Phototherapy is, in its broadest sense, the use of light for any kind of surgical or nonsurgical treatment, but it is the athermal and atraumatic therapeutic application of light which is now accepted as the working definition of phototherapy. The early light-emitting diodes (LEDs) were unsuitable for clinical applications because of low unstable output powers, broad wavebands and very high angles of divergence. In the late 1990’s, the Space Medicine Programme in the United States National Aeronautics and Space Administration (NASA), developed the ‘NASA LED’ with much higher output powers, a much narrower divergence and quasimonochromatic output. With the ability to mount multiple LEDs in planar arrays, large areas of tissue can be irradiated in one hands-off session, unlike the time-consuming and therapist-intensive punctal application with laser diodes. These arrays deliver almost laser-like wavelength specificity and with clinically useful penetration depths and intensities, three of the most important considerations when considering cellular targets in the light of the first law of photobiology which states that without absorption, there can be no reaction. In the past few years, LED-based systems have been successfully applied in an increasingly large number of fields, and three major wavelengths have emerged with a good photobiological basis and proven clinical utility: blue, around 415 nm; red, around 633 nm, and near infrared, around 830 nm. Each has its own specific cellular target or targets and biological action spectrum and reaction, but it has become even more clear that no single wavelength can accomplish everything and combination LED therapy has proved necessary for greatest efficacy. The application of LEDs has ushered in a new and exciting era in phototherapy, and offers a versatile and inexpensive therapeutic modality either as a stand-alone therapy, or as an adjunctive approach to enhance the good results of existing surgical modalities.

Key words: Photobiomodulation, mast cell, macrophage, skin-homing T-cell, photodynamic therapy, cytochrome c oxidase

Introduction

Phototherapy, from the Greek words meaning ‘treatment with light’, has been a valid therapeutic modality since at least the days of the Ancient Egyptians, when the sun was used in what the Ancient Greeks later termed heliotherapy, and was still being actively used in Europe in the late 19th and early 20th century, particularly red light therapy carried out with the patient placed in a room with red-tinted windows. Entities treated included the eruptive skin lesions of rubella and rubeola, and even ‘melancholia’, now recognised as clinical depression. The latter application concurred with the views of Hippocrates, who also prescribed sunlight for depressive patients, and believed that the Greeks were more naturally cheerful than their northern neighbours because of the greater exposure to the sun. Red light therapy was also examined in cells under the newly-invented microscope by Fubini and colleagues in the late 19th century, who were able to show that visible red light selectively activated the respiratory component of cellular mitochondria. However, the sun is a fickle medical tool, particularly in northern Europe, and phototherapy as we know it started around the turn of the last century with Finsen’s electric arc lamp-based system, giving phototherapy at the turn of a switch, independent of the sun. Apart from the use of blue light therapy for neonatal bilirubinemia, phototherapy was, in the majority of its applications, overtaken by better medication or treatment techniques. A new lease of life was given to light therapy, however, by the successful development of the first...
ruby laser in 1960, followed in the next 4 years by the argon, neodymium:YAG and carbon dioxide lasers. The first commercially available noncoherent light-emitting diode (LED) was also developed in this period. Clinicians using the laser in surgery, particularly the CO2 laser, reported less pain and better wound healing compared with incisions made with the conventional scalpel: this was found to be a light-mediated effect due to athermal reactions from low photon densities reaching the tissues at the periphery of the thermal range of reactions, and classified more recently by Ohshiro as ‘autosimultaneous laser treatment’. This interesting finding with the CO2 laser prompted more research into athermal and atraumatic levels of reaction in target tissue well below the cellular survival threshold, and led to the evolution in the 1980’s of laser diode-based systems which were used in what was termed, amongst others, low reactive-level laser therapy (LLLT), low incident laser therapy (LILT), or simply ‘laser therapy’, as distinct to laser surgery. This very journal was established in 1988 by John Wiley and Sons, Chichester, UK, as the first dedicated forum for work on laser therapy and associated clinical and basic research, under the Masthead ‘Laser Therapy’, the name it retains till the present, although the submasthead has been changed from; ‘An international journal for laser therapy and photobiomodulation’ to; ‘An international journal for phototherapy and photobiomodulation’. This has reflected the additional light sources now used to deliver phototherapy in addition to the laser diode-based systems, and also the evolution of the meaning of phototherapy itself to encompass athermal and atraumatic changes brought about in light-irradiated tissue. One of the most useful of these new non-laser light sources is the LED, which has evolved from the previous generation of low and unstable powered LEDs with a very large angle of divergence and broad waveband, all of which characteristics combined to make them unsuitable for clinical applications, even though they were very cheap and bright. In the late 1990’s, however, Whelan and colleagues working in the Space Medicine program in the United States National Aeronautics and Space Administration (NASA) developed a new generation of super-powerful, quasimonochromatic LEDs, the so-called NASA LED, which very quickly proved useful in the clinical field, including wound healing. This development gave clinicians and researchers the basis of a new phototherapeutic tool, much less expensive than lasers, IPLs and even laser diodes.

