LASER PRIMER

VASCULAR LESIONS, PIGMENTED LESIONS & RESURFACING

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The word laser is an acronym for "light amplification by stimulated emission of radiation". Lasers generate light energy as a beam of photons, and current commercially available lasers emit wavelengths ranging between the ultraviolet to near-infrared portions of the electromagnetic spectrum. Devices transfer their energy into the skin and produce a desired biological effect depending on the amount of energy delivered and its rate of absorption, usually creating heat within tissue. Lasers are distinct from regular light as they produce monochromatic (single or narrow wavelength, determined by the medium present in the optical cavity), coherent (all waves are in phase with each other in space and time) and collimated (waves travel in parallel with little divergence) light [1].

Parameter	Unit	
Wavelength	Nanometers (nm)	Dictates absorption by different tissues and depth of penetration
Pulse duration	Seconds (s)	Span of time over which the laser interacts with skin
Energy	Joules (J)	Energy contained within laser light
Fluence	J/centimeter$(cm)^2$	Energy delivered per unit area
Power	Watts (W)	The rate at which energy is emitted from the laser (W = J/s)
Irradiance	W/cm^2	Rate of energy delivery per unit area
Spot size	cm	The radius of the laser beam

Table 1: Basic device parameters describing laser energy delivered to tissue [2-4].

The main biological targets (chromophores) for laser light in skin are oxyhemoglobin, deoxyhemoglobin, melanin and water; which absorb light differently and have optimum absorption spectra depending on the wavelength of the photon received [5]. Sebaceous glands, adipocytes, aminolevulinic acid and tattoo pigments may also be targeted when treating the skin with lasers.

The principle of selective photothermolysis (SPT) is the cornerstone behind the use of lasers in medicine, allowing the destruction of tissues containing a chromophore that absorbs a specific wavelength of light whilst minimizing damage to surrounding tissues by using high powers and short pulse widths. Anderson, et al. stated that SPT relies on a wavelength that is preferentially absorbed by the desired target structures; an exposure duration less than or equal to the time necessary for cooling of the target structures; and sufficient energy to damage the target [6].

The thermal relaxation time (TRT) of a tissue is the time required for a target tissue to cool. The theory of thermal relaxation states that when a target structure is heated to a certain temperature, heat escapes to the surrounding tissues via conduction. If a chromophore is heated over a long period of time, the temperature rise in the tissue being targeted is limited due to conduction into surrounding tissues. If, however, the chromophore is heated over a short period, the temperature rises quickly as heat does not diffuse, known as thermal lock-in, allowing selective thermal destruction of the target. Whether or not thermal lock-in is achieved depends on the TRT, which is dependent on the absorption coefficient and heat diffusion coefficient of the structure [7]. Therefore, the pulse duration is selected to be equal or less than the TRT of the target. Smaller targets have a shorter TRT than larger ones, for example the TRT of a melanosome is roughly 1μs, whereas that of a large caliber blood vessel may be as long as 20ms [1].

Intense pulsed light (IPL) differs from laser in that devices emit polychromatic, incoherent light via a flash lamp. Light is emitted in the visible spectrum range of 420-1,400nm; however filters can be used to isolate predetermined wavelengths to target specific chromophores. The principles of IPL therapy also rely on SPT to treat a wide range of skin disorders [8, 9].

Specific clinical endpoints can be observed when light is absorbed by its chromophore, and depend on multiple factors including wavelength, target, pulse duration and fluence. Endpoints vary depending on the specific interaction between the histologic target and laser being used and should be used to guide the clinician in ensuring that a therapeutic dose of energy has been delivered [10]. Importantly, endpoints may vary between patients, particularly when treating those with darker skin phototypes, and therefore each patient must be treated as an individual rather than using a "one size fits all" approach with parameters.

