laser use on darker skin (Newman JB et al. 2000).

The long-pulsed 1320-nm Nd:YAG laser was the first nonablative laser to reach the commercial market. It functions by avoiding damage to the epidermis and instead targeting the dermal layers to stimulate new collagen growth. The water in the skin absorbs the 1320-nm wavelength in particular, creating an even distribution of energy without damaging melanin or hemoglobin. As such, this laser is effective on all skin types without producing changes in pigment (Preissig J, et al. 2012). The laser accelerates the productive capacity and vitality of fibroblasts, as seen in its promotion of the two major secretory factors they produce: basic fibroblast growth factor (bFGF) and inhibiting transforming growth factor β1 (TGF-β1) (Zhenxiao Z et al. 2011). The laser actively reverses visible and histopathologic signs of skin aging as it stimulates collagen types I, III, and VII, and tropoelastin production (El-Domyati M et al. 2011). The laser has been noted as safe and effective in the treatment of acne and related scarring by shrinking sebaceous glands and minimizing sebum production which prevents future acne lesions (Yaghmai D et al. 2005).

The 1319-nm pulsed energy laser is a member of the mid-infrared laser class, which is effective at treating fine facial wrinkles. It resurfaces the skin to improve the appearance of wrinkles, acne and related scarring, skin tone, and texture. Like other nonablative lasers, the 1319-nm pulsed energy laser thermally targets the fibroblasts that reside in the dermal layer to stimulate production of collagen (Bogle MA 2008). These lasers are not beneficial for treating pigment discolorations or vascular abnormalities, although they are designed to safely treat all skin types and shades (Preissig J, et al. 2012).

The 1450-nm diode laser is effective for the treatment of facial acne by partially damaging sebaceous glands to reduce sebum secretions, as well as for improving the appearance of scarring (Friedman PM et al. 2004). It has demonstrated greater scar response after treatment than the nonablative 1320-nm Nd:YAG laser by targeting sebaceous glands in the upper dermis while sparing the epidermis, reducing downtime (Paithankar DY et al. 2002). Downtime is minimal and is restricted to temporary erythema, edema, and hyperpigmentation after treatments (Tanzi EL et al 2003).

7.3. Fractional resurfacing

The search for laser rejuvenation alternatives was prompted by the high complication rates associated with traditional ablative resurfacing. The concept of fractional resurfacing was introduced in 2004 by Manstein et al. Fractional resurfacing produces clinical and histologic changes comparable to ablative lasers, but spares most of the skin and is characterized by rapid reepithelization and mild side effects just like nonablative resurfacing (Štulhofer Buzina D et al. 2010).

The term "fractional" refers to treating a portion or fraction of the skin, without specification of laser type, spot size or wavelength. By treating only microscopic areas in one session, healing time is greatly reduced. Each treated area is surrounded by normal viable skin from which migration of keratinocytes occurs. Each treatment spot is termed a microscopic treatment zone (MTZ) which heals via migration of the normal surrounding epidermis, as opposed to healing via differentiation. Very high energies can be tolerated without bulk heating, and epidermal healing is completed within 36 hours. This rapid healing time reduces the incidence of infections, pigment alterations, and scarring (Baumann L 2009). The higher the density, the closer together the MTZ will be, and the more agressive the treatment. Fractional devices come in two varieties: ablative and nonablative (Baumann L 2009).

7.3.1. Ablative fractional lasers

The most recent generation of ablative lasers are the fractional ablative lasers, with the start of usage around 2007. These lasers have been able to reduce the trauma of the treatment and decrease downtime while retaining resurfacing power. They are significantly safer than their nonfractionated counterparts, but they still retain a high risk of potential damage in the form of scarring, discoloration, and skin infection (Chwalek J and Goldberg DJ 2011).

The main use of these lasers is for mild skin tightening to battle laxity and rhytides. However, they can also treat photodamage, atrophic acne scars, hypopigmented scars, and dyspigmentation (Karsai S et al. 2010). Overall, patients can expect moderate down time and moderate risk of complications (Preissig J, et al. 2012).

