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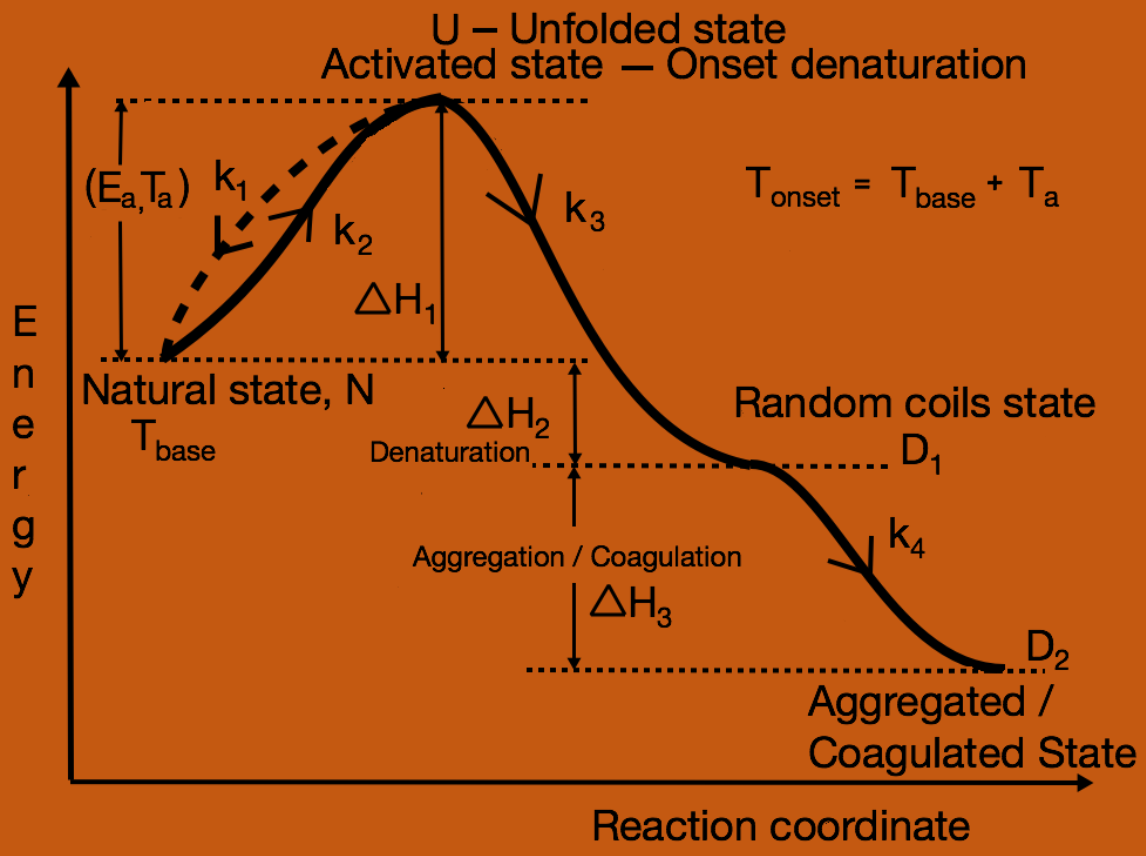

Michael J Murphy

THE LASER-IPL GUYS

The biophysics of photothermal treatments with lasers and intense pulsed light systems

Lasers and intense pulsed lights are commonly used for many skin applications today. An understanding of the basic biophysics is essential to achieve good clinical outcomes. Yet, the author's training experiences demonstrate that many users do not have a good grasp of some of these concepts. In this article, Mike Murphy will address these issues, and the most important parameters that need to be considered when treating the skin with high-energy devices will be identified

How light interacts with skin is actually very complicated (Jacques, 2013; Lister and Wright, 2017), and it depends on the wavelength (colour) of the light, energy, delivery time, spot diameter, repetition rate, skin thickness, contents and absorption characteristics. Reactions in absorbing targets range from a very subtle chemical reaction inside cells, to thermal reactions where proteins denature and physical disruptive processes that tear apart tissues or other targets (Baranoski and Krishnaswamy, 2004).

Possessing a good understanding of these processes is critical in achieving good clinical results. Many laser operators achieve 'adequate' results, simply because they do not fully understand what they are trying to do in the skin with the technology that is available.

Even with a good understanding, many laser operators are unsure how to set up the correct parameters, such as fluence, pulse width and spot size, when tackling skin conditions.

Light energy and the skin

There are many processes—optical and thermal—that may occur as light penetrates deep into the skin.

However, before continuing, it should be considered why light is fired at the skin in the first place. Well, light is a form of energy. When something in the skin is targeted, it is usually to change or alter it in some way. Patients may wish for some unwanted tissue (or another target, such as tattoo ink) to be destroyed, or they may want to enhance something.

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Usually, this means that it should be heated up in a controlled manner. When light energy is absorbed by something in the skin, the energy is mostly converted into heat energy (Mckenzie, 1990). So, in essence, light is being used to transfer energy into the targets in the skin in a safe and controlled fashion.

The journey of light in the skin

So, what happens to the light as it makes its journey into the skin?

Firstly, some of the light that hits the skin surface is reflected back. These are called Fresnel reflections, and may account for up to 5–7% of all light hitting the skin surface.

Secondly, as soon the light enters the stratum corneum (topmost skin layer), it begins to scatter. This can be thought of as photons of light bouncing off atoms and molecules. Consequently, the photons can move in many directions, including back out of the skin, which is known as back-scattering. At the same time, the wavelength of the light changes by shortening. This is due to the change in the refractive index between the air and the skin.

Next, the light enters the epidermis. This layer is around 0.06–0.1 mm thick and comprises of several layers of different cell types. It takes around 0.3 picoseconds for the light to travel through these layers (0.3 trillionths of a second). The light will encounter some melanin granules in this part of the skin. Depending on the colour of the light (wavelength), some will be absorbed by this melanin, which will raise its temperature.

The remaining light enters the basal layer, which is where most of the melanocytes and melanin granules are found (in non-black skin). As above, some of the light energy will be absorbed by the melanin in this layer, raising its temperature. This layer is only around 10 microns thick (0.01 mm), which can cause problems. If there is a lot of absorption of the light energy, this layer can become very hot. Since it is so

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Many laser and intense pulsed light treatment problems are caused by excessive heating of the basal layer

thin, it will lose its heat very rapidly into the epidermal layer above and the upper dermis below. This is where blisters are usually formed, due to excess heating.

Most skin temperature and pain receptors are near the basal layer (both above and below), which explains why such treatments can be painful. Once the local temperature exceeds 45°C, pain is felt instead of heat.

The dermis

Many laser and intense pulsed light (IPL) treatment problems are caused by excessive heating of this basal layer, simply due to absorption in the melanin. Surface skin cooling is essential to reduce the damaging effects of this heating. Proper cooling will greatly reduce any likelihood of skin damage by drawing out any excess heat energy from this layer. It will also make the treatments more comfortable.

Any light that is not absorbed in the basal layer may then propagate into the dermis below. By this stage, there may be anything between 70–90% of the original light energy left, depending on the amount of melanin in the basal and epidermal layers, and epidermal back-scattering (Murphy, 2020). This layer can be between 3–5 mm thick, depending on the body area and ethnicity of the patient.

Now, the interesting thing about the dermis is that it is a highly scattering medium—much more than the epidermis. So, any light entering the dermis will bounce around excessively. This has two very important effects:

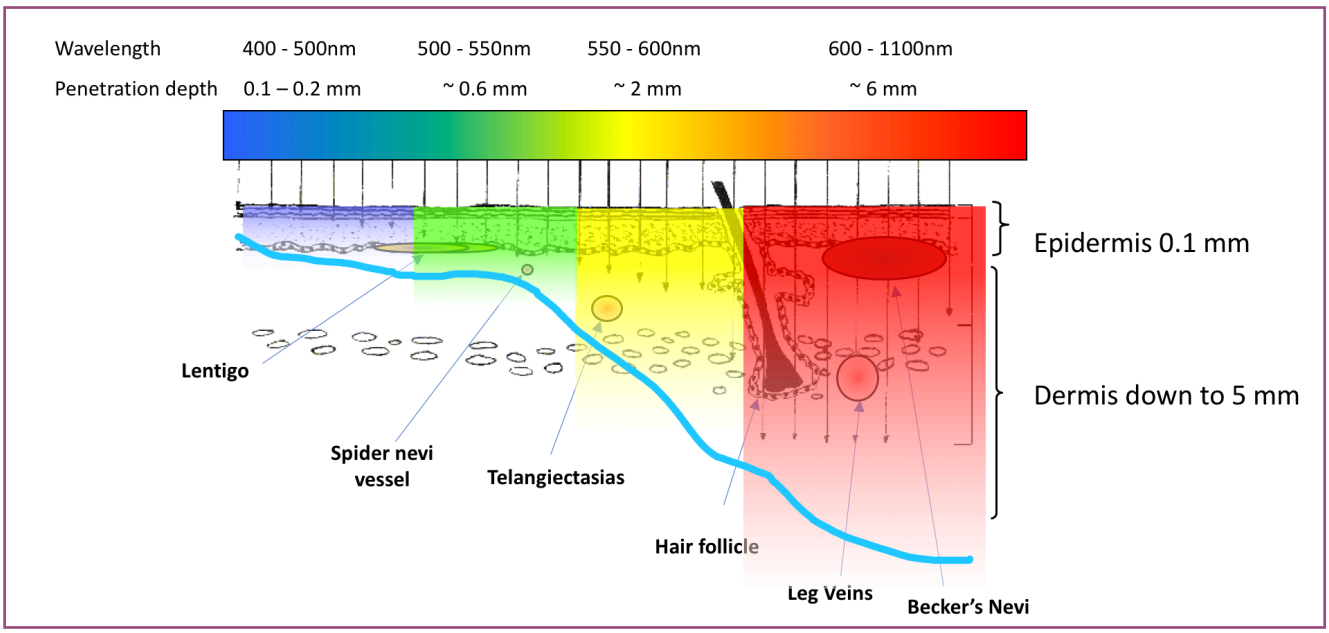
- Firstly, as the light progresses into the dermis, it spreads out, due to scattering. In other words, the beam diameter increases, thereby reducing the fluence (the fluence is the energy divided by the spot size area, measured in Joules/cm^2). This can significantly affect the outcome of any treatment
- Secondly, a proportion of this scattered light may be turned through 180°, which may cause it to leave the skin completely, thereby reducing the total amount of energy left for any treatment.

Scattering in the dermis is hugely significant in many laser and IPL treatments (Jacques, 2013; Lister and Wright, 2017). It can easily reduce the effectiveness of treatment, simply through loss of light energy and reduced fluences.

The dermis also contains many potential absorbing sites: haemoglobin, tissue water, melanin, keratin and bilirubin, etc. Consequently, much of the light energy will be absorbed in this layer. All of these absorptions will raise the temperature of those sites.

It is a simple fact of physics that many sites within the dermis will heat up, regardless of the chosen wavelength.

Supplied by the author



Light penetration in the skin

The heating of some absorption sites can be maximised by carefully choosing the wavelength of the device, but there will always be unintended absorption in adjacent areas.

If the wavelength is chosen properly, then the temperature of the intended targets can be raised specifically, compared with the surroundings. This is the basic principle of selective photothermolysis—a theory which has proved to be very useful in light-skin therapies for nearly 40 years (Anderson and Parrish, 1981; Altshuler et al, 2001; Murphy and Torstensson, 2013).

If some of the light gets through the dermis without being absorbed, then it may continue its journey to deeper layers, such as the fatty tissues. By this point, the energy will be very low compared with the surface value. This is known as transmission through the dermis.

An interesting fact about laser light penetrating the skin is that it cannot be regarded as 'laser' light as soon as it enters the skin. Scattering causes it to lose its directionality almost immediately, and it also loses its coherence. These are two of the main defining features of laser light, and the third is its monochromaticity (single wavelength/colour).

If the scattering events in the skin are 'elastic'—meaning that the photons do not lose any energy in each event—then the scattered light will retain the original wavelength. So, while the light entering the skin may be 'laser', it rapidly loses two of its main features, meaning that it cannot be considered 'laser light' once it is in the skin.

As mentioned above, light undergoes a series of processes when it is in the skin. Much of it may be lost through back-scattering, unwanted absorption or transmission. In fact, calculations show that less than 0.5–2% of the light energy used for hair removal is absorbed by hair follicles in the dermis. This means that the remaining 98–99.5% may be lost to back-scattering or unintended absorptions, leading to a general heating of the dermis and epidermis. This explains why skin cooling is so critical in all photo-thermal treatments.

Choosing the correct laser and intense pulsed light parameters

Choosing the correct parameters for IPL removal of hair (or blood vessels or pigmentation) can be difficult and cannot be fully covered in this article. However, factors that are important to consider will be identified.

First, what are the critical parameters? Many laser and IPL systems allow a number of parameters to be selected, including the wavelength, fluence, pulse width, spot size and skin cooling (*Table 1*) (Babilas et al, 2020; Barikbin et al, 2010; Adamic et al, 2007). However, in the author's experience, most laser and IPL users do not fully understand how to select these properly, particularly when faced with certain skin conditions.

Considerations

If all the parameters that are detailed in *Table 1* are properly selected, then the desired result should always be achieved, without damaging the surrounding tissues. Knowing how to choose the best parameters for any given situation is down to training and experience. Unfortunately, the author's experience is that most practitioners are not adequately trained.

Other important issues that must be considered when treating the skin with lasers and IPLs include leaving appropriate time between repeat sessions (which depends strongly on the skin repair processes), properly diagnosing skin conditions and laser and IPL calibration (many systems do not output what they claim on the screens).