The present article will examine and attempt to justify the use of LEDs from photobiological principles, looking at the benefits of LEDs as a phototherapeutic source, the importance of wavelength, the targets for LED phototherapy including cellular action spectra, a discussion on appropriate intensity, and finally a brief overview illustrating the range of current practical applications in the clinical field.

**LEDs as a Phototherapy Light Source**

If we accept the definition of phototherapy as beneficial athermal and atraumatic reactions in tissue brought about by irradiation with light energy, then any of the photothermally-based light sources are ruled out when used at their normal parameters, including surgical lasers, intense pulsed light (IPL) sources and nonablative skin rejuvenation lasers. However, as has often been argued in this journal, a surgical laser of an appropriate wavelength can definitely be used as a phototherapeutic light source by sufficient defocusing of the beam. For example, a CO2 laser with an incident power at the tissue of 20 W, when defocused to give a spot size 10 cm in diameter, delivers an incident spectral irradiance (power density) of just over 800 mW/cm2, well below the level required even merely to heat the target tissue, and therefore with true phototherapeutic potential. This example shows very clearly the total inaccuracy of the popular but erroneous term of ‘low power laser’ used by many people who should know better, because 20 W is certainly not low power! However, CO2 lasers are rather expensive, and unless a clinic or practitioner has one already, with all the safety requirements firmly in place for a class IV laser, they should not be used as a primary phototherapeutic light source.

LEDs, on the other hand, are very inexpensive even compared to laser diodes, with the price of a single laser diode equal to 200 or more of the new generation LEDs. These LEDs can be mounted in adjustable planar arrays, attached via an articulated arm to a free-standing base unit complete with control console, so that the arrays can be adjusted to fit very well the contours of, for example, a face, leg, hip or other anatomical treatment site. Once set up, the system can be turned on and the therapist or clinician can leave the patient during their treatment session and attend to other matters. The new generation of LEDs has wavebands only a few nm either side of
the rated wavelength, so although they are not mono-
chromatic, as is a laser diode, they are quasimonochromatic, still delivering all of their output power over a very few nanometres (nm). This is very important when considering target/wavelength specificity, as will be discussed in detail in the next section.

Finally, the anatomy of a typical LED is totally solid state, with no filaments, gases or flashlamps, and is shown diagrammatically in Figure 1. Note the small parabolic reflector which makes up part of the chip cathode, helping to ensure that all of the photons generated by the chip are directed out of the envelope tip with a much smaller angle of divergence than previous generation LEDs, typically in the region of 60° steradian. This solid state construction also gives a very high current/photon generation efficiency, meaning that much less power into the LED is required to give a good output power, and hence photon intensity, with minimum generation of heat in the LED itself.

Looking to the future, envelope optics could be altered to incorporate condensers to collimate the beam better, lenses to focus the beam, or polarization filters to deliver polarized light of the desired polarity, should any or all of these factors be judged to increase the treatment efficacy of the beam. LEDs are thus much more economical than other phototherapy sources, very important in this age of spiralling health costs; are quasimonochromatic; can be used in a hands-off manner to free up the clinician during therapy time; are much more energy-efficient; and have the potential for future and further optical quality development.

The Importance of Wavelength

The first law of photobiology, the Grotthus-Draper Law, states that only energy which is absorbed in a target can produce a photochemical or photophysical reaction. However, any such reaction is not an automatic consequence of energy absorption. It may be simply converted into heat, or re-emitted at a different wavelength (fluorescence). The prime arbitrator of this ‘no absorption-no reaction’ is not the output power on the incident photons, but their wavelength, and this comprises two important considerations: wavelength specificity of the target, or the target chromophore; and the depth of the target. Based on these two considerations, the wavelength must not only be appropriate for the chosen chromophore, but it must also penetrate deeply enough to reach enough of the target chromophores with a high enough photon density to induce the desired reaction. In theory, a single photon can activate a cell, but in actual practice multiple photon absorption Specific targets will be dealt with in the following section, but in general, shorter wavelengths penetrate less than longer wavelengths, up to a given waveband, depending on the absorbing chromophore.

