REVIEW

Future Prospects in Dermatologic Applications of Lasers, Nanotechnology, and Other New Technologies☆

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Abstract   We review novel technologies with diagnostic and therapeutic applications in dermatology. Among the diagnostic techniques that promise to become part of dermatologic practice in the future are optical coherence tomography, multiphoton laser scanning microscopy, Raman spectroscopy, thermography, and 7-T magnetic resonance imaging. Advances in therapy include novel light-based treatments, such as those applying lasers to new targets and in new wavelengths. Devices for home therapy are also appearing. We comment on the therapeutic uses of plasma, ultrasound, radiofrequency energy, total reflection amplification of spontaneous emission of radiation, light stimulation, and transepidermal drug delivery. Finally, we mention some basic developments in nanotechnology with prospects for future application in dermatology.
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Perspectivas de futuro en láseres, nuevas tecnologías y nanotecnología en dermatología

Resumen   Presentamos una revisión actualizada en materia de avances en la aplicación de la tecnología al proceso diagnóstico y terapéutico en dermatología. Respecto a las técnicas de diagnóstico, realizamos una breve reseña sobre la tomografía de coherencia óptica, la microscopia láser multifotónica, la espectroscopia, la termografía y la resonancia magnética nuclear de 7 tesla, siendo que estas últimas también prometen incorporarse al arsenal diagnóstico en el futuro. En cuanto a los avances en terapéutica, la aplicación de tecnologías basadas en la luz,

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como el láser, ven ampliar sus aplicaciones con nuevas dianas y longitudes de onda, además de desarrollarse dispositivos de uso casero. Comentamos también el uso de plasma, ultrasonidos, radiofrecuencia, *traser*, fotoestimulación y administración transepidérmica de fármacos con fines terapéuticos. Finalmente, mencionamos los aspectos básicos de la nanotecnología y su proyección futura en el campo de la dermatología.

Introduction

The diagnostic process was traditionally based on information acquired through a meticulous medical history and physical examination. Doctors would use their senses to examine patients and obtain objective information about the state of their health. The stethoscope—the first instrument designed to improve the physician's diagnostic abilities—was invented in 1816 by Dr René Laënnec.[1] With the development of anatomic pathology in the 19th century, biopsy of diseased organs became a widespread practice. In 1895, the German physicist Wilhelm Röntgen discovered x-rays and their potential in medicine after accidentally taking a radiograph of his wife's hand. By the end of the 19th century, with Marie and Pierre Curie's discovery of radium in 1898, ionizing radiation started to be used in the treatment of various diseases.[2] Since then, the application of the latest discoveries in physics, chemistry, and molecular biology has shaped the technological development of Western medicine. In dermatology, the introduction of histopathology improved the diagnostic process considerably. Although the skin is an organ that is easily accessible for visual inspection and for the collection of biopsy specimens, in recent years there has been a growing demand for new real-time in vivo diagnostic techniques that can be coupled with minimally invasive therapeutic processes and which have acceptable toxicity. The role of dermoscopy as such a technique is now well-established, and confocal microscopy is making its way into routine practice. In the future, the diagnosis and treatment of dermatology patients will require a multidisciplinary approach and the application of advances in physics, chemistry, and molecular biology, which will complement and even surpass techniques that are currently very useful, such as pulsed light and photodynamic therapy (PDT). In this review, we discuss diagnostic and therapeutic techniques that are not yet routinely applied in health care practice, as well as devices for home-based cosmetic treatments, a trend that we believe is worth highlighting (Table 1).

Diagnostic Techniques

Optical Coherence Tomography

Optical coherence tomography (OCT) is an imaging technique that was first used to examine the retina. OCT measures the intensity of the light reflected by tissue by means of a process called low-coherence interferometry. This technique uses infrared light (1300 nm).

Table 1 Technologies in Development for Diagnosis and Treatment in Dermatology.

Diagnostic techniques
Optical coherence tomography
Multiphoton laser scanning microscopy
Raman spectroscopy
Thermography
7-T magnetic resonance imaging
Therapeutic techniques
New targets in laser therapy
Sebaceous glands
Lipids
Sweat glands
Exogenous pigments and tattoos
Bacteria and fungi
Immunotherapy
Nonmelanoma skin cancer
New wavelengths in laser therapy
1565 nm
1940 nm thulium laser
Other energy-administration techniques
Plasma
Ultrasound
Fractional radiofrequency
TRASER
Light stimulation

Abbreviation: TRASER, total reflection amplification of spontaneous emission of radiation.

Unlike reflectance-mode confocal laser scanning microscopy (RCLSM), OCT creates virtual images of vertical cross-sections in the plane defined by the incident beam, and it also has higher imaging depth (up to 2 mm). However, OCT has lower lateral resolution (10-15 μm) than RCLSM, which prevents the technique from distinguishing cellular structures and cytologic details.[3-8]

Multiphoton Laser Scanning Microscopy

Multiphoton laser scanning microscopy (MPLSM) is based on the autofluorescent properties of the skin. MPLSM excites the endogenous fluorophores in the dermis and epidermis (melanin, keratin, and nicotinamide adenine dinucleotide phosphate), which are normally excited by wavelengths in the UV spectral range. However, this technique uses a femtosecond pulsed laser (1 fs = 1×10^{-15} s) with near-infrared (IR) light, which is less prone to scattering than visible light. Because the laser emits such a large number of photons in

such a short amount of time, 2 photons of infrared light occasionally strike the same fluorophore of the skin practically simultaneously. Behaving as though they had been struck by a single photon of UV light, these fluorophores become excited and emit visible fluorescence, which is detected by the optical system of the microscope.

Like RCLSM, MPLSM creates high-resolution images at the cellular and intracellular level in planes horizontal to the skin surface. In dermatology, most studies involving this technique have been performed ex vivo, but systems for in vivo skin studies are now available on the market.[9–11]

Raman Spectroscopy

Raman spectroscopy (RS) is a method for identifying the chemical composition of a sample using a laser. RS makes it possible to classify skin lesions by molecular composition. This technique has been shown to differentiate malignant skin lesions with a sensitivity of > 90%, although its specificity is lower.[12–14] RS provides information about the biochemical composition of the analyzed tissue but offers little information about its structure and anatomic site. Nevertheless, by combining RS with OCT—which provides complementary spatial information—it is possible to conduct a combined biochemical and morphological analysis. Given that neoplastic cells have a spectroscopic signature different from that of healthy tissue, RS could be useful in defining surgical margins in Mohs surgery.[15,16]

Thermography

Thermography provides infrared images of the human body that have been used in medicine for diagnostic purposes. This technique can identify areas of the body that have irregular blood flow (either increased or decreased) because these irregularities translate into changes in temperature. Thermography has been used, for example, in herpes zoster and in the monitoring of hemangiomas.[17–19]

7-T Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a noninvasive technique for obtaining high-resolution anatomic images. The image resolution of MRI makes it possible to differentiate the stratum corneum, the epidermis, and the dermis.[20] The use of MRI in dermatology remains experimental, although its potential for use has been noted in many publications since the 1990s. However, conventional MRI machines cannot produce magnetic fields greater than 3 T; because the cells in the stratum corneum and the dermis have low signal intensity, this limitation translates into poor image resolution.[21] Some current research has focused on the use of various contrast methods, such as magnetization transfer contrast (MTC). This method is especially useful for evaluating how the various layers of skin tissue interact with the interstitial fluids.[22]

Recently, MRI scanners with higher-powered magnets that create ultra-high-field (UHF) magnetic fields (greater than 3 T) have been developed. The resolution of these scanners is similar to or greater than that of histologic images.

The current limitations of this technique are mainly related to cost and infrastructure, because machines capable of generating such strong magnetic fields must be housed in very large and extremely expensive facilities.