Table 1: Laser treatment fundamentals	
Wavelength	The wavelength must be chosen according to two important criteria: first, the wavelength must be preferentially absorbed by the target (significantly more than by the surroundings); and second, the wavelength must be able to penetrate the skin sufficiently and with enough energy to do the task in hand
Fluence	Fluence is the energy per unit area (in J/cm^2). This can be thought of as the concentration of light energy into a spot. It determines the temperature rise in the target tissues, and also in the surrounding tissues. Too high a fluence will cause unwanted damage, while too a low a value will not achieve the end result
Pulse width	The pulse width (also known as the pulse duration or pulse length) is how long the energy is applied for. It is a critical parameter, because it determines whether the desired clinical end point will be achieved
Spot size	This may seem obvious, but it is not. Contrary to popular misconception, larger spot diameters result in a deeper penetration of light energy, compared to smaller sizes. So, to target particularly deep tissues, as large a spot size as possible must always be used, while maintaining the required fluence
Cooling	When sending light energy into the skin, a thermal response (in photothermal treatments) is deliberately being created. This means that excess heat is being generated in the tissues. This is where problems begin, and it must be mitigated against by good surface cooling. Too much heat will result in too much tissue damage and scarring. A balance should always be considered—the more energy that is applied, the more cooling must also be applied. This not only reduces the pain that is felt by the patient, but it also reduces the risk of scarring

Conclusion

A good understanding of the considerations detailed in this article will greatly assist in achieving good clinical results. Many treatments go wrong, simply because of a poor understanding of the condition or the technology. Laser and IPL treatments can be quite complex, and obtaining good, consistent results can be difficult. However, it is much more difficult if the basics are not properly understood.

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Plume control in medical and cosmetic laser clinics: a practical guide

In this article, Godfrey Town and Mike Murphy review risk assessments that aim to control the dangers of plume and make recommendations that laser specialists can use to make their practice safe and secure

Infection control requirements driven by the COVID-19 pandemic now require the laser and intense light source—for example, intense pulsed light (IPL)—services provider to have a policy and procedure for hygiene, infection and cross-infection control that is supported by a risk assessment against virus transmission. Of course, this includes airborne transmission through water and saliva droplets, and has driven the need for pre-treatment infection control protocols and increased use of personal protective equipment (PPE) (for example, respirator masks and face shields) (Fox-Lewis et al, 2020; Pavan et al, 2020; Vuorinen et al, 2020).

Improved room ventilation is recommended to reduce risk of exposure to airborne virus transmission (Carpenter and Poitrast, 1990; Hatcher, 2020; Poplett, 2021).

Plume control and risk assessment

The potential hazards of other airborne particulates and noxious plumes that are generated by the interaction of laser and IPL beams on human tissue must also be identified by the laser and IPL services provider, as well as procedures considered to mitigate the risks. Published guidelines from the Medicines and Healthcare products Regulatory Agency (MHRA) and British Medical Laser Association (BMLA) should always be followed (MHRA, 2015; Madan, 2020).

'Plume' can be defined as any emissions from tissues following laser, IPL, electrosurgical, harmonic scalpel, plasma or radiofrequency intervention that contains any form of contaminant, including smoke (water vapour), tissues, bacteria, viruses, chemicals, gases or particulate matter, etc. The types of hazard and level of risk to laser and IPL operators and patients depends on the intended application, the laser or IPL and settings being used, the method of delivery and environmental factors, in particular, ventilation and filtration.

It is the legal duty of establishment owners to manage health and safety in the establishment (Legislation.gov.uk, 1999), but a certificated laser protection adviser (LPA) will have the competencies and indemnity insurance to advise about the specific laser and IPL risks in the workplace and recommend control measures that are proportionate and reasonably practical (Health and Safety Executive (HSE), 2021).

A laser and IPL plume risk assessment should include the following considerations.

Identify the hazards

Certain surgical and aesthetic techniques can generate plume as a by-product, particularly from procedures that rely on the ablation or mechanical manipulation of target tissue by devices such as laser and high-power pulsed broadband light sources.

Plume can contain a variety of contaminants, including viable bacteria, viruses, cellular debris, particulates, noxious and toxic aerosols, gases, vapours and fumes. The gases can include toxic substances, such as benzene, formaldehyde and hydrogen cyanide. Laser and IPL contact with skin preparations will also produce additional chemicals.

Plume can also contain aerosolised blood (plasma and blood cells or fragments of cells) and bloodborne pathogens in the form of bacteria and viruses. Thus, plume poses a hazard to exposed individuals and can transmit infections.

The contaminants in plume can cause respiratory problems or have mutagenic or carcinogenic effects. They can also cause mucous membrane, ocular, respiratory and skin irritations and reduce the practitioner's ability to visualise the operative field, resulting in unsafe operating conditions (CSA Group, 2020) Furthermore, Ilçe et al (2016) found that exposure to electrosurgery-generated plume resulted in headaches, coughing, nausea and drowsiness in 81 clinical personnel.

Decide who might be harmed and how

For each hazard, it needs to be clear who might be harmed, as it will help to identify the best way of managing the risk.

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Table 1: Example of a simple laser plume hazard risk assessment for a small hair reduction service provider

People at risk	How?	Existing controls	OK?	Risk factors	Action required
Laser operator	Extended exposure to mutagenic particulate and gases in laser plumes (disease cross-infection and allergies, etc)	▸ Extractor fan to the outside that is switched on through the day to ensure air exchanges ▸ The patient always shaves the treatment area before the laser appointment (maximum 1 mm stubble) ▸ Using diode laser in skin contact with thermoelectric skin colling and minimum 2 mm thick refrigerated transparent gel ▸ All persons present in the treatment room use FFP2/ N95 respirator masks during the treatment.	OK	Low/very low	Always ensure that the extractor fan is turned on
Patient/any observer who is present	Brief exposure to mutagenic particulate and gases in laser plumes (disease cross-infection and allergies, etc)		OK		Always ensure that the treatment area is clean shaven to reduce carbonising the hair follicles
			OK		Always ensure that transparent gel is refrigerated and applied 2 mm thick minimum
			OK		Always ensure FFP2/ N95 masks are used during treatments (except the patient if treating facial areas)

This risk assessment will be reviewed yearly or following any significant changes that are made (for example, new laser equipment or changes to the room's layout)

Date of risk assessment: Name:

Risk assessment perfomed by: Signature:

For example, this might include laser therapists, patients, an observer in the laser room, cleaners and contractors.

In each case, identify how they might be harmed (i.e. what type of injury or ill health might occur). For example, bloodborne pathogens from laser tattoo removal might transmit human immunodeficiency virus (HIV) and infect others, or airborne bacterial contaminants from ablative skin procedures might transmit and infect others with disease.

COVID-19 viral transmission aside, the risk of chronic disease transmission through airborne particulates during laser and IPL procedures is low. While many in vitro studies have shown the existence of viable airborne pathogens in surgical plume, a literature search produced only two cases, with the first detailing actual laryngeal papillomatosis transmission in a laser surgeon after repeated laser therapy to patients with anogenital condylomas (Hallmo and Naess, 1991), and the second describing transmission of laryngeal papillomatosis in an operating room nurse (Calero and Brusis, 2003).

It has also been suggested that noxious gases from laser and IPL hair reduction odour might reach toxic levels and affect the health of regular users (see laser hair reduction plume risks below).

The long-term cumulative effects of inhaling potentially harmful plumes from laser and IPL use are unknown.

Evaluate the risks and decide on precautions

The law requires practitioners to do everything that is 'reasonably practicable' to protect people from harm. The easiest way is to compare current practice with established good practice.

The UK HSE published a list of workplace exposure limits for potentially harmful plumes for use with the Control of

Table 2. Standards for respirators in the EU and US			
EU: European Standard EN 149:2001 + A1:2009		**US: National Institute for Occupational Safety and Health standards**	
FFP1	Minimum filtration – 80% Maximum leakage – 22% May be used as a 'dust' mask	Class N	'Non-oil' meaning that it must be used in an environment where no oil-based particulates are present in the atmosphere.
FFP2	Minimum filtration – 94% Maximum leakage – 8% Used as protection against influenza viruses	Class R	Means that the mask is resistant to oil-based particulates for eight hours.
FFP3	Minimum filtration – 99% Maximum leakage – 2% Protects against very fine particles such as asbestos	Class P	Indicates that the mask is oil proof.
		Rating: 95 99 100	These ratings apply to Classes N, R and P: Filters out at least 95% of particles down to 0.3 microns in size 99% filtration down to 0.3 microns 99.97% filtration

Substances Hazardous to Health Regulations 2002 (HSE, 2020). This list can be used to guide those responsible for controlling exposure to hazardous substances at work. Short-term exposure limits (15 minutes) are set to help prevent effects such as eye irritation, which may occur immediately after exposure, and long-term limits (8 hours) for delayed effects.

Exposure to surgical smoke is considered hazardous and is well-documented in guidance documents (MHRA, 2015; Madan, 2020), regulations and standards (British and International Standards Institution, 2014; CSA Group, 2020; HSE, 2020) and in the scientific and clinical literaturei. A number of measures may be taken to minimise exposure to unwanted plume (see how to minimise plume below).

Record findings and implement them

Putting the results of the risk assessment into practice will make a difference when looking after patients, colleagues and yourself.

When writing down results, keep it simple. For example, 'check the room carbon dioxide (CO_2) monitor before each patient enters the laser treatment area and increase room ventilation if required'.

A risk assessment does not have to be perfect, but it must be suitable and sufficient. Practitioners need to be able to show that:

- A proper check was made (protocol and/or check list)
- It was established who might be affected (perhaps the therapist, patient or an observer)
- All the obvious significant hazards were dealt with, while taking into account the number of people who could be involved
- The precautions are reasonable, and the remaining risk is low
- Colleagues or staff were involved in the process.

Review risk assessments and update if necessary

Regarding risk assessments, practitioners should consider if there have been any changes or any improvements that still need to be made. Furthermore, questions should be considered, including whether other people have spotted a problem. Has anything been learnt from accidents or near misses? Make sure that risk assessments stay up to date.

Laser hair reduction plume risks

A 2016 study analysed plume generated by laser hair reduction therapy, reporting significant airborne contaminants (Chuang et al, 2016) type of laser, the technique used and the body area treated (Eschleman et al, 2017).

An alexandrite laser delivering comparatively short (3 ms), high-energy pulses through free space to tissue with cryogen spray cooling was compared with a diode laser using 30 ms pulses, contact delivery and a laser optical transmission lotion/gel, which resulted in up to 60% lower plume emissions than those measured with the alexandrite laser. Pre-shaving of the treatment area, reduced charring, contact delivery, lower energy density and the use of a cooled transparent gel all appear to mitigate the risk of exposure to airborne contaminants.

In 2016, Chuang et al analysed plume using gas chromatography, following exposure of discarded whole adult terminal hairs to 3 ms pulses of a high-energy alexandrite laser fired through free space. By-products produced in this simulation were compared with US Occupational Safety and Health Administration OSHA permissible limits. Data showed

that limits were exceeded by several hazardous chemicals and gases. US OSHA and the UK HSE maximum permissible limits in EH40/2005 Workplace exposure limits are broadly similar (HSE, 2020).

However, values for harvested and irradiated whole adult terminal hairs in vitro bears little resemblance to the clinical setting where patients are routinely expected to present with the treatment area shaved to the infundibulum or to a maximum stubble height of 2 mm.

To further illustrate the point, Eschleman et al (2017) demonstrated that hair reduction laser plume was reduced by up to 60% compared with alexandrite lasers when a diode laser was used in conjunction with chilled transparent laser lotion, gel or contact delivery and cooling.

Therefore, laser hair reduction service providers should develop a risk assessment that is appropriate for the technology that they are using. An example of a simple risk assessment is given in *Table 1*.

Minimising plume

There are a number of steps that can be easily implemented to minimise the amount of plume in the air.

Increased ventilation

Good practice will always dictate adequate room ventilation for general comfort. An obvious and simple method to reduce plume is simply to open windows, which allows for contaminated air to be replaced by new, cleaner air. However, this method cannot be relied on to reduce contaminants to an acceptable level. The minimum total air exchange rate for the room should be 20 air changes per hour to ensure a safe working environment (CSA Group, 2020).

Use a plume and smoke evacuator

It should be identified if there is a significant risk of exposure to noxious laser plumes through frequent ablative or surgical procedures. Best practice might include the use of a plume scavenging evacuator, with the evacuator nozzle kept as close as possible to the operative site (for example, no greater than the diameter of the nozzle), and respiratory protection by all present in the treatment room. Evidence shows that this is a very important issue—moving the evacuator nozzle only 2 cm away from the laser site can reduce its efficiency by 50%, allowing more particulate material to escape in the local air (International Standards Organisation, 2016).

Such systems use filters that must be changed on a regular basis, with the frequency of change depending on the usage. These filters must be treated as hazardous waste, as they may contain viable bacteria and/or viral particles (Coxon, 2015).

Use high-efficiency particulate air or ultra-low particulate air filtration systems

In facilities where energy-based devices generate plume, the room air is exhausted directly to the outdoors or returned to the air circulation system through a high-efficiency particulate air (HEPA) or ultra-low particulate air (ULPA) filtration unit. HEPA filters are designed to remove airborne particles down to a 0.3 micron size, with an efficiency of 99.95% (British Standards Institution, 2001), while ULPA filters can remove particles down to 0.1 microns to an efficiency of 99.999%.

Good practice requires that, if the hazard cannot be removed entirely where noxious plumes may arise from laser and IPL treatments, measures should be reviewed to control the risks so that harm is unlikely. For example, pre-treatment preparation of the patient, the use of plume-absorbing accessories such as transparent cooling gel, perfluorodecalin (PFD) patches or clear hydrogel sheets, glass slides or cling film, laser beam guards and increased exhaust ventilation of the room, etc.

Ultraviolet-C light

Ultraviolet-C (UVC) light has been used to neutralise viruses in clinical settings for many years (US Food and Drug Administration, 2021). It has also been found that UVC energy was useful in reducing the levels of airborne COVID-19 virus particles (Beggs and Avital, 2020; Nogueira, 2020). Furthermore, Simmons et al (2020) found significant deactivation in the SARS-CoV-2 virus following irradiation with pulsed UVC energy.

However, many UVC systems cannot be used routinely while people are present, because of the hazard to tissues (D'Orazio et al, 2013). Recent developments have produced 'upper-room' devices that irradiate room ceiling spaces with UVC but that result in sub-damage threshold fluences in the 'working area' below (Beggs and Avital, 2020). This begs the question whether such devices would prove efficacious during normal working periods.

An alternative device (Sanispaces 60H, Sanispaces ApS, Denmark) draws room air through a chamber where it is irradiated with a controlled dose of UVC and ozone to deactivate viruses and resistant bacterial contamination most efficiently. The unit can be used in any working area where people are present, without any risk of unwanted tissue damage, on a 24-hour per day basis, if required.

