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Future Considerations in Cutaneous Photomedicine

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Laser and light technology and their use in dermatology are rapidly advancing. Radiofrequency devices have recently integrated lasers to augment the beneficial effects of both while minimizing potential complications of each. Laser-assisted liposuction is becoming more commonplace, and new investigations into the noninvasive selective destruction of fat with lasers have been undertaken. A better understanding of photobiology has generated renewed interest in the effects of low-level laser therapy on skin and wound healing. Lasers also are being used in novel ways for the purposes of in vivo diagnosis, producing some incredible imaging that may prove useful in the early diagnosis and evaluation of cutaneous disease. Finally, more recent work in the field of photochemical tissue bonding may be bringing us closer to sutureless and scarless surgery. Although not an exhaustive review, this article explores some recent advances in laser and light technologies for dermatologic applications and diagnosis.

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Lasers have been in clinical application in the field of dermatology since Leon Goldman's work in the 1960s.[1] The theory of selective photothermolysis introduced in 1983 by Anderson and Parrish provided direction for the development and application of lasers and light therapies.[2] The recent developments in the delivery of visible and infrared electromagnetic energy offer a variety of treatment options that can more predictably achieve a balance of efficacy, safety, and reduced downtime.

The majority of new laser and light devices are modifications of older technology. By drastically reducing the spot size of infrared nonablative and ablative lasers, the fraction lasers were introduced. Further advancing fractional technology has been the development of highly user-friendly handpieces and laser interfaces that make efficacy and safety more predictable. Applications of low-level laser light are experiencing renewed interest as the underlying mechanism of action is better elucidated and photobiologic effects in tissue are better appreciated. Radiofrequency devices alone, or integrated with lasers or intense pulsed lights, continue to vie for a niche in the treatment of skin laxity.[3] More recent applications of laser and light are holding promise for noninvasive diagnostic imaging of dermatologic lesions. New advances in photochemical tissue bonding may allow sutureless wound closure with the potential for reduced scarring. This article will review some of the most recent developments in the field lasers and light, as well as some potential future applications as they apply to the field of dermatology.

Radiofrequency

Radiofrequency (RF) devices—monopolar, bipolar, and the soon-to-be approved tri-polar devices—are still used by many dermasurgeons to achieve a modest tissue tightening of the face, forehead, and periorbital areas. While RF technology depends on the generation of heat to create changes in the skin, heating is achieved by the flow of ions rather than the absorption of photons as in laser and light modalities. Heating of tissue is based on the tissue's resistance to the flow of ions within an RF field.[4] Unipolar RF devices use a monopolar system in which an electrical current is introduced to the skin through a contact electrode and a ground electrode is placed at a distant site on the body. Electrical energy dissipates rapidly from the point of contact. These systems have a high power density and relatively deep penetration in the skin, properties that make them somewhat painful with the potential to burn tissue.[5] They have been used successfully in tissue tightening and in the treatment of acne.[6-9] Bipolar devices allow electrical energy to flow between 2 electrodes placed at a fixed distance. The propagation of electrical energy is confined to the space between the 2 electrodes. This spacing allows for a more precise application of RF current within the tissue and limits the depth to approximately half

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the distance between the electrodes. These devices have also been shown to be effective in the treatment of skin laxity.[5]

More recently, the use of a tripolar device has been explored for the treatment of skin laxity and cellulite.[10] These devices are currently available and used in Europe and Asia, but are pending Food and Drug Administration (FDA) approval in the United States. Pollogen Ltd. (Tel Aviv, Israel) has developed a device with 3 probes that exploits the benefits of both unipolar and bipolar RF to treat tissue. Marketed as TriPollar™ RF technology, there are 2 devices that have been touted primarily as advanced treatments for cellulite and wrinkles. Although bipolar devices rely on active integrated cooling devices to avoid damage to the epidermis, the tripolar device advertises simultaneous moderate deep and superficial heating of tissues that does not require protective cooling for the epidermis. The device is endorsed by Pollogen as being painless. Temporary posttreatment erythema is reported as the only adverse effect. The first device introduced by Pollogen, called the Regen™ system, became available in Europe in 2006. Most recently, a device marketed as the Apollo™ (Fig. 1) advertises faster treatment times than the Regen™ and claims more immediate results.