Phototherapy is athermal and atraumatic, hence achieving selective photothermolysis is of no concern as it would be for surgical or other photothermal
applications. On the contrary, penetration of light into living tissue is, however, extremely important in phototherapy, and very frequently displays characteristics which are often in discord with results produced by mathematical models, a point often totally ignored by some researchers. A favourite, but false, axiom is that ‘all light is absorbed within the first millimeter of tissue’. Anyone who has shone a laser pointer through their finger, transilluminating the entire fingertip and completely visible on the other side, has already disproved that statement. Figure 2 is based on a transmission photospectrogram of a human hand captured in vivo over the waveband from 500 nm (visible blue/green) to 1100 nm in the near infrared. The photospectrometer generator was positioned above the hand, delivering a ‘flat spectrum’ of ‘white light’, and the recorder placed beneath it. The wavelength is shown along the x-axis, and the calculated optical density (OD) is on the y-axis, from lower ODS to higher. The higher the OD, the greater is the absorption of incident light, and hence the lower the transmission, or penetration depth into the tissue. It must also be remembered that the OD is not an arithmetic but a logarithmic progression, so that the difference between an OD of 4 and one of 6 is not simply 2, but 2 orders of magnitude, i.e. a factor of 100.

From 500 to 595 nm (blue-green to yellow), the OD was from 8.2 to approximately 7.6, respectively. At 633 nm, the wavelength of the helium neon (HeNe) laser, the photobiological efficacy of which is well recorded, the OD is approximately 4.5. In other words, red light at 633 nm penetrated living human tissue by 3 orders of magnitude better than yellow at 595 nm, because of the pigment-specific absorption characteristics of the 2 wavelengths. Visible yellow at 595 nm is at the peak of the oxyhaemoglobin absorption curve, and is also much higher absorbed in epidermal melanin than 633 nm, which is why the yellow light in the spectrogram did not penetrate at all well into the tissue. Accordingly, cellular and other targets in the mid to deep reticular dermis will be inaccessible to yellow light. The deepest penetration was achieved at 820-840 nm in the near infrared. At this waveband, pigment is not a primary chromophore with proteinous targets as the major chromophore, and this 820-830 nm waveband coincides with the bottom of the water absorption curve. The most successful of the laser diode systems gave a wavelength of 830 nm for this very reason, and was shown to penetrate living hands, and even bone, very successfully. After around 1000 nm, water absorption once again starts to play a significant role, and in the curve in Figure 2 the OD was seen to increase thereafter.

Following these findings, it made a great deal of sense to source LEDs at wavelengths already tried, tested and proven in laser therapy application for LED systems, so LED systems delivering 633 nm or thereabout in the visible red and 830 nm in the near infrared, and at high enough photon densities, have been reported as having significant effects on their target tissues at a good range of depths well into the mid and even the deep reticular dermis. The visible blue wavelengths were chosen for different reasons, which will be covered in the following section.

Finally, the different wavebands, visible light and invisible infrared light, have different primary mechanisms. Absorption of visible light photons at appropriate levels induces a photochemical reaction, and a primary photochemical cascade occurs within the cell, usually instigated by the mitochondria, the adenosine triphosphate-producing power-houses of the cell. Infrared photons, on the other hand, are primarily involved in photophysical reactions which occur in the cell membrane, changing the rotational and vibrational characteristics of the membrane molecules. Through subsequent activation of the various membrane-located transport mechanisms, such as the Na⁺/Ca⁺ and Na⁺/K⁺ pumps and changes in the cell permeability, changes occur in the chemical and osmotic balance in the cytosol, finally resulting in the induction of a secondary chemical cascade which gives more or less the same endpoint as the visible light photons, namely cellular activation or proliferation. These considerations are schematically illustrated in Figure 3.

To sum up, the wavelength of a therapeutic source therefore has a double importance, namely to ensure absorption of the incident photons in the target chromophores, and to be able to do so at the depths at which these chromophores exist. The waveband in which the wavelength of the incident photons is located determines not only which part of the cell is the target, but also the primary photoaction. Wavelength is thus probably the single most important consideration in phototherapy, because without absorption, there can be no reaction.