Personal protective equipment

It is important to understand the difference between masks and respirators. Surgical masks are medical devices that are designed to reduce the transmission of particles larger than 5 microns from the wearer (Barrett and Garber, 2003). Masks are specifically designed to minimise the potential of contamination from exhaled air. Consequently, any infected person who may be shedding viral particles will be less likely to contaminate the local air when wearing a mask (since the viral particles sit on aerosolised saliva droplets >5 µm). However, masks provide relatively poor protection against the inhalation of viruses or bacteria.

Respirators (for example, FFP2/FFP3, N95/N99 or KN95/KN99) are specifically designed to reduce the probability of inhaling potentially hazardous materials, such as viruses and bacteria. These devices must be properly fitted to maximise efficiency. All such devices must comply with the British and European Standard EN 140:2001 and A1:2009 (British Standards Institution, 2001). In the US, all respirators must comply with National Institute for Occupational Safety and Health (NIOSH) standards (*Table 2*).

Conclusions

When working in clinical situations where significant levels of plume may exist, respirators should be worn by staff and surgical masks be worn by patients whenever possible.

All of the aforementioned methods should be implemented to reduce the amount of plume in any working area, in addition to PPE and standard hygiene policies. While these techniques may not reduce the total amount of airborne particulate and noxious gases to zero, they can significantly minimise the risk of inhalation of unwanted contaminants and, therefore, the risk of cross-infection.

Health and safety in all clinical situations is everyone's responsibility, especially in these unprecedented times. Extra precautions are now necessary to minimise the cross-infection potentials that currently exist. This requires a more robust assessment of the possible hazards, including plume contaminants and airborne aerosolised viruses.

While PPE provides some level of protection, it cannot be relied upon to ensure suitably high levels of filtration alone. Technology, such as HEPA and ULPA filtration systems and UVC devices, should be seriously considered to reduce potential exposure to hazards for staff and patients alike.

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BRIEF REPORT

Resumption of laser/IPL skin services post COVID-19 lockdown—British Medical Laser Association (BMLA) guidance document

Vishal Madan [1,2]

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Abstract

The COVID-19 pandemic has had a significant negative impact on the global health economies. As health care resources have been prioritised to cater for patients affected by COVID-19, routine health care services have remained suspended. In an effort to slow the spread of SARS-CoV-2 virus, the UK introduced a country-wide lockdown which came into effect on the 23rd March 2020. Since then, clinics offering laser and intense pulsed light services have remained closed for business. As the rate of COVID-19 infection slows, the UK government has issued guidance for lifting of the lockdown in a cautious and phased manner. With this in view and to facilitate safe resumption of laser and intense pulsed light services, the British Medical Laser Services has issued this guidance document, based on best available and current scientific evidence.

Keywords Aerosol · Coronavirus · COVID 19 · Guidance · Laser · Pandemic · Plume · SARS-CoV-2 virus

Introduction

As strategies to relax the COVID-19 lockdown that commenced in the UK on the 23rd March 2020 are being discussed and implemented, many laser practitioners will seek to resume their services after a period of 10–12 weeks.

This document specifically addresses challenges laser practitioners and clinic managers face while reopening their clinics to offer laser and IPL services, taking into account that the reproduction rate 'R0 number' for transmission of COVID-19 is 0.7–1 at the time of issuance of this guidance[1].

Several clinics offer a complement of aesthetic treatments of which lasers and IPL form a component. As this document specifically addresses the challenges in resumption of laser/IPL skin services, the reader should refer to general guidance/publications issued by other organisations such as the Joint council for cosmetic practitioners on commencing non-laser treatments and non-dermatological laser/IPL services (https://www.jccp.org.uk/NewsEvent/covid-19-preparing-for-return-to-work)[2].

Pre-treatment screening

Proper pre-treatment screening should substantially reduce the risk of contact with symptomatic patient displaying the commonest signs and symptoms of COVID-19 infection such as high temperature, new and persistent cough, loss or change to sense of smell or taste[3]. Until such time that antibody testing becomes routinely available, all patients attending for laser treatments should be presumed COVID-19 positive.

Excluded from this document are precursory checks and screening of potential patients for signs of COVID-19, general and COVID-19-specific hygiene in clinic reception etc. which are covered in detail elsewhere (https://www.jccp.org.uk/NewsEvent/covid-19-preparing-for-return-to-work)[2].

Guidance

1. Risk assessment: lasers, aerosols and COVID

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2. Risk management

A. General hygiene
B. PPE
C. Ventilation
D. Smoke evacuation systems
E. Laser equipment

Risk assessment: lasers, aerosols and COVID

Aerosols are particles of respirable size generated by both human and environmental sources and that can remain viable and airborne for extended periods in indoor air[4].

The SARS-CoV-2 virus which is the causative agent of COVID-19 pandemic is thought to spread mainly from person-to-person through respiratory droplets produced when an infected person breathes, coughs, sneezes or talks. Infection with SARS-CoV-2 occurs primarily by inhalation of aerosolised virus or secondarily by contact with droplets and contaminated fomites such as garments, instruments and furniture.

SARS-CoV-2 virus has a size of 0.06–0.14 μm with mean size of 0.1 μm[5]. During a sneeze or a cough or while talking, "droplet sprays" of virus laden respiratory tract fluid, typically greater than 5 μm in diameter, impact directly on a susceptible individual. Alternatively, a susceptible person can inhale microscopic aerosol particles (droplet nuclei) consisting of the residual solid components of evaporated respiratory droplets, which are tiny enough (< 5 μm) to remain airborne for hours, particularly in enclosed spaces with poor or no ventilation[4].

Lasers and intense pulsed light (IPL) treatment of tissues generates plumes and aerosols which include both combustion and non-combustion-generated products including tissue(s), gases, particulate materials, steam and carbonised material (smoke). All ablative and non-ablative laser procedures can generate potentially hazardous plumes.

In a recent study, gas chromatography-mass spectrometry of plume during laser hair removal showed presence of 377 chemical compounds comprising suspected carcinogens and environmental toxins[6]. Ablative laser-generated plume has been shown to contain intact human papillomavirus DNA, viable bacteriophages and viable human immunodeficiency virus[7]. Similarly, micron-sized tattoo ink particles potentially contaminated with aerosolised blood products have been detected following laser tattoo removal[8].

Results of polymerase chain reaction (PCR) and viral RNA testing for SARS-CoV-2 from blood samples of most patients with COVID-19 infection have been negative and viraemia is very uncommon[9]. This is an important finding which should reassure practitioners that the risk of viable SARS-CoV-2 in aerosol generated from laser treatments of asymptomatic COVID-19 patients should be very low. As of date, no studies looking at SARS-CoV-2 viral RNA on intact skin or hair follicles or the effect of laser treatments on viral particles have been published. For this reason, all laser treatments should be considered potentially COVID-19 aerosol-generating procedures (AGP) and all necessary precautions should be followed.

Based on the above, and until such time that evidence to the contrary is available, one could assume that the main route of COVID-19 infection in laser/IPL procedures remains patient-generated respiratory aerosol but still considers laser-generated plume/aerosol as potentially infective.

Risk management

General hygiene and enhanced infection control procedures In any setting, hand hygiene remains the most important defence against spread of COVID-19. Practitioners should also focus on surface decontamination procedures. These form the basis of reduction of virus transmission. Guidance regarding this is freely available[2, 3].

PPE—personal protection equipment comprises face masks, gloves, gowns/aprons, face shields and caps Barrier precautions such as masks and respirators are regarded as the last line of defence against viral transmission secondary to hand washing and other hygiene measures. In the case of laser/IPL treatments, proper eye protection is imperative and should not be ignored. Resources detailing correct methods of donning and doffing of PPE are freely available[10].

Face masks and respirators

Face masks protect against aerosol spread from inside out. They are tested in the direction of expiration (from inside to outside). They offer minimal protection to the wearer from inhalation of droplets. Face masks can simply be classified as surgical and non-surgical. Surgical masks worn by the practitioner protect the patient and the environment (air, surfaces, equipment, surgical site). If worn by patients, they prevent contamination of the patients' surroundings and environment. Standard surgical masks offer no protection to the practitioner undertaking laser procedures. If available, surgical masks or three ply cotton masks should be offered to patients undergoing non-facial laser procedures.

Filtering facepiece respirators (FFP), which are sometimes called disposable respirators protect from aerosol inhalation. FFP are tested in the direction of inspiration (from outside to inside). The tests take into account the efficiency of the filter and leakage to the face. FFP are subject to various regulatory standards around the world. FFP2 and FFP3 conform to EU standard EN149:2001. The FFP3 standard is often considered broadly equivalent to the US N99 standard and Chinese KN99 standard. The FFP2 standard is often considered broadly

equivalent to the US N95 standard and Chinese KN95 standard.

Respirators are often more comfortable for the wearer when fitted with a valve exhalation feature, but this feature has the effect of elevating wearer safety over that of patients and others in the vicinity, and therefore is generally discouraged (Table 1)[11].

The World Health Organisation recommends that health care workers should wear a particulate respirator at least as protective as a N95/ FFP2, or equivalent, when performing aerosol-generating procedures on patients suspected or confirmed of being infected with COVID-19[12].

The BMLA also recommends that until proven otherwise, all patients should be considered suspected of being infected with COVID-19. All practitioners should wear N95 respirators as a minimum when undertaking any laser or IPL procedures. This should in addition be complemented by a reusable cleanable face shield. For all above-clavicle procedures, where risk of exposure to patient-generated respiratory aerosol is higher, where available, FFP3 respirators should be used instead (Chart 1**).**

Practitioners should be fit-tested for all respirators and should receive PPE training comprising proper hand hygiene practices, correct fit, donning and doffing to avoid cross-contamination(https://www.hse.gov.uk/respiratory-protective-equipment/fit-testing-basics.htm).

Concerns about availability and costs of respirators should be taken into account. Unlike surgical masks which are single use (3–8 h maximum), FFP can be reusable or disposable. While the BMLA does not recommend extended use or reuse of disposable FFPs, when availability is an issue and, if unavoidable, it may be possible to extend the life of single use FFPs. The use of reusable, cleanable face shields may enhance the life of single-use FFPs. Thorough decontamination and safe storage of FFP are incumbent upon the user and are beyond the scope of this guidance. Practices ranging from UV radiation (260–285 nm), 70 °C dry heat, 70% ethanol and vaporised hydrogen peroxide (VHP) can reduce SARS-CoV-2 on N95 respirator with VHP treatment exhibiting the best combination of rapid inactivation of SARS-CoV-2 and preservation of N95 respirator integrity[13, 14].

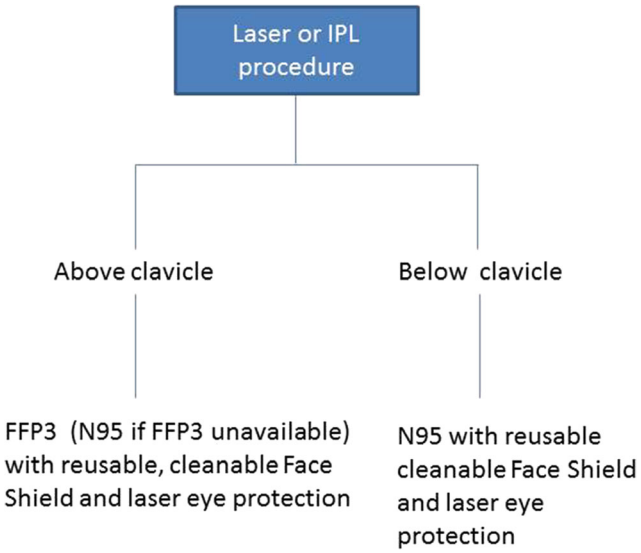

Chart 1 Recommendations for facial personal protection equipment during laser/IPL procedures

Ventilation

As the SARS-CoV-2 spreads mainly through aerosol during AGP in enclosed spaces and as particle aerosol (< 10 μm) remains airborne for long durations in the laser treatment room and adjacent rooms, adequate ventilation is important to ensure appropriate air handling, containment and evacuation of contaminated air[15].

Table 1 Differences between FFP2 and FFP3 filtering face piece respirators (source; https://www.finder.com/uk/ffp2-vs-ffp3-face-masks] FFP2 FFP3

	FFP2	FFP3
Example		
Conforms to	EUROPE: EN 149:2001+ A1:2009	EUROPE: EN 149:2001+ A1:2009
Minimum filter efficiency requirement	94%	99%
Filter efficiency tested using	Sodium chloride and paraffin oil	Sodium chloride and paraffin oil
Filter efficiency test flow rate	95 l/min	951/min
Filter efficiency test particle diameter	0.3 μm (approx.)	0.3 μm (approx.)
Maximum total inward leakage requirement	8%	2%
Maximum permitted inhalation resistance	0.7 mbar at 301/min 2.4 mbar at 95 l/min	1.Ombar at 30I/min 3.0 mbar at 951/min
Maximum permitted exhalation resistance	3.0 mbar at 160I/min	3.0 mbar at 1601/min

Standard in-room air cleaners alone are not effective at protecting staff and preventing the spread of COVID-19. A HEPA (high-efficiency particulate air) filter uses mechanical filtration to remove airborne particles greater than or equal to 0.3 μm in diameter at a minimum 99.97% efficiency and such filters are used in vacuum cleaners and in office buildings air management systems. Used alone, they are not adequate for medical practices.

ULPA (ultra-low particulate air) filters offer up to 99.9995% efficiency on particles down to 0.12 μm. ULPA filters in air filtration systems and ductless fume hoods may help drawing in the airborne drops to capture and remove most of them from the airflow.

Where possible, air conditioning units should be serviced and set at exhaust to extract air from the room to outside the building rather than in air circulation modes. If required, air filters should be replaced in line with device manufacturers' recommendations. Negative-pressure rooms help control the spread of airborne-transmitted infections in health care facilities such as hospitals, but will not be readily available in high street clinics. If available, laser treatments should ideally be undertaken in negative pressure rooms[11].

Smoke evacuation systems

Smoke evacuation systems are useful to reduce aerosol and plume generated during laser procedures but should be considered as an adjunct to hand hygiene, PPE and adequate ventilation. Laser smoke evacuation systems should have sub-micron filtration capability. Several smoke evacuation systems exist in the market but all offer certain common features such as ULPA filters and minimum flow rate of 25 cfm (cubic feet per minute) with variable flow rate to accommodate various levels of smoke.