Therapeutic Techniques

Laser Devices and New Targets

For years, dermatologic laser therapy has targeted 3 classic chromophores—hemoglobin, melanin, and water—that have allowed the removal of hair follicles as well as the successful treatment of acne scars, some signs of skin aging, and various vascular and pigmented lesions. However, it could be possible to add new therapeutic targets and to act on subcellular structures and cytoplasmic organelles in addition to macroscopic structures such as hair follicles and blood vessels.[23]

Sebaceous Glands

Recent studies have attempted to identify more precisely the most effective wavelengths for the treatment of sebaceous glands, which are directly involved in the pathophysiology of acne. With a free electron laser, which can be tuned to any wavelength on the electromagnetic spectrum, we find absorption peaks in the sebaceous glands at 1210, 1728, 1760, 2306, and 2346 nm. With pulses of 100-125 ms in the range of 1700 nm, a free electron laser can induce selective thermal damage to sebaceous glands.

PDT has also been shown to cause some degree of inhibition of the sebaceous glands, which has a beneficial effect on inflammatory acne lesions. To avoid excessive damage to the keratinocytes, exposure to low-power red light (635 nm) or blue light (420 nm) has been used successfully during incubation with aminolevulinic acid (ALA), thereby preventing the massive accumulation of protoporphyrin IX. Protoporphyrin IX causes cytotoxic damage to keratinocytes on exposure to high-energy red light. The use of PDT with low-power red or blue light has been called inhibition photodynamic therapy (I-PDT).[24]

Lipids

Among the absorption peaks for the various cutaneous lipids, the 1210 nm wavelength stands out for its ability to cause selective thermal damage to subcutaneous tissue when used in combination with epidermal cooling systems. At this wavelength, a new therapeutic concept called selective photothermostimulation (SPS) occurs. SPS could have the capacity to stimulate the adipocytes and mesenchymal cells in the subcutaneous tissue, making it useful for treating cellulite and even large lipomas. Satisfactory results have also been obtained with fibers placed laterally underneath the skin surface that deliver 1440 nm laser pulses to the dermal-hypodermal interface.[25]

Sweat Glands

Various wavelengths (Nd:YAG, 924/927 nm diode, 800 nm diode) have been used to destroy eccrine sweat glands in axillary hyperhidrosis. Radiofrequency and ultrasound systems have also been used to induce thermal damage in these glands. In 2011, the US Food and Drug

Administration approved a microwave-based device for the treatment of axillary hyperhidrosis.[26–31]

Exogenous Pigments and Tattoos

Ultra-short-pulse (picosecond) lasers appear to be superior to nanosecond-pulse lasers in pigment removal, especially for colors—such as blue and green—that are resistant to removal with current systems.[32–36] These devices operate on familiar wavelengths. Alexandrite and Nd:YAG lasers are used to remove black, blue, and green pigments, while 532 nm Nd:YAG lasers are used to remove red, yellow, and orange pigments.

Bacteria, Fungi, and Other Cutaneous Pathogens

Research has shown that exposing *Trichophyton rubrum* to 42.5 °C for 2 minutes can inactivate the fungus. However, the conclusions of this in vitro study cannot be extrapolated to the conditions of clinical practice. Q-switched pulsed Nd:YAG lasers and 1320, 870, and 930 nm lasers have been used in the treatment of onychomycosis.[37–41] Studies of PDT have demonstrated that this technique is useful even in onychomycosis caused by nondermatophyte fungi, which tend to respond very poorly to conventional pharmacotherapies.[42,43]

Lasers in Immunotherapy

The efficacy demonstrated in some studies by vascular laser treatment in diseases such as lupus erythematosus, psoriasis, and inflammatory rosacea may be due not only to the effect of the lasers on the vessels but also to the suspected involvement of certain immune modulation mechanisms.[44,45]

Nonmelanoma Skin Cancer

Recent studies have demonstrated the efficacy of vascular laser treatment against basal cell carcinoma.[46–50] However, it has been suggested that this technique could increase the risk of multifocal growth in recurrent tumors, as occurs in recurrences following cryotherapy.

Laser Devices and New Wavelengths

Among the most recent advances is the discovery of the potential application of ''old'' wavelengths for the treatment of new targets. For example, long-pulse alexandrite lasers, used primarily in hair removal, can be used in the treatment of vascular lesions.[51] The combination of lasers and antiangiogenic agents has also been investigated as a treatment that holds promise in the short term. One example is the use of pulsed dye lasers in combination with topical rapamycin in capillary malformations.

New Wavelengths

- 1565 nm. A nonablative fractional laser that emits 1565 nm infrared light with greater penetration than 1540 or 1550 nm light has been approved, but it is still too soon to know whether it is more effective than previous lasers.
- Thulium 1940 nm laser. Nonablative fractional 1940 nm lasers operate at a new wavelength with a water absorption coefficient that is higher than that found at other nonablative wavelengths (1410-1550 nm) but lower than that of ablative lasers.

Other Energy-Administration Techniques

Plasma

Plasma—defined as the fourth state of matter—consists of highly ionized gas that transforms into a radiating material. In fact, plasma accounts for 99% of the observable matter in the universe and is found, for example, in stars, the aurora borealis, and lightning.

Plasma can be classified as either cold or hot. Cold plasmas can be used in rejuvenation treatments to induce controlled thermal damage in the skin, which results in new collagen production and the restructuring of the dermal architecture. Cold plasma devices have also been used to improve wound healing, to induce hemostasis, and to treat infectious dermatoses, atopic dermatitis, and other conditions. Today, cold plasmas are mainly used routinely for skin rejuvenation in cosmetic dermatology.[52,53]

Ultrasound

In addition to its diagnostic applications, ultrasound may have new therapeutic uses. In recent years, ultrasound cavitation has been developed for ultrasonic body contouring[54] and the selective destruction of sweat glands as treatment for axillary hyperhidrosis.[55,56]

Several articles have underscored the utility of ultrasound as a means of enhancing the transcutaneous penetration—and therefore increasing the bioavailability—of various drugs by means of the sonophoresis effect.[57–65] Other therapeutic uses of this technique involve focusing the ultrasonic waves at different depths in the skin tissue. In rejuvenation therapies, for example, due to the effect of ultrasonic waves on collagen, this technique is used to heat the dermis and cause dermal tightening.

Radiofrequency Energy

Radiofrequency equipment is less expensive to manufacture—and therefore more accessible—than laser devices. One development in this area is the use of fractional radiofrequency devices that induce microlesions on the skin surface similar to those caused by fractional CO_2 lasers. The radiofrequency energy is delivered by a roller tip that is moved across the surface of the skin. Some fractional radiofrequency devices use a system of needles to deliver the energy to deeper tissue planes.[66–70]

Total Reflection Amplification of Spontaneous Emission of Radiation

Total reflection amplification of spontaneous emission of radiation (TRASER) is a concept introduced by Morgan Gustavsson. In this technique, fluorescent dyes are excited by the sudden, flash-like release of energy, generally from a light source. After absorbing light of a precise wavelength, the fluorescent dye molecules become excited and reemit a narrow band (peak) of fluorescence at a nearby wavelength (Stokes shift phenomenon). This peak of intensity varies depending on the fluorescent dye used. TRASER is neither a laser (it lacks an optical resonator and induces non-coherent, non-collimated light) nor a pulsed light (it has no filters). TRASER is simpler than those systems and therefore less expensive to manufacture. Because it uses

cheap, nontoxic, long-lasting dyes, TRASER is a very attractive technology for future development.