Four to five treatments with treatment times ranging from 5 to 30 minutes (depending on amount of surface area being treated) is the recommended protocol for optimal results. The maximum output of the device is 50 W, equaling the energies of current unipolar and bipolar devices.[11] There are several white papers regarding the efficacy of the Regen™ device in the treatment of facial skin laxity, reduction of hip circumference, and reduction of circumference on facial neck and arm skin in an Asian population.[12-14] Overall, the reports lack objective data and include small numbers of patients or single case reports. To date, there have not been any studies published in peer-reviewed journals regarding the efficacy of these devices. The prospect of a more refined, efficacious and faster device, however, remains appealing.

Newer devices have combined RF and laser into a single application. In combination, these devices are able to target specific tissues and work synergistically to achieve the desired clinical outcome. The light component is target specific, creating a thermal injury to a particular tissue. RF energy can be delivered into a region of tissue, albeit in a less precise fashion, based on the distance between electrodes. By using these modalities in conjunction, the practitioner is able to use lower levels of optical energy, making the treatment of darker skin types safer and theoretically compensating for any optical energy that may not be able to penetrate or achieve enough absorption in the target tissue to induce the desired clinical effect.[15,16] Sadick and Trelles[16] investigated the use of a bipolar frequency device in combination with a 900-nm diode laser for the treatment of wrinkles on the face and neck. Patients received up to 3 treatments at 2- to 3-week intervals. They performed one pass over the face and neck and 3 total passes over wrinkled areas. More than 50% of patients enrolled in this study had a 50% or greater improvement in the appearance of wrinkles.[16] Combination devices have also been shown to be effective in the removal of light colored hairs, a problem that cannot be adequately addressed with laser alone due to the lack of melanin as a chromophore.[17]

Figure 1 (a) The Apollo tripolar device and (b) medium applicator (Courtesy of Pollogen Ltd.).

Unfortunately, all RF devices now contend with their reputation of poor interprovider consistency and the niche of skin tightening remains an area of numerous controversies, mainly around predictable efficacy. Various techniques have been used including devices that combine radiofrequency with broad spectrum or monochromic devices, radiofrequency with vacuum handpieces, mono/bipolar combinations, and low pulse fluence/high cumulative energy treatments with near and mid-infrared lasers and intense pulsed light.

Anecdotally, there is no question that results can be achieved with many of these devices and when selecting patients properly they achieve a high rate of satisfaction. I use a monopolar RF device (ThermaCool, Thermage, Hayward, CA) on many of my liposuction patients, especially neck cases, either at the time of liposuction or 2 to 6 weeks postoperatively. Those that are most satisfied with the results are thinner patients who are postliposculpture that subsequently have Thermage treatments 3 to 6 months postoperatively. Nevertheless, numerous attempts to capture photographic confirmation of a significant increased skin “tightening” with RF postliposculpture have been fruitless.

Newly developed techniques and treatment tips are now marketed that have been reported to induce more predictable results. Time will tell whether this technology will produce a clinical effect that is predictable, less operator-dependent, and relatively cost effective.

Treatment of Fat and Cellulite

Laser-assisted lipolysis was introduced in the 1990s and has undergone several refinements since its inception. There are currently 3 devices that are marketed in the United States for laser-assisted lipolysis. The Smartlipo (Cynosure Inc., Westford, MA) uses a 1064-nm Nd:YAG laser. The rival device, Coollipo (Cooltouch, Roseville, CA), uses 1320-nm Nd:YAG laser and was approved by FDA for use in January 2008.[18] It offers a laser-integrated handpiece, marketed as the CoolBlue Duet (Cooltouch, Roseville, CA), that allows for administration of laser energy and lipoaspiration simultaneously, avoiding the need for a second pass cannula to remove irradiated fat. The makes of the Smartlipo MPX (Cynosure Inc., Westford, MA) have taken the next step of integrating the 1064-nm and 1032-nm wavelengths into a single device.

Each wavelength may be used separately or in sequence.[19] By integrating the 2 wavelengths, it is proposed that the surgeon can create a thermal and photomechanical effect that heats collagen and liquefies fat in sequence. Laser lipolysis is discussed in further detail by Parlette in this issue of the journal (pages 259-263).