Some devices offer multistage filtration to ensure adequate removal of all contaminants. Charcoal filter comprises activated charcoal which absorbs gas and vapour. It helps in elimination of strong-smelling gases such as those released from laser hair removal. The optimised primary HEPA filter collects over 99.9% of all vaporised tissue and secondary ULPA filter removes solid and biological particles down to 0.01 μm[16, 17].

It is important that smoke capture device (e.g. smoke evacuation pencil capture port, tubing) is positioned as close to the surgical site as possible to effectively collect all traces of surgical smoke. It has been shown that when the smoke extraction tip is moved only 2 cm from the treatment area, up to 50% of the particulate matter escaped into the local environment[18, 19]. Used smoke evacuator filters, tubing and wands must be handled using standard precautions and disposed of as biohazardous waste[20].

Smoke evacuation systems should be serviced as per manufacturer's recommendations to ensure that they function at maximum efficiency.

Laser equipment and treatments

Prior to resuming clinical services, practitioners much endeavour to switch on the lasers to check for any faults that may be addressed in good time. Additionally, as the lockdown has lasted for well over 10 weeks, it would be prudent for practitioners to spend some time for reorientation with laser protocols.

As SARS-CoV-2 can persist on inanimate surfaces such as metal, glass or plastic for up to 9 days, cleaning of laser equipment, display unit, hand pieces, guiding tips, patient goggles and practitioners' laser eyewear should be meticulously decontaminated after every treatment and as per manufacturer's recommendation[21]. SARS-CoV-2 is efficiently inactivated by surface disinfection procedures with 62–71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 min. Practitioners must refer to manufacturer-issued COSHH advice to ensure safety of use of these products on laser equipment[21].

Although COVID-19 is not known to transmit through skin, pre-treatment skin cleansing should be meticulous as per local guidelines to reduce aerosolisation of the virus, if present on treatment site.

Additional measures can be employed to reduce the aerosol generation during laser treatments. To avoid the excessive dispersal of aerosol and plume during laser treatment, wherever possible, positive cold air flow used during laser treatments for the purpose of skin cooling should be substituted by alternative methods such as gels and disposable ice packs, which should in turn be appropriately disposed of as clinical waste and sapphire tips thoroughly cleansed post-procedure. It has been demonstrated that cold sapphire skin cooling with gel suppresses plume during laser hair removal[22].

Similarly, use of hydrogel packs or cling film can reduce tissue splatter and aerosolisation during laser tattoo removal[23].

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Not applicable.

Declaration of interests Vishal Madan servers as honorary president of the British Medical Laser Association.

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Summary Aerosols can carry viruses—these can be generated by coughs, sneezes and talking.

Laser/IPL procedures may also generate aerosols.

All patients should wear surgical masks (or similar) when in the clinic.

All laser/IPL operators should wear FFP2/N95 or FFP3/N99 respirators during treatments, preferably with face shields.

High efficiency smoke evacuation systems should be used to reduce plume generated during laser procedures.

All equipment and work surfaces should be decontaminated between procedures.

Good air ventilation should be used to clean the air between patients.

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LETTER TO THE EDITOR

Back-scattered light during laser-tattoo removal treatments is hugely significant

Michael J. Murphy [1]

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Laser energy can be dangerous to the retina, particularly invisible wavelengths which will not stimulate the 'blink response'. Healthy skin naturally reflects up to around 5–7% of any incident light energy—diffuse Fresnel reflections due to the change in refractive index between air and the skin [1]. However, a significant amount of additional light energy can come from back-scattered radiation which leaves the skin in all directions.

Wearing the appropriate laser safety glasses will protect users from any harmful exposure. But how much power would a laser operator's eyes be exposed to if they were not wearing the correct glasses, assuming no major absorbers in the skin?

There are two stages to this calculation—firstly, the reflected/back-scattered light power emanating from the treatment site; secondly, the amount of this power entering the eyes. This method will calculate the maximum possible exposure. In reality, targets within the skin, such as (oxy)haemoglobin, melanin, water or tattoo ink, will absorb some of the light energy before it can be back-scattered.

With a typical Q-switched laser using standard outputs to treat tattoos (energy of 1 J in a 5-mm spot diameter with a 10-ns pulsewidth), the power per pulse directed at the skin may be routinely up to 100 million W. This may be considerably higher with some current picosecond lasers. The reflected power, solely due to Fresnel reflections, is around 5 to 7 MW.

Assuming the operator's eyes are, on average, between 50 and 100 cm from the treatment site, then, the light emanating from the skin fills a hemisphere of surface area 2π*(distance) [2] which is 15,700–62,800 cm^2. Hence, the average power per unit area at this distance is simply the reflected power divided by the surface area of the hemisphere, in the range 80–318 W/cm^2 (in reality, this distribution will not be homogeneous across the surface, but this first approximation will do for this analysis). These values exceed the maximum permissible exposure (MPE) for the eyes for some wavelengths between 400 and 1400 nm (according to BS EN207 [2]). As a comparison, on a clear day, the amount of sunlight reaching the Earth's surface at noon can be around 1000 W/m^2 (0.1 W/cm^2).

If we take the human eye pupil diameter with a maximum of 7 mm, then, the aperture of an eye is approximately 0.385 cm^2. Consequently, the amount of laser power entering an eye, due to Fresnel reflections, is simply the reflected light power per unit area leaving the skin surface (in all 'upward' directions) times the aperture area of the pupil which equals around 31 to 123 W in each eye, per pulse. While this may not sound like much, the light entering the eye from a standard, domestic 100-W light bulb is around 1.2 mW, at a distance of 50 cm, and 0.3 mW at a distance of 100 cm.

However, this assumes that the only light energy leaving the skin are Fresnel reflections. This is not true since back-scattered light will also leave the skin surface, into a hemisphere. Most back-scattered light originates in the dermis where photons undergo many deflections as they interact with tissue and water molecules [3]. Some of these end up turning sufficiently to leave the skin. Recent Monte Carlo calculations, in an 8-layer skin model, by PA Torstensson (unpublished data) show that the amount of laser power back-scattering from the skin is significant—up to 59.4% at 755 nm, 55.5% at 1064 nm, and 29.1% at 532 nm (these percentages are of the remaining light power entering the skin after deducting the Fresnel reflections and assuming no major absorbers in the skin).

This reveals that back-scattering is a serious issue when considering eye protection.

The curves in Fig. 1 show the maximum amount of power which can enter the eye when the pupil diameter is 7 mm. This indicates that up to more than 1590 W of laser power may enter each eye from reflected and back-scattered light, at 755

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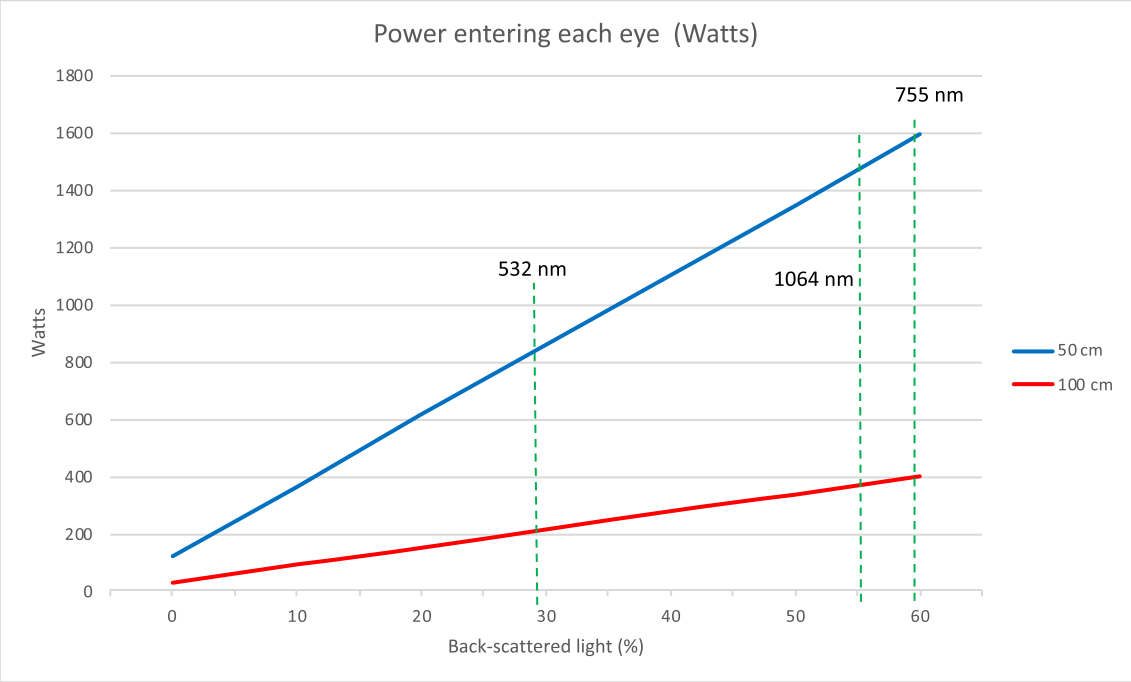

Fig. 1 The power entering an eye from Fresnel and back-scattered Q-switched laser light for two distances from the skin, 50 and 100 cm

nm. With visible wavelengths, this would be immediately obvious (see Fig. 2). However, with invisible Q-switched or picosecond laser light such as 755 nm (alexandrite), 1064 nm, and 1320 nm (Nd:YAG), this becomes a potentially serious issue, especially at close quarters.

It is known that exposure to high levels of visible and near-infrared (400–1400 nm) laser energy can lead to flash blindness or retinal burns [4] since most of the energy in this wavelength range is transmitted to the retina. The absorption of such energy may result in a rise of anything from less than 1 °C to several hundred degrees Celsius, depending on the incident energy and pulsewidth of the light source.

Some laser users have reported having painful eyes or heads after a laser treatment session. This usually indicates an issue with their safety glasses. It has been my experience that such users are wearing the wrong glasses, or none at all.

There are at least three situations when exposure to these high power levels may be a problem—wearing glasses with the wrong safety specifications; wearing damaged safety glasses; or wearing no glasses. In each case, the eye will be liable to damage, especially as retinal cellular damage will accumulate over a sequence of laser pulses (in the wavelength range 400–1400 nm[4]). With some tattoos, thousands of shots may be fired in a single session. If the user is not properly protected, they will most likely experience accumulative and permanent ocular damage.

These calculations show that the amount of light energy which may interact with the operator's eyes or skin can be higher than previously thought, and hence, higher levels of protection may be necessary, especially with invisible outputs. They also indicate that the amount of energy retained by tissues, such as the skin, or its components, may be lower than previously calculated.

Fig. 2 Reflected and back-scattered Q-switched laser energy at 532 nm during a treatment of a tattoo. The extreme intensity of this green light without the use of any safety filters is clearly obvious

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High Speed Ink Aggregates Are Ejected from Tattoos During Q-switched Nd:YAG Laser Treatments

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Introduction: Dark material has been observed embedded within glass slides following Q-switched Nd:YAG laser treatment of tattoos. It appears that these fragments are ejected at high speed from the skin during the treatment.
Method: Light microscopic analysis of the slides reveals aggregates of dark fragmented material, presumably tattoo ink, with evidence of fractured/melted glass. Photomicrographs reveal that the sizes of these aggregates are in the range 12 μm to 0.5 mm.
Results: Tattoo ink fragments were clearly observed on the surface and embedded within glass slides. Surface aggregates were observed as a fine dust and were easily washed off while deeper fragments remained *in situ*. The embedded fragments were not visible to the unaided eye. Some fragments appeared to have melted yielding an "insect-like" appearance. These were found to be located between approximately 0.2 and 1 mm deep in the glass.
Conclusion: Given the particle masses and kinetic energies attained by some of these aggregates their velocities, when leaving the skin, may be hundreds to thousands of metres per second. However, the masses of the aggregates are minuscule meaning that laser operators may be subjected to these high-speed aggregates without their knowledge. These high-speed fragments of ink may pose a contamination risk to laser operators. Lasers Surg. Med. © 2018 Wiley Periodicals, Inc.

Key words: bacteria; contamination hazard; glass slide technique; high speed ejected particles; laser tattoo removal; Q-switched Nd:YAG laser

INTRODUCTION

Q-switched laser removal of tattoos is a well proven technique since its inception in the 1980s [1–8]. A number of processes occur around the ink aggregates which are induced by absorption of the laser energy. One reaction results in the generation of a photoacoustic shockwave, causing the brittle ink aggregates to fracture. (Note, in this report "particles" refer to individual ink particles, around 10–40 nm in size, while 'aggregates' refer to clumps of these particles).

Plume or splatter, has been observed throughout the years since laser treatment of tattoos was first investigated [1,7–12]. Goldman and Kitzmiller [11,12] observed plumes from tattoos treated with normal mode ruby and Nd:YAG lasers and a Q-switched ruby laser, in the late 1960s, and suggested that this was the method of tattoo removal. Splatter had also been identified previously by other researchers including reports of expelled viable cells/tissues following laser treatments of other clinical targets [13,14].

One study found potentially harmful particles of material including hydrogen cyanide, benzene, and aerolized biological matter from bacteria and viruses in plume [15,16]. Indeed, petechiae is a relatively common occurrence although it was originally thought to be due to photomechanical disruption of the papillary vessels during treatment [8,17]. Various splatter "guards" have been used as barriers to prevent potential cross-infection between patients and laser operators including acetate films [7] and commercially available products such as Tegaderm® [7,18], Second Skin® [18] or Vigilon® [10], and, more recently, perfluorodecalin-infused patches [15,16]. Clearly these guards were used to "protect" the laser operators during treatments suggesting that they had concerns about the contents of the splatter. This study will show that tattoo ink aggregates are also leaving the skin during these treatments with a Q-switched Nd:YAG laser.

