

## ADVANCES IN DERMATOLOGY

# Recent Advances in Laser Therapy and Other Technologies

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**Abstract.** Laser technology and other energy sources are rapidly finding a place in dermatology clinics. In the field of skin rejuvenation by fractional photothermolysis, although few controlled studies have been undertaken, several devices have emerged in recent years that appear less effective than laser ablation techniques but that are safer. The aim of this short article is to provide an introduction, though not treat in depth, the different emerging technologies in dermatology. We will focus particularly on lasers and light sources in improving applications such as the treatment of vascular lesions, acne, and encapsulated ink tattoos; light-emitting diodes; developments in the treatment of cellulitis; photodynamic therapy; suction methods; scarring; and finally the recent and doubtlessly future introduction of home devices for use in a range of dermatologic applications (depilation, rejuvenation, treatment of acne, etc).

**Key words:** laser, fractional, vascular, light emitting diode, tattoos, acne, review.

## RECIENTES AVANCES EN LÁSER Y OTRAS TECNOLOGÍAS

**Resumen.** La tecnología láser y otros tipos de fuentes energéticas se están incorporando rápidamente a la consulta del dermatólogo. En el campo del rejuvenecimiento fraccional han aparecido en los últimos años varios equipos, aun habiéndose realizado escasos estudios controlados, inferiores en eficacia a los láseres ablativos pero con mayor grado de seguridad. Este breve artículo sólo pretende introducir, pero no desarrollar de forma exhaustiva, las diferentes tecnologías emergentes en Dermatología, especialmente láseres y fuentes de luz para el tratamiento de lesiones vasculares, acné y tatuajes con tintas encapsuladas y cicatrices; las aplicaciones de los diodos emisores de luz (LED), las novedades en el tratamiento de la «celulitis», terapia fotodinámica, métodos de succión, y por último la reciente y sin duda futura introducción de los dispositivos caseros para el tratamiento de diversos problemas dermatológicos (depilación, rejuvenecimiento, acné, etc.).

**Palabras clave:** láser, fraccional, vascular, LED, tatuajes, acné, revisión.

## Skin Rejuvenation by Fractional Photothermolysis, Plasma Techniques, and Other Advances

Several devices for fractional skin rejuvenation have come onto the market in recent years and are beginning to enjoy strong sales figures even though few controlled trials have been performed (Table). These devices were developed with a view to avoiding the side effects of the ablative (CO<sub>2</sub> and

Eryttrium-aluminum-garnet [YAG]) lasers that had been used and that, despite their proven effectiveness, had the drawbacks of slow healing and the risk of scarring and hypopigmentation. It should be remembered that techniques based on fractional photothermolysis are less effective than ablative lasers, which require a single session, eliminate epidermal lesions, have predictable outcomes, and induce greater skin tightening.

Fractional laser systems produce many small regions of lesioned skin (microthermal zones), each of which affects a fractional part of the tissue while sparing the skin around the lesion for a faster epithelization. Minimal posttreatment care is required and the side effects associated with ablative laser therapy do not occur. Each lesioned region covers an area of approximately 50 to 70  $\mu\text{m}$  and is surrounded by viable tissue, which ensures complete reepithelization within 24 hours. Lasers currently available on the market include the Fraxel laser at 1550 nm (2004, Reliant Technologies), Lux IR (IPL) at 1540 nm, erbium laser (2005, Palomar),

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Affirm Laser at 1440 nm (2006, Cynosure, which is now associated with 1320 nm light to produce greater skin tightening), Pixel at 2940 nm (Alma), Reliac at 10 600 nm (Lumenis), Mosaic at 1550 nm (Lutronic), Profractional at 2940 nm (2007, Sciton), Active Fx at 10 600 nm (Lasering), Fraxel Re:Pair (10 600 nm), and Fraxel Re:Fine (1410 nm).

The term *fractional* can be applied to any energy source that delivers high fluence and has a small spot diameter that produces pixels of skin damage measuring less than 500 nm in diameter without harming surrounding tissue to ensure rapid reepithelization within 24 to 48 hours. The risk of infection is therefore reduced and less time off work is required. Thus, an annular coagulation of dermal collagen occurs that increases skin tightening.

