DERMATOLOGIC LASERS: THREE DECADES OF PROGRESS
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Thirty years have passed since the creation of the first laser. Although significant applications for lasers were forecast immediately, many subsequent developments in their diagnostic and therapeutic uses in medicine took decades to be realized. Laser technology has improved, and will continue to improve, health care delivery, diminishing the time, cost, and invasion of many procedures. This review of the use of lasers in dermatology will survey past and present developments and will outline and preview the possibilities of laser techniques.

HISTORY OF LASERS

The word laser was coined as an acronym for Light Amplification by the Stimulated Emission of Radiation. While ordinary light is emitted spontaneously by excited atoms or molecules, laser light occurs when an atom or molecule retains excess energy until it is “stimulated” to emit it.

Albert Einstein was the first to suggest the existence of stimulated emission.1 Scientists believed that atoms and molecules were more likely to emit light spontaneously, and that stimulated emission would be much weaker. After World War II, however, physicists attempted to make stimulated emission dominate, seeking ways for one atom or molecule to stimulate many others to emit light, amplifying it to much higher powers. The first to succeed was Charles H. Townes, who instead of working with light, worked with microwaves, which have a much longer wavelength. Townes built a device he called a “maser,” which stood for Microwave Amplification by the Stimulated Emission of Radiation.

Together with Arthur Schawlow, Townes outlined the key concepts of stimulated emission in 1958.2 In 1960, Theodore Maiman at Hughes Aircraft Research Laboratories actually developed the first laser, a ruby laser.3 Many other types of lasers have subsequently been developed, but Maiman’s original ruby laser manifested all the important properties we associate with today’s lasers: it emitted light in a narrow, tightly concentrated beam (collimated), all the light was the same wavelength (monochromatic), and the light waves were all aligned with each other (coherent).

In 1963, Leon Goldman and co-workers4 performed the initial experiments demonstrating the effects of lasers on human skin, using the only available laser at the time, the ruby laser. Initially, normal white and black skin was irradiated, with and without the addition of various superficial black substances.5 Subsequently, laser treatment of seborrheic keratoses and hemangiomas was attempted.6 While it became evident that the damage inflicted was nonspecific thermal destruction of the irradiated site, laser treatment had one major advantage over other destructive treatment methods, the ability to focus high intensity energy onto very small sites. This precision did not enhance target selectivity, but it was inferred from these initial experiments that more damage was induced by equivalent laser pulses in darker lesions. This observation was important to the future development of lasers specifically designed to treat certain cutaneous lesions.

LASER PRINCIPLES AND LASER-TISSUE INTERACTION

Fundamental to the diverse applications of laser light are its unique properties: (1) coherence, (2) monochromaticity, (3) high intensity, (4) “compressibility” into ultra-short pulses, and (5) tunability. Light waves are said to be coherent if they are each in phase with the other (the peaks and valleys of the light waves are aligned). Monochromaticity involves emission of a single wavelength of light. Most known energy sources emit radiation that consists of many different wavelengths. Lasers are also capable of emitting radiation of extremely high intensity, thereby providing a high concentration of light energy in the substance being irradiated. The ability to compress the light energy into ultra-short pulses allows for the excitation of high-energy levels in the molecules specifically being irradiated, while tunability of the wavelength in the range from infrared to ultraviolet permits selective excitation
of certain molecular species depending on the absorption spectrum of that molecule. A single laser can provide a combination of several of the above properties to suit a particular application.

The concept of "selective photothermolysis" was born from the idea that special properties inherent in laser radiation could be adjusted and selected to confine thermal damage to a few pathologic lesions while minimizing the destruction of normal tissue.8 One control of laser–tissue interaction involves matching the wavelength of laser light to the absorption spectrum peak of the target tissue. The absorbing molecules (or chromophores) within the skin include hemoglobin, melanin, carotenoid, and bilirubin.7 While no cutaneous lesions contain primarily carotenoid or bilirubin, there are pathologic lesions that are composed primarily of hemoglobin or melanin. The naturally occurring optical absorptive advantage of certain tissues, therefore, can be used to optimize laser–tissue interaction. For instance, the beta 577 nm peak of oxyhemoglobin has been shown to correspond most closely to the wavelength demonstrating the best clinical and histologic response in the treatment of vascular lesions5–10 because the absorption of melanin weakens toward the longer visible wavelengths (Fig. 1).