Through the use of different dyes, TRASER can be tuned to different wavelengths of pulsed light ranging from UV-A to near-infrared. Experiments have been carried out with various dyes, including sulforhodamine 640, which emits a peak wavelength of 658 nm and has been shown to be effective in hair removal, and pyrromethene 556, which emits fluorescence with a peak of 543 nm and is useful for vascular treatments. The utility of TRASER in these 2 applications has been investigated in clinical and histologic studies. This technique could have medical, domestic, and industrial uses. It will soon be seen whether TRASER is capable of replacing laser technology in a single device.[71]

Home Devices

Most of the techniques mentioned in the previous sections remain under development and are not yet applied in routine health care practice. In this section, however, we will briefly review the home devices for the treatment of cosmetic problems that have invaded the market in recent years. Most of these devices target 5 therapeutic areas:

1) Hair removal (Epila, Silkin, Gillette, Philips, Boots, Palomar, Tria Beauty, etc.).
2) Rejuvenation (PaloVia, Solta, Syneron, etc.).
3) Acne (Blue Light, Omnilux, etc.).
4) Hair stimulation.
5) Cellulite treatment.

Although these devices are affordable for the general public, they are much less effective than professional equipment and are therefore no substitute for it. Nevertheless, they can be useful in many cases. The safety profile of these devices is not fully established. Moreover, the safety profile is largely determined by the patient's level of instruction in the use of the device.[72–75]

Light Stimulation

Light-emitting diodes (LEDs) are used to stimulate the dermal fibroblasts, which then increase procollagen synthesis. Although this technique has been widely studied in animals, there have been very few controlled clinical trials that provide evidence of its efficacy. However, LED PDT has been proven effective in dermatology and is used in photorejuvenation and the treatment of erythema, scarring, acne, and alopecia. There have been a few recent studies on the use of LED PDT in alopecia, and various systems for LED emission through hat-, helmet-, comb-, and brush-like devices are now commercially available.[76–78]

Transepidermal Delivery

Ablative fractional CO_2 laser treatment makes it possible to open the epidermal barrier by forming dermal-epidermal channels, which can be used to deliver biomolecules (antioxidants, hyaluronic acid, and proteins), drugs (retinoids), photosensitizing agents for PDT, and stem cells for
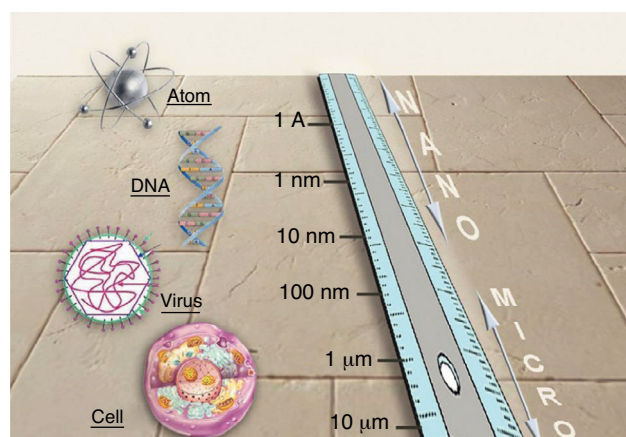
Figure 1 Size comparison of nanometric objects in the context of the biological sciences. DNA indicates deoxyribonucleic acid.

regenerative therapies. Ultrasound compression systems have been developed to accelerate and increase the penetration of drugs and biomolecules. These dermal-epidermal channels could also be used for the extraction of intradermal substances.[79–81]

Tissue Soldering

Several studies have demonstrated the possibility of soldering tissues with photomechanical soldering techniques that reach temperatures of around 60 °C and use light-activated adhesives. Tissue soldering could be improved through nanotechnology, specifically, the design of nanofibers and nanoparticles. This technique has been used in the skin, nervous tissue, and vascular tissue.[82–85]

Nanotechnology

Nanotechnology consists in manipulating matter at the atomic and molecular scales. The conceptual foundation of nanotechnology can be traced back to Richard Feynman, winner of the 1965 Nobel Prize in Physics. In 1959, in a celebrated lecture entitled ''Plenty of Room at the Bottom,'' Feynman described the possibility of material synthesis processes based on the direct manipulation of atoms. Although there are great expectations surrounding the development and the possible applications of new nanometric technologies, this technical revolution is still in its infancy. Nanotechnology is based on the advantages of manufacturing materials at the nanometric scale (1-100 nm) (Fig. 1), the scale of biomolecules. Many of the optical, mechanical, magnetic, electrical, and chemical properties of a material change when it is manipulated at the nanometric scale. This is due to the fact that nanoparticles (NPs) have an exponentially greater surface-area-to-volume ratio than larger particles and therefore interact with the surrounding environment to a greater degree. Consequently, the laws of quantum physics are better able to predict their properties than the laws of classical physics. Nanotechnology will make it possible to create new materials that open up a vast range of applications in medicine and in daily life: earlier

diagnoses and new treatments for cancer; faster microprocessors and computers; flexible mobile telephones; harder and more flexible materials; batteries; new industrial fabrics (self-cleaning, invisible to the human eye, extremely strong and elastic); and other industrial applications currently under development.

Nanotechnology and the Health Sciences: Nanomedicine

Nanomedicine is the application of nanotechnological knowledge in health care. It is already possible to design NPs capable of functioning in a coordinated manner as biosensors for diagnosing, monitoring, and treating disease in early stages when it is still curable. Nanomedical researchers predict a new age of medicine (Fig. 2) in which diseases such as cancer, diabetes, atherosclerosis, Alzheimer disease, and human immunodeficiency virus infection will be cured or will become chronic conditions. Behind these ideas is the hope of offering a personalized form of medicine in which treatment regimens can be adapted to each patient and each stage of disease evolution. From the beginning, nanomedicine has aimed to revolutionize therapeutics by using nanostructures as vehicles for transporting drugs to molecular targets, thereby increasing the efficacy of the drugs while decreasing their toxicity.[86–90]

Nanoparticles

NPs can be either organic (liposomes and dendrimers) or inorganic (quantum dots, nanospheres, carbon nanotubes, and metallic NPs). The basic structure of an inorganic NP consists of a core and a shell. Each of these components offers various possibilities for designing contrast media, drug carriers, and selective drug release systems.

Shell

The optical, magnetic, electronic, and fluorescent characteristics of a NP are determined by its shell. The shell can be coated with fluorescent materials that make it possible to detect the presence of the NP, which is useful for diagnostic and therapeutic purposes. If the shell is coated with certain monoclonal antibodies that have an affinity for 1 or more specific cell receptors, it could be possible to direct the NP precisely to an organ or tissue, or even to a type of cellular target (neoplastic cells, cells infected by viruses or intracellular bacteria, populations of specific inflammatory cells, etc.). It is also possible to coat the NP surface with molecules that increase the stability of the particle and prevent degradation and uptake by macrophages, thereby increasing the half-life and bioavailability of the drugs associated with the NP[91] (Fig. 3).

Core

The core of a NP can be used to transport drugs, modified viruses, proteins, genetic material, vaccines, or cosmetics to precise target sites (Fig. 4).

Nanometric Devices for Diagnostic Use

Quantum dots are crystals several nanometers in diameter made from semiconductor materials such as cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs). The special optical, electrical, and thermal properties of quantum dots are determined by quantum confinement—that is, the spatial confinement of the charged particles (electrons) of the nanocrystal.