Fractional technology was first developed in use with CO_2 lasers. Side effects are rarer than with nonfractional lasers, and only a few cases of scarring following fractional CO_2

therapy have been reported (Fife Djet al. 2009). Currently, the main representatives of ablative fractional CO_2 lasers are the Lumenis UltraPulse Encore, and Fraxel re:pair (Preissig J, et al. 2012).

Fractional technology can be applied to Er:YAG lasers in the same way that it was developed for CO_2 lasers. Similar to the comparison between nonfractionated CO_2 and Er:YAG lasers, the fractionated versions of these two laser types have similar postoperative and comparable cosmetic improvement (Preissig J, et al. 2012).

7.3.2. Nonablative fractional lasers

The 1410-nm Laser (Solta Fraxel Re:Fine) is nonablative fractional laser designed to resurface the skin, reducing the appearance of superficial rhytides. It requires 3 to 5 treatments to see results with a minimal downtime of 3 to 5 days. The laser is safe in all skin types, making it very versatile for a broad spectrum of patients.

The 1440 Nd:YAG Laser (Cynosure Affirm and Palomar StarLux) improves the appearances of rhytides by microrejuvenation, which is brought about by the induction of microcolumns of even heating. The StarLux system employs an additional cooling system to improve patient comfort while allowing for a higher power treatment, increasing efficiency. The Affirm laser distinguishes itself via its combined apex pulse (CAP) technology, which evenly distributes energy across a 300-μm depth, focusing the laser on the desired dermal skin layers. This laser also utilizes a cooling system for patient comfort.

The 1540-nm (PalomarStarLux 1540 and Palomar Icon) and 1550-nm (Solta Fraxel re:store) erbium fiber lasers and the 1927-nm thulium fiber laser (Solta Fraxel re:store DUAL) are fractional lasers with ablative and nonablative capabilities that allow them to treat both epidermal and dermal skin imperfections. This laser class safely and effectively treats epidermal pigmentation, photoaging, melasma, rhytides, atrophic, surgical, and acne-related scarring and additional textural imperfections. The fractionated component of the laser allows for a spatially precise, regular pattern of columns of tissue injury to be created across the treated region, retaining the healing function of the epidermis even while targeting both skin layers. Through the fractionated treatment pattern that targets both the dermis and epidermis,

these lasers provide the significant skin resurfacing capabilities of an ablative laser while retaining the downtime profile of a nonablative laser. However, because the laser can only target a fraction of the patient's skin at a time, more treatments are typically required at 2 to 4 week intervals for the best outcomes (Preissig J, et al. 2012).

8. SAFETY MEASURES

The use of lasers in medical practice has seen great expansion in the past decades. However, these devices may also pose a significant hazard. Laser hazards are generally divided into beam hazards and nonbeam hazards. Beam hazards inflict ocular and cutaneous injury, whereas nonbeam hazards stem from the laser device itself or its interaction with materials within the surgical environment. The latter include laser plume hazards and electrical hazards inherent in a high voltage system that is a laser device (Dudelzak J and Goldberg DJ 2011)

8.1. Operator education

The laser should be operated only by a person who has had training in laser theory, techniques of control, and operation of the laser. It is the physician's responsibility to select appropriate settings such as power, spot sizes, power density, fluences, operating modes, pulse times and accessory operation during each procedure. If the physician designates and trains appropriate office personnel to perform the dermatological procedures themselves, he should provide instructions on the selection of these settings. The laser should be placed in the standby mode whenever it is not being fired, to prevent accidental firing into the field, and preclude accidents that could occur if the laser and other footpedals are confused and fired during a procedure.

8.2. Eye protection

Ocular injury is a very serious complication arising from the use of a laser. Usually operating in the millisecond range of pulse duration, a laser beam cannot effectively be shielded by the eyelid blink reflex, which takes a tenth of a second to complete. Furthermore, lasers operating in the infrared spectrum do not emit a bright visible light necessary to elicit a blink reflex (Friedman NR et al. 1987).