In those cases where a pathologic lesion does not have a naturally occurring optical absorptive advantage over normal tissue, an exogenous chromophore (i.e., hematochromophyrin) can be administered that is preferentially taken up by the pathologic lesion, thereby simulating an absorptive advantage.12,13 Exogenous chromophore administration in the treatment of various dermatologic conditions, particularly tumors, is still experimental, but has great potential.

Another aspect of tissue optics that must be taken into account when trying to optimize laser parameters is the depth of penetration of light into the skin. In general, the longer the wavelength of laser light, the deeper the penetration into tissue. More recently, it has been shown that spot size is also an important parameter to consider when monitoring laser–tissue interaction.14,15

Regardless of what tissue is absorbing the laser energy, once this energy is converted to heat, it will spread throughout the surrounding tissue. If the energy source continues for too long, damage to normal stroma may occur from heat dissipation, and the relative optical absorptive advantage gained by choosing the appropriate wavelength and spot size will be lost. This can be prevented by consideration of a target's thermal relaxation time. The thermal relaxation time is defined as the time required for a target to cool from the temperature achieved immediately after laser irradiation to half that temperature.7 For example, the time that it takes for an organelle to cool is in the order of a microsecond, whereas cell layers will cool in a millisecond, and large abnormal vessels in portwine stains may take tens of milliseconds. If the exposure duration is long compared with the time required for diffusion of heat to surrounding structures, thermal damage will be extensive and nonspecific regardless of how specifically the laser light is absorbed and heats a target structure.16 Confining the pulse duration of the laser to the thermal relaxation time of the target tissue limits the extent of thermal damage and demonstrates the advantage of pulsed lasers (with short exposure time) over continuous wave lasers (with longer exposure times).

Laser Types

Lasers can be categorized into one of three major groups based on their active medium: solid, liquid, or gas (Table 1). Each laser has predominant wavelength and specific chromophore interaction capabilities. Several different lasers have been used for a wide array of dermatologic conditions. Each will be briefly summarized, but without detailing the laser mechanics involved.

Argon Laser

The argon laser emits visible blue-green light with wavelength peaks at 488 and 514 nm. It is a continuous wave system, although there are now “pulsed” systems available, which use a mechanical or optical shuttering device to break up a steady output beam. Absorption of the blue-green light is achieved by chromophores of its complementary colors, such as hemoglobin.

The argon laser has been used primarily in the treatment of vascular lesions, including portwine stains (Figs. 2 and 3),7–25 telangiectasias,17,18,25–27 spider varicosities,28–30 pyogenic granulomas,17 cherry angiomas,17 venous lakes,17 angiookeratomas,31 and Kaposi’s sarcoma.17 Theoretically, there should be selective absorption of the light by hemoglobin within the blood vessels.
comprising the lesion; however, several histologic studies have cast doubt on the specificity of the damage, showing the argon laser effects possibly due to nonspecific thermal destruction of skin. It has been shown that the exposure intervals used are too long and exceed the thermal relaxation time of the target tissues, thereby increasing the risk of scarring and dyspigmentation. Several clinicians have, nevertheless, reported excellent results with lesion regression and minimal scarring, especially in those protocols using very low energies. With the advent of newer, more vascular-specific systems (pulsed dye lasers), however, the argon laser is falling out of favor as the laser of choice for treatment of vascular lesions.

Because the wavelength of light is well absorbed by melanin, the argon laser has been used to treat pigmented lesions such as lentigo maligna and benign nevi, "café-au-lait" spots, nevus of Ota, and chloasma. Tattoos have also been treated with some success, but there have been reports of significant postoperative scarring. Nonpigmented lesions reported to be successfully removed by argon laser have included granuloma faciale and lymphocytoma cutis, both having a reddish-purple hue that may selectively absorb the blue-green light.

Tunable Dye Laser

The tunable dye lasers contain fluorescent dyes (of various composition) that absorb light at one wavelength and then emit laser light at another. The output wavelength of these systems may be varied or tuned by the operator by adjusting the dye used (ranging from approximately 400 to 1000 nm). They may be powered by a number of systems, such as a flash lamp or another laser (i.e., argon). The continuous wave dye laser systems provide a steady output of light, while the pulsed dye laser system provides intermittent pulses of light.