Targets in LED Phototherapy
Just as was the case with selecting the optimum wavelengths for sourcing LEDs to use in phototherapeutic systems, selecting the targets for LED
Fig 3: Schematic depicting photoreception (absorption) of light in a cell, and the subsequent waveband-specific response. The basic reaction as defined by Karu is absorption, which is followed by signal transduction and amplification within the cytosol, and leads to the photoreponse, such as cell proliferation. In the case of visible and infrared light, the former (A) induces a primary photochemical cascade initiated in the mitochondrion, whereas the latter (B) produces a primary photophysical response, initiated in the cell membrane, which leads directly to intra/extracellular exchange: this is transformed into a secondary photochemical cascade similar to that induced by visible light. In both cases, there is a dramatic rise in intracellular ATP, the cell’s ‘fuel’, calcium ions (Ca^{++}), very important for intercellular signaling and another driving force to boost mitochondrial action, and protons (H^+), also important for intercellular signaling and for energy generation from ATP. The end result is virtually the same: namely cell proliferation; enhanced cell function, for example, collagen synthesis in the case of fibroblasts; or repair of damaged or compromised cells.

NAD, nicotinamide adenine dinucleotide, an important coenzyme functioning as a hydrogen carrier in a wide range of redox (reduction-oxidation) reactions; the H is carried on the nicotinamide residue; NAD^+, the oxidized form of NAD; ATP, adenosine triphosphate, a high energy phosphate molecule required to provide energy for cellular function; NaKATPase, sodium potassium adenosine triphosphatase, required for the function of the sodium/potassium pump in the membrane; CA^{++}, calcium ions; H^+, protons, elementary particles carrying a positive electric charge, the flow of which is used to generate energy from ATP via ATPase; DNA, deoxyribonucleic acid; RNA, ribonucleic acid.

Table 1: Literature-based summary of the phototherapeutic wavelength-specific efficacy in raising the action potentials of specific cells

<table>
<thead>
<tr>
<th>Nominal wavelength (nm)</th>
<th>Mast</th>
<th>Neutrophil</th>
<th>Macrophage</th>
<th>Fibroblast</th>
<th>Fibro-Myo</th>
<th>Keratinocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>630-670</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>790</td>
<td>++</td>
<td>?</td>
<td>?</td>
<td>++</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>830</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>904</td>
<td>-</td>
<td>+</td>
<td>±</td>
<td>-</td>
<td>-</td>
<td>?</td>
</tr>
<tr>
<td>1,064</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>10,600</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

Fibro-myo: Fibroblast to myofibroblast transformation *: True pulsed diode laser, rest are C/W
Action levels: -, retardation; ±, no reaction; +, noted reaction; ++, significant reaction; ++++, highly significant reaction
phototherapy was largely based on the existing knowledge gleaned from over 20 years of the laser therapy and photobiomodulation literature. Table 1 shows in the left hand column a selection of investigated wavelengths, in increasing length from the top, and along the top of the table can be found the most important cellular targets. These cells can be sub-grouped into 4 types. The first three subgroups are concerned with the wound healing process. Subgroup 1 consists of mast cells, neutrophils and macrophages, which are associated with the inflammatory stage of wound healing; subgroup 2 consists of fibroblasts, associated with the proliferative stage; and subgroup 3 are the transformational cells associated with the remodeling stage. In subgroup 4 can be found epidermal keratinocytes, which, when photo-activated, are an extremely important source of cytokines and other chemokines which can descend into the dermis and are involved in either proinflammatory or anti-inflammatory reactions.

From the various wavelengths reported, two are notable for their effect on raising the action potential of target cells, but they do so in different ways. Visible red at 633 nm has been reported to have profound effects on fibroblasts, inducing fibroplasia with increased numbers of highly active mitochondria, medium effects on mast cell degranulation and macrophage activation, and some apparent effects on neutrophil activation. Near IR 830 nm, on the other hand, has some apparent effects on fibroblasts, but profound effects on all three of the inflammatory stage cells.