The retina is particularly vulnerable to visible and near infrared spectrum optical radiation, even that emitted by low powered light devices, as a result of focusing by the ocular refractive

media. Retinal injury from optical radiation is in large part related to the absorption by the melanin chromophore and, to a lesser degree, xanthophyll and hemoglobin (Barkana Y and Belkin M 2000). Depending on the site of retinal injury, the insult may range from insignificant in the periphery, to a perceptible deterioration of visual acuity and color discrimination in the foveal region. The degree of visual loss is determined by the number of lost photoreceptor cells in the fovea. The inflammation and edema resulting from a laser injury in the parafoveal region may extend into the fovea, resulting in transient reduction in visual acuity that may recover over a period of days to weeks.

Certain lasers have the ability to inflict injury on multiple ocular structures. For instance, the 1,320 nm neodymium - doped yttrium aluminum garnet (Nd:YAG) laser may damage the lens and cornea, as well as the retina. The 755 nm alexandrite, 810 nm diode, and the 1,064 nm Nd:YAG lasers endanger the retina and the lens; the 2,940 nm erbium:YAG (Er:YAG) laser may damage the lens as well as the cornea (Youker SR and Ammirati CT 2001). Q-switched near infrared lasers, such as the Q-switched alexandrite and Nd:YAG lasers present an even greater threat through a mechanism of photoacoustic waves in addition to their thermal effects (Cao LY et al. 2010). Light emitted in very short pulse durations, on the order of pico and nanoseconds, results in a photoacoustic laser-tissue interaction, a mechanical, rather than a thermal, process that is not pigment dependent. The extremely high temperatures (exceeding 10,000°C) generated within the tissue lead to electron stripping, resulting in plasma formation, the rapid expansion of which produces tissue damaging photoacoustic waves. Retinal injury resulting from photoacoustic waves may culminate in perforation (Barkana Y and Belkin M 2000).

Ocular protection is, therefore, of outmost importance when operating a laser device. Any person that may possibly be exposed to optic radiation must wear appropriate protective eyewear, including the laser operator, support staff, patients, and visitors. Protective eyewear is chosen based on the wavelengths of light emitted by the laser (Dudelzak J and Goldberg DJ 2011).

Ocular injury may occur not only from a direct laser beam exposure, but also from exposure to the light reflected or scattered off glass, glossy metal, or plastic surfaces. Thus, all windows and mirrors in the room should be covered with opaque material, all jewelry removed, and all instruments anodized, roughened, and ebonized with black fluoropolymeric coating (Cao LY et al. 2010).

A warning sign should clearly be displayed on the door of the room where laser surgical procedures take place, informing potential visitors and staff of the potential ocular hazard inside.

8.3. Skin and teeth protection

Cutaneous injury from a laser beam may be significant and its spectrum may range from redness to overt burns and scarring. Lasers may also be a hazard to oral health. Dental enamel, in particular, is vulnerable to ultraviolet and infrared light. Thus, lasers operating in these wavelengths, including the CO_2 and Er:YAG, pose a particular threat. Avoiding oral injury can be achieved by keeping the mouth closed or by covering it with a moistened gauze or a protective mouthpiece (Pogrel MA et al. 1993).

8.4. Plume hazards

The interaction between a heat producing device and the treated tissue has the potential to produce surgical smoke or plume. The evaluation of laser plume as a hazard has centered on its mutagenic and carcinogenic capacity, as well as the possible role it may play in disease transmission. Plappert et al. in 1999 have found substances released in CO_2 laser pyrolysis of tissue to be cytotoxic, genotoxic, clastogenic, and mutagenic. Numerous chemical substances, some carcinogenic, have been detected in the laser plume, including carbon monoxide, hydrogen cyanide, ammonia, formaldehyde, acrolein, toluene, and benzene (Barrett WL and Garber SM 2003).

Laser procedures utilizing lower irradiance energies carry the risk of liberating cellular clumps and red blood cells that may be carried in the laser plume. It is believed that laser plume may harbor a greater infectious potential compared to electrosurgical smoke (Sawchuk WS et al.1989). The presence of viral particles in the laser plume has been documented in the literature. For instance, intact human papillomavirus DNA has been isolated from laser plume generated in the CO_2 laser treatment of verruca plantaris and respiratory tract papillomatosis. Human immunodeficiency virus (HIV) DNA capable of infecting cultured cells has also been recovered from a laser plume (Dudelzak J and Goldberg DJ 2011).