The "glass slide technique" was discussed in the QS Nd:YAG laser treatment of tattoos by the author in 2014 [19]. This technique reduces the perception of pain reported by patients during treatments due to compression of the skin in the treatment area during application of the laser energy. In addition, the compression also reduces capillary damage [20] and petechiae (due to the blood being occluded within the capillary plexus in the papillary dermis during compression), epidermal disruption, and post-treatment oedema. Disruption of capillaries was observed by Taylor [8] during Q-switched ruby laser treatment of tattoos and by Ferguson and co-workers [17] during Nd:YAG laser treatment of black tattoos. Light microscopy revealed rupturing of capillary vessels in an "upward" direction without any evidence of thermal coagulation or wall necrosis, suggesting a mechanical process was occurring. This appears to agree with the idea

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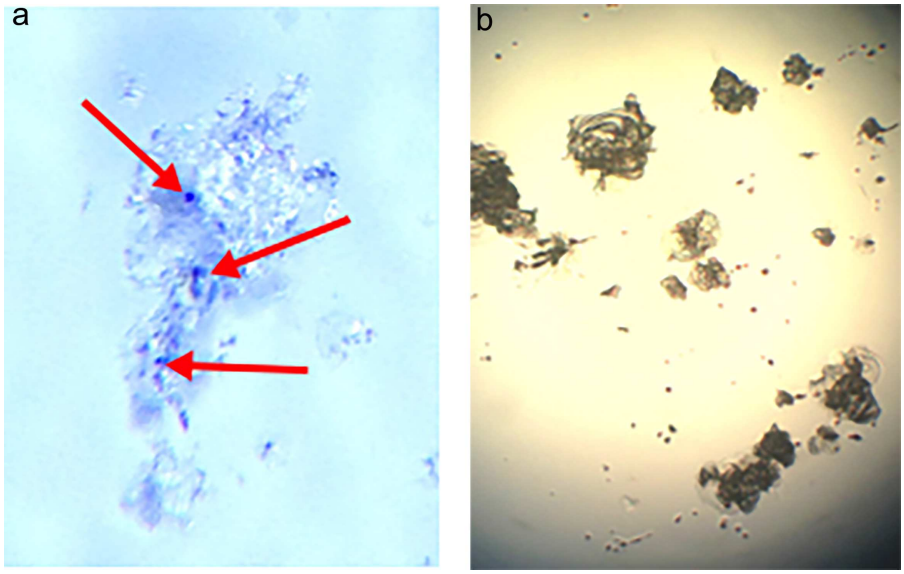

Fig. 1. Glass slide with pitting marks under light microscope with magnifications at ×60 (a), and at ×47 (b). The dark dots in (a) are tattoo ink fragments. The pits were typically found to be between <0.1 and 1 mm in size.

that some ink aggregates are perforating vessels following an explosive reaction within the deeper ink fragment surfaces.

However, following a number of treatments during the original study [19] the author noticed "pitting" on some of the glass slides (Fig. 1). The purpose of this subsequent study was to determine the origin and contents of these pits in the slides used in the original study.

The pits were originally assumed to be due to physical stresses in the glass caused by the very high optical irradiances at 1064 nm (typically 3.5–5.1 J/cm^2 in an 8 ns pulsewidth yielding an irradiance range of 440–640 MW/cm^2) impinging upon the slide. This was found not to be the case, however, when the slides were exposed to the same irradiances with the slides positioned above non-tattooed skin or plain white paper. In addition, the pitting only occurred on the surfaces which were in contact with tattooed skin.

None of the embedded ink aggregates within the glass slide were visible to the unaided eye. Given that the resolution of the human eye is around 40–50 μm, this indicates an upper limit on the size of the aggregates embedded within the glass. Further evidence of the origins of these pits can be clearly seen in Figure 2 where

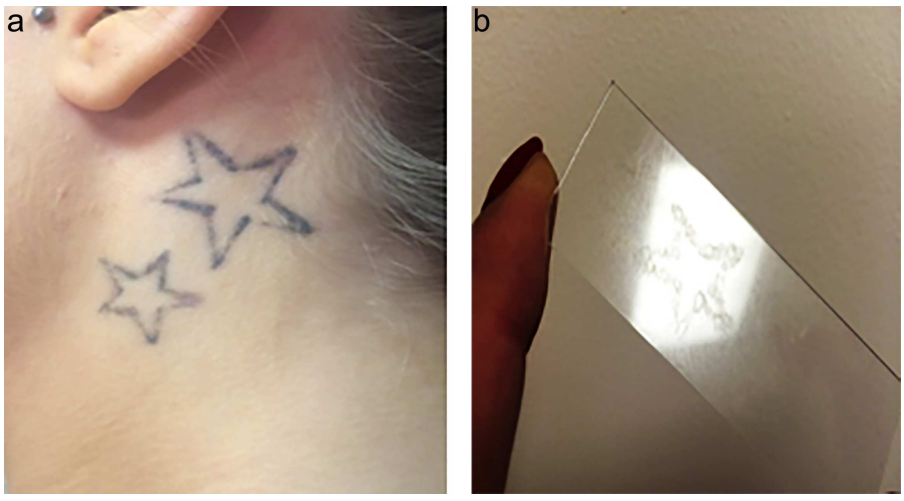

Fig. 2. The glass slide exhibits an "image" of the original professional tattoo following treatment using the "glass slide technique." The dark particles on this slide were clearly on its surface as they were easily washed off. These particles had not penetrated into the glass. (Photographs used with the kind permission of Lesley Murphy).

the glass slide used to treat the tattoo showed an "image" of the treated tattoo on its surface (4.5 J/cm^2, 4 mm spot diameter, 1064 nm, Fitzpatrick skin type 2, 26 y.o. female, first treatment).

MATERIALS AND METHODS

More than 60 slides from the original study [19] were studied for evidence of pitting. Of these, 23 slides were chosen for further microscopic examination as each showed indications of embedded ink aggregates. A GS S.E.R.B. P2 light microscope with a range of magnifications between $\times$47 and $\times$70 was used to study the pits more closely. The depths of the pits were estimated from visual inspection through the side of the slides with a back-light to highlight the deformations. Their impact crater areas were calculated from taking measurements of the surface deformations using the microscope's built-in graduation marks (spaced at 12 μm intervals). It was noted that a large variation in pit areas was observed indicating a large range of impact energies, as should be expected.

RESULTS

Figure 3 shows photomicrographs of tattoo ink within the glass slides. Figure 3a displays a large range of fragment sizes on the glass surface with both very small clumps and larger, aggregated masses ranging in dimensions from less than 12 μm to more than 500 μm, while Figures 3b–e show "smeared" patterns (the image resolution at this magnification is approximately 12 μm).

Figure 3c–e show the same site at different depths of focus revealing the difference in penetration distances between aggregates. It is interesting to note the resemblance of the "smeared" aggregates with insects. However, it is difficult to gauge the size of the ejected aggregates as they likely disintegrate or melt on impact with the glass.

The smeared "insects" were all deep within the glass, with none detected on the surfaces. Their depths ranged between 0.2 and 1 mm, approximately, and they ranged in dimensions from $<$0.05 mm to approximately 0.9 mm across (measured using the optical microscope).

The "insect-like" patterns appeared only within those slides where a tattooed area had been irradiated. They did not appear at all in unused slides, nor in the slides which were tested over non-tattooed skin. This clearly indicates that these marks are created as a result of the laser energy interaction with tattoo ink. However not all slides exhibited evidence of tattoo ink ejecta (only around 35% of the tested slides showed embedded ink particles), indicating the lower kinetic energies of those flying fragments.

DISCUSSION

Optical microscopic analysis revealed that the pits ranged from $<$100 μm up to 1 mm in size, and were created by the impact of high energy particulate matter (Fig. 1a). All of the pit marks were clearly on the surface of the glass. This is easily confirmed with the use of a fingernail. It is highly unlikely that human skin tissues would be sufficiently hard to scratch the surface of the glass slides. (Note, that the depths of these pits were not accurately measureable in this study—only a visual inspection was used). In every examination (more than 60 sites) the only colour observed was black, regardless of the colour of the treated tattoo ink, except in one instance when a distinct blue colour was observed. The lack of other colours may be due to their relatively low absorption of the laser energy resulting in less aggressive ablation, compared with black ink.

The expansion of tissue water adjacent to the ink aggregates into steam is rapid, and may provide a source of kinetic energy to "launch" smaller ink aggregates throughout the dermis, including through the epidermis. Histological evidence clearly shows tattoo ink aggregates on the surface of the steam bubbles [1,8,17] within the irradiated dermis.

Alternatively, the origin of the ejected ink fragments may be due to the rapid thermal expansion of the dermal ink aggregates during laser energy absorption. In laser welding, the phenomenon of "spattering" is a well-known issue when applying light energy to various materials [21]. The same process may be occurring on the ink aggregate surfaces during laser tattoo removal. Ready [22] describes an experiment where an aluminium target was irradiated with a Q-switched ruby laser pulse at 2 J and a pulsewidth of 30 ns (66.6 MW per pulse). Photographic measurements show that a high velocity plume can be observed leaving the surface of the target at around 10,000 ms^{-1}. This is described as the velocity of expansion of the luminous front of the ionised material. Using a 200 MW Q-switched Nd: YAG laser, the luminous edge of the "blowoff material" was measured at a velocity of 63,000 ms^{-1}. Modern lasers used for tattoo removal can easily exceed peak powers of 200 MW, especially the picosecond variety.

Using a simple, first-approximation calculation of the kinetic energy of the ink aggregates impacting the glass slides, it can be shown that low mass aggregates are impinging on the glass at velocities up to thousands of metres per second (see Appendix, Fig. 4). These calculations are in reasonable agreement with Ready's observations. However, the masses of these aggregates are sufficiently small that they are not readily observed or felt by laser operators. Anecdotal evidence indicates that some laser operators do occasionally feel "impacts" on their necks and lower faces during Q-switched laser treatments, which may be due to these high-velocity ejected ink particles.

Both Taylor [8] and Ross et al. [23] reported a "stippling" of ink aggregates post-treatment using electron microscopy. It was noted that stippling occurred in the superficial region of the dermal ink aggregates. It is possible that this stippling indicates sites where smaller ink aggregates have been explosively removed from the larger aggregates during the rapid thermal expansion phase.

It might appear obvious, with hindsight, that initiating small "explosions" within the skin on the tattoo particle surfaces will inevitably result in high speed ejection of ink aggregates. Tattoo inks may be composed of a wide range of materials including iron oxides, carbon (both black), cinnabar, cadmium (both red), chromium oxide (green), azure, and cobalt blues, lead carbonate (white) plus a wide

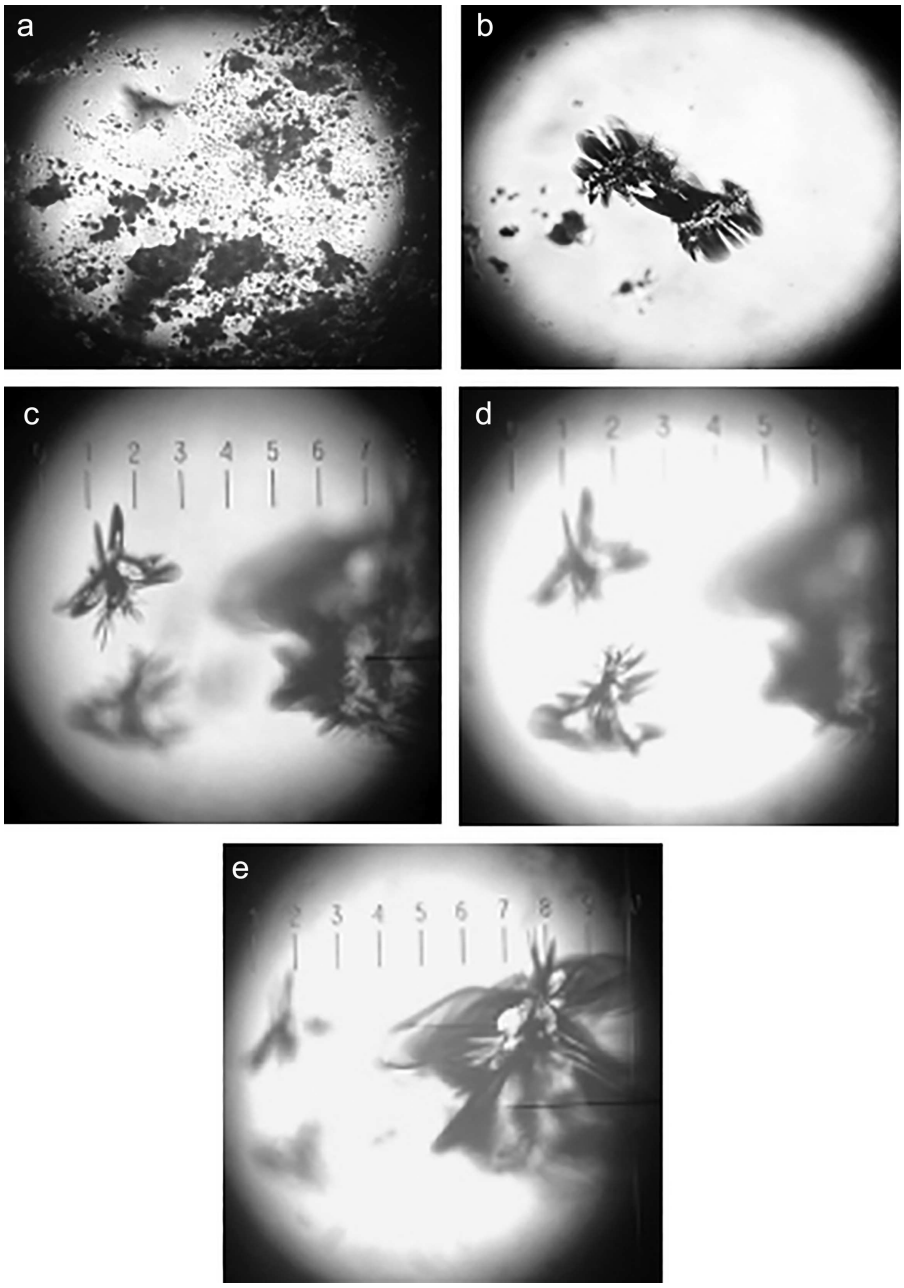

Fig. 3. Microscope images of the pits in the glass slides. The aggregates in (a) range from <0.012 to ≈ 0.5 mm in size. Typical smear patterns (b–e) measured in the range <0.05 to ≈ 0.9 mm (the graduated marks in the above photographs are 0.12 mm apart). All of the above photographs were taken at the same magnification of $\times 70$.

range of other metal salts and plastics. Consequently, tattoo ink has a large range of melting points while glass typically melts in the range 1,425–1,600°C [24].