Newer noninvasive laser techniques have been and are currently being explored for the treatment of unwanted fat and cellulite. Anderson and coworkers investigated the use of selective photothermolysis of lipid-rich tissue in a porcine model using a free electron laser. After evaluating and comparing the absorption spectra of fat and water, they were able to determine that fat absorbs infrared light greater than water at 1210 nm and 1720 nm. Armed with this information, the group treated fresh porcine skin with intact subcutaneous fat using a free electron laser at an exposure time of 16 seconds, a beam power of 14 to 18 W, and a spot size of 1.7 cm. Anderson and his colleagues were able to demonstrate selective damage of fat of several millimeters depth without damage to overlying epidermis and dermis when used in conjunction with parallel cooling. There was speculation on the part of the investigators that the 1210-nm waveband may be useful in treating disorders of the sebaceous gland due to the triglyceride and other lipids that they produce, although this was not evaluated.[20]

On the basis of this work, an abstract presented at the American Society for Laser Medicine and Surgery provided some results for the application of 1210-nm laser to test spots on the abdomen of 20 human subjects. Each subject was exposed to a 3-second pulse duration of 70 J/cm^2, 80 J/cm^2, and 90 J/cm^2 using a 10-mm spot size, 5 seconds of precooling, and parallel cooling with the delivery of the laser pulse. Biopsies of test sites in 10 subjects at 1 to 3 days after exposure revealed epidermal damage in only 2 of 30 sites. Investigators attributed to the damage to inadequate cooling. At 4 to 6 weeks after treatment, biopsies revealed a focal panniculitis but no other evidence of a laser-induced effect. The group anticipates that larger spot sizes with longer exposure duration and more aggressive cooling will produce selective damage to fat in future trials.[21] These results hold some promise for the possible clinical application of this wavelength for the selective treatment of fat and sebaceous gland disorders in the future.

Low-Level Laser Therapy

Low-level laser or light therapy (LLLT) has been investigated for multiple applications for several decades and the current use and applications of light-emitting diode (LED) therapy is discussed in detail by Barolet (pages 227-238) in this journal. LLLT is defined as light that is delivered with a power range of 10^{-3} to 10^{-1} W, an intensity of 10^{-2} to 10^{0} W/cm^2, a fluence of 10^{-2} to 10^{2} J/cm^2, a wavelength of 300 to 10,600 nm, a pulse duration of 1 to 500 milliseconds, an interpulse interval of 1 to 500 milliseconds, and a total irradiation time of 10 to 3000 seconds.[22] There are multiple devices using low-level laser that are currently available. Although the efficacy of these devices has been in question for many years, there is some more recent evidence that suggests and supports its use in some clinical settings.

The theory of photobiostimulation involves multiple factors and processes that occur at the subcellular level. One of the primary proposed mechanisms is the increased formation of ATP after absorption of optical energy by the mitochondria. It has been proposed that the primary chromophore in this process is the molecule known as cytochrome c oxidase. There are 2 copper-based centers within the molecule, known as Cu_a and Cu_b. Cu_a has an absorption peak at 830 nm in its oxidized form. It delivers photons across the inner membrane of the mitochondria and drives the formation of ATP by oxidative phosphorylation. Cu_a may also initiate secondary cell signaling pathways. Stimulation via this mechanism leads to increased cell viability, more efficient use of energy, and prevention of apoptosis.[23] Direct photostimulation also appears to result in photodissociation of inhibitory nitric oxide from cytochrome c oxidase, leading to an increased rate of electron transport and production of ATP. Low-level light may also stimulate the expression of many genes related to the proliferation and migration of cells, as well as the production of cytokines and growth factors.[23]

One of the most compelling recent uses of LLLT is in the treatment of ischemic stroke was reported by Lampl and coworkers in 2007.[24] In this study, an 808-nm laser was used to transcranially irradiate 79 patients of 120 enrolled within 24 hours of presentation of acute ischemic stroke. Patients in the active treatment group received approximately 1 J/cm^2 delivered at 20 sites on the scalp for 2 minutes each. Patients in the treatment group had significantly more successful outcomes based on standard outcome scales used to assess patients who have had a stroke. Although not a dermatologic application of light therapy, it well illustrates the potential for light in multiple systems and encourages further investigation of applications in medicine as a whole.