The main application of quantum dots in the biomedical sciences is their use as fluorescent markers of molecules in cells and tissues. Illuminated by a laser, they produce intense fluorescence that is useful for locating tumors. Quantum dots have been injected into tumors in mice and used to identify the sentinel lymph node, achieving more precise sentinel lymph node mapping.[92–98] This application could be useful for the selective marking of tumor cells with tumor-specific antibodies—which would facilitate Mohs surgery—as well as for the early diagnosis of tumors and PDT, given that quantum dots can generate O_2 radicals without the need for photosensitizer molecules. Quantum dots are therefore capable of acting as new active agents in PDT. However, quantum dots—which, remember, are made of heavy metals—have an important limitation: their toxicity is unknown.[99]

Drug Transport and Release Systems

Another solution offered by nanomedicine is the development of systems for the transport and controlled release of drugs. The idea consists in using nanostructures to transport the drug and release it in response to a particular stimulus only after recognizing the target. Systems of this sort could reduce toxicity in healthy tissue and increase therapeutic effectiveness.

Nanoemulsions

Nanoemulsions are a very promising system for administering drugs in dermatology.[100] Applications include the administration of antioxidants, nonsteroidal anti-inflammatory drugs, photosensitizing agents for PDT, antimicrobial agents, and sunscreens in the form of nanoemulsions. Physical sunscreens containing titanium dioxide and iron oxide are already commercially available as topical sun protection. Because they are transparent, these sunscreens do not disperse incident light, leading to better patient acceptance and adherence.

Nanoparticles

NPs can transport a drug and, on recognizing the target, release it in response to a particular stimulus, thereby providing enormous selectivity and therapeutic precision. The vehicles of these drugs can be liposomes, polymeric NPs, or dendrimers (Fig. 5). An example is the encapsulation of minoxidil in liposomes to increase absorption in pilosebaceous follicles, thereby increasing the bioavailability of the drug in the root of the follicle. Solutions involving antioxidant vitamins encapsulated in liposomes—which increases the dermal bioavailability of the vitamins and prevents them from oxidizing on contact with air—are now
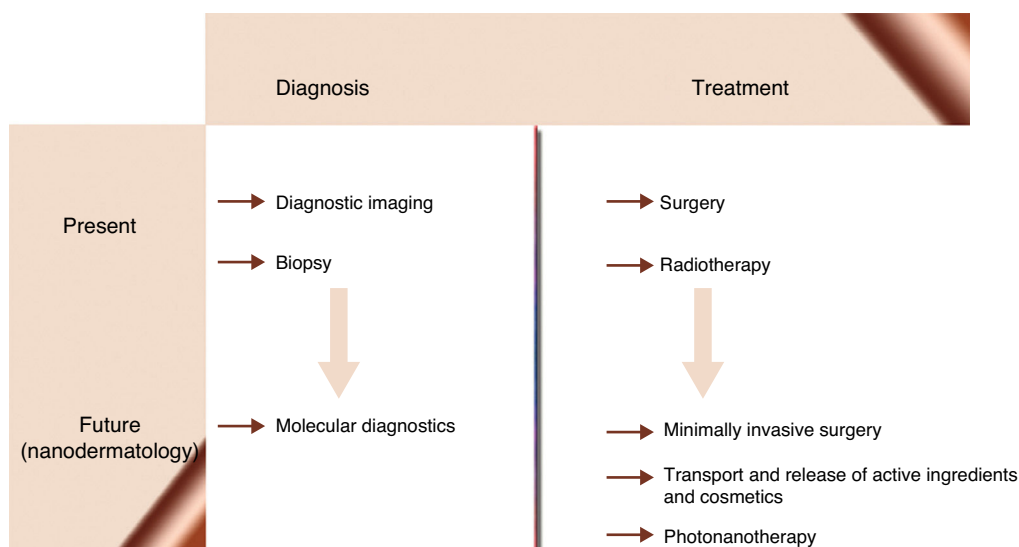
**Figure 2**   Areas of application of nanomedicine in dermatology.

commercially available. Antiandrogenic substances, finasteride, and retinoids can also be encapsulated, making it possible to reduce the side effects associated with systemic administration of these drugs.[101-107]

Photothermal Ablation With Metallic Nanoparticles

Thanks to their photothermal properties, metallic nanostructures are candidates for use in ablative laser treatment. A laser of appropriate wavelength could be used to excite the plasmons on the metallic surface of a nanostructure consisting of a metallic shell over a glass surface, producing heat. This technology could revolutionize light-source-based therapies, mainly those which involve red or near-infrared light, which is capable of penetrating tissues to a depth of several centimeters.

By using appropriate surface molecules (antibodies), it could be possible to select specific molecular targets that would allow the selective thermal destruction of malignant cells and/or the blood vessels supporting the skin tumor. In therapeutics, it could be possible to use lasers or light sources on any area of the skin surface and target cell populations that do not contain any of the classic chromophores. In mice, gold NPs conjugated with anti-EGFR antibodies have been used in the treatment of squamous cell carcinoma to destroy malignant cells with half the energy required for benign cells. Selective photothermal ablation of melanomas has also been achieved in mice using gold NPs attached to
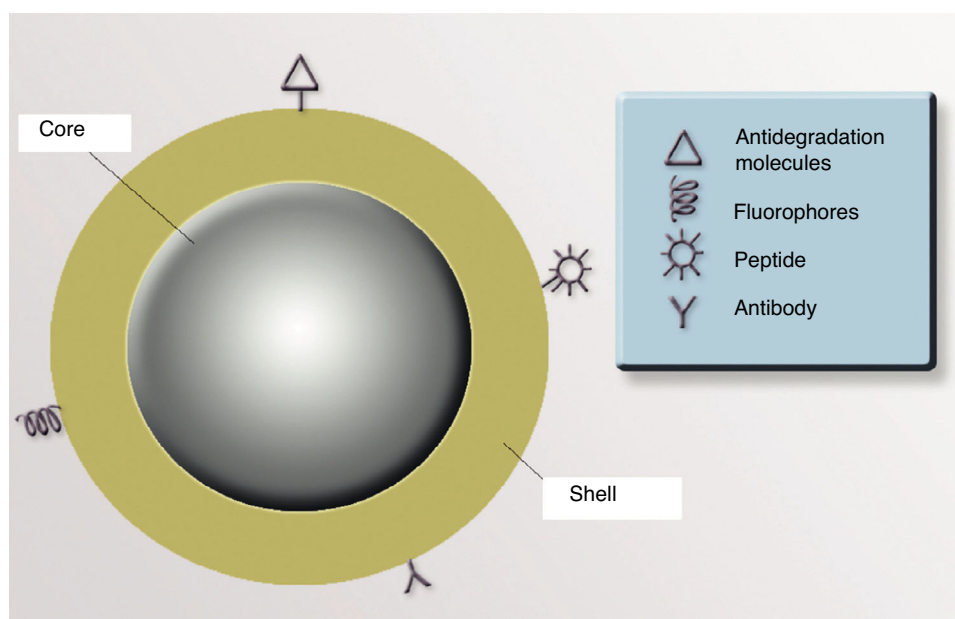
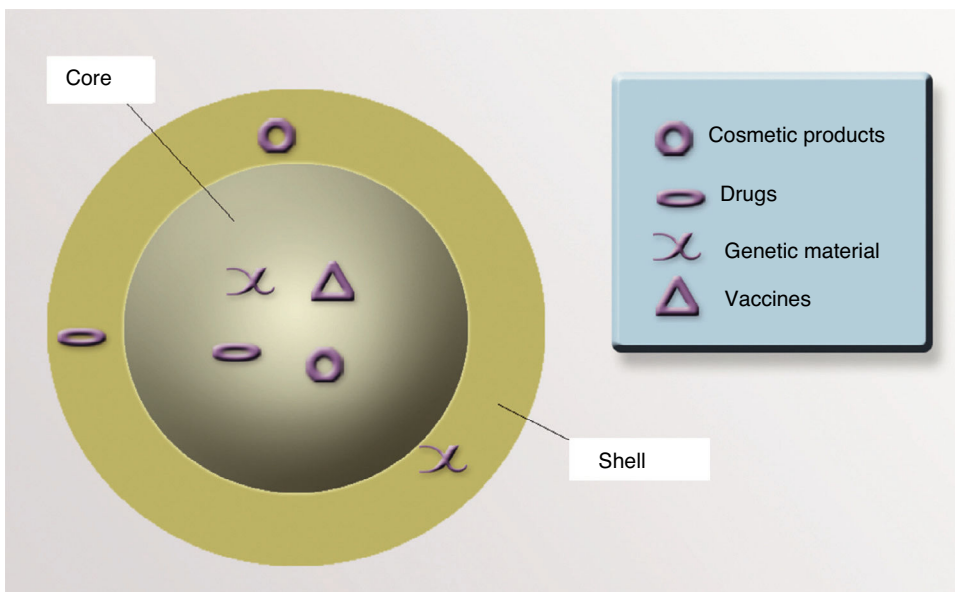**Figure 3**   Possible modifications to the surface of nanoparticles.