Microscopic analysis indicates that some of the ejected particles appear to have melted while others remain intact (Fig. 1a). During the energy absorption/photomechanical explosive process some of the ink aggregates will rise in temperature significantly (up to more than 1,000°C [1,8,17]) and will be ejected from the skin. With a sudden deceleration on the surface of the glass slide the kinetic energy will rapidly reduce to zero resulting in a further rise in the aggregates' temperatures, possibly above the melting point of some of the ejected inks (the kinetic energy will be converted into mechanical and thermal energy as the aggregates hit the glass, resulting in the generation of heat, sound, and pressure.)

With at least two independent temperature rises in this process, coupled with the high-pressure impact, it is conceivable that some of the ink will melt within the impact crater, while also potentially melting a region of the impact

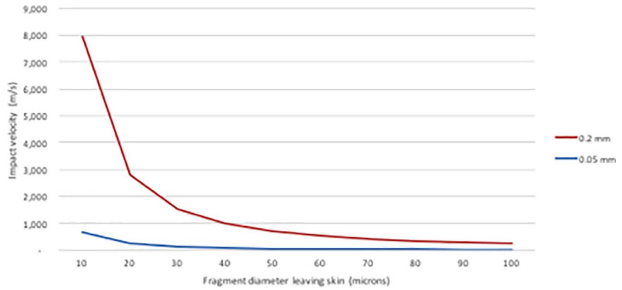

Fig. 4. Impact velocities on the glass slide as a function of penetration depths into the glass slides.

site glass. This may be evident in Figure 5 where the optically distorted peripheral areas appear to indicate a melting and/or fracturing of the glass. The melted ink and glass then mix forming the observed "insects," before the glass rapidly solidifies. Note the significant degree of symmetry suggesting a fairly homogeneous diffusion of ink.

Only around 35% of the tested slides exhibited embedded ink fragments following treatments. Not all treatment sites appear to eject ink particles which may be due to deeper ink targets. These tattoos will receive less energy than superficial ones and, consequently, will generate less powerful explosive photoacoustic reactions, with lower kinetic energies within the fragments. In addition, non-black ink will generate lower kinetic energies due to their lower energy absorption. This may explain why coloured inks were not seen within the slide samples.

CONCLUSION

It appears that "splatter" includes aggregates/particles of tattoo ink and may also carry epidermal and dermal tissue [15,16], including blood, with the high velocity ink particles providing a transmission mode. The possibility of transmitted viable bacterial and viral particles must also be a concern for all QS and picosecond laser operators (although no evidence has been found of this to the author's knowledge, as yet). The use of physical barriers such as Tegaderm®, Second Skin®, and Vigilon® suggests that this concern is not new. However, the speed of ejection of these particles was not previously known and it is possible that these barriers may prove ineffective, under these conditions. It is entirely possible that the high temperatures within the hot ink aggregates destroy the viability of any potential viruses/bacteria. Clearly, further work needs to be done to determine the potential biohazard risk from these ejected aggregates.

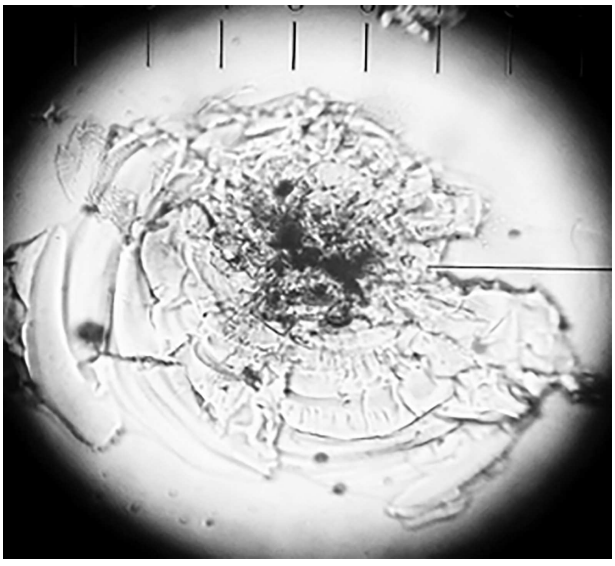

Fig. 5. An impact zone in a glass slide following laser treatment (×70 magnification). The darker areas are ink aggregates with clear evidence of alterations, probably mechanical and thermal, to the glass surrounding the central impact zone.

It appears that the glass slide method [19] may be the best way to prevent possible transmission of these particles. However, a glass "harder" than that used in this study may need to be used routinely to prevent contamination of the treatment site with glass particles from the slides. No patients reported any undue effects or irritations following the use of this technique. One downside to this technique is the extra time required to treat larger areas, using a glass slide, however, with a larger glass slide (55 × 100 mm) this was not found to be significant.

It is probable that, in some cases, ink aggregates may have become embedded in the skin of laser operators. While this may pose a very small probability of cross-infection, it is still a risk. Conventional surgical masks may not offer suitable protection due to the very small size and high speed of the ejected particles. Given that there are currently thousands of Q-switched lasers across the world today, carrying out potentially millions of tattoo removal treatments every year, the risk is very real. The same is true for the newer picosecond lasers which generate higher peak powers than the Q-switched variety.

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APPENDIX

THE KINETIC ENERGY/VELOCITY OF THE ESCAPING AGGREGATES—A FIRST APPROXIMATION:

The following calculations are a first approximation and are based on a number of approximations and measurements. The compressive strain, ε, within the glass slide following ink fragment impact may be calculated from the ratio of the depth of penetration, Δl, of the fragment to the thickness of the slide, l (2 mm). Knowing this and the Young's Modulus, E, of glass (65 GPa) the compressive stress, σ, may be found.

Multiplying σ by the area of the impact zone, A, gives the impact force, F. The product of this force with the depth of penetration, Δl, yields the kinetic energy, KE, of the impact fragment.

Let us assume that the observed black ink particles are carbon ink aggregates, with the density of the carbon as 2,250 kg/m^3. From the dark material in Figure 5 we can see that the aggregates leaving the skin have diameters in the range 1–10 μm (below the resolution of the human eye and, therefore, invisible). Assuming that the aggregates strike the glass and shatter into much smaller pieces, the sizes of the aggregates striking the glass might be in the range 10–100 μm. Assuming spherical aggregates, as a first approximation, this yields aggregates masses of between approximately 1.2×10^{-12} to 1.2×10^{-9} kg.

It was not possible to accurately measure the penetration depth of the aggregates into the glass, but a visual inspection revealed craters with a maximum depth of 0.2 mm. Note that the smeared portions of ink were found to be significantly deeper than this (up to approximately 1 mm).

Knowing the masses we can calculate a range of corresponding impact velocities as a function of the penetration depth according to the equation:

$$v = \sqrt{\left(\frac{2\,E\,A\,\Delta l^2}{m\,l}\right)}$$

where v is the velocity of the aggregates on impact (metres/second), E is Young's modulus for glass (Pascals), A is the area of the impact zone (m^2), Δl is the depth of the impact zone (m), m is the mass of the fragment (kg) and l is the thickness of the glass slide (m).

Note that these calculations are a very simple, first approximation based on relatively low-tech measurements of the samples.

TABLE 1. Parameters Used in the Calculation of Escape Velocities

Δl	0.05–0.2 mm
Fragment size	10–100 μm
Impact area	$8 \times 10^{-13} - 3 \times 10^{-11}$ m^2

Table 1 shows a range of parameters taken from the photomicrographs, which yields a range of impact velocities for the above penetration depths (0.05 and 0.2 mm):

The lower end impact velocities, below 5 ms^{-1}, (which correspond to the larger mass, lower kinetic energy aggregates) will result in minimal surface damage on the glass, if any. This may account for the image in Figure 3a where it appears to show tattoo aggregates on the glass surface. The upper end of these impact velocities appears to be rather high but they are theoretically possible given the explosive nature of photomechanical reactions and the very small mass of the particles. The range of ink fragment masses will inevitably be large yielding a large range of kinetic energies, and hence escape velocities. However, given the number of assumptions in this very rough calculation the actual velocities may be in a much larger range than shown above.

Given that Ready [22] observed velocities around 10,000 ms^{-1} of ejecta from an aluminium target it appears the above calculations are in the same range. It should be noted that these calculations are based on the impact kinetic energies. The kinetic energy of individual ink particles will be higher as they leave the donor site but the surrounding dermal collagen will inevitably absorb some of that energy, thereby slowing down those aggregates.

Research letter

Q-switched 532-nm laser energy causes significant vascular damage in the capillary plexus: how does this affect laser tattoo removal?

DOI: 10.1111/bjd.16130

Dear Editor, Tattoos can be effectively removed using Q-switched and picosecond lasers at four wavelengths: 1064, 755, 694 and 532 nm.[1–4] However, there are two particular problems with the 532-nm line. Firstly, it is well absorbed by the melanin in the epidermis, because of its relatively high absorption coefficient,[5] (μ_{a_mel} = 56 cm^{-1} for typical white skin). Secondly, 532 nm is also strongly absorbed in the oxyhaemoglobin located in the capillary plexus[5] (μ_{a_HbO} = 260 cm^{-1}).

In this small study, I compared the effects of Q-switched pulses using all four of the above wavelengths on nontattooed skin. In particular, the effects of absorption in the blood layer was studied. The results indicate that treatments with 532 nm may be slightly more complicated than first thought.

A Lynton Q+ Ruby/Nd:YAG laser (Lynton Lasers, Holmes Chapel, U.K.) generated the 532-, 694- and 1064-nm wavelengths and a Candela Trivantage Q-switched alexandrite laser (Syneron Candela Corp., Wayland, MA, U.S.A.) was used to generate the 755-nm wavelength. I subjected myself to these tests (Fitzpatrick type 2). Both dorsal forearms were irradiated – the right forearm was treated with all four wavelengths at 10 J cm^{-2} in 3 mm diameter spots, except for the 532-nm wavelength, which was set at its maximum output of 5·5 J cm^{-2}. The left forearm was treated with 532 and 1064 nm at 5·5 J cm^{-2} in 3-mm spots, to compare them directly at the same radiant exposure (fluence).

The 'glass-slide technique' has previously been discussed in 2014.[6] This technique comprises the compression of a tattooed skin site by a standard microscope glass slide through which the laser energy is delivered. Half of the irradiated areas were compressed with a glass slide, whereas the other half were treated directly.

The difference between the sites irradiated with the 1064-, 755- and 694-nm wavelengths and the 532-nm wavelength was marked. The 532-nm sites all instantly displayed the telltale 'whitening' or 'frosting' often seen during laser tattoo removal treatments, much more so than with the other wavelengths. Note that there was no tattoo ink present in any of the above sites and no blood appeared on the skin surface. It is likely that the whitening appearance is mostly as a result of absorption of the 532-nm laser energy by the melanin in the epidermis.[1,7,8]

Twelve minutes after irradiation the initial whitening had faded significantly. However, 3 h after irradiation there was a clear difference between the compressed and the noncompressed spots. The compressed areas showed significantly less erythema and oedema than the uncompressed set. Figure 1 shows the extent of this erythema with a marked rise in the blood-filled spots 48 h after irradiation. Clearly, there is a significant difference between the two sets of spots.

At 48 h there appeared to be only a very marginal difference between the uncompressed and compressed sets of laser irradiated spots with the 1064-, 755- and 694-nm wavelengths. Only the 532-nm spots showed any obvious difference, with significantly more sub-surface vascular damage occurring in the uncompressed skin regions. This is because of the relatively low absorption coefficients for 1064, 755 and 694 nm compared with 532 nm in blood.[5] This indicates that much of the incident 532-nm laser energy is absorbed by the blood layer leaving significantly less energy available to deeper levels, where large amounts of tattoo ink may be located.[1,2,7,8]

The use of 532 nm is commonplace in laser tattoo removal. The cumulative absorption of this wavelength in both melanin and blood reduces the total amount of energy that can reach the reticular dermis, while also mechanically damaging melanin granules and capillary vessels.[2,7,8]

Compressing the skin with glass slides appears to be sufficient to occlude many of the vessels in the superficial capillary

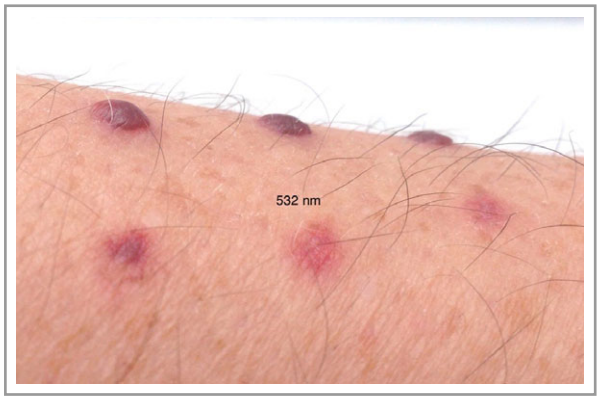

Fig 1. Irradiation spots 2 days after 532-nm laser energy irradiation of nontattooed skin. The upper set of spots were irradiated without the use of the glass-slide compression technique, and the lower set were the compressed areas (5·5 J cm^{-2}, 3-mm diameter).

plexus. By doing so, the 532-nm laser energy absorption in blood is reduced significantly as can be seen in the 'compressed' irradiated spots (Fig. 1), leaving more energy available for deeper targets. Anecdotal evidence from the patients also appeared to indicate enhanced healing rates following treatment using the glass slide method.