Both visible red and near IR wavelengths photomodulate the mechanisms of epidermal keratinocytes, producing an increased amount of inter-leukins such as IL1, 2, and 6 and also tumor necrosis factor alpha (TNFα). Both wavelengths also encourage the recruitment of skin-homing T-cells into the irradiated area, both T-1 and in particular T-2 cells. Both IR and visible red light are well-associated with increased local blood flow post-radiation. This is important when considering that this not only increases the flow of nutrients and oxygen into the treated area, but also provides a gradient between areas of low and high oxygen tension which can act as ‘highways’ for the wound-healing cells into the target area, particularly those associated with the inflammatory stage of wound healing.

The central reaction in all the above instances is athermal and atraumatic, and involves a direct energy exchange between the incoming photons and their target, so that the level of energy of the irradiated cell is increased following absorption of the incident photons and their energy. This activates or modulates the cell’s activity, and is referred to as photoactivation therapy (PAT). PAT can result in cell proliferation, better cell function, repair of injured or compromised cells or any combination of these.

Wavelength again determines the target in PAT. In the case of visible red light the main target is the respiratory chain of the mitochondrion in the fibroblast, and specifically cytochrome c oxidase (CCO), which is the terminal electron acceptor in the electron transfer redox chain, taking 4 reducing equivalents from cytochrome c and converting molecular oxygen to water. In the process, in which copper ions play an important role, it translocates protons, helping to establish a chemiosmotic potential that the ATP synthase then uses to synthesize ATP. One of the major peaks in the absorption spectrum of CCO is in the visible yellow, but bearing in mind the poor penetration of yellow light in living human tissue, it is not possible for yellow light to reach deeply enough into the reticular dermis to affect the activity of fibroblasts in that zone so the yellow waveband is not ideal for any phototherapeutic application involving fibroblasts. Another major peak in the CCO absorption spectrum is around 633 nm, and that wavelength does offer much deeper penetration, and thus potentially greater applications in phototherapy involving fibroblast activity, such as wound healing and even skin rejuvenation.

Light at 633 nm does have a similar but lesser influence on the mitochondria of the inflammatory cells, as seen from Table 1, but near IR at 830 has a very pronounced effect on the activity of these cells. Wound healing cells have their own cycle during the wound healing process, all peaking in number at different times. The inflammatory phase of wound healing is extremely important for the subsequent proliferative phase, because macrophages and mast cells produce large amounts of trophic factors, in addition to the proinflammatory components, which make for a beneficial environment for the fibroblasts. The inflammatory cells peak in number during the inflammatory stage usually recognized as occurring from day zero to day 4 or 5, together with neutrophils, and then return to normal baseline levels. From day 4 to around day 21, both fibroblasts and endotheliocytes increase in number, peak, and
decrease, being responsible for matrix regeneration and neovascularization, respectively. Some of the fibroblasts then undergo transformation into myofibroblasts, literally fibroblasts with muscles, and are responsible for the tight alignment of new collagen fibres during the remodeling process by aligning with the fibres and exerting a linear force on them. The timing and cell cycles are shown in Figure 4.

Given the difference in the peak of the cell numbers and the timing of their appearance, it could be argued that these considerations should affect or determine the timing of the irradiation of target tissue with the two wavelengths known to activate these cell groups, namely 830 for the inflammatory stage cells and 633 nm for the fibroblasts and endotheliocytes. It would make strong photobiological sense in photoactivation therapy to irradiate first with 830 nm when the inflammatory cells are present, and then to follow up with 630 nm when fibroblasts are in the majority. Near IR at 830 nm has a very strong anti-inflammatory effect, despite activating the inflammatory cells, but the action turns out to be more of a controlled inflammatory phase, peaking the cells harder and faster, and then lowering the numbers while leaving a very beneficial environment for the fibroblasts. Photoactivated macrophages are known to release much larger amounts of fibroblast growth factor (FGF), and to internalize phagocytosed materials faster. Near IR-irradiated pooled human neutrophils have been shown to develop significantly increased chemotactic and phagocytic properties. Many reports have shown increased fibroblast function and collagen formation both in vitro and in vivo following 633 nm irradiation, so 830 nm phototherapy and collagen formation might well be enhanced with another set of 830 nm treatment sessions. It is apparent that for wound healing itself, or any process which depends on the wound healing process such as skin photorejuvenation, the ideal combination is the sequential application of 830 nm followed by 633 nm LED phototherapy, with a final 830 nm LED session to establish the remodeling process.