Figure 4 Diagram of a transport nanosystem.

a peptide that is an agonist for the melanocortin 1 receptor overexpressed in melanoma.[108–113]

Carbon nanotubes—molecules in the fullerene family consisting of sheets of graphite arranged in a tubular structure—also absorb light in the near-infrared spectral range and are capable of generating heat. As in the case of NPs, it could be possible to take advantage of the fact that, due to their greater permeability, carbon nanotubes accumulate in the tumor stroma through the capillary vessels that form in order to nourish the tumor. Following the

application of a laser or other light source, the tumor could be destroyed by photoablation.[114–116]

Cutaneous vascular lesions such as telangiectasias and capillary malformations are another interesting area for exploration. If metallic nanostructures are designed that are capable of accumulating in the periphery or endothelial coating of these lesions, photothermal ablation could be used thanks to the surface plasmonic properties of the nanostructures following irradiation with a light energy source.
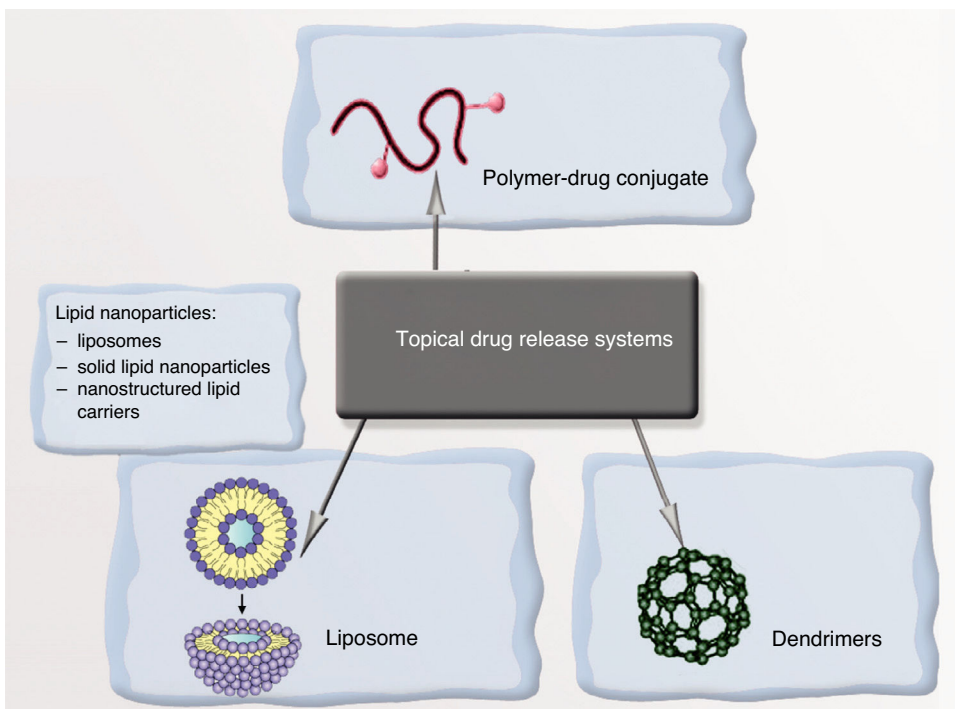

Figure 5 Nanosystems for the transport and release of active ingredients in dermatology.

Nanobiosensors

NPs can act as biosensors that allow the adjustment of dosage and treatment regimen, thereby reducing systemic toxicity without relinquishing the maximum therapeutic effect.

As the reader may have deduced, research on the biomedical applications of nanotechnology is filled with possibilities for improving techniques for diagnosis, monitoring and treatment in dermatology. This field is poised to revolutionize our specialty in the coming decades.

New Toxicities

The development of new technologies is inseparable from the appearance of new toxicities that affect both patients and health care workers. Gas chromatography—mass spectrometry studies of smoke plumes from laser hair removal have demonstrated the presence of more than 14 potentially toxic substances including 2-methylpyridine, diethyl phthalate, and trimethyl disulfide.[117]

As new technologies with therapeutic and, especially, cosmetic applications have spread and demand for them has grown, these techniques have been widely and almost indiscriminately applied to all sorts of skin lesions before their real possibilities and side effects are fully understood.

The high reactivity of NPs could also alter other biological mechanisms besides those identified during the design of the particles; this phenomenon has become known as nanotoxicity. NPs could also become new irritants and allergens. Quantum dots contain heavy metals and could therefore have cytotoxic effects, especially if they are not designed with a hydrophilic coating. Moreover, they remain inside the cells for weeks or months, and we know almost nothing about their excretion pathways or how they are metabolized. In fact, some nonbiodegradable particles could remain in the body indefinitely and cause permanent activation of the immune system as the body attempts to eliminate them, possibly triggering autoimmune diseases. The following factors are essential to determining the safety profile of NPs[118]:

1) How the NP enters the body.
2) Size (the smaller the NP, the more toxic it is).
3) Biocompatibility.
4) Biodegradability.

Therefore, in our opinion and that of experts, more exhaustive studies are needed to ensure the safety of these techniques.

Scientific and technical advances are gradually making their way into the routine practice of dermatologists. Concepts and terms that are strange to us today may become the standard diagnostic and therapeutic methods of tomorrow. We have reviewed some recent advances that are currently experimental or have limited applications, but which in the future could complement or even replace present techniques.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