A review of literature with regard to the effects of LLLT on wound healing was done by Posten and coworkers.[25] In the sum of studies that were reviewed from 1965 to 2003, there were some supportive, but inconsistent results for the role of LLLT. Some studies on cell cultures suggested an increase of collagen deposition and proliferation of fibroblasts, keratinocytes, and endothelial cells after LLLT whereas others show no effect. Several animal studies in rat models showed some benefit, but these results were not able to be reproduced in a porcine model that more closely resembles human skin. Human studies have been inconsistent and poorly controlled. A variety of devices with different parameters have been used, making comparisons among studies even more difficult.

Sobanko and Alster[26] recently examined the literature on the efficacy of LLLT in the treatment of chronic cutaneous ulcers in humans. They concluded that the available data do not support the role of LLLT in the treatment of chronic ulceration and that it should not be recommended in most circumstances.

In contrast to the studies discussed already, a low-level light study investigating its effects in the healing of excision wounds in mice was undertaken by Demidova-Rice and coworkers.[27] They examined the utility of 3 light sources using variable wavelengths and fluences to irradiate sites on BALB/c, SKH1 hairless and C57BL/6 mice 30 minutes after wounding. They then measured wound areas throughout healing and evaluated tissue using immunofluorescence staining for CD31 and SMA. In this study, the BALB/c and SKH1 hairless mice demonstrated significant stimulation in wound healing and an increased number of cells positive for α-smooth muscle actin at the wound edges. Eight hundred-twenty nanometer light seemed to produce the best results when compared with 635, 670, and 720 nm light. When looking at the light source, there was no significant difference between a coherent and noncoherent light source. Finally, although the BALB/c and SKH1 hairless mice showed similar beneficial effects with exposure to LLLT, the C57BL/6 strain did not show any improvement after illumination. This study certainly produced some quantifiable improvements with low level illumination. However, it also illustrates the variability and difficulty in determining parameters and predicting outcomes with LLLT.[27] Multiple unknown variables exist with the light source as well as within the target tissue that can lead to varied outcomes.

It is likely that as these mechanisms are better understood, new applications of existing lasers used with lower energies and greater frequencies of treatment will be used to treat common conditions. New, low fluence home-use devices are now available for the treatment of unwanted hair. Although they do not generate sufficient energy or heat to destroy the hair bulb, they do seem to induce anagen growth arrest and transition of the follicle into a catagen-like state, reducing the amount of hair that is visible.[28] By using the devices at regular intervals, a significant amount of growing hair is eliminated. Conversely, IPL treatment has been reported in some instances to induce a paradoxical growth of hair, though not at low level energies.[29] There are practitioners that use LLLT to