However, the optimum depth of skin damage for each lesioned area and the volume of coagulated or necrotized tissue have not been determined. We also do not have a clear idea of what percentage of skin area should be covered or treated in each session or the total number sessions necessary, and the most appropriate parameters have yet to be optimized for each system. At present, there is evidence that fractional techniques are effective,<sup>1,2</sup> with one of the most important indications being acne scarring (primary indication), fine and moderate wrinkles, melasma<sup>4-6</sup> (still the subject of some debate), rejuvenation, and actinic keratosis. What does seem clear is that all these techniques are effective and their usage will depend on the level of training and judgment when selecting the appropriate parameters in each case.

Another promising option is a plasma-based system (Portrait plasma skin regeneration [PSR]).<sup>7</sup> It operates on a different principle to fractional techniques and is effective for rejuvenation. Unlike other systems, PSR is not based on laser light or radiofrequency radiation. The energy source is a combination of nitrogen gas and high-frequency electromagnetic radiation that forms a plasma, which is applied through a handheld device to give a 6-mm spot size with a uniform energy distribution and without the need for physical contact with the target skin surface. The energy is delivered in pulses and the depth of penetration and fluence can be tailored to the needs of each patient. The stratum corneum remains intact after treatment, thereby reducing the risk of infections and side effects. Forty-eight hours after treatment, fine uniform peeling takes place where the skin has been treated. Epidermal regeneration takes place in 7 days. This system has the advantage of requiring a single application and the effect is similar to that of peeling techniques, but in this case, skin tightening is induced thermally and few days off work are required, depending on the energies used. In addition, the technique does not rely on chromophores and can be used in all phototypes. Histologic studies have shown that a decrease in solar elastosis persists even up to 1 year after treatment,

**Table.** Rejuvenation by Fractional Thermolysis, Plasma Techniques, and Other Advances

<i>CO<sub>2</sub>/Er</i>
Ablative
Major improvement
More time off work
Greater risk of adverse effects
<i>Plasma Techniques</i>
Partially ablative
Single session
Better tolerated
Better than chemical peeling
Less improvement than the previous technique
<i>Fractional</i>
Nonablative
Repeat sessions required
Hardly any time off work
Excellent for acne scars
Less skin tightening

with a narrowing of the collagen band close to the dermal-epidermal junction.<sup>8</sup>

## Acne: Advances in Conventional Laser and Light Therapies and Photodynamic Therapy

In recent years, there have been many advances in the treatment of acne and new techniques have been introduced, but it is too early to tell whether these will be effective and inexpensive enough to replace the conventional ones. The mechanisms of action are still theoretical and confirmation of their effectiveness has yet to be obtained. For the time being, few rigorous randomized controlled trials of their effectiveness have been done, and so they cannot be used alone as single therapy. The bewildering range of devices, protocols, and parameters for the different types of acne makes it very hard to tailor protocols to each individual patient.

If the effect of these devices at a molecular level could be determined, the therapies could be better targeted, but it still has not been shown that they really work. Among the many systems used for acne therapy, we shall highlight 4:

1. Blue, red, and UV light with an endogenous photosensitizer<sup>9</sup>
2. Pulsed dye lasers<sup>10,11</sup>
3. Infrared lasers for selectively damaging sebaceous glands<sup>12-14</sup>
4. Photodynamic therapy (with exogenous photosensitizer)<sup>15,16</sup>

The outcomes are probably better when more energy is delivered, more treatment sessions are performed, and different therapies are combined. In addition, devices for home use are under development and will probably flood the market in the coming years.

### Advances in Skin Pigment Insertion and Removal (Including Tattoos)

Different types of laser usually have to be combined in order to eliminate tattoo pigments. So if a certain pigment cannot be eliminated using an appropriate fluence of energy from a Q-switched laser, we should therefore change system (ruby 694 nm laser, alexandrite 755 nm laser, or the Nd:YAG 1064 and 532 nm laser, which is particularly effective) but never excessively increase fluence because this would also increase the risk of side effects. Lasers with nanosecond pulses (Q-switched systems) are the most appropriate. These pulses produce shock waves that literally rupture the pigment through a photoacoustic mechanism whereas millisecond pulses can cause scarring. Particular care is necessary in suntanned patients, who should wait before starting treatment and, whenever possible, undergo an initial test or use topical bleaching agents before treatment.