The dye laser systems have been applied to the treatment of vascular lesions, since the damage is highly specific to blood vessels, with sparing of adjacent tissue elements. The tunable dye laser, utilizing the yellow dye rhodamine 6G, can emit at 577 nm, which corresponds to the third absorption peak of oxyhemoglobin. When a very brief pulse duration (400 μs) is delivered, precise and localized vascular injury occurs, with a histologic appearance resembling vasculitis. More recently, it has been demonstrated that a laser emitting at 585 nm is even more effective in the treatment of vascular anomalies, with deeper vascular injury and continued vascular specificity. Scar formation and pigment alteration, which has been seen with the use of the argon laser, has been eliminated when the combination of laser parameters in the pulsed dye laser system is used.

Table 1. Characteristics of Lasers

<table>
<thead>
<tr>
<th>Laser</th>
<th>Medium</th>
<th>Wavelength</th>
<th>Chromophore</th>
<th>Lesions Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argon</td>
<td>Gas</td>
<td>488 nm, 514 nm</td>
<td>Hemoglobin, Melanin</td>
<td>Vascular, Pigmented</td>
</tr>
<tr>
<td>Dye</td>
<td>Liquid</td>
<td>Variable, depends on dye</td>
<td>Variable</td>
<td>Vascular, Pigmented</td>
</tr>
<tr>
<td>Ruby</td>
<td>Solid</td>
<td>694 nm</td>
<td>Melanin, Tattoo pigment</td>
<td>Pigmented, Tattoo</td>
</tr>
<tr>
<td>Nd:YAG</td>
<td>Solid</td>
<td>1060 nm</td>
<td>—</td>
<td>Vascular</td>
</tr>
<tr>
<td>CO₂</td>
<td>Gas</td>
<td>10,600 nm</td>
<td>Water</td>
<td>Epidermal, Dermal, Excision</td>
</tr>
</tbody>
</table>

Figure 2. Portwine stains on the nose and medial canthus of a 21-year-old female with prior argon laser test site (mid-nose).

Figure 3. Portwine stain of same patient (Fig. 2) 8 weeks after three pulsed dye laser treatments.
The portwine stain is the most common vascular lesion treated with the pulsed dye laser, but hemangiomas, facial telangiectasias (Figs. 4 and 5), poikiloderma, lymphangioma circumscriptum, Kaposi's sarcoma, and blue rubber bleb nevi have also been treated successfully using this laser system. One of the most important advances in the treatment of portwine stains is the fact that the pulsed dye laser can be safely used without scar formation in children. Recently, there has been renewed interest in treating spider varicosities of the legs with the pulsed dye laser, but hyperpigmentation (both persistent and transient) following treatment remains a common complication. Pigmented lesions such as “café-au-lait” spots have been treated with a dye laser tuned to a wavelength of 504 nm, with selective melanocyte damage seen on histologic examination of laser-treated skin.

The continuous tunable dye laser has been used in photodynamic therapy. This procedure involves the systemic administration of a photocytotoxic agent (usually hematoporphyrin derivative), which is selectively taken up and retained by malignant cells, followed by delivery of laser light, resulting in a toxic reaction that kills the malignant cell population. The hematoporphyrin derivative is photoactive when exposed to 630 nm light, which is most often derived from a tunable dye laser, although a nonlaser source may be used. Its antitumor effect is thought to result from singlet oxygen production with subsequent necrosis of the irradiated tumor. Basal cell carcinoma has been reported to respond to photodynamic therapy, but prolonged photosensitivity reactions following photoactivation of the hematoporphyrin derivative have been encountered, limiting its practicality as a treatment modality.

Ruby Laser

The ruby laser emits a visible red light with a wavelength of 694 nm. The red light can be delivered via a long-pulse system or a Q-switched (short pulse) system and is preferentially absorbed by blue or black pigments. On histologic examination, melanosomal disruption with alteration of both epidermal and dermal pigment has been observed when the ruby laser is used. The ruby laser has, therefore, been used successfully in the treatment of lentigines, nevocellular nevi, nevus of Ota, and tattoos (Figs. 6 and 7). Although initially used in the treatment of vascular lesions, it is no longer indicated for such lesions because of excessive scar formation. This is due to minimal absorption by both oxyhemoglobin and deoxyhemoglobin at 694 nm.