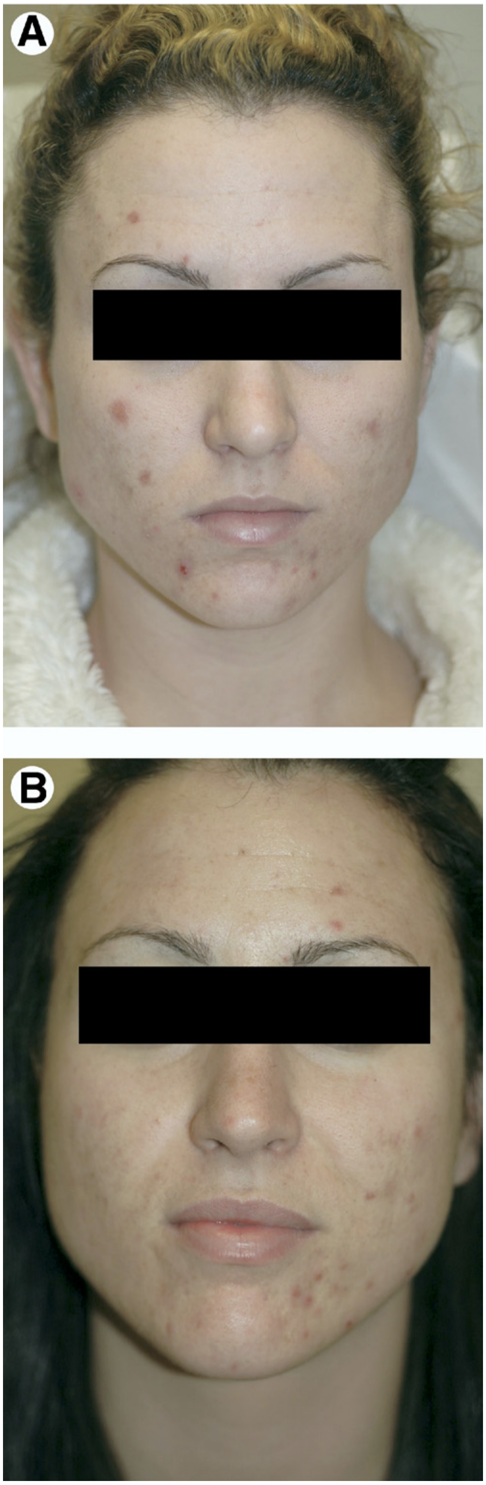

Figure 2 (A) Pretreatment photo of acne patient. (B) Posttreatment photo after 5 weekly treatments of 1064-nm Nd:YAG using 12-mm spot size, 10 J/cm^2, 20-millisecond pulse duration, and no cooling. Approximately 500 pulses delivered on treatment side (right) per treatment session. (Photos courtesy of Jonathan Baker, MD and Nathan Uebelhoer, DO.)

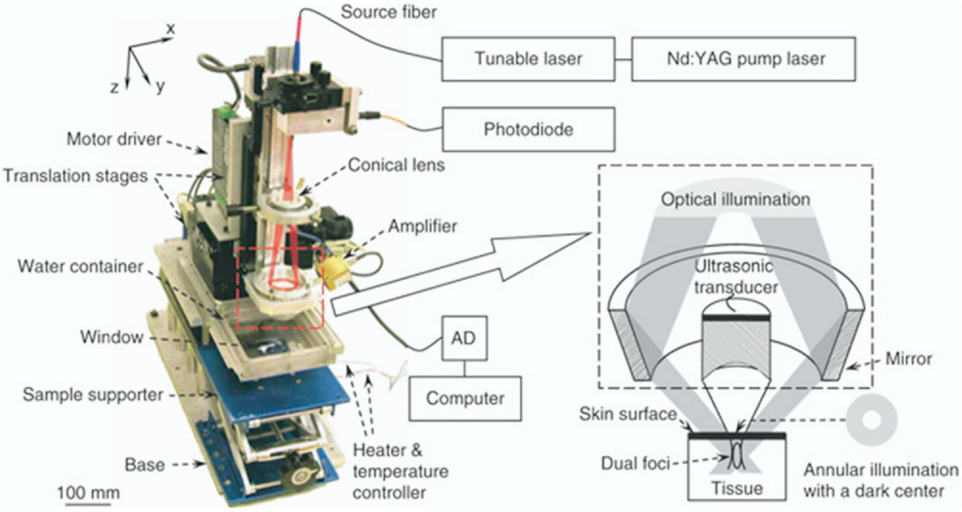

Figure 3 Experimental fPAM system. The components within the dashed box in the photograph are mechanically translated along an x-y plane with the bottom of the mirror and the ultrasonic transducer immersed in water. A window at the bottom of the water container is sealed with an optically and ultrasonically transparent disposable polyethylene membrane (thickness, 0.044 mm). After commercially available ultrasound gel is applied to the region of interest on the sample for acoustic coupling, the sample is placed between the water container and the sample supporter for imaging. (Reprinted by permission from MacMillan Publishers Ltd: Nature Biotechnology, Zhang and coworkers: Functional photoacoustic microscopy for high resolution and noninvasive in vivo imaging. Nat Biotechnol 24: 848-851, 2006.)

induce hair growth in individuals with androgenetic alopecia, although rigorous study and data do not yet support this application.

Some preliminary data from our study being conducted at the Naval Medical Center in San Diego for the treatment of acne using low-fluence 1064 nm Nd:YAG are encouraging. Patients have been treated at regular intervals using 10J/cm^2 with a 12-mm spot, 20-millisecond pulse duration, and 4 to 5 pulses per lesion with visible improvement (Fig. 2).

Further investigations are necessary but may yield a new approach of multiple low-fluence, high-frequency treatments for patients who do not respond to or cannot tolerate conventional medical treatments.

Lasers in Diagnostics

Lasers have been used not only in therapeutics but also in a novel way in diagnostic technology that will have implications for the dermatologist. Imaging of cutaneous lesions through techniques such as ultrasound, magnetic resonance imaging, dermoscopy, and optical coherence tomography (OCT) all offer in vivo evaluation, but not with the precision of standard histology. In vivo confocal scanning laser microscopy and functional acoustic microscopy are technologies that have been used in the evaluation of pigmented lesions, epithelial tumors and multiple other skin lesions. Improvement in optics and speed of image capture is bringing these modalities closer to the forefront of regular use in diagnosing skin lesions.[30,31] Additional work done with optical frequency domain imaging may also yield real-time, noninvasive dynamic imaging that may some day replace invasive biopsies of skin lesions.