1. Roguin A. Rene Theophile Hyacinthe Laënnec (1781-1826): The man behind the stethoscope. Clin Med Res. 2006;4:230–5.
2. Scatliff JH, Morris PJ. From Roentgen to magnetic resonance imaging: The history of medical imaging. N C Med J. 2014;75:111–3.
3. Gambichler T, Plura I, Kampilafkos P, Valavanis K, Sand M, Bechara FG, et al. Histopathological correlates of basal cell carcinoma in slice and enface imaging modes of high-definition optical coherence tomography. Br J Dermatol. 2014;170:1358–61.
4. Boone MA, Norrenberg S, Jemec GB, del Marmol V. High-definition optical coherence tomography imaging of melanocytic lesions: A pilot study. Arch Dermatol Res. 2014;306:11–26.
5. Banzhaf CA, Themstrup L, Ring HC, Welzel J, Mogensen M, Jemec GB. In vivo Imaging of *Sarcoptes scabiei* infestation using optical coherence tomography. Case Rep Dermatol. 2013;5:156–62.
6. Alawi SA, Kuck M, Wahrlich C, Batz S, McKenzie G, Fluhr JW, et al. Optical coherence tomography for presurgical margin assessment of non-melanoma skin cancer —a practical approach. Exp Dermatol. 2013;22:547–51.
7. Sattler E, Kästle R, Welzel J. Optical coherence tomography in dermatology. J Biomed Opt. 2013;18:061224.
8. Gambichler T, Jaedicke V, Terras S. Optical coherence tomography in dermatology: Technical and clinical aspects. Arch Dermatol Res. 2011;303:457–73.
9. Paoli J, Smedh M, Ericson MB. Multiphoton laser scanning microscopy —a novel diagnostic method for superficial skin cancers. Semin Cutan Med Surg. 2009:190–5.
10. Prow TW. Multiphoton microscopy applications in nanodermatology. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2012;4:680–90.
11. Paoli J, Smedh M, Wennberg AM, Ericson MB. Multiphoton laser scanning microscopy on non-melanoma skin cancer: morphologic features for future noninvasive diagnostics. J Invest Dermatol. 2008;128:1248–55.
12. Smith L, Macneil S. State of the art in non-invasive imaging of cutaneous melanoma. Skin Res Technol. 2011;17:257–69.
13. Lademann J. Optical methods of imaging in the skin. J Biomed Opt. 2013;18:61201.
14. Calin MA, Parasca SV, Savastru R, Calin MR, Dontu S. Optical techniques for the noninvasive diagnosis of skin cancer. J Cancer Res Clin Oncol. 2013;139:1083–104.
15. Khan KM, Krishna H, Majumder SK, Rao KD, Gupta PK. Depth-sensitive Raman spectroscopy combined with optical coherence tomography for layered tissue analysis. J Biophotonics. 2014;7:77–85.
16. Freudiger CW, Pfannl R, Orringer DA, Saar BG, Ji M, Zeng Q, et al. Multicolored stain-free histopathology with coherent Raman imaging. Lab Invest. 2012;92:1492–502.
17. Park J, Jang WS, Park KY, Li K, Seo SJ, Hong CK, et al. Thermography as a predictor of postherpetic neuralgia in acute herpes zoster patients: A preliminary study. Skin Res Technol. 2012;18:88–93.
18. Mikulska D, Maleszka R, Parafiniuk M. The usefulness of thermography as a diagnostic method in dermatology on the basis of clinical trials in 2001-2005. Ann Acad Med Stetin. 2006;52:91–7.

19. Garcia-Romero MT, Chakkittakandiyil A, Pope E. The role of infrared thermography in evaluation of proliferative infantile hemangiomas. Results of a pilot study. Int J Dermatol. 2014;53:216–7.

20. Aubry S, Leclerc O, Tremblay L, Rizcallah E, Croteau F, Orfali C, et al. 7-Tesla MR imaging of non-melanoma skin cancer samples: Correlation with histopathology. Skin Res Technol. 2012;18:413–20.

21. Sharma R. Microimaging of hairless rat skin by magnetic resonance at 900 MHz. Magn Reson Imaging. 2009;27:240–55.

22. Mirrashed F, Sharp JC. In vivo morphological characterization of skin by MRI micro-imaging methods. Skin Res Technol. 2004;10:149–60.

23. Fabi SG, Metelitsa AI. Future directions in cutaneous laser surgery. Dermatol Clin. 2014;32:61–9.

24. Sakamoto FH, Doukas AG, Farinelli WA, Tannous Z, Anderson R. Introduction of I-PDT: A new phenomenon able to reduce side-effects of photodynamic therapy (PDT) with Ala and Ala Derivatives. Lasers Surg Med. 2010;42 Suppl 22:30.

25. DiBernardo BE:. Treatment of cellulite using a 1440-nm pulsed laser with one-year follow-up. Aesthet Surg J. 2011;31:328–41.

26. Kotlus BS. Treatment of refractory axillary hyperhidrosis with a 1320-nm Nd:YAG laser. J Cosmet Laser Ther. 2011;13:193–5.

27. Goldman A, Wollina U. Subdermal Nd-YAG laser for axillary hyperhidrosis. Dermatol Surg. 2008;34:756–62.

28. Bechara FG, Georgas D, Sand M, Stücker M, Othlinghaus N, Altmeyer P, et al. Effects of a long-pulsed 800-nm diode laser on axillary hyperhidrosis: a randomized controlled half-side comparison study. Dermatol Surg. 2012;38:736–40.

29. Johnson JE, O'Shaughnessy KF, Kim S. Microwave thermolysis of sweat glands. Lasers Surg Med. 2012;44:20–5.

30. Glaser DA, Coleman WPJ 3rd, Fan LK, Kaminer MS, Kilmer SL, Nossa R, et al. A randomized, blinded clinical evaluation of a novel microwave device for treating axillary hyperhidrosis: The dermatologic reduction in underarm perspiration study. Dermatol Surg. 2012;38:185–91.

31. Nestor M, Hyunhee P. Randomized, double-blind, controlled pilot study of the efficacy and safety of micro-focused ultrasound for the treatment of axillary hyperhidrosis. American Society for Laser Medicine and Surgery Conference; 2013 Abril 4-6. Boston: American Society for Laser Medicine and Surgery; 2013.

32. Ibrahimi OA, Sakamoto FH, Anderson RR. Picosecond laser pulses for tattoo removal: A good, old idea. JAMA Dermatol. 2013;149:241.

33. Sierra R, Mirkov M. Impact of pulse duration from nanoseconds to picoseconds on the thermal and mechanical effects during laser interaction with tattoo targets. American Society for Laser Medicine and Surgery Conference; April 4-6, 2013. Boston: American Society for Laser Medicine and Surgery; 2013.

34. Saedi N, Metelitsa A, Petrell K, Arndt KA, Dover JS. Treatment of tattoos with a picosecond alexandrite laser: A prospective trial. Arch Dermatol. 2012;148:1360–3.

35. Brauer JA, Reddy KK, Anolik R, Weiss ET, Karen JK, Hale EK, et al. Successful and rapid treatment of blue and green tattoo pigment with a novel picosecond laser. Arch Dermatol. 2012;148:820–3.

36. Luebberding S, Alexiades-Armenakas M. New tattoo approaches in dermatology. Dermatol Clin. 2014;32:91–6.

37. Kalokasidis K, Onder M, Trakatelli MG, Richert B, Fritz K. The effect of switched Nd:YAG 1064 nm/532 nm laser in the treatment of onychomycosis in vivo. Dermatol Res Pract. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3875102. Accessed March 28, 2014.

38. Ortiz AE, Avram MM, Wanner MA. A review of lasers and light for the treatment of onychomycosis. Lasers Surg Med. 2014;46:117–24.

39. Noguchi H, Miyata K, Sugita T, Hiruma M, Hiruma M. Treatment of onychomycosis using a 1064 nm Nd:YAG laser. Med Mycol J. 2013;54:333–9.

40. Gupta AK, Simpson FC. Laser therapy for onychomycosis. J Cutan Med Surg. 2013;17:301–7.

41. Nenoff P, Grunewald S, Paasch U. Laser therapy of onychomycosis. J Dtsch Dermatol Ges. 2014;12:33–8.

42. Calin MA, Parasca SV. Light sources for photodynamic inactivation of bacteria. Lasers Med Sci. 2009;24:453–6042.

43. Souza LW, Souza SV, Botelho AC. Distal and lateral toenail onychomycosis caused by Trichophyton rubrum: treatment with photodynamic therapy based on methylene blue dye. An Bras Dermatol. 2014;89:184–6.

44. Chen X, Wu MX. How effective could laser-based approaches be in assisting dendritic cell immunotherapy? Immunotherapy. 2012;4:983–5.

45. Truchuelo MT, Boixeda P, Alcántara J, Moreno C, de las Heras E, Olasolo PJ. Pulsed dye laser as an excellent choice of treatment for lupus tumidus: A prospective study. J Eur Acad Dermatol Venereol. 2012;26:1272–9.