Implications of these findings on viral disease transmission have been a subject of debate, with emerging evidence supporting infectivity potential. In light of these findings and concerns, effective methods should be employed to combat the laser plume hazard. These include a smoke evacuator and laser masks. Most surgical masks only filter particles to approximately 0.5 μm in size. However, about 77% of particles in the laser plume are 1.1 μm or smaller. Therefore, wellfitted high filtration, or laser masks that filter particles larger than 0.1 μm by means of electrostatically charged synthetic fibers should be employed in place of standard surgical masks. These must be frequently changed as condensate moisture eliminates their polarity (Youker SR and Ammirati CT 2001). The importance of proper operation of a smoke evacuator cannot be overemphasized. The effectiveness of the device is drastically reduced from 99 to 50% when the distance from the laser treated site is increased from 1 to 2 cm (Sawchuk WS et al.1989).

8.5. Fire and electrical hazard

Laser fires may result from ignition of combustible material in the vicinity of a laser procedure, resulting in burns. Common sources of fuel include flammable materials used during a laser surgical procedure, including gauze, towels or drapes, and respiratory devices, including face masks and nasal cannulae. Flammable materials, including makeup and hair spray, should be removed prior to a laser procedure. Alcohol should never be utilized to prepare a laser surgical field. Caution should be exercised when performing laser procedures in hair- bearing areas, as hair can ignite and cause skin burns. In order to mitigate the risk of ignition of potentially combustible materials, the prepping with saline of the surgical area and supplies, including drapes, gauze, and tubing, is appropriate. A water reservoir, such as a bowl or an irrigation syringe, as well as fire extinguisher should always be within easy reach during a laser procedure to combat combustion fires on the surgical field.

Given the high voltage high current electrical nature of lasers, these devices carry a significant hazard of electrocution, and should only be maintained and repaired by specially trained and authorized personnel (Youker SR and Ammirati CT 2001).

9. CONCLUSION

Laser therapy is one of the fastest expanding and most exciting fields in dermatology. Although lasers have been used in dermatology for nearly 50 years, only in the last decade they gained the widespread acceptance in this field of medicine. Through selective targeting of skin chromophores, they revolutionized cosmetic dermatology, providing safe and effective means for treating various cutaneous problems. As emphasized in previous chapters of this thesis, lasers become the preferred treatment for benign pigmented and vascular lesions, tattoos, scars, unwanted hair, and aging skin.

The technology and design of lasers continue to evolve, allowing greater control of laser parameters and resulting in increased safety and efficacy for patients. With the correctly established indications and adequate preoperative and postoperative care of the patient, laser therapy nowadays has many advantages in comparison to conventional methods. Still, additional research in this area is ongoing and warranted, as are increased regulations in laser training and operation, which will ensure the safe and effective treatment of all laser patients.

Taking into account the continuing technical advances, as well as the growing number of skin problems amenable to laser treatment, lasers are becoming irreplaceable tools of modern medicine.

10. REFERENCES

Alajlan A, Shapiro J, Rivers JK, et al. (2005) Paradoxical hypertrichosis after laser epilation, J Am Acad Dermatol 53:85-8.

Alster TS (2000) Laser treatment of pigmented lesion. In: Manual of cutaneous laser techniques 2nd ed. Philadelphia: Lippincott-Williams & Wilkins, p.53-70.

Alster TS, Lupton JR (2001) Lasers in dermatology: An overview of types and indications. Am J Clin Dermatol 2: 291-303.

Alster TS, Lupton JR (2001) Laser therapy for cutaneous hyperpigmentation and pigmented lesions. Dermatol Ther 14:46-54.

Anderson RR, Parrish JA (1983) Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. Science 220:524-7.

Anderson RR, Ross E (2000) Laser – tissue interactions In: Fitzpatrick RE, Goldman MP (eds) Cosmetic Laser Surgery. Mosby, St. Louis p.1-30.

Barčot Z, Župančić B (2010) Pulsed Dye Laser Treatment of Vascular Lesions in Childhood. Acta Dermatovenerol Croat 18:201-208.

Barkana Y, Belkin M (2000) Laser eye injuries. Surv Ophthalmol 44:459– 478.