Warning endpoints may be observed in the skin soon after delivery of laser energy and suggest tissue injury. Appearance of the Nikolsky sign signals keratinocyte necrosis and is likely to be followed by an open wound. Most frequently, this occurs as a result of treating tanned or pigmented skin with the incorrect settings, pulse stacking or

inadequate cooling. Skin shrinkage is an indication of significant thermal injury to the dermis resulting from structural changes to collagen. Charring of the skin signals that energy is being applied to tissue after its water content has been removed, leading to partial combustion. Occurrence of any warning endpoints should lead the clinician to pause treatment and reassess the situation [2].

Despite the many advantages of lasers in the field of dermatology, laser energy can injure both the patient and operator; therefore, safety protocols should be followed at all times and only those with sufficient experience should operate energy-based devices. Appropriate eye protection is mandatory for all in the treatment room. Chlorhexidine should be avoided when preparing the skin, as it is toxic to the cornea when vaporized. Alcohol should also be avoided due to risk of ignition [11]. Skin around the target area should be protected with damp drape or gauze, due to the risk of dry materials being ignited by the laser beam [12]. The smoke plume is carcinogenic may contain potentially harmful substances including viable viral particles, and therefore a smoke extractor is essential [13].

VASCULAR LESIONS

The target chromophore for vascular lesions is hemoglobin, as oxy-hemoglobin or deoxy-hemoglobin. The major absorption peaks are 418, 542 and 577-59 nm; the 418nm wavelength has the strongest absorption peak however is also absorbed by melanin and therefore may result in post-treatment pigmentary changes [14]. The 577-595nm wavelength is therefore a desirable target in the treatment of vascular lesions.

Oxyhemoglobin in the superficial blood vessels of the face and neck has a maximum absorption peak at 540nnm and 580nnm, however vessels on the legs are typically deeper and contain more deoxyhemoglobin. This shifts the absorption curve to the right and a longer wavelength is required to penetrate more deeply into the skin. Very high energy levels and longer pulse durations are required to coagulate these deep vessels [15].

Treatment of vascular lesions relies on the theory of SPT. Laser energy is absorbed by hemoglobin in circulating red blood cells resulting in vascular injury with coagulation, vessel wall necrosis and damage to perivascular collagen with minimal damage to the epidermis and surrounding tissues [15]. The TRT of the treated blood vessel is dependent on the diameter of that vessel, and longer pulse durations should be employed for larger-caliber vessels [16].

In general, the treatment principles for vascular lesions are:

Pulse duration: Smaller vessels can be treated with shorter pulses (as small as 0.4-3ms in infantile hemangiomas), whereas large vessels require longer pulse durations as more time is required for thermocoagulation: up to 50ms in large adult facial telangiectasia. The TRT of a vessel in seconds is roughly equal to the square of the vessel diameter in millimeters. Excessively long pulse durations may lead to diffusion of heat into surrounding tissues and thermal damage [17].

Spot size: The deeper the location of the blood vessel, the larger the spot size required.

Temperature control: Heat may conduct to the epidermis during treatment causing damage, and therefore selective cooling is important at all stages of treatment; allowing high temperatures to occur in target tissues without epidermal damage. However, epidermal cooling may result in dyspigmentation when treating darker skin types.

For effective treatment of vascular lesions, the correct wavelength, pulse duration and fluence must be chosen, with pulse duration equal to the TRT of the target vessel.

Therapeutic Endpoints for vascular lesions [10]:

- Port wine stains: Purpura limited to the confines of the spot size
- Infantile hemangiomas: Subtle purpura, which may be transient
- Telangiectasia: Immediate vessel darkening or disappearance
- Cherry angiomas: Purpura without petechiae
- Venous lakes: Vessel darkening or disappearance