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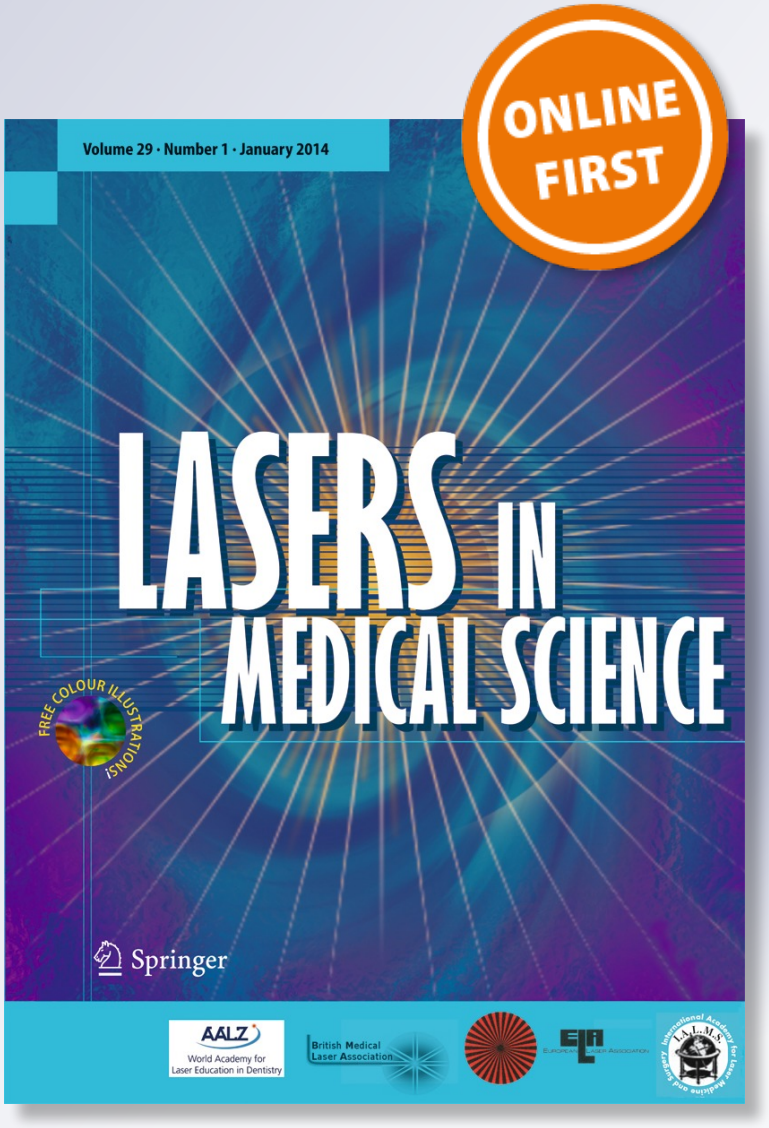

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ORIGINAL ARTICLE

A novel, simple and efficacious technique for tattoo removal resulting in less pain using the Q-switched Nd:YAG laser

Michael J. Murphy

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Abstract A new yet simple technique has been tested on patients seeking tattoo removal by Q-switched Nd:YAG laser based on an observational study. The technique involves application of a glass microscope slide on the treatment area with a firm pressure to compress the skin which results in evacuating the blood from the capillary plexus. Results from a survey of 31 patients revealed that most felt less pain and reported less epidermal damage post-treatment. This new technique is easy to apply and inexpensive, using standard, conventional Q-switched lasers.

Keywords Nd:YAG laser · Tattoo removal · Pain reduction · Q-switched · Glass slide

Introduction

Q-switched lasers have been routinely used for tattoo removal since the mid-1980s when the ruby laser was found to generate excellent scar-free results [1–5]. Since that time, many of these lasers have been used all around the world on many thousands of patients. Three types of QS laser have been found to be useful for this application—the ruby, neodymium yttrium aluminium garnet (Nd:YAG) and alexandrite [6–12]. Each has its advantages and disadvantages [8–10].

Previous attempts to reduce the pain sensation include the application of topical anaesthesia and a vacuum technique [13, 14]. Both of these techniques have yielded limited results.

This report will detail a simple and effective technique which has a number of significant benefits for patients. This technique involves the use of standard microscope glass slides placed over the tattooed area with a moderate pressure applied to the skin. The laser energy is then fired through the glass slide to the ink beneath. Note that no difference in the efficacy of the treatment was observed using this new technique.

Materials and methods

Before each treatment, the tattooed area and the glass slide were cleaned with alcohol swabs to remove any surface dirt and hence improve optical coupling.

Immediately prior to the treatment, a thin layer of a water-based gel (ECG Gel from Camcare Gels, Ely, Cambridgeshire, UK) was applied to the skin surface. This was applied to minimise reflection losses between the glass and the skin surface (due to index mismatching). In addition, the water gel fills some of the air gaps found in the stratum corneum, making it more optically conductive.

A fresh microscope glass slide (IMED Microscope Slides; clear glass, 1–1.2-mm thick) was then placed on the surface above the tattoo and firmly pressed against the skin to compress it during the treatment. A DermaLase DLY600 Q-switched Nd:YAG laser was used to treat the tattooed sites using the 1,064-nm wavelength with a fluence range of 3.5–5.1 J/cm^2 in a 5-mm spot diameter and a pulse width of 8 ns, with a repetition rate of 6 Hz.

Patient survey results

A short survey was carried out on 31 patients who had been subjected to the treatment with and without the glass slide in the same treatment session. All patients were from the West of Scotland and presented skin type 2 or 3 (according to the Fitzpatrick scale) with 12 males and 19 females in an age range from 18 to 53 (mean age of 35.5). Of the tattoos, 94 %

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were professionally applied, and the majority, 62 %, were blue/black with a smaller number presenting colours such as red, green, light blue and purple. Patients were typically treated at 4 to 6-week intervals (note, no anaesthesia was used in any of these treatments).

Each patient was asked to rate their opinion on the pain sensation on a scale of 1 to 10 (1 being minimal, 10 being maximal) with both the conventional technique and the newer glass slide method, during the same treatment session.

Results

As with any optical transition, there will be a loss of energy due to refractive index mismatching when the laser energy traverses the two sides of the glass slide. Fresnel reflections typically account for around a 4 % loss at each optical surface. Measurements of the energy through the glass slide, with a thin film of gel on one side, revealed an energy loss of 7.8±0.3 %. These measurements were carried out using an Ophir DGHH meter with a detector head designed for nanosecond laser pulses.

In tattoos which have not previously been treated by lasers, there is an immediate whitening of the treated areas. This is presumed to be due to the formation of many minute steam 'bubbles' on the surface of the ink particles [2–5]. Tattoos which have been treated previously may also exhibit whitening immediately after irradiation, but this effect diminishes with an increasing number of treatments.

The most immediate difference between this technique and the previously used conventional technique is a reduction in the sensation felt by the patient. Virtually every patient reported a reduction in the sensation (or pain) felt during the laser application (see Table 1).

Table 1 Results of patient survey with 31 patients

	Pain sensation, mean (SD)
Without slide	6.97 (1.9)
With slide	3.84 (1.8)

Patients were asked to comment on each category on a scale of 1 to 10. In both cases, $p<0.005$ (statistics calculated using Minitab 16 software)

A common occurrence with the older conventional technique is the appearance of punctate bleeding immediately post-treatment, particularly with tattoos with no previous treatment history. This has been almost completely eliminated with the glass slide technique, suggesting less mechanical damage to the capillary plexus and epidermis. This can be explained by the evacuation of blood from the capillaries during the compression by the glass slide.

It is interesting to note that the impact of shattered fragments of ink can be felt during the treatment, through the glass slide. This may be verified by firing at non-tattooed skin where no such impacts can be felt.

In addition, the vast majority of patients (>93.5 %) also reported less epidermal damage and oedema in the weeks following treatment.

Figure 1 shows the raw data from each condition, with and without the glass slide. It is clear that the shift in the data points, when applying the glass slide, to the lower end of the pain scale shows how effective this technique is.

Discussion

The reduction in pain felt by patients during the treatment is statistically significant. Pain is typically caused when the ink

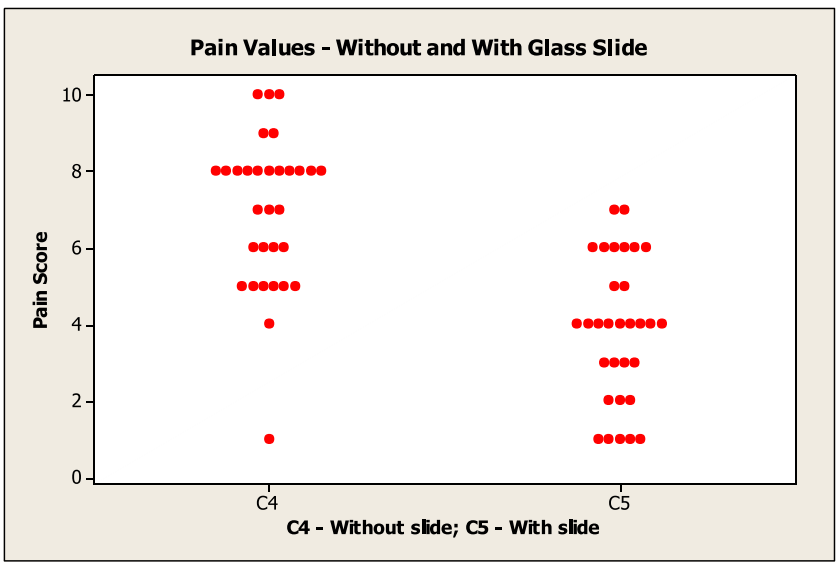

Fig. 1 Distribution of the raw data—the left hand column (*C4*) shows the pain data when the glass slide is not applied, while the right hand column (*C5*) shows the pain data when the slide is applied

particles shatter during the photomechanical reaction induced by the nanosecond pulse. This is easily verified when laser energy is exposed to non-pigmented skin and virtually no sensation is felt (author's observations). In fact, quite often the ink-shattering process can be felt by the operator through the glass slide as a slight 'thud' sensation. By compressing the skin, the pain sensation is reduced as a consequence of "afferent inhibition of pain transmission due to the dermal A-beta fibres being stimulated by the compression force" (Melzack's gate theory [15]).

A technique had been previously developed using a vacuum chamber to minimise pain during treatments [13, 14]. However, this technique involves considerably more expense and technology than the simple glass slide method presented here.

A note of caution must be included—since the laser energy is being fired through a glass slide, there is a potential for around 8 % of the incident fluence to be reflected towards the eyes of the laser operator or patient. While this may initially appear to be insignificant, the reflected power density potentially may be up to 80 MW/cm^2—more than enough to inflict serious damage on the retina. Extreme care must be taken when choosing the appropriate safety glasses to prevent any unwanted ocular exposure.

An interesting, although not clinically significant, observation was the lack of the burning smell usually associated with the vapourisation of surface hair during laser treatments. Clearly, the gel and glass slide 'trap' vapourised particles thereby preventing them from engaging the nostrils of the treatment room's occupants. While this does not add to the efficaciousness of the treatment, it does improve the general atmosphere.

Using the same arguments as above, the glass slide technique may also yield improved results with the Q-switched ruby and alexandrite lasers. It may also help to improve other light-based treatment applications such as the laser/IPL removal of hair, blood vessels and other unwanted tissues/targets plus other applications such as skin rejuvenation and resurfacing, and similar.

Conclusion

Patient feedback was immediate, in particular, with the pain sensation during laser application dropping from a mean of 6.97 to 3.84. This result is very important since many patients find the treatment uncomfortable and can often lead to unfinished treatment programmes.

The reduction in punctate bleeding and epidermal damage was also significant. Not only does this make the whole process more comfortable for the patients but it also ensures a better outcome with less chance of post-treatment infection.

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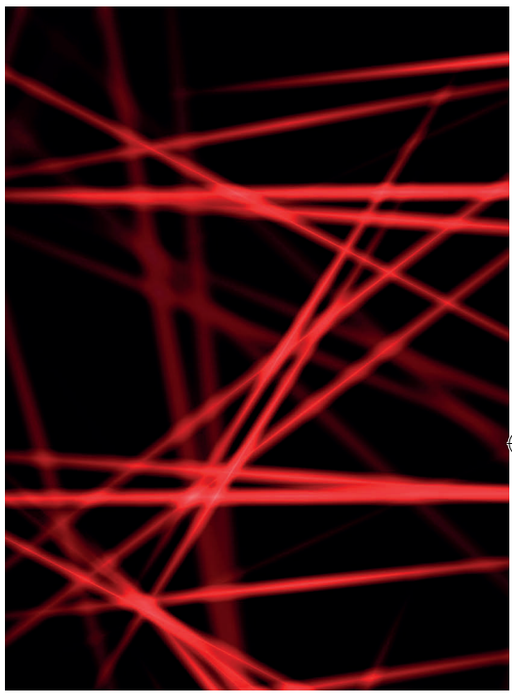
Thermal relaxation times

Target destruction while minimising damage to surrounding tissues during photothermal treatments relies on the theory of thermal relaxation. But the concept focuses on target cooling rather than destruction, write MIKE MURPHY and PER-ARNE TORSTENSSON, leading to poor results and repeat treatments



Lasers and IPLs have long been used to treat a range of unwanted blemishes on the skin. The theory of selective photothermolysis was devised in 1981 by Anderson and Parrish and was based on the pulsed laser technology of the day. This idea involved heating the target tissues without over-heating the surrounding tissue, by restricting the time in which laser energy was applied, thereby minimising collateral damage and scarring.

They applied the heat diffusion equation to a cylinder (to approximate for a blood vessel). A short energy pulse heats a cylinder then cools. Anderson and Parrish surmised that as long as the total pulse duration was less than the cylinder's "relaxation time", then no significant damage to adjacent tissues would occur outside the vessel.

By careful choice of wavelength and fluence, the selected targets could be successfully targeted and selectively destroyed. A major part of this theory was the concept of thermal relaxation time (TRT).

This is defined as the time taken "for the central temperature of a Gaussian temperature distribution with a width equal to the target's diameter to decrease by 50%". TRT is calculated, in cylinders as a first approximation, as the following; where d is the target diameter (in mm) and α is the tissue diffusivity (mm²/s):

$$\mathbf{TRT = d^2 / 16\,\alpha}$$

This definition describes the cooling time of the target. It is only dependent on the size of that target and the local heat conduction properties. By choosing pulse durations less than the TRT of the target, it was believed that a successful outcome would be produced without damaging adjacent tissues. While this is essentially true, there is a significant problem with this idea. To explain this we need to re-examine the basic physics and biology behind the light-tissue interactions.

Target destruction

The purpose of delivering light energy and, hence, generating localised heat energy in a target tissue, is to selectively destroy that target. To achieve this goal, the target must be irreversibly denatured. If the target is not damaged sufficiently, there is the probability that the tissue will simply regenerate. Consequently, the important goal is to damage the target such that it cannot regrow.