Barrett WL, Garber SM (2003) Surgical smoke: a review of the literature. Is this just a lot of hot air? Surg Endosc 17:979–987.

Baumann L (2009) Lasers and light devices, Cosmetic Dermatology, 2nd ed: The McGraw-Hill, p. 212-220.

Bekhor P (2006) Long-pulsed Nd:YAG laser treatment of venous lakes: report of a series of 34 cases. Dermatologic Surgery 32:1151–4.

Bernstein EF (2006) Laser treatment of tattos. Clin Dermatol 24:43.

Bernstein EF (2007) Laser Tattoo Removal, Semin Plast Surg 21: 175–192.

Bogle MA (2008) Fractionated mid-infrared resurfacing. Semin Cutan Med Surg 27:252–258.

Brnjas Kraljević J (2001) Struktura materije i dijagnostičke metode. Zagreb, Medicinska naklada, p. 56-58.

Bukvić Mokos Z (2006) Uklanjanje pigmentiranih lezija Q-switched ruby (694nm) laserom. In: Primjena lasera u dermatologiji, Zagreb, Medicinska naklada, p.43-47.

Bukvić Mokos Z, Lipozenčić J, Čeović R, Štulhofer Buzina D, Kostović K (2010) Laser Therapy of Pigmented Lesions: Pro and Contra, Acta Dermatovenerol Croat 18:185-189.

Bukvić Mokos Z, Lipozenčić J, Pašić A, Fattorini I (2006) Laser therapy for solar lentigines: review of the literature and case report. Acta Dermatovenerol Croat 14:81-5.

Cao LY, Taylor JS, Vidimos A (2010) Patient safety in dermatology: a review of the literature. Dermatol Online J 16:3.

Chiller KG, Passaro D, Frieden IJ (2002) Hemangiomas of infancy. Clinical characteristics, morphologic subtypes, and their relationship to race, ethnicity and sex. Arch Dermatol 138:1567-76.

Chwalek J, Goldberg DJ (2011) Ablative skin resurfacing. Curr Probl Dermatol 42:40–47.

Ciocon DH, Doshi D, Goldberg DJ (2011) Non-ablative lasers. Curr Probl Dermatol 42:48–55.

Čeović R (2006) Primjena Nd:YVO4 (532 nm) lasera u uklanjanju vaskularnih lezija kože In: Lipozenčić J, Bukvić Mokos Z. Primjena lasera u dermatologiji, Zagreb, Medicinska naklada, p.31-34.

Dehkor PS (2006) Long-pulsed Nd:YAG laser treatment of venous lakes: Report of series of 34 cases. Dermatol Surg 32:1151-1154.

Dierickx C, Grossman MC, Farinelli W, Anderson RR (1998) Permanent hair removal by normal-mode ruby laser. Arch Dermatol 134:837-842.

Dover JS, Arndt KA (2000) New approaches to the treatment of vascular lesions. Lasers Surg Med 26:158-63.

Dudelzak J, Goldberg DJ (2011) Laser Safety. Bogdan Allemann I, Goldberg DJ (eds): Basics in Dermatological Laser Applications. Curr Probl Dermatol. Basel, Karger, vol 42, p 35–39.

Eifert S, Villavicencio JL, Kao TC, Taute BM, Rich NM (2000) Prevalence of deep venous anomalies in congenital vascular malformations of venous predominance. J Vasc Surg 31:462-71.

El-Domyati M, El-Ammawi TS, Medhat W, Moawad O, Mahoney MG, Uitto J (2011) Effects of the Nd:YAG 1320-nm laser on skin rejuvenation: clinical and histological correlations. J Cosmet Laser Ther 13:98–106.

Fife DJ, Fitzpatrick RE, Zachary CB (2009) Complications of fractional CO2 laser resurfacing: four cases. Lasers Surg Med 41:179–184.

Fitzpatrick RE, Goldman MP (1994) Tatto removal using the alexandrite laser. Arch Dermatol 130:1508.

Fitzpatrick RE, Goldman MP, Ruiz-Esparza J (1993) Laser treatment of benign pigmented epidermal lesions using a 300 nanosecond pulse and 510 nm wavelength. J Dermatol Sur Oncol 18:341-347.