46. Jalian HR, Avram MM, Stankiewicz KJ, Shofner JD, Tannous Z. Combined 585 nm pulsed-dye and 1,064 nm Nd:YAG lasers for the treatment of basal cell carcinoma. Lasers Surg Med. 2014;46:1–7.

47. Minars N, Blyumin-Karasik M. Treatment of basal cell carcinomas with pulsed dye laser: A case series. J Skin Cancer. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3532878/. Accessed March 27, 2014.

48. Tran HT, Lee RA, Oganesyan G, Jiang SB. Single treatment of non-melanoma skin cancers using a pulsed-dye laser with stacked pulses. Lasers Surg Med. 2012;44:459–67.

49. Ballard CJ, Rivas MP, McLeod MP, Choudhary S, Elgart GW, Nouri K. The pulsed dye laser for the treatment of basal cell carcinoma. Lasers Med Sci. 2011;26:641–4.

50. Konnikov N, Avram M, Jarell A, Tannous Z. Pulsed dye laser as a novel nonsurgical treatment for basal cell carcinomas: response and follow up 12-21 months after treatment. Lasers Surg Med. 2011;43:72–8.

51. Tierney EP, Hanke CW. Alexandrite laser for the treatment of port wine stains refractory to pulsed dye laser. Dermatol Surg. 2011;37:1268–78.

52. Heinlin J, Morfill G, Landthaler M, Stolz W, Isbary G, Zimmermann JL, et al. Plasma medicine: Possible applications in dermatology. J Dtsch Dermatol Ges. 2010;8:968–76.

53. Heinlin J, Isbary G, Stolz W, Morfill G, Landthaler M, Shimizu T, et al. Plasma applications in medicine with a special focus on dermatology. J Eur Acad Dermatol Venereol. 2011;25:1–11.

54. Kleinerman R, Whang TB, Bard RL, Marmur ES. Ultrasound in dermatology: Principles and applications. J Am Acad Dermatol. 2012;67:478–87.

55. Commons GW, Lim AF. Treatment of axillary hyperhidrosis/bromidrosis using VASER ultrasound. Aesthetic Plast Surg. 2009;33:312–23.

56. Garcia J. Treatment of axillary hyperhidrosis/bromidrosis using VASER ultrasound. Aesthetic Plast Surg. 2010;34:120.

57. Escobar-Chávez JJ, Bonilla-Martínez D, Villegas-González MA, Rodríguez-Cruz IM, Domínguez-Delgado CL. The use of sonophoresis in the administration of drugs throughout the skin. J Pharm Pharm Sci. 2009;12:88–115.

58. Issa MC, de Britto Pereira Kassuga LE, Chevrand NS, do Nascimento Barbosa L, Luiz RR, Pantaleão L, et al. Transepidermal retinoic acid delivery using ablative fractional radiofrequency associated with acoustic pressure ultrasound for stretch marks treatment. Lasers Surg Med. 2013;45:81–8.

59. Trelles MA, Martínez-Carpio PA. Attenuation of acne scars using high power fractional ablative unipolar radiofrequency and

ultrasound for transepidermal delivery of bioactive compounds through microchannels. Lasers Surg Med. 2014;46:152–9.

60. Trelles MA, Leclère FM, Martínez-Carpio PA. Fractional carbon dioxide laser and acoustic-pressure ultrasound for transepidermal delivery of cosmeceuticals: A novel method of facial rejuvenation. Aesthetic Plast Surg. 2013;37:965–72.

61. Suh DH, Oh YJ, Lee SJ, Rho JH, Song KY, Kim NI, et al. A intense-focused ultrasound tightening for the treatment of infraorbital laxity. J Cosmet Laser Ther. 2012;14:290–5.

62. Chan NP, Shek SY, Yu CS, Ho SG, Yeung CK, Chan HH. Safety study of transcutaneous focused ultrasound for non-invasive skin tightening in Asians. Lasers Surg Med. 2011;43:366–75.

63. Escobar-Chávez JJ, Bonilla-Martínez D, Villegas-González MA, Revilla-Vázquez AL. Electroporation as an efficient physical enhancer for skin drug delivery. J Clin Pharmacol. 2009; 49:1262–83.

64. Azagury A, Khoury L, Enden G, Kost J. Ultrasound mediated transdermal drug delivery. Adv Drug Deliv Rev. 2014;72: 127–43.

65. Park D, Park H, Seo J, Lee S. Sonophoresis in transdermal drug deliverys. Ultrasonics. 2014;54:56–65.

66. Harth Y, Frank I. In vivo histological evaluation of non-insulated microneedle radiofrequency applicator with novel fractionated pulse mode. J Drugs Dermatol. 2013;12:1430–3.

67. Shin MK, Park JM, Lim HK, Choi JH, Baek JH, Kim HJ, et al. Characterization of microthermal zones induced by fractional radiofrequency using reflectance confocal microscopy: A preliminary study. Lasers Surg Med. 2013;45:503–8.

68. Cho SI, Chung BY, Choi MG, Baek JH, Cho HJ, Park CW, et al. Evaluation of the clinical efficacy of fractional radiofrequency microneedle treatment in acne scars and large facial pores. Dermatol Surg. 2012;38:1017–24.

69. Lolis MS, Goldberg DJ. Radiofrequency in cosmetic dermatology: A review. Dermatol Surg. 2012;38:1765–76.

70. Seo KY, Kim DH, Lee SE, Yoon MS, Lee HJ. Skin rejuvenation by microneedle fractional radiofrequency and a human stem cell conditioned medium in Asian skin: A randomized controlled investigator blinded split-face study. J Cosmet Laser Ther. 2013;15:25–33.

71. Zachary CB, Gustavsson M. TRASER-Total Reflection Amplification of Spontaneous Emission of Radiation. PLoS One. 2012;7:e35899.

72. Metelitsa AI, Green JB. Home-use laser and light devices for the skin: an update. Semin Cutan Med Surg. 2011;30:144–7.

73. López-Estebaranz JL, Cuerda E. Medical-cosmetic devices for home use: Present and future considerations. Actas Dermosifiliogr. 2010;101:223–9.

74. Wheeland RG. Permanent hair reduction with a home-use diode laser: Safety and effectiveness 1 year after eight treatments. Lasers Surg Med. 2012;44:550–7.

75. Thaysen-Petersen D, Bjerring P, Dierickx C, Nash JF, Town G, Haedersdal M. A systematic review of light-based home-use devices for hair removal and considerations on human safety. J Eur Acad Dermatol Venereol. 2012;26:545–53.

76. Lanzafame RJ, Blanche RR, Bodian AB, Chiacchierini RP, Fernandez-Obregon A, Kazmirek ER. The growth of human scalp hair mediated by visible red light laser and LED sources in males. Laser Surg Med. 2013;45:487–95.

77. Kim WS, Calderhead RG. Is light-emitting diode phototherapy (LED-LLLT) really effective? Laser Ther. 2011;20:205–15.

78. Avci P, Gupta GK, Clark J, Wikonkal N, Hamblin MR. Low-level laser (light) therapy (LLLT) for treatment of hair loss. Lasers Surg Med. 2014;46:144–51.

79. Beltraminelli H, Dietrich N, Hunziker T. Fractional transepidermal delivery: a histological analysis. Dermatology. 2011;223:321–4.

80. Lee WR, Shen SC, Al-Suwayeh SA, Yang HH, Li YC, Fang JY. Skin permeation of small-molecule drugs, macromolecules,

and nanoparticles mediated by a fractional carbon dioxide laser: The role of hair follicles. Pharm Res. 2013;30:792–802.