Neodymium Yttrium Aluminum Garnet (Nd:YAG) Laser

The Nd:YAG laser emits in the invisible near-infrared portion of the spectrum at 1060 nm. It is a continuous wave laser system without color specificity in its absorption. It tends to be a high energy system with deep tissue penetration, leading to a large amount of nonselective thermal destruction. Despite its nonselectivity, the Nd:YAG laser has found its way into dermatology. Large cavernous hemangiomas of the skin and mucosal surfaces have been treated successfully, as have dark nodular portwine stains. In addition, the Nd:YAG laser has been used for tattoo removal. Even with the recent development of a frequency-doubled variant of this system in which a crystal placed in the beam path...
halves the wavelength (giving a green color similar to the argon laser output and, thus, slightly better absorption by hemoglobin), there remains a significant amount of nonspecific tissue destruction, with possible resultant scarring.

Perhaps the most interesting future application of the Nd:YAG laser in dermatology will be that of wound closure by laser welding. Laser welded wounds have been shown to heal similarly (by tensile strength measurements) to conventionally sutured wounds, with less tissue manipulation and without introduction of foreign material into the wound, thus decreasing the risk of infection and/or foreign body reaction.

Carbon Dioxide (CO₂) Laser

The CO₂ laser is the most commonly used laser system. The laser system is usually a continuous wave laser, emitting light at the invisible far-infrared portion of the spectrum at 10,600 nm. The energy from the CO₂ laser is delivered to tissue through sealed tubes and angled mirrors because it cannot be delivered through optical fibers. The energy emitted by a CO₂ laser is nonselectively absorbed by both intracellular and extracellular water, and, because soft tissue is 80 to 90% water, total absorption of the CO₂ laser is a handy tool because it enables the surgeon to incise or ablate tissue, the outcome depending on the mode in which it is used. Whether the laser is used in either a defocused mode to vaporize tissue or a focused mode to incise tissue, its other unique properties, such as the ability to seal blood vessels and lymphatics up to 1.5 mm in diameter and the ability to seal nerve endings, allow for better hemostasis and less postoperative pain and edema than with conventional techniques.

The CO₂ laser is best suited to treat epidermal lesions, because it works by tissue vaporization. The most common dermatologic conditions treated by the CO₂ laser are verruca vulgaris and condyloma acuminatum, especially when they are large and/or recalcitrant to other forms of treatment. A variety of epidermal and dermal lesions, including syringomas, adenoma sebaceum, epidermal nevi, xanthelasma, trichoepitheliomas, apocrine hidrocystomas, myxoid cysts, and neurofibromas have been treated with the CO₂ laser. Successful CO₂ laser treatment of actinic cheilitis, lentigines, and superficial penile lesions, such as balanitis xerotica obliterans, erythroplasia of Queyrat, and Bowenoid papulosis has been achieved with excellent cosmetic results and minimal postoperative swelling and morbidity because the pathologic changes in these lesions are confined to the squamous epithelium of the epidermis.

Tattoos and keloids have also been treated with the CO₂ laser. Hypertrophic scarring and pigmentary loss are common complications when this laser is used in the removal of tattoos. While CO₂ laser excision of keloidal tissue showed promising initial results, subsequent reports with long-term follow-up of these same patients have shown high recurrence rates.
The combination of vaporization and excision using the CO\textsubscript{2} laser in the defocused and focused modes, respectively, is useful in the treatment of rhinophyma\textsuperscript{121,122} and acne scars. The surface remodeling using the defocused lower irradiance vaporization technique is akin to a superficial dermabrasion and yields excellent cosmetic results. In addition, cosmetic and functional improvement of nail plate abnormalities may be seen when the CO\textsubscript{2} laser is used in a focused mode to modify the nail matrix.\textsuperscript{123}

The CO\textsubscript{2} laser has also been used in the treatment of portwine stains\textsuperscript{124,125} and hemangiomas.\textsuperscript{126,127} The mechanism by which the CO\textsubscript{2} laser works in these conditions is through conduction of heat from the hot epidermis to the upper dermal blood vessels, producing full-thickness epidermal damage. This has been shown to result in hypertrophic scarring.\textsuperscript{128,129} Those clinicians who favor the use of the CO\textsubscript{2} laser now reserve its use for debulking large hypertrophic portwine stains and hemangiomas.