In vivo confocal scanning laser microscopy (CSLM) has been explored as an imaging technique for several years. It exploits the backscatter of light from a point light source to produce a high resolution en-face representation of the skin. To produce an image, an isolated point is targeted within the skin at a chosen depth. A near infrared low-power laser is focused on that spot within the region of interest and reflected scattered photons are focused through an objective lens to a pinhole aperture. This allows only reflected light from the point of interest to pass through to a detector. The apparatus can be moved to adjacent points within the skin to scan points along the x and y axis. Adjusting the depth of focal plane allows for examination of different levels of tissue in the z axis. In this way, a volume of tissue can be imaged and reconstructed.

Recent work by Ahlgrimm-Seiss and coworkers[32] examined the correlation of CSLM with the dermoscopic and histologic appearance of benign nevi with different pigmentation patterns. They found that architectural features observed with CSLM correlate well with different dermoscopic pigment patterns, suggesting that CSLM may be a useful tool in the future for distinguishing between benign nevi and early melanomas. Currently, this is a time-consuming process, can be somewhat cumbersome, and is expensive. These devices are limited by their depth of penetration, currently 200 to 300 um, that only allows visualization of the epidermis and the superficial papillary dermis. Cell ultrastructure on images is somewhat obscured and nonspecific. With technological and methodological improvements, the future holds the prospect of using such devices to replace biopsies, to monitor response to therapy, to delineate lesions more precisely for