As with all energy-based devices, the risk of side effects depends on the choice of parameters and experience of the operator. Treatment of vascular lesions may produce moderate pain, and this may be limited by topical or local anesthesia. Purpura and ecchymoses are common and will usually fade over 7-10 days. Bleeding and hemangiomas may occur when high energies are delivered with a short pulse duration. Edema is common within a few minutes of treatment and subsites within 3-5 days. Grey or white discoloration of the skin is an indicator of early damage and may be followed by blistering and epidermal necrosis; if grey/white discoloration of the epidermis is seen the fluence should be reduced and the pulse duration increased as well as using epidermal cooling. Bacterial infection and HSV reactivation may also occur. Hyperpigmentation occurs more frequently in patients with Fitzpatrick skin phototypes III-V and pretreatment with hydroquinone may reduce this risk. Hypopigmentation may occur as a result of overtreatment and repigmentation is usually observed within 3-6 months. Scarring may occur when high fluences or overlapping spots are used [15]. Use of epidermal cooling with direct contact, forced cold air or cryogen spray allow higher temperatures to occur in target structures without damage to the epidermis.

Condition	Choice of energy-based device
Facial telangiactasia	PDL, KTP, IPL
Rosacea	PDL, KTP, IPL
Infantile hemangioma	PDL, IPL, Nd:YAG, KTP
Vascular malformation (port wine stain)	PDL, IPL, Nd:YAG, KTP
Blue rubber bleb syndrome	Nd:YAG, IPL, CO_2, diode
Hereditary hemorrhagic telangiactasia	Nd:YAG, diode
Spider angioma	KTP, PDL, IPL, Nd:YAG
Poikiloderma of Civatte	PDL, IPL
Pyogenic granuloma	Nd:YAG, IPL
Venous lake	KTP, Nd:YAG, PDL, IPL
Cherry angioma	KTP, Nd:YAG, IPL, PDL
Leg veins (isolated small)	KTP, PDL, Nd:YAG, IPL
Leg veils (large deep)	Nd:YAG, alexandrite, diode, IPL

Table 2: Lasers frequently used for the treatment of different vascular lesions

PDL: pulsed dye laser; KTP: potassium-titanyl-phosphate; IPL: intense pulsed light; Nd:YAG: Neodymium:yttrium-aaluminium-garnet; CO_2: Carbon dioxide

PDL

Pulsed dye laser (PDL) emits a wavelength or 585-595nm (yellow spectrum) and was specifically developed for the treatment of vascular lesions of the skin. Longer wavelengths of 595-600nm allow deeper penetration of laser light to a depth of 1.2mm. The active medium of the PDL is an organic rhodamine dye energized by a short pulse of light from a flash lamp. The pulse duration of 450μs-1.5ms is shorter than the TRT of the vessels present in most cutaneous lesions [14]. PDL is an effective treatment for telangiactasiae, superficial strawberry hemangiomas, venous lakes, poilikoderm of Civatte, hypertrophic scars, flushing/erythema and port wine stains [18]. Short pulse durations may result in purpura which can last 1-2 weeks after treatment. PDL is safe to use in skin types I-IV, however use in darker skin types carries a risk of hyperpigmentation and epidermal cooling is essential for most treatment indications [14]. Other possible adverse events include erythema, purpura, blistering, edema and scarring.

KTP

A potassium-titanyl-phosphate (KTP) crystal doubles the frequency of the Neodymium:yttrium-aluminium-garnet (Nd:YAG) to 532nm (green), near the first absorption peak of hemoglobin [19]. This short wavelength is effective at targeting superficial vessels, however is also absorbed by melanin. Long-pulsed KTP laser is commonly used for treatment of facial telangiectasia and rosacea without the risk of purpura, however it can only be used in skin types I-III due to risks of absorption by melanin [20]. Edema is common following use of the KTP laser, particularly when treating the cheeks and forehead, and usually subsides within a few days.

Alexandrite

Blue lesions are typically deeper in the dermis and have a higher concentration of deoxyhemoglobin. The alexandrite laser emits a wavelength of 755nm (red) and targets the deoxyhemoglobin absorption peak; its long pulse width allows deeper dermal penetration to target larger diameter vessels [21].

Diode

The diode laser can emit wavelengths between 800-980nm (near infrared) and may be used for deep or thick vascular lesions [22]. Diode is less safe for use in darker skin phototypes than other vascular lasers.