Frieden IJ, Eichenfield LF, Esterly NB, Geronemus R, Mallory SB (1997) Guidelines of care for hemangiomas in infancy. American Academy of Dermatology Guidelines/Outcomes Committee. J Am Acad Dermatol 37:631-7.

Friedman NR, Saleeby ER, Rubin MG, Sandu T, Krull EA (1987) Safety parameters for avoiding acute ocular damage from the reflected CO2 (10.6 microns) laser beam. J Am Acad Dermatol 17:815– 818.

Friedman PM, Jih MH, Kimyai-Asadi A, Goldberg LH (2004) Treatment of inflammatory facial acne vulgaris with the 1450-nm diode laser: a pilot study. Dermatol Surg 30:147–151.

Geronemus RG (1995) Argon laser for the treatment of cutaneous lesions. Clin Dermatol 13:55-8.

Goldberg DJ (1999) Laser treatment of pigmented lesions. In: Alster TS, Apfelberg DB, eds. Cosmetic laser surgery, 2nd ed. New York: Wiley-Liss, p. 279-288.

Goldman L, Wilson RG, Hornby P et al. (1964) Radiation from a Q-switched ruby laser: effect of repeated impacts of power output of 10 megawatts on a tattoo of man. J Invest Dermatol 44:69-71.

Gravelink JM, Casparian JM, Gonzales E et al. (1993) Undesirable side effects associated with treatment of tatoos and pigmented lesions with Q-switched lasers at 1064 nm and 694 nm: the MGH experience (abstract). Lasers Surg Med Suppl. 5:53.

Grekin RC, Shelton RM, Geisse JK, Frieden I (1993) 510 nm pigmented lesion dye laser. Its characteristics and clinical uses. J Dermatol Surg Oncol 19:380-387.

Gross AJ, Herrmann TRW (2007) History of lasers In: World J Urol 25:217-220.

Hague JS, Lanigan SW (2008) Laser treatment of pigmented lesions in clinical practice: a retrospective case series and patient satisfaction survey. Clin Exp Dermatol 33:139-41.

Houk LD, Humphreys T (2007) Masers to magic bullets: an updated history of lasers in dermatology. Clinics in Dermatology 25:434-442.

Iyer S, Fitzpatrick RE (2005) Long-pulsed dye laser treatment for facial teleangiectasias and erythema: evaluation of a single purpuric pass versus multiple subpurpuric passes. Dermatol Surg 31:898-902.

Kapur N, Lambiase P, Rakhit RD, Pearce J, Orchard G, Calonje E (2002) Local and systemic expresion of basic fibroblast growth factor in a patient with familial glomangioma. Br J Dermatol 146:518-22.

Karrer S, Hohenleutner U, Szeimies RM, Landthaler M, Hruza GJ (1999) Amiodarone-induced pigmentation resolves after treatment with the Q-switched ruby laser. Arch Dermatol 135:251-254.

Karsai S, Czarnecka A, Jünger M, Raulin C (2010) Ablative fractional lasers (CO(2) and Er:YAG): a randomized controlled double-blind split-face trial of the treatment of peri-orbital rhytides. Lasers Surg Med 42:160–167.

Kaufmann R (2006) Basic principles of lasers in dermatology. In: Lipozenčić J, Bukvić Mokos Z. Primjena lasera u dermatologiji. Zagreb, Medicinska naklada, p.15-17.

Kelly KM, Nelson JS, Lask GP, Geronemus RG, Bernstein LJ (1999) Cryogen spray cooling in combination with nonablative laser treatment of facial rhytides. Arch Dermatol 135:691-694.

Kilmer SL, Alster TS (1996) Laser treatment of tatoos and pigmented lesions In: Cosmetic laser surgery. New York: John Wiley and Sons, p.111-128.

Kilmer SL, Wheeland RG, Goldberg DJ, Anderson RR (1994) Treatment of epidermal pigmented lesions with the frequency-doubled Q-switched Nd:YAG laser: a controlled, single-impact, dose response, multicenter trial. Arch Dermatol 130:1515-1519.

Knoell KA, Milgraum SS, Kutenplom M (1996) Q-switched ruby laser treatment of minocycline-induced cutaneous hyperpigmentation. Arch Dermatol 1251-1252.