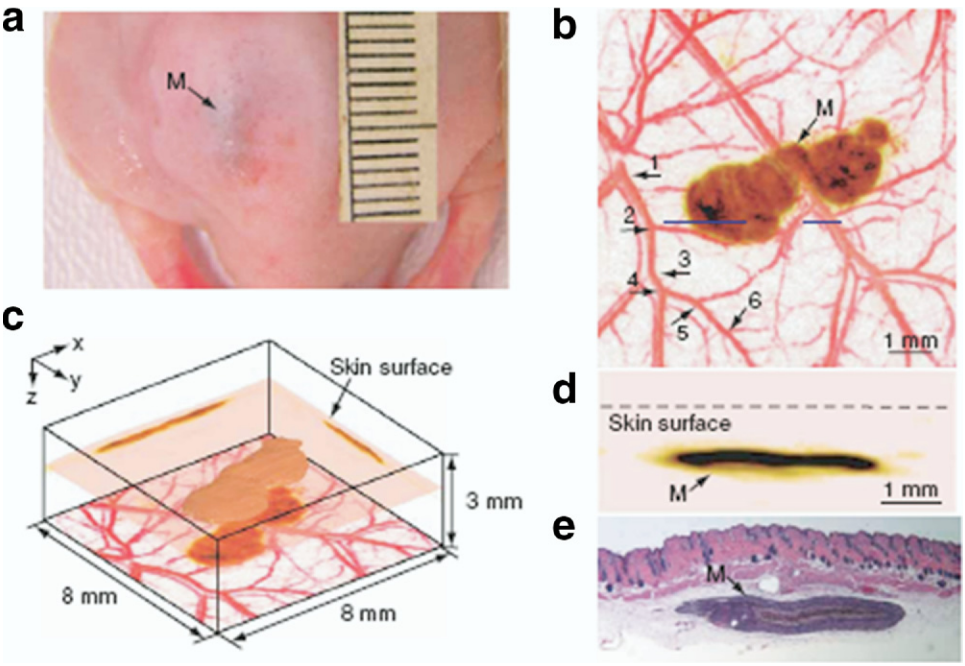

Figure 4 In vivo imaging of a subcutaneously inoculated B-16 melanoma in an immunocompromised nude mouse using fPAM at 584 nm and 764 nm. (a) Photograph of melanoma. (b) A composite of the t2 maximum amplitude projection (MAP) images projected along the z axis, where a MAP image is formed by projecting the maximum photoacoustic amplitudes along a direction to its orthogonal plane. Here, blood vessels are pseudocolored red in the 584-nm image and the melanoma is pseudocolored brown in the 764-nm image. As many as 6 orders of vessel branching can be observed in the image as indicated by the numbers 1 to 6. (c) Three-dimensional image rendering of the melanoma from the data acquired at 764 nm. Two MAP images at this wavelength projected along the x and y axes are shown on the 2 side walls, respectively. The composite image shown in a is redrawn at the bottom. The top surface of the tumor is 0.32 mm below the skin surface, and the thickness of the melanoma is 0.3 mm. (d) An enlarged cross-sectional (B-scan) image of the melanoma parallel with the z-x plane at the location marked with a dashed line in a. (e) hematoxylin-and-eosin (HE) stained section at the same marked location. M, melanoma. (Reprinted by permission from MacMillan Publishers Ltd: Nature Biotechnology, Zhang and coworkers: Functional photoacoustic microscopy for high resolution and noninvasive in vivo imaging. Nat Biotechnol 24:848-851, 2006.)

surgical excision, and to evaluate dynamic processes such as blood flow.[31,32]

A more recent development in diagnostic imaging is that of functional photoacoustic microscopy (fPAM). It involves the use of short pulses of laser light that are transmitted into tissue. As the light is absorbed and converted to heat, an expansion of the target tissue occurs that results in the formation of an acoustic wave. An ultrasound transducer is then used to detect these waves (Fig. 3).

In reconstructing them, a three dimensional image can be made that represents the optical absorption of specific tissues.[33] A recent letter by Zemp and coworkers[34] describes a photomicroscopy system that uses a high-frequency (30-MHz) ultrasound array photoacoustic device to visualize microvasculature in rats in situ. The system was demonstrated to achieve resolution at depths of 3 mm. This depth is not obtainable with optical microscopic techniques such as confocal and 2-photon microscopy due to the scattering of light. The proposal is made that this will have utility not only in dermatologic disorders, but other diseases that involve microvasculature such as atherosclerosis and vascular complications associated with diabetes.

Zhang and coworkers describe the use of fPAM in the evaluation of an inoculated B16-melanoma in an immunocompromised nude mouse. Using a 584-nm laser, they were able to visualize the melanotic lesion and its relationship to surrounding blood vessels (Fig. 4).

Because of inadequate penetration of visible light through the melanotic lesion, they used a 764-nm laser to gauge tumor thickness. By combining these images, they were able to construct a 3D image of the melanoma and the surrounding vasculature. In addition, they were able to use fPAM to functionally measure the sO^2 levels of single blood vessels, which they propose may have some utility in studying tumor physiology in the future.[35]

Functional fPAM offers better evaluation at deeper levels of tissue than those that can be achieved with optical in vivo imaging techniques. It is a safe modality that offers excellent resolution and has the capability of functional imaging using multiple wavelengths.[36] Current technology limits the rate at which images can be acquired. Through the use of higher pulse-repetition rate lasers in conjunction with parallel data acquisition electronics, real-time imaging will be possible.[37]

Finally, OCT is a technology that has undergone refinements recently that has potential dermatologic application. A basic OCT system focuses a beam of light that is directed through a beam splitter, dividing the light into 2 beams. One beam is sent to a reference mirror while the other beam is sent to the tissue sample of interest. Reflected light from the reference mirror and the tissue sample are sent back through the beam splitter and to a detector, where interference between the two light beams occurs (interferometer). A computer is then used to interpret the signals and reconstruct a picture of the tissue of interest.[36,37] Although the technology itself was invented in the early 1990s, it has been limited by the light sources available and the acquisition speeds of the cameras and photodetectors necessary to produce a usable image. More recent advancements in the capability of the hardware have resulted in improvements of this modality that may prove to be a viable and valuable tool in noninvasive imaging of the skin.

An iteration of this technology is known as swept-source OCT or optical frequency domain imaging (OFDI). Although the details of this device are beyond the scope of this review, it employs the use of a wavelength tunable laser with standard photodetectors and is able to provide a significant signal-to-noise ratio gain over standard OCT.[37] With optical frequency domain imaging, investigators have been able to achieve resolutions at the submicrometer level, allowing for the potential of imaging at the subcellular level. It has been used in the evaluation of esophageal mucosa and coronary arteries in vivo in a study by Yun and coworkers with good microscopic resolution. It has the potential for offering a noninvasive, rapid acquisition modality for imaging and analyzing lesions of the skin.[36]