In the future, lasers with shorter pulse durations (picoseconds and femtoseconds) and a potential for improved therapeutic effectiveness may well appear on the market. These considerations notwithstanding, we should always begin therapy with the longest wavelength available.

Allergic reactions within tattoos should not be treated with Q-switched lasers due to the risk of systemic allergic reactions,<sup>17</sup> which have also been described using continuous-wave lasers (CO<sub>2</sub> lasers).<sup>18</sup>

Recently, permanent but removable tattoo inks, which can be eliminated in a single laser session, have become available commercially. These biodegradable and microencapsulated inks are made up of polymethylmethacrylate.<sup>19</sup>

Fractional lasers are also starting to be used, particularly for resistant tattoos, but this indication is still the subject of much debate. This technique has also been used for superficial melasma and may find its place among the therapeutic options. In other diseases such as lentiginos, Q-switched lasers or intense pulsed light can be used.

### Light-Emitting Diodes: Do They Work?

Light emitting diodes (LEDs) are inexpensive light sources that have been introduced into dermatology for indications such as photorejuvenation<sup>21-23</sup> (yellow light at 570-600 nm and red light at 630-635 nm) and for treating conditions such as acne (blue light at 415 nm and yellow light at 570-600 nm) and several types of dermatitis.<sup>24</sup> Theoretically, they act through a photobiostimulation mechanism. There is still much debate about their effectiveness. The devices can emit wavelengths of light between 630 and 850 nm, which has a high penetrating power. Examples of systems on the market include Gentlewave, Omnilux, and Active FX. Although more data are required to understand the exact cellular mechanism, they seem to exert their effect primarily by increasing the permeability of the mitochondrial membrane and thereby raising the pH, activating cyclic adenosine monophosphate (cAMP), and increasing DNA/RNA synthesis. Until now, most clinical studies have centered on lasers and other energy sources that selectively destroy a cutaneous target, and so few data are available to support the effectiveness of LEDs for dermatologic applications.

They still have a long way to go before they can compete with effective rejuvenation techniques such as ablative rejuvenation.

On the basis of a probable anti-inflammatory effect caused by the emitted light, such therapy has been tried in certain conditions in which, in theory, benefit might be obtained, such as rosacea, pityriasis rubra pilaris, and cases of erythema and edema after use of certain types of laser (fractional or CO<sub>2</sub> lasers). Moreover, heating of the skin induces collagen remodeling, and so this therapy might be effective in preventing hypertrophic scarring and in treating skin ulcers. Potential applications in conditions that involve metabolic pathways in which the p53 protein is implicated have also been studied with LEDs at 660 nm. An example is the treatment of postinflammatory hyperpigmentation.

Photodynamic therapy could also benefit from LED technology through the use of wavelengths with deeper penetration (infrared at 830 nm).

A role in the prevention of UV damage (photoprophylaxis) has also been suggested. Potential targets of such therapy would be cytochrome C oxidase, p53,<sup>25</sup> G protein, cAMP activation, increased DNA or RNA synthesis, and protoporphyrin IX.

### Advances in the Treatment of Cellulitis

There are currently many different systems on the market that combine laser systems,<sup>26,27</sup> radiofrequency sources,<sup>28</sup> pulsed light sources, suction, and ultrasound. They are still not as effective as liposuction but they are beginning to

emerge as a clear alternative for the future. As always in this field, technology is getting ahead of the basic science, and although systems are marketed with the approval of the US Food and Drug Administration (FDA), there is an insufficient body of supporting literature. Among the most widely used systems are VelaSmooth (Syneron), which combines a radiofrequency energy source, pulsed light sources, and suction; Accent (Alma), which uses a unipolar radiofrequency source; Thermage, Sciton, Titan, and TriActive (Cynosure), which combine a laser light source with suction; Ultrashape (acoustic effect due to ultrasound); LipoSonic (thermal and lipoacoustic ultrasound effect); SmartLipo (Cynosure), which comprises a minimally invasive Nd:YAG fiber lasing at 1064 nm that "liquidates" the fat through lipolysis by direct action of laser light on adipocytes and contraction of collagen in the fibrous septa and dermis; and Cool Lipo (Cooltouch) at 1320 nm, which acts in the same way as SmartLipo. Their effectiveness is often unpredictable, with good and even excellent outcomes in some cases. They seem to be more effective in patients with very flaccid abdominal skin, apparently because of the resulting skin tightening and elimination of fat.