Kostović K (2006) Preoperativni i postoperativni postupak kod primjene lasera. In: Lipozenčić J, Bukvić Mokos Z. Primjena lasera u dermatologiji. Zagreb, Medicinska naklada, p.19-22.

Landthaler M, Hohenleutner U (2006) Laser therapy of vascular lesions. Photodermatol Photoimmunol Photomed 22:324-332.

Lin RL, Schwartz RA (2006) Hemangiomas of infancy – a clinical review. Acta Dermatovenerol Croat 14:109-16.

Lipozenčić J, Bukvić Mokos Z (2010) Dermatologic Lasers in the Treatment of Aging Skin. Acta Dermatvenerol Croat 18:176-180.

Manstein D, Herron GS, Sink RK et al. (2004) Fractional photothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med 34:426.

Milgraum SS, Cohen ME, Auletta MJ (1995) Treatment of blue nevi with Q-switched ruby laser. J Am Acad Dermatol 32:307-10.

Nehal KS, Levine VJ, Ashinoff R (1996) The treatment of benign pigmented lesions and tatoos with the Q-switched ruby laser: a comparative study using the 5.0 and 6.5 mm spot size. Dermatol Durg 36:683-686.

Newman JB, Lord JL, Ash K, McDaniel DH (2000) Variable pulse erbium:YAG laser skin resurfacing of perioral rhytides and side-by-side comparison with carbon dioxide laser. Lasers Surg Med 26:208–214.

No D, Dierick C, McClaren M (2003) Pulsed alexandrite treatment of bulky vasculat malformations. Lasers Surg Med 15:26.

Paithankar DY, Ross EV, Saleh BA, Blair MA, Graham BS (2002) Acne treatment with a 1,450 nm wavelength laser and cryogen spray cooling. Lasers Surg Med 31:106–114.

Plappert UG, Stocker B, Helbig R, Fliedner TM, Seidel HJ (1999) Laser pyrolysis products – genotoxic, clastogenic and mutagenic effects of the particulate aerosol fractions. Mutat Res 441:29– 41.

Pogrel MA, Muff DF, Marshall GW (1993) Structural changes in dental enamel induced by high energy continuous wave carbon dioxide laser. Lasers Surg Med 13:89– 96.

Railan D, Parlette EC, Uebelholer NS (2006) Laser treatment of vascular lesions. Clin Dermatol 24:8-16.

Rao J, Goldman MP (2005) Prospective, comparative evaluation of three laser systems used individually and in combination for axillary hair removal. Dermatol Surg 31:1671.

Rosenbach A, Williams CM, Alster TS (1997) Comparison of the Q-switched alexandrite (755 nm) and Q-switched ND:YAG (1064 nm) lasers in the treatment of benign melanocytic nevi. Dermatol Surg 36:683-686.

Sawchuk WS, Weber PJ, Lowy DR, Dzubow LM (1989) Infectious papillomavirus in the vapor of warts treated with carbon dioxide laser or electrocoagulation: detection and protection. J Am Acad Dermatol 21:41– 49.

Stratigos AJ, Dover JS, Arndt KA (2000) Laser treatment of pigmented lesions - 2000. How far have we gone? Arch Dermatol 136:915-21.

Suzuki H, Anderson RR (2005) Treatment of melanocytic nevi. Dermatol Ther 18:217-26.

Štulhofer Buzina D (2006) Laserski resurfacing primjenom Er:YAG (2940 nm) lasera In: Lipozenčić J, Bukvić Mokos Z. Primjena lasera u dermatologiji. Zagreb, Medicinska naklada, p.39-42.

Štulhofer Buzina D, Lipozenčić J, Bukvić Mokos Z, Čeović R, Kostović K (2010) Ablative Laser Resurfacing: Is It Still the Gold Standard for Facial Rejuvenation? Acta Dermatovenerol Croat 18:190-194.

Tan OT, Morelli JG, Kurban AK (1992) Pulsed dye laser treatment of benign cutaneous pigmented lesions. Lasers Surg Med 12:538-42.