Nd:YAG

Nd:YAG produces light at 1,064nm (near infrared), which penetrates deep into the dermis with almost no melanin absorption. However, at this wavelength deoxyhemoglobin and surrounding tissues absorb laser energy equally effectively, leading to an increased risk of scarring [23].

IPL

IPL employs high-intensity polychromatic light in a broad spectrum of 500-1,100nm at energies up to 80 J/cm^2. Filters are used to isolate different wavelengths and light is delivered in the millisecond range; 580-590nm light is generally filtered out for the treatment of vascular lesions. Devices also have large, cooled, application tips allowing for rapid and effective treatment of larger areas. Conditions including benign cavernous hemangiomas, venous malformations, facial telangiectasia, poikiloderma of Civatte, port wine stains and leg telangiectasia respond well to IPL. Mild, transient, erythema is usually the only observed side effect, however dyspigmentation, blistering, crusts and atrophic scarring may occur [14, 24].

PIGMENTED LESIONS

Melanin is the target chromophore for pigmented lesions and is targeted by a number of wavelengths from different energy-based devices. Although absorption of light by melanin decreases as the wavelength increases, longer wavelengths may be employed to target melanin deeper in the skin whilst minimizing the risk of pigmentation in patients with darker skin types [25]. Between 630-1,100nm, light is preferentially absorbed by melanin over hemoglobin and penetration into the dermis occurs [14].

Melanocytes contain intracytoplasmic melanosomes, in which melanin biosynthesis occurs. After melanin is produced by melanocytes, the melanosomes are transferred to keratinocytes. Melanosomes measure approximately 1μm and have a TRT of between 50-500ns, therefore extremely short pulse durations must be used to target melanosomes whilst reducing damage to surrounding tissue [26].

As lasers have evolved, Q-switched (QS) lasers have been introduced to produce short (typically in the nanosecond range) high-energy light pulses that match the TRT of small melanin particles. More recently, picosecond lasers with pulse durations in the range of 300–900 picoseconds (one trillionth of a second) have been developed. The rapid temperature changes resulting from picosecond pulses are able to shatter tattoo pigment and cellular melanosomes, allowing clearance of pigment by macrophages whilst reducing the risks of dyspigmentation.[27]

The target endpoint for the treatment of benign pigmented lesions is transient whitening of the lesion with no change in the surrounding skin. When using long pulses in the millisecond range, subtle darkening of pigmented lesions may be observed, corresponding to necrotic melanocytes in the epidermis which persist for several days [10]. Use of nanosecond lasers for treatment of pigmented lesions in patients with darker skin types carries a greater risk of postinflammatory hyperpigmentation (PIH), whereas use of long pulses may reduce this risk. Evidence has shown that use of a picosecond laser reduces the risk of PIH significantly [27].

Pigmented lesions may be separated into epidermal, dermal or mixed. Epidermal lesions include café au lait macules, solar lentigines, Becker's nevus, nevus spilus and ephelides. Dermal and mixed lesions include PIH, nevus of Ota, nevus of Ito and melasma. Longer wavelength lasers should be used for dermal lesions as the light energy is able to penetrate deeper into the skin [28].

Condition	Choice of Energy-Based Device
Lentigines	KTP (QS/ps), ruby, alexandrite, IPL
Ephelides	KTP (QS in light skin, LP in darker phototypes)
CALM	QS Nd:YAG, ruby, KTP; QS/LP alexandrite
Becker nevus	LP ruby, alexandrite
Nevus of Ota/Ito	QS Nd:YAG
PIH	With caution
Melasma	PDL, IPL (in light skin photoypes)

Table 3: Lasers frequently used for the treatment of different vascular lesions [29].