## Advances in Vascular Laser Treatment

In the field of vascular laser treatment, the main advance was made in 2006 with the sequential use of a pulsed dye laser at 595 nm followed by a Nd:YAG laser at 1064 nm (Cynergy Multiplex, Cynosure).<sup>29,30</sup> The pulse from the pulsed dye laser induces a  $\beta$ -chromatic shift in the absorption spectrum of oxyhemoglobin, with the production of methemoglobin, which leads to an exponential increase in the absorption of the Nd:YAG laser pulse at 1064 nm. The result is that much lower fluences are required to produce a deep thermal effect. The greater therapeutic effects associated with using multiple pulses at the same wavelength from a pulsed dye laser are well known.<sup>31,32</sup>

For dark, hypertrophic port wine stains (nevus flammeus or capillary vascular malformations) resistant to pulsed dye laser treatment, this system seems to provide a novel therapeutic option that improves outcomes. In adults with treatment-resistant port wine stains, we use a 10-mm diameter spot from a pulsed dye laser (6-10 ms, 8-10 J/cm<sup>2</sup>) followed by a second Nd:YAG pulse of 15 ms and 30-45 J/cm<sup>2</sup>, with optimal air cooling and ice packs. In resistant cases, a further dye laser pulse of 0.5 ms duration is applied with a spot size of 10 mm and a fluence of 7-9 J/cm<sup>2</sup> after 1 minute has elapsed.<sup>30</sup>

In any case, the pulsed dye laser is still the technique of choice for this type of lesion in children<sup>33</sup> due to the risk of scarring associated with Nd:YAG lasers. Even with the larger beam diameters (10 mm), fluence is optimal (for example, 10 mm, 0.5 ms, 6-9 J/cm<sup>2</sup> with intense epidermal

cooling) for treatment in children. The treatment therefore acts much more quickly and may sometimes help avoid the need for general anesthetic. It remains to be seen whether suction techniques can improve outcomes in refractory patients. The new generations of pulsed light sources such as AcuTip 500 (Cutera) and Lux G (StarLux System Palomar) have much improved vascular applications in pigmented lesions and in rejuvenation.

## For What Types of Scarring Does Laser Therapy Work?

Types of scarring may be varied, for example, erythematous, hyperpigmented, hypopigmented, hypertrophic, and atrophic. Treatment of hypertrophic and keloid scars remains a difficult challenge for the dermatologist. We should always ensure that the patients' expectations correspond to what can actually be achieved, as the effectiveness of lasers in this field is still a long way from that obtained in depilation or elimination of vascular and pigmented lesions or tattoos. In general, several therapies should be combined (dressing, corticosteroid instillation, bleomycin, intralesional 5-fluorouracil, imiquimod, retinoic acid, interferon, cryotherapy, surgery, etc) with the use of different light sources. Pulsed dye laser light alone will only be partially useful in recent or erythematous hypertrophic scars almost flush with the surrounding skin and even then not in all patients.<sup>34-36</sup> Sequential techniques have started to be used (pulsed dye laser-Nd:YAG, Cynergy Multiplex), but conclusive data on their efficacy have yet to be obtained. It should be remembered that these lesions improve spontaneously over time and that few rigorous controlled studies have been done. Some patients with hyperpigmented scars may benefit from treatment with Q-switched lasers,<sup>37</sup> whereas hypopigmented scars might improve with use of fractional lasers or UV light sources such as a 308-nm excimer laser.

Ablative lasers (CO<sub>2</sub> and Er:YAG),<sup>38-40</sup> fractional lasers,<sup>3,41,42</sup> and PSR systems are good options in the case of atrophic scars caused by acne but not for the treatment of keloid scars. The outcomes with nonablative lasers have been poor. With ablative lasers (CO<sub>2</sub>), there is a risk of relapse.