Photochemical Tissue Bonding

The prospect of closing surgical wounds without producing a scar is an exciting one in the field of dermatology. Practitioners have made many attempts using photothermal tissue welding during the past 2 decades. This technique involves the localized heating of skin to denature collagen. The resultant tissue bonding is thought to occur as a result of the intertwining of collagen from the wound edges as the tissue cools. Results have been inconsistent and complications have arisen due to excessive peripheral tissue heating and damage. Topical application of dyes that absorb laser light, such as indocyanine green and India ink, have allowed for a smaller areas of thermal damage by allowing for selective absorption and heating of wound edges. In combination with protein-based tissue solders, stronger tissue bonds have been achieved in an ex vivo porcine model.[38]

A newer technique, involving the use of photoreactive dyes in conjunction with laser irradiation, obviates the thermal denaturation of collagen and avoids collateral tissue damage. Immediate tissue bonding occurs as a result of absorption of light energy by the photoreactive dye that initiates the formation of covalent crosslinks between proteins of apposed tissue surfaces. Several recent studies have demonstrated the feasibility of this procedure and the potential for multiple clinical applications. Johnson and coworkers,[39] at the Wellman Center for Photomedicine at Harvard, demonstrated functional recovery rates equivalent to the conventional technique of epineural suture repair in rats with transected sciatic nerves. Related work by O'Neill and coworkers[40] evaluated the use of photochemical tissue bonding (PTB) in microvascular anastomosis. Using ex vivo porcine brachial arteries, the group was able to demonstrate a higher resistance to leaking of PTB-treated vessels versus those vessels that had undergone suture repair. In a second, in vivo portion of the same study using femoral arteries of rats, O'Neill and coworkers showed patency rates among PTB-treated femoral arteries to be the same as sutured arteries 8 weeks after repair with no increase in adverse events such as aneurysm formation. More specific to dermatology, work done by Kamegaya and coworkers,[41] also at the Wellman Center for Photomedicine, explored the use of Rose Bengal and 1,8 naphthylamide in conjunction with a 532-nm laser to close incisional and excisional wounds in vivo in a pig model. Incisions were irradiated with 100J/cm^2 and excisional with treated with 75, 100, or 150 J/cm^2. Standard sutures and tissue adhesive groups were included as comparisons in the cosmetic and histologic evaluation of resultant scars. The cosmetic results were similar between all groups and there were no adverse effects such as thermal damage, dehiscence, local tissue reaction to the PTB dye, or infection. One could theorize that further refinements in this technique may lead to a safe, quick, technique for wound closure with clinically superior results.

Lasers and Medicine

As the underlying mechanisms of laser interaction with tissue are better understood, so are the reasons that some modalities may produce inconsistent or short-lived results. As an example, the paradoxical response of skin to pulsed dye laser therapy of port wine stains was recently discussed by Dr. Nelson at the "MauiDerm: Advances in Cosmetic and Medical Dermatology" meeting. Using a rodent window chamber model to study the blood vessel response to light induced injury, Nelson and colleagues have been studying the long-term effects of light-induced injury to the superficial vasculature of skin. Initial treatment with the pulsed dye laser (PDL) results in loss of blood flow on post operative day 1, but by day 11 the port wine stain blood vessel reformation and revascularization has occurred. They have attempted to determine if this wound healing response could be altered after PDL therapy by targeting the hypoxia-inducible factor-1-α and vascular endothelial growth factor. Using Rapamycin topically after PDL irradiation, they found that this response was altered sufficiently to prevent reformation of the blood vessels. Obviously, this holds major implications for the future of cutaneous vascular treatment. At this point it appears promising and could dramatically change the course duration of laser treatment of port wine stains as well as other vascular lesions on and off the face.[42]

Conclusion

The application of lasers and other light sources in dermatology is rapidly advancing. Improvements in technology and understanding of light interaction with tissues have led to some astounding developments in the treatment of the skin and the ability to perform in vivo diagnostic tests. New applications for existing lasers as well as new devices that integrate multiple wavelengths and modalities are continuously being developed. The approach of low level treatments has experienced a renewed interest as subtle photobiologic effects are better understood and treatment approaches are optimized. Forays into arenas such as PTB, once seen only in science fiction, are producing results that have practical application in many fields of medicine. Regardless of which direction the future takes in the field of dermatology, lasers and light will continue to illuminate the path.

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