The visible blue wavelength of 415 nm has already been mentioned above, and it has specific ap-
Applications only in the treatment of acne vulgaris, with a totally different mechanism from the PAT (photactivation therapy) associated with 633 nm and 830 nm light energy. Active inflammatory acne lesions contain a bacterium, *Propionibacterium acnes* (*P. acnes*), which in turn contains endogenous porphyrins protoporphyrin IX (pp IX) and coproporphyrin III (cp III) (Figure 5). Both of these porphyrins have a very strong absorption peak at 415 nm in the Soret waveband, so that irradiation with sufficient photon density at 415 nm will generate reactive oxygen species (ROS) such as singlet oxygen within the *P. acnes* cells through the process known as endogenous photodynamic therapy (PDT), and destroy them via apoptosis. However, PDT only destroys the *P. acnes*, but does not address the associated inflammatory problem, which is also known to include an immune complement of rogue T-cells. Red light at 633 nm (PAT) has a recognized anti-inflammatory effect, is known to recruit large numbers of normal T-cells, and is moreover the optimum wavelength to activate fibroblasts to repair the matrix damaged by the acne lesions. The combination of 415 nm and 633 nm LED phototherapy, applied sequentially, should therefore be the ideal endogenous PDT/PAT approach in light-only therapy for the physiologically unpleasant and psychologically disturbing inflammatory lesions of acne vulgaris.

**Intensity in Phototherapy**

Wavelength as already argued will determine both the target, and the depths at which the desired targets can be reached, but the photon intensity will help to ensure that either PAT or PDT is successfully achieved with the selected wavelength or sequential wavelengths to get the desired clinical result. The third law of photobiology, the Bunsen-Roscoe Law of reciprocity, states that any appropriate combination of incident power and treatment time to deliver the same dose will achieve the same effect. However, it has been shown that this holds true only for a comparatively narrow range of high-powered photosurgical applications, and ceases to be true at very low incident powers such as are used in phototherapy. If we consider a single laser diode, because of its specific laser characteristics in particular a very high photon intensity, it can have recognized phototherapeutic effects on the target cells. However, it is capable of treating only one point at a time, and multiple treatments would be necessary to treat a large area such as the face. On the contrary, one single LED, even one of the new generation of LEDs, when used on its own, will not achieve anywhere near a clinically useful photon intensity in the target tissue. When multiple LED’s are mounted close together in a planar array, however, and correctly positioned according to the angle of divergence of the beam, the interaction where the beams impact with each other gives an extremely intense photon density due to the phenomenon of interference, particularly with the physical forward- and backward scattering characteristics of red and near IR light. If the distance between the LEDs is too great, however, then the intensity will drop off dramatically. This is illustrated schematically in Figure 6.

Using a large enough head made up of several planar arrays will also solve the problem of the need to set up the LEDs at a precise distance from the surface of the target tissue to maintain the ideal photon intensity. In the case of the face, for example, this would be virtually impossible due to the degree of protrusion of the nose. If the surface area of the irradiating source is large enough compared with the area being irradiated, then the distance at which the ideal intensity would be generated is flexible, allowing a range of distances between the LED head and the target tissue to obtain a viable photon intensity. The ability to adjust the planar arrays of which the head is constructed to accommodate anatomically curved target tissue will further maintain the photon intensity, rather than allowing it to diminish at the outer zones of a curved target such as the face (Figure 7).

In short, to achieve the ideal photon intensity, an LED-based head must be large enough to ensure good coverage of a large target area, must have multiple LEDs precisely mounted in the arrays to achieve the interference phenomenon in overlapping beams, and should consist of several flat arrays which are adjustable to allow even irradiation of a curved surface, such as the face.

**LED Phototherapy in Practice**

This section will briefly show the results obtained and published using an LED-based phototherapy system based on representative examples. All examples shown used the Omnilux™ system of LED heads, manufactured by Photo Therapeutics of Fazely, UK. This system, illustrated in Figure 8, has three interchangeable heads based on blue (415 nm), red (633 nm) and near infrared (830 nm) LEDs. All heads are designed around multiple adjustable planar...
arrays. Two geographically remote studies with significantly large numbers of patients have illustrated
that the combination of blue and red LED therapy has had good results in the treatment of inflammatory
acne, with a final clearance rate in inflammatory lesions of over 80%, at an assessment point 12 weeks
after the final treatment of a 4-week, 8-treatment
regimen.\(^{22,23}\) Figures 9 and 10 show representative
results, but the interesting point is that the treatment
effect in both studies continued to improve well after
the final treatment, suggesting the strong latency ef-
fect associated with LED phototherapy at appropriate
doses and wavelengths. In the photorejuvenation of
photo-and chronologically aged skin, the combina-

Fig 6: When a single LED is irradiated onto target tissue, the photon intensity in the tissue is very low, and probably of
little clinical utility (left panel). The angle of divergence is 60°. In the right-hand panel, however, when all of the
LEDs are illuminated, the beams interact with each other, and in the areas of interaction the interference phe-
nomenon develops an extremely high photon intensity in the tissue which does have clinical utility, and which is
even higher than the rated output power because of the forward and backward scattering characteristics par-
ticularly of visible red and near IR light.