QS: Q-switched; ps: picosecond; LP: long-pulsed; KTP: potassium-titanyl-phosphate; IPL: Intense pulsed light; Nd:YAG: Neodymium:yttrium-aluminium-garnet; CALM: Café-au-lait macules; PIH: postinflammatory hyperpigmentation

Ruby

The ruby laser emits a wavelength of 694nm (red) and is able to penetrate deep into the dermis. The ruby laser may be long-pulsed (milliseconds pulse duration) or Q-switched (QSR). The QSR was the first laser used to treat dermal pigmented lesions without scarring with and a fluence of 4-10 J/cm^2 with pulse duration of 20 to 40ns is considered ideal for selective absorption by melanin [30]. A white frost appears immediately after treatment, lasting for approximately 30 minutes, followed by edema and erythema, with healing within 12 days. QSR has been reported to be effective for the treatment of solar lentigines, ephelides and nevus of Ota/Ito. Becker's nevus, nevus spilus and café au lait macules are reported to have high rates or recurrence following treatment. PIH and melasma are reported to

respond poorly [28, 30]. In patients treated with systemic gold, chyriasis (a permanent blue-grey discoloration of the skin) may be induced following treatment with a ruby laser [2].

Alexandrite

The alexandrite laser emits light at 755nm (red) and may be used with long-pulsed, Q-switched (QSA) or picosecond pulse durations. Long-pulsed alexandrite is more commonly used for treatment of vascular lesions and hair removal whereas QSA has pulse durations of 50-100ns and is used for pigmented lesions and tattoo removal [28]. Picosecond alexandrite lasers have also been reported as safe and effective for treatment of dermal pigmentary disorders in patient with skin of color [27].

Nd:YAG & KTP

Nd:YAG emits light at 1,064nm (near-infrared) or frequency-doubled at 532nm (green) (KTP). The 532nm wavelength is effective at targeting epidermal pigmented lesions and QS or picosecond pulses are used for this indication. There is a low incidence of scarring and hyperpigmentation, however purpura is reported to occur frequently [28].

IPL

IPL has been shown to be effective in the treatment of multiple pigmentary disorders [31]. In contrast to QS devices, an immediate darkening of pigmented lesions is observed following treatment with subsequent sloughing [8].

RESURFACING

ABLATIVE

CO_2

The carbon dioxide (CO_2) laser emits light at 10,600nm, targeting water as its chromophore. Since 80% of the skin is composed of water, this leads to rapid heating and vaporization of water resulting in destruction of cells and connective tissue [11]. Due to residual thermal damage at the borders of the CO_2 ablated zone, thermocoagulation of small blood vessels occurs achieving hemostasis.

Traditional continuous-wave laser results in extensive conduction of heat from the impact zone resulting in damage to depths of up to 1mm, slowing wound healing and increasing the risk of scarring. To reduce the size of the thermal damage zone, short-pulse, high peak CO_2 lasers have been developed to emit pulses of durations shorter than 1ms with power two to 10 times that of a continuous-wave laser. In order to generate fluences high enough to achieve tissue vaporization (5 J/cm^2), pulses must occur at a rate of 100 Hz or more [12].

In the 1990s, CO_2 was first utilized for photorejuvenation. Continuous-wave energy was used to fully ablate the epidermis, with subsequent regrowth. In addition, a zone of partially coagulated tissue is produced in the dermis known as residual thermal damage, stimulating collagenesis and dermal remodeling [32]. Fully-ablative resurfacing remains the gold standard for facial rejuvenation, however comes at the cost of increased downtime, prolonged erythema, scarring, dyspigmentation and risk of both bacterial and viral infection [33].

Erythema and oedema are the most frequently observed side effects after treatment, with the mean duration of erythema reported to be between 6.3-12.3 days. Pain is also a significant disadvantage of ablative laser and topical and local anesthesia, nerve blocks and cryoanasthesia are frequently employed. Herpes simplex virus (HSV) reactivation is also a risk and antivirals are therefore used prophylactically before and following treatment [11].