81. Lavon I, Kost J. Ultrasound and transdermal drug delivery. Drug Discov Today. 2004;9:670–6.

82. Gabay I, Abergel A, Vasilyev T, Rabi Y, Fliss DM, Katzir A. Temperature controlled two-wavelength laser soldering of tissues. Lasers Surg Med. 2011;43:907–13.

83. Tabakoğlu HO, Gülsoy M. In vivo comparison of near infrared lasers for skin welding. Lasers Med Sci. 2010;25:411–21.

84. Schöni DS, Bogni S, Bregy A, Wirth A, Raabe A, Vajtai I, et al. Nanoshell assisted laser soldering of vascular tissue. Lasers Surg Med. 2011;43:975–83.

85. Esposito G, Rossi F, Matteini P, Scerrati A, Puca A, Albanese A, et al. In vivo laser assisted microvascular repair and end-to-end anastomosis by means of indocyanine green-infused chitosan patches: a pilot study. Lasers Surg Med. 2013;45: 318–25.

86. Nasir A. Nanotechnology and dermatology: Part I—potential of nanotechnology. Clin Dermatol. 2010;28:458–66.

87. Gupta S, Bansal R, Gupta S, Jindal N, Jindal A. Nanocarriers and nanoparticles for skin care and dermatological treatments. Indian Dermatol Online J. 2013;4:267–72.

88. DeLouise LA. Applications of nanotechnology in dermatology. J Invest Dermatol. 2012;132:964–75.

89. Basavaraj KH. Nanotechnology in medicine and relevance to dermatology: Present concepts. Indian J Dermatol. 2012;57:169–74.

90. Blecher Paz K, Friedman A. Nanotechnology and the diagnosis of dermatological infectious disease. J Drugs Dermatol. 2012;11:846–51.

91. Papakostas D, Rancan F, Sterry W, Blume-Peytavi U, Vogt A. Nanoparticles in dermatology. Arch Dermatol Res. 2011; 303:533–50.

92. Walther C, Meyer K, Rennert R, Neundorf I. Quantum dot-carrier peptide conjugates suitable for imaging and delivery applications. Bioconjug Chem. 2008;19:2346–56.

93. Michalet X, Pinaud FF, Bentolila LA, Tsay JM, Doose S, Li JJ, et al. Quantum dots for live cells, in vivo imaging, and diagnostics. Science. 2005;307:538–44.

94. Pons T, Pic E, Lequeux N, Cassette E, Bezdetnaya L, Guillemin F, et al. ACS cadmium-free CuInS2/ZnS quantum dots for sentinel lymph node imaging with reduced toxicity. ACS Nano. 2010;4:2531–8.

95. Ravizzini G, Turkbey B, Barrett T, Kobayashi H, Choyke PL. Nanoparticles in sentinel lymph node mapping. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2009;1:610–23.

96. Tez S, Tez M. Topical application of luminescent nanoparticles for sentinel lymph node imaging. Surg Innov. 2008;15:334–5.

97. Wu Y, Li YH, Gao XH, Chen HD. The application of nanoemulsion in dermatology: An overview. J Drug Target. 2013;21: 321–7.

98. Ballou B, Ernst LA, Andreko S, Harper T, Fitzpatrick JA, Waggoner AS, et al. Sentinel lymph node imaging using quantum dots in mouse tumor models. Bioconjug Chem. 2007;18: 389–96.

99. Kim S, Lim YT, Soltesz EG, De Grand AM, Lee J, Nakayama A, et al. Near-infrared fluorescent type II quantum dots for sentinel lymph node mapping. Nat Biotechnol. 2004;22:93–7.

100. Collins A, Nasir A. Nanotechnology and dermatology: Benefits and pitfalls. G Ital Dermatol Venereol. 2011;146:115–26.

101. Tsujimoto H, Hara K, Tsukada Y, Huang CC, Kawashima Y, Arakaki M, et al. Evaluation of the permeability of hair growing ingredient encapsulated PLGA nanospheres to hair follicles and their hair growing effects. Bioorg Med Chem Lett. 2007;17:4771–7.

102. Shim J, Seok KH, Park WS, Han SH, Kim J, Chang IS. Transdermal delivery of mixnoxidil with block copolymer nanoparticles. J Control Release. 2004;97:477–84.

103. Jain B, Singh B, Katare OP, Vyas SP. Development and characterization of minoxidil-loaded liposomal system for delivery to pilosebaceous units. J Liposome Res. 2010;20:105–14.

104. Kumar R, Singh B, Bakshi G, Katare OP. Development of liposomal systems of finasteride for topical applications: Design, characterization, and in vitro evaluation. Pharm Dev Technol. 2007;12:591–601.

105. Münster U, Nakamura C, Haberland A, Jores K, Mehnert W, Rummel S, et al. RU 58841-myristate-prodrug development for topical treatment of acne and androgenetic alopecia. Pharmazie. 2005;60:8–12.

106. Bernard E, Dubois JL, Wepierre J. Importance of sebaceous glands in cutaneous penetration of an antiandrogen: Target effect of liposomes. J Pharm Sci. 1997;86:573–8.

107. Li L, Hoffman RM. Topical liposome delivery of molecules to hair follicles in mice. J Dermatol Sci. 1997;14:101–8.

108. Pitsillides CM, Joe EK, Wei X, Anderson RR, Lin CP. Selective cell targeting with light-absorbing microparticles and nanoparticles. Biophys J. 2003;84:4023–32.

109. Dickerson EB, Dreaden EC, Huang X, el-Sayed IH, Chu H, Pushpanketh S, et al. Gold nanorod assisted near-infrared plasmonic photothermal therapy (PPTT) of squamous cell carcinoma in mice. Cancer Lett. 2008;269:57–66.

110. El-Sayed IH, Huang X, el-Sayed MA. Selective laser photothermal therapy of epithelial carcinoma using anti-EGFR antibody conjugated gold nanoparticles. Cancer Lett. 2006; 239:129–35.

111. Wei L, Xiong C, Zhang G, Huang Q, Zhang R, Zhang JZ, et al. Targeted photothermal ablation of murine melanomas with melanocyte-stimulating hormone analog-conjugated hollow gold nanospheres. Clin Cancer Res. 2009;15: 876–86.

112. You J, Zhang G, Li C. Exceptionally high payload of doxorubicin in hollow gold nanospheres for near-infrared light-triggered drug release. ACS Nano. 2010;4:1033–41.

113. Chatterjee DK, Fong LS, Zhang Y. Nanoparticles in photodynamic therapy: An emerging paradigm. Adv Drug Deliv Rev. 2008;60:1627–37.

114. Rastogi V, Yadav P, Bhattacharya SS, Mishra AK, Verma N, Verma A, et al. Carbon nanotubes: An emerging drug carrier for targeting cancer cells. J Drug Deliv. 2014;2014, 670815.

115. Mundra RV, Wu X, Sauer J, Dordick JS, Kane RS. Nanotubes in biological applications. Curr Opin Biotechnol. 2013; 28C:25–32.

116. Zhang H, Hou L, Jiao X, Yandan J, Zhu X, Hongji L, et al. In vitro and in vivo evaluation of antitumor drug-loaded aptamer targeted single-walled carbon nanotubes system. Curr Pharm Biotechnol. 2014. Forthcoming.

117. Chuan G, Farinelli W, Avram M, Anderson RR. Smoke plume from hair laser removal. Gas-chromatography analysis. American Society for Laser Medicine and Surgery Conference; 2013 Abril 4-6. Boston: American Society for Laser Medicine and Surgery; 2013.

118. Keck C, Müller R. Nanotoxicological classification system (NCS) —A guide for the risk-benefit assessment of nanoparticulate drug delivery systems. European Journal of Pharmaceutics and Biopharmaceutics. 2013;84:445–8.