Fig 7: The single flat LED panel on the left delivers a higher dose to the nose and front of the
face than the sides, because of the contour of the human head. By setting up articu-
lated panels, the head can be adjusted to give an even dose over the entire face. This
can be applied to any contoured area of the

Fig 8: The Omnilux LED phototherapy system, from Photo
Therapeutics, Ltd, Fazeley, UK.
Fig 9: A 19-year-old female, Skin Type II, with severe inflammatory acne, before (a) and 12 weeks after the final treatment session in a 4-week course of sequential Onmilux blue (415 nm) and revive (633 nm). Seventy-three percent clearance of the lesions has been obtained. Photographs courtesy of Dr Bruce Russell, Reference 22.

Fig 10: A 20-year-old Asian male, skin type IV, with moderately severe inflammatory acne (Burton Grade 4) before (a) and 8 weeks after the final treatment of the 4-week sequential blue/red light regimen. Clearance obtained was 79%, with a downshift in the Burton grade to Grade 2. Photographs courtesy of Dr Seung-yoon Lee, Reference 23.

Fig 11: A 28-year-old Asian female before (a) and 12 weeks after the final session of a 4-week sequential Onmilux plus (830 nm) and revive (633 nm) treatment regimen for photorejuvenation. The improvement in the periorcular wrinkles and fine lines is very clear, and the patient was extremely satisfied. Photographs courtesy of Dr Seung Yoon Lee, Reference 24.

Fig 12: Haematoxylin and eosin stained specimens from the face of the same patient as in Fig 11, before (a) and two weeks after the final treatment session (b). The baseline histology shows typical elastotic skin with poorly-organized collagen fibres. In the post LED therapy histology, the collagen fibres are plump and much better aligned in a well-organized matrix. The Grenz layer of linearly-oriented collagen can be seen running under and attached to the dermoepidermal junction. The epidermis is thicker with closely packed ascending daughter keratinocytes, and the stratum corneum is also better organized. (Original magnification X 200) Photomicrographs courtesy of Dr Seung Yoon Lee, Reference 24.
tion of sequential 830 nm and 633 nm LED therapy has proved very effective, although there is only 1 study based on hemifacial LED therapy with a large patient population and suitable intra-patient and inter-group controls, (24) and Figures 11 and 12 illustrate typical findings from this study. In frank wound healing, the 830 nm/633 combination has reportedly proved very effective in burn wounds in children, (25) and also in accelerating wound healing and reducing downtime, erythema and pain following full-face laser ablative resurfacing in a controlled retrospective/prospective study. (26) While on the interesting subject of pain attenuation, papers have already appeared in Laser Therapy on 830 nm LED therapy for sports pain and post-mastectomy pain. (27,28)

Conclusions

Phototherapy has definitely arrived in the clinical field for the treatment of inflammatory acne, wound healing, skin rejuvenation, and the treatment of pain. The new generation of quasimonochromatic and powerful LEDs has emerged as the main phototherapeutic modality used in treatment heads consisting of adjustable, hands-off planar arrays in systems which offer relatively inexpensive but effective therapy in all the above fields, with more emerging at national and national meetings. Basic science is elucidating mechanisms at tissue, cellular and subcellular levels, proving what clinicians and therapists have already found in patients. The combination of one LED wavelength with another, used sequentially, has appeared as the best and most effective approach. LED therapy may be used as a stand-alone light therapy, but has very interesting effects when used in an adjunctive manner to improve and speed up the already good results achieved with other light sources, or conventional surgery. There is no doubt that LED phototherapy, when used based on the solid photobiological precepts of appropriate wavelength, target and photon intensity, is a safe, flexible, effective and comparatively inexpensive modality, very welcome in this era of ever-spiralling costs for both practitioners and patients.

References

19: Niimikoski J: Current concepts of the role of oxygen in