Tan OT, Scherwood K, Gilchrest BA (1989) Treatment of children port-wine stains using the flashpump-pumped tunable dye laser. N Engl J Med 320:416-21.

Tanna N (2014) Skin Resurfacing - Laser Surgery at http://emedicine.medscape.com/ article/838501-overview

Tanzi EL, Lupton JR, Alster TS (2003) Lasers in dermatology: four decades of progress. J Am Acad Dermatol 49:1-31.

Tanzi EL, Williams CM, Alster TS (2003) Treatment of facial rhytides with a nonablative 1,450-nm diode laser: a controlled clinical and histologic study. Dermatol Surg 29:124–128.

Taylor CR, Anderson RR (1994) Ineffective treatment of mlasma and post-inflammatory hyperpigmentation by Q-switched ruby laser. J Dermatol Surg Oncol 20:592-7.

Taylor CR, Gange RW, Dover JS, et al. (1990) Treatment of tatoos by Q-switched ruby laser. A dose-response study. Arch Dermatol 126:893.

Tenzel EL, Alister TS (2003) Single-pass carbon dioxide versus multiple-pass Er:YAG lasers skin resurfacing: a comparison of postoperative wound healing and side efect rates. Dermatol Surg 29:80-4.

Uebelhoer NS, Bogle MA, Stewart B et al. (2007) A split-face comparison study of pulsed 532-nm KTP laser and 595-nm pulsed dye laser in the treatment of facial teleangiectasias and diffuse teleangiectatic facial erythema. Dermatol Surg 33:441.

Wang HW, Wang JB, Liu YH, Zuo YG, Jin HZ, Jiang GT, Li HC, Ma DL (2006) Clinical efficacy of Q-switched Alexandrite laser for pigmentary skin diseases in 4656 patients Zhongguo Yi Xue Ke Xue Yuan Xue Bao 28:202-5.

Watanabe S (2008) Basics of laser application to dermatology. Arch Dermatol Res 300:S21-S30.

Watanabe S, Flotte TJ, McAuliffe DJ, Jacques SL (1988) Putative photoacoustic damage in skin induced by pulsed ArF excimer laser. J Invest Dermatol 90:761-766.

Weller R, Hunter J, Savin J, Dahl M (2011) Clinical Dermatology, Blackwell Publishing, p.284-296.

Wheeland RG (2005) Basis laser physics and safety. In: Goldberg DJ. Laser Dermatology. Berlin Heidelberg: Springer-Verlag, p.1-10.

Wolff K, Johnson RA (2009) Adverse cutaneous drug reactions. In: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology. New York: McGraw Hill, p.551-581.

Yaghmai D, Garden JM, Bakus AD, Massa MC (2005) Comparison of a 1,064 nm laser and a 1,320 nm laser for the nonablative treatment of acne scars. Dermatol Surg 31:903–909.

Youker SR, Ammirati CT (2001) Practical aspects of laser safety. Facial Plast Surg 17:155–163.

Zhenxiao Z, Aie X, Yuzhi J. et al (2011) Exploring the role of a nonablative laser (1320 nm cooltouch laser) in skin photorejuvenation. Skin Res Technol 17:505–509.

Zollnet TM, Stracke S, Neumeister B et al. (1996) Treatment of minocycline-induced hyperpigmentation with the Q-switched ruby laser. Arch Dermatol 132:1250-1251.

11. BIOGRAPHY

Kristina Žužul was born on June 19th 1990 in Zagreb. In her hometown she finished primary and all the grades of high school with the average of 5.0. During that time, she actively played tennis and was a member of Croatian Tennis Association. In 2006 she was awarded as a best young host in Croatia by the Rhetoric school of Croatian Philological Society.

In 2008, she enrolled the Medical Studies in English, at the University of Zagreb, School of Medicine, where in 2011 she received Dean's Commendation, an award for a distinguished academic record.

In 2008, she completed the specialist year training at Business Academy Experta and gained the title of a spokesman. In the same Academy, she also gained the title of a Host in TV and radio shows in 2009.

Kristina Žužul is currently a student of 6^{th} year at the Medical Faculty in Zagreb, demonstrator at the Physics department, and is among top 3% of students in generation. She is fluent in English and Spanish, and has a good level in German and Italian.