Utilizing laser technology, many cutaneous disorders are being treated more effectively and with less morbidity than with conventional therapies. When determining the appropriate laser for use in a particular condition, it is best to categorize the lesion into one of the following groups: vascular, pigmented, tattoo, epidermal process, or dermal process. The laser chosen should correspond to the predominant chromophore or absorbant tissue in the lesion being treated (Table 2).

### COMPLICATIONS OF LASER SURGERY

Lasers are versatile instruments that are associated with an acceptable risk profile. A survey of complications encountered with cutaneous laser surgery found the rate to average 2.8 to 4.2\% of procedures.\textsuperscript{130} Hypertrophic scarring is the most frequently reported complication, while infection carries a low occurrence rate, estimated at 0.2 to 0.6\%. Reports of unintentional burns to personnel or patients have also been rare. Perhaps the most worrisome disadvantage of laser use is the unknown risk of inhalation of laser smoke. “Lung-damaging dust” consisting of particles with diameters between 0.1 and 1.0 \(\mu\)m has been found in laser plume and can penetrate into distal lung branches.\textsuperscript{131} In addition, intact human papillomavirus DNA\textsuperscript{132,133} and HIV-virus\textsuperscript{134} have been isolated in laser smoke, and standard surgical masks do not filter out particles of the size seen in the laser plume of irradiated tissue, raising the obvious concern of infectivity of laser vapor.\textsuperscript{135} Smoke evacuation systems are necessary during laser therapy, especially when using the CO\textsubscript{2} laser, because copious amounts of vaporized material are generated.\textsuperscript{136}

### Table 2. Specific Dermatologic Lesions Treated with Laser Surgery

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Lasers Used</th>
</tr>
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<tbody>
<tr>
<td>Vascular</td>
<td>Dye (585 nm)</td>
</tr>
<tr>
<td>Portwine stains</td>
<td>Argon (488, 514 nm)</td>
</tr>
<tr>
<td>Telangiectasias</td>
<td></td>
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<tr>
<td>Hemangiomas</td>
<td></td>
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<tr>
<td>Blue rubber bleb nevi</td>
<td></td>
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<tr>
<td>Cherry angiomas</td>
<td></td>
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<tr>
<td>Spider veins</td>
<td></td>
</tr>
<tr>
<td>Pigmented</td>
<td>Dye (504 nm)</td>
</tr>
<tr>
<td>Lentigines</td>
<td>Argon (488, 514 nm)</td>
</tr>
<tr>
<td>“Café-au-lait” spots</td>
<td>Ruby (694 nm)</td>
</tr>
<tr>
<td>Nevocellular nevi</td>
<td></td>
</tr>
<tr>
<td>Tattoos</td>
<td>CO\textsubscript{2} (10,600 nm)</td>
</tr>
<tr>
<td></td>
<td>Ruby (694 nm)</td>
</tr>
<tr>
<td>Epidermal</td>
<td></td>
</tr>
<tr>
<td>Verrucae</td>
<td>CO\textsubscript{2} (10,600 nm)</td>
</tr>
<tr>
<td>Linear epidermal nevi</td>
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<tr>
<td>Actinic cheilitis</td>
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<tr>
<td>Rhinophyma</td>
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<tr>
<td>Nail plate abnormalities</td>
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<tr>
<td>Dermal</td>
<td></td>
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<tr>
<td>Keloids</td>
<td></td>
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<tr>
<td>Appendageal tumors</td>
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</table>
FUTURE USES OF LASERS IN DERMATOLOGY

While laser surgery of dermatologic conditions has been based primarily on the principles of selective photothermolysis, there are other areas of intellectual intrigue that may further the use of lasers both in treatment and diagnosis.

The use of low-energy lasers to accelerate wound healing, presumably by stimulation of dermal fibroblasts137 or by some other biostimulative process138-145 is but one area generating much interest in the scientific community. Laser induced photodynamic therapy (PDT) is another expanding area, which is already showing promise as a tool for selective cytotoxicity using newer, less toxic, but more photosensitizing substances.146 Additionally, liposomal147-149 or monoclonal antibody delivery systems with laser-induced release of drugs, may aid in the diagnosis and subsequent treatment of neoplastic or proliferative conditions.

In conclusion, the future practice of dermatology will be greatly benefited by laser technology. We are just now beginning to manipulate laser effects on tissue in order to maximize desired laser-tissue interactions and design new therapeutics and diagnostics. The benefits of lasers to medicine and mankind in the next 30 years are eagerly anticipated.

REFERENCES