## What is New in Photodynamic Therapy?

The most appropriate choice of wavelength for photodynamic therapy has yet to be determined. LED systems, which do not emit heat, are spreading quickly in this application. Such systems might avoid the thermal effect of photosensitizers and also allow progressive photoactivation. With dual LEDs (2 wavelengths of light—

red light at 630 nm and blue light at 405 nm), superficial and deep structures can be treated (for example, sebaceous glands in acne).

In addition, cheaper new photosensitizers (besides Metvix and Levulan) with a better performance are likely to be become available.

Besides the indication of nonmelanoma skin cancer,<sup>43,44</sup> additional indications for topical photodynamic therapy are being approved and the technique can now be used for conditions such as erythroplasia, lichen sclerosis, warts, alopecia areata, extramammary Paget disease, epidermodysplasia verruciformis, lichen planus, photorejuvenation, acne, and depilation.<sup>45,46</sup>

## New Suction Methods

Recently, several systems have appeared on the market that use laser light, pulsed light, or radiofrequency radiation in combination with suction of the skin.<sup>47</sup> The suction process helps bring the target area closer to the energy source, reduce the melanin and hemoglobin concentration in the target area, and take advantage of the most effective part of the light spectrum. The main objective of these devices is to lower pain associated with therapy, reduce side effects through avoiding competition with other chromophores (hemoglobin and melanin), and increase the effectiveness of treatment.

There are 2 types of device: those that suction and raise the skin to produce a pneumatic flattening of it, thereby decreasing the blood volume in the target region (pneumatic skin flattening<sup>48</sup> or PSF [Inolase]), and those, known as photopneumatic therapy, that only suction the skin without compressing it (PPX [Aesthera, Lumenis–Alumna]). These systems have been used mainly in laser depilation and also in the treatment of acne, in which mechanical extraction of sebaceous material from the pores would occur at the same time.

Some systems have yet to be approved by the FDA as clinical study data are not available to support their effectiveness. In actual fact, at present, their effectiveness and the most appropriate parameters have yet to be determined, and so this approach should not be considered more than an interesting idea worthy of further study.

## Conclusions: Will Home Devices Be Used in the Future?

We have seen how, in recent times, technology is outpacing the basic science, and so there are many systems on the market whose mechanism of action has only been hypothesized. Studies that support the effectiveness of these devices and define how best to use them are often lacking.

Another recent phenomenon has been the proliferation of home devices for treatment of different skin problems. The number of such devices will increase sharply in the coming years. The fields in which these types of system are being developed are mainly laser depilation with Epila Laser SI808 (Beauty Korea World Co), with a diode laser at 808 nm, Rio Laser Hair Remover (Dezak, UK), SpaTouch (Radiancy), and ABC Hair removal system (Palomar), which emits light between 400 and 1200 nm; acne with Zeno (Tyrell, Inc), Clear Touch Lite (Radiancy), ThermaClear Device (Dermacare, Inc), and EsteLux (Palomar), which emits pulsed light between 500 and 1200 nm; skin rejuvenation with NuLase, Clear Touch Lite, Facial Toning Device (Radiancy), and Syneron (with radiofrequency radiation and pulsed light); capillary growth with a light brush for androgenetic alopecia (HairMax LaserComb [Lexington International, LLC] with 9 LEDs); and cellulitis. The technology was first used in dermatology clinics and spread to plastic surgery and general medicine clinics, and then beauty centers and spars. It will finally reach the consumer directly with home devices in view of the huge market and enormous profits to be made. The large laser companies are even beginning to form alliances with cosmetic companies to develop these devices (for example, Palomar and Gillette/P&G).

The problem with all these devices is that the effects of laser and pulsed light depend essentially on the energy delivered reaching an effective thermal threshold. However, these devices have and will continue to have low powers, some will be of limited effectiveness, and they can only be used through direct contact to avoid eye damage. In the case of depilation, some of these devices may attenuate hair growth even though definitive hair removal proves impossible. It should however be remembered that, at times, unwanted hair growth may be induced, particularly in facial areas and on the back. A visit to the FDA website is an interesting exercise to see what criteria are used for approval of these types of system.

In short, this is a new and rapidly developing field in which dermatologists should strive to keep their knowledge up to date.<sup>49</sup>

## Conflicts of Interest

The authors declare no conflicts of interest.

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