Indications for CO_2 laser:

- Warts and condyloma acuminatum [34]
- Seborrheic keratoses
- Actinic keratoses
- Epidermal / sebaceous nevi [35]
- Intradermal naevi [36]
- Benign skin appendageal lesions
- Xanthelasma[37]
- Rhinophyma
- Scars
- Photorejuvenation

Ablative resurfacing using a CO_2 laser remains the gold standard for facial photorejuvenation, however the complication rate is high. In order to reduce the risks of scarring and decrease downtime, ablative fractional photothermolysis (AFP) was developed to enable coagulative injury to the dermis without ablation of the entire epidermis. Fractionated lasers “drill” holes known as microscopic treatment zones (MTZ) from the stratum corneum to the reticular dermis in a grid-like pattern, which promotes neocollagenesis with rapid wound healing [38]. The result is tissue shrinkage and an improvement in skin texture [39]. The safety profile of AFP is superior to that of fully-ablative laser, with complete re-epithelialization seen at 3-6 days, versus 2-3 weeks in traditional systems [38]. This leads to reduced incidence of infections and a shorter duration of postoperative erythema.

CO_2 laser has limited penetration into tissue due to its high absorbance by water but by using a small spot size such as 120μm in AFP, depths of over 2mm can be achieved, allowing treatment of thicker lesions such as keloid scars [12]. The AFP approach also allows treatment of areas other than the face, as abundant pilosebaceous units are not required for epidermal healing.

Whilst complications of AFP are generally lower than that of fully ablative laser, they have been reported in the literature. It is important that conservative parameters are chosen, particularly in areas with thin dermis and a paucity of pilosebaceous units such as the neck [38]. Commercially available AFP devices allow the user to adjust the energy, density and pulse duration:

Energy: Increasing the device's energy results in deeper tissue injury, and higher energies result in a longer duration of edema and erythema post-procedure. Lower energies should be chosen for areas with thin dermis such as the eyelids and neck.

Spot size: Smaller spot sizes also allow for deeper penetration into tissue. Larger spot sizes should be chosen for the treatment of superficial skin conditions, whereas smaller spot sizes should be used in the management of rhytids and scars.

Density: The distance between each MTZ is the device's density. Higher densities result in prolonged erythema and edema, and low density should be chosen in areas with fewer pilosebaceous units.

Pulse duration: Longer pulse durations result in more collateral damage to adjacent tissues, and therefore durations shorter than 2ms are desirable.

There are no specific therapeutic endpoints for ablative fractional lasers. Bleeding correlates to the depth of thermal injury and is more common with shorter pulse widths, however is not a therapeutic endpoint [10].

Er:YAG

The Erbium:Yttrium-aluminium-garnet (Er:YAG) emits light at a wavelength of 2,940nm; leading to increased uptake by water by a factor of 12 to 18 when compared to a CO_2 laser. Increased absorption by the superficial layers of skin produces a thermal damage zone of less than 10μm. However, due to the limited thermal damage zone, hemostasis is not achieved limiting its use to ablation above the level of the papillary dermis [12].

NONABLATIVE

Nonablative fractional resurfacing (NFR) was initially developed to reduce the post-procedural recovery period and limit adverse effects observed with ablative resurfacing. Lasers target dermal water and create MTZs whilst maintaining the integrity of the stratum corneum with epidermal cooling [9, 40]. It is now acknowledged that a level of epidermal damage is required for photorejuvenation and therefore results from NFR may be disappointing for some patients. Nevertheless, nonablative technology has a place for the resurfacing of delicate skin and in patients for whom extended downtime is not acceptable and adverse effects are usually minimal. A recent meta-analysis reported no differences in effectiveness between ablative and non-ablative lasers for photorejuvenation [41]. Indications for NFR include acne scarring, photoageing, scar revision, striae and melasma [40].

Lasers commonly employed for NFR include:

- Diode (980 and 1,450nm)
- Nd:YAG (1,064nm)
- Erbium:glass (1,540nm)
- Erbium Fiber (1,550nm)
- Erbium:Thulium (1,550/1,927nm)
- Thulium (1,927nm)

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