This is extremely important since it is the basis for many treatments. The TRT simply describes the target's cooling time. It has no relevance in terms of denaturing or destroying it. While the TRT may be important in minimising collateral damage, it ignores the most important task—to destroy the main target.

The key problem with this approach has been observed in poor clinical results with short-pulsed lasers and the treatment of aberrant blood vessels. Consequently, many treatment programmes were abandoned once a "plateau" in the results had been reached. Recent developments with IPL technology have improved clinical outcomes resulting from the longer pulsewidths available from these devices.

Arrhenius Damage Equation

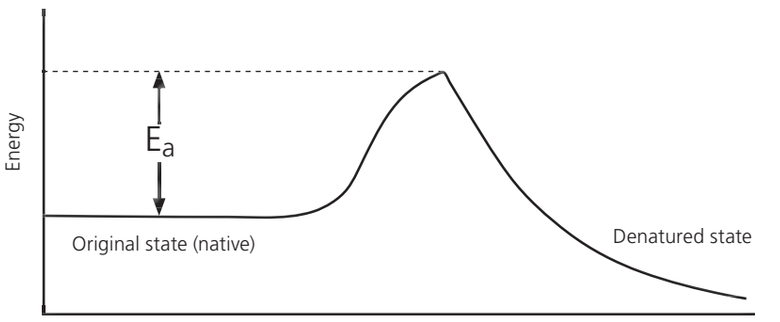
To consider how much damage a target sustains during the heating process, we need to consider the Arrhenius Damage Equation. The amount of tissue damage, Ω, at any point can be calculated as:

$$\mathbf{\Omega = A\,\delta t\,\exp(-E_a/RT)}$$

where A is the frequency of decomposition of the molecules (or damage rate factor, s^{-1}), E_a is the activation energy per mole between the native and the denatured states of tissue (J/mole), δt is the time that the energy within the target tissue is at or above the activation energy, T is the tissue temperature (in degrees Kelvin) and R is the molar gas constant (8.314 J/mole K).

This model is based on the tissue molecules absorbing an amount of energy at or above E_a followed by decomposition of the molecules at a rate determined by A. The terms E_a and A are generally known as the Arrhenius parameters.

The equation shows that the amount of tissue damage, Ω, is exponentially proportional to the temperature, T, attained by those cells and linearly with the time, δt, maintained at that temperature. Note that the time, δt, is not necessarily the same time as the pulse duration of the energy—it is the time the tissue is at, or



The activation energy required to denature tissue molecules

above, the temperature corresponding to the activation energy, or E_a.

The activation energy of any tissue differs according to the molecules in question and the denaturation pathways. This is the energy required to break molecular bonds within the tissues and is often referred to as the barrier energy.

It induces a change of state from "native" to "denatured" (see "The activation energy required to denature tissue molecules").

In essence, E_a determines the temperature at which denaturation of the tissue proteins begins, while the frequency factor, A, dictates the rate at which that denaturation occurs.

The determination of tissue damage was calculated by Diller and Pearce as the logarithm of the relative concentration of un-denatured tissue.

The level of damage may be calculated by the ratio of the concentration of native tissue, c_t, at the end of the thermal insult, at time t_1, to the concentration of native tissue prior to any denaturation, c_0, at time t_0.

Diller and Pearce showed that the logarithm of the relative concentration of undenatured collagen is the same quantity as Ω in the equation above.

The accumulated damage is defined by the dimensionless parameter Ω with the threshold for irreversible damage at a point being defined as Ω = 1. The quantity c_t / c_0 represents the proportion of undamaged tissue at the end of the applied thermal energy. This, therefore, dictates that the proportion of damaged protein may be found as follows:

$$\Omega = -\log_e(c_t / c_0) = 1$$
$$\text{i.e. } c_t / c_0 = 0.368$$

Therefore, the proportion of damaged protein, $(1 - c_t / c_0)$, is 63.2% of the initial concentration. Hence the threshold for irreversible damage, or tissue necrosis, is assumed to occur in tissue when 63.2% of the target tissue has been denatured by the thermal process.

With the definition of Ω = 1 being the threshold for irreversible protein denaturation, it is worth considering what happens when Ω is greater or less than one (see "Variation of % damaged tissue versus damage level Ω"). This shows the relationship between as Ω and the percentage of denatured proteins.

The chart below clearly shows that an Ω of one corresponds with a 63.2% damage level, while a value of three is required to achieve 95% damage. Diller and Pearce suggest that values of Ω above one are essentially meaningless since irreversibility has already been achieved in that tissue.

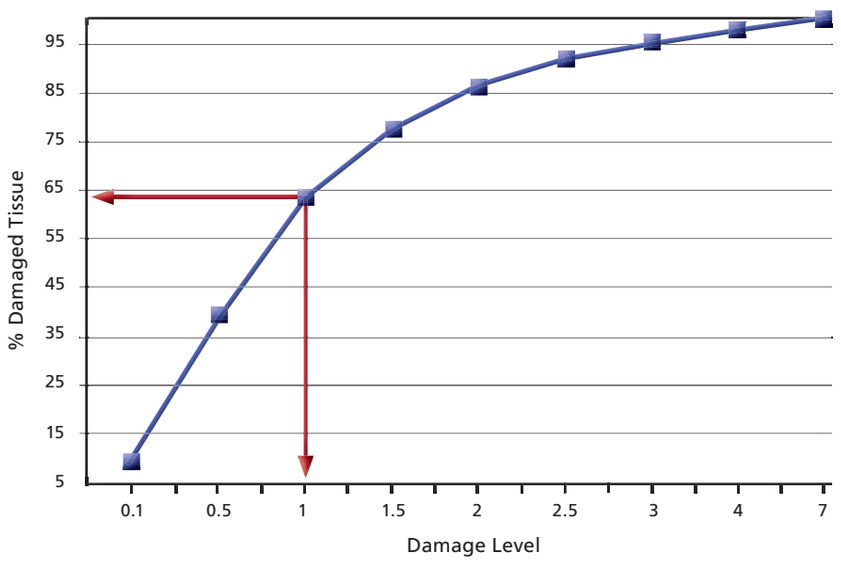
Interestingly, Takata et al suggest an Ω of 10,000 is equivalent to "third degree burns", yet calculations show that an Ω of only seven will result in 99.9% tissue damage. However, this definition is purely arbitrary. There is no clinical or histological evidence available in the literature to confirm that this assumption is accurate.

It may be that an Ω of two (equivalent to 86.5% denaturation), three (95.0%), four (98.2%) or somewhere else in that range, may actually be necessary to prevent sufficient protein re-naturation or regrowth of the existing structure occurring. We shall continue with the accepted definition of the onset of irreversible denaturation (ID) at an Ω value of one.

However, it may be that total denaturation is not required to induce the desired response. In the case of generating new collagen growth, it appears that the existing collagen merely needs to be stimulated by the application of external heat.

Our calculations reveal that the actual amount of level of damage, Ω, may be as low as only 0.1 to 0.2. Yet, even this low damage level appears to be sufficient to stimulate the fibroblasts to produce neocollagenesis.

Below: Variation of % damaged tissue versus damage level Ω



Irreversible denaturation

It is clear that the target cells must attain a temperature, T, which must be maintained for a minimum time, t, to achieve ID (Ω = 1). Consequently, it is not sufficient to simply describe a desired temperature to ensure a successful treatment outcome. The associated time for that temperature must also be indicated. The temperature-time combination is a "coupled pair"—quoting one without the other is meaningless.

So, what are the typical (T,t) combinations required to achieve ID in hair or blood vessels? These depend on the Arrhe-

	E_a	A
	(J/mole)	**(s^{-1})**
Bulk Skin	3.27×10^5	1.8×10^{51}
Blood	4.55×10^5	7.6×10^{66}

Arrhenius Parameters for bulk skin and blood (data from Diller and Pearce). The activation energy for blood is higher than that for 'bulk skin', but once it is achieved blood will denature at a much faster rate than bulk skin.

nius parameters for the tissue in question. These parameters must be found through experiment; they cannot be calculated. Many researchers have carried out such experiments for a wide range of human tissues but the data produced by Diller and Pearce will be used in this article.

The graph below shows the temperature-time combinations required to achieve ID for bulk skin and blood. The curves shows the thresholds for ID where the volume of tissue denaturation reaches 63.2% ($\Omega = 1$).

The areas above each curve therefore show all the temperature-time combinations that will induce ID for each tissue. Any temperature-time pairing which lies within those areas will exceed the damage threshold of 63.2% and render the tissue necrosed. The areas below the curves represent $\Omega < 1$ and, hence, may result in tissue re-growth.

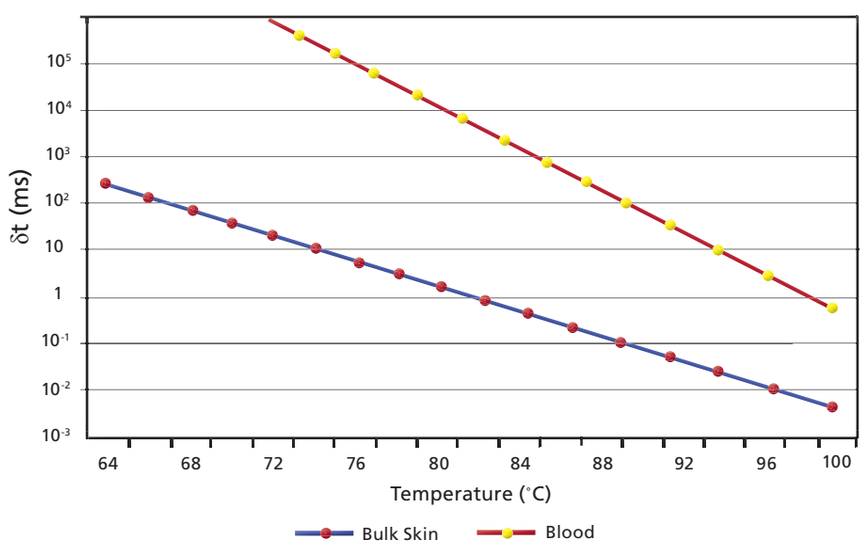
Higher temperatures require less time to induce ID compared with low temperatures. Note that the time axis in the graph below is logarithmic.

It is clear from the Arrhenius Damage Equation that the desired goal of most photothermal treatments is the attainment of irreversible denaturation. If this does not occur then tissue regrowth is possible. The time required to achieve this state is entirely dependent on the temperature achieved in the tissue. The cooling time, or TRT, is essentially irrelevant. There is no direct link between the denaturation time and the relaxation time—they describe two completely separate processes.

The Arrhenius equation shows the relationship between time and temperature. Simply achieving a desired temperature in tissue to induce a particular response is not sufficient. That temperature must be maintained for the appropriate time to achieve the desired end result. If either the temperature or the time is not attained then the response will fall short of what is clinically required, leading to poor results or excess repeat treatments.

Most importantly the equation shows that the damage achieved, Ω, due to denaturation of proteins by heat is, for any given tissue: linearly dependent on time (i.e. pulse duration); and exponentially dependent on temperature (i.e. input energy/fluence). Therefore, as long as sufficient energy has been deposited into the target then damage to the proteins can be controlled by careful selection of exposure time. Denaturation will not occur in the tissue proteins until the activation energy has been input; thereafter, a small increase in energy density (fluence) will have a major effect on the rate of the denaturation process. This strongly indicates that careful control of tissue damage is more easily achieved by judicious choice of pulsewidths, as this will result in a linear progression of denaturation.

Thresholds of irreversible damage for "bulk skin" and "blood" (Ω =1) as functions of temperature and time. The areas above each curve show the temperature-time combinations which will ensure ID. Combinations below the curves will result in less than 63.2% tissue destruction.



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Thermal energy levels

Heating of the skin triggers different processes at different temperatures, resulting in a variety of outcomes. MIKE MURPHY AND PER-ARNE TORSTENSSON discuss the effects of heat shock proteins and collagen denaturation when treating the skin at variable temperatures

It is a fundamental law of physics that electric current always seeks the path of least resistance. So when radiofrequency (RF) probes are placed on the skin surface, the current will 'seek' a path which offers the lowest possible resistance, regardless of the distance between electrodes.

The stratum corneum is mostly composed of dead, flat skin cells, lipids, air pockets and very little moisture. It therefore has a very high electrical impedance (or resistance to an AC current), potentially up to 100,000 ohms. Wet skin, either due to external water or perspiration, will have a much lower impedance.

In skin, the path of least resistance is most likely a direct route from the emitter electrode through the stratum corneum to the epidermis—which has a much lower impedance compared to the stratum corneum—along the top of the epidermis, then back through the stratum corneum to the collecting electrode.

As electric current flows through these tissues, heat is generated due to the resistance to the current flow. The amount of heat generated is directly proportional to the tissue impedance, the power applied and the time for which it is applied.

Radiofrequency

The heating that takes place using typical non-invasive RF systems in the low megahertz region (0.5 – 5MHz) with skin contact electrodes is known as Joule heating. The temperature rise results from purely resistive heating resulting from electrons colliding with ions within the tissues.

Dielectric heating is also possible, as a result of friction losses from the rotation of dipole molecules induced by magnetic and or electrical field oscillations. Dielectric heating is typically an order of magnitude smaller than Joule heating in the above frequency range.

Dipole heating is proportional to the field frequency and also proportional to the tissue permittivity. At frequencies greater than 10MHz, dielectric heating is no longer negligible in human tissues.

The absorbed electrical energy is converted into thermal energy in resistive tissues according to the following equation:

$$\mathbf{E_{avg} = I^2_{rms}\, Z\, t}$$

$\mathbf{E_{avg}}$ is the heat energy (J) averaged over a number of cycles, $\mathbf{I_{rms}}$ is the root mean squared current (amps), **Z** is the tissue impedance (ohms) and **t** is the current application time in seconds. Clearly high impedance tissues will generate higher temperatures per unit current.

The electrical impedance of the dermis is typically around 290 ohms while that of fatty tissue is almost 7.5 times that, at around 2180 ohms. Hence any current flowing through the fat layer will generate more heat than the dermal tissue above and so RF energy may also be used to induce lipolysis.

RF current typically generates relatively low temperatures in the skin compared to high energy lasers and IPL systems. Since the heat is generated through electrical impedance, the colour of the tissue is irrelevant. If the heat is sustained for a sufficiently long period, collagen fibres can contract and thicken during the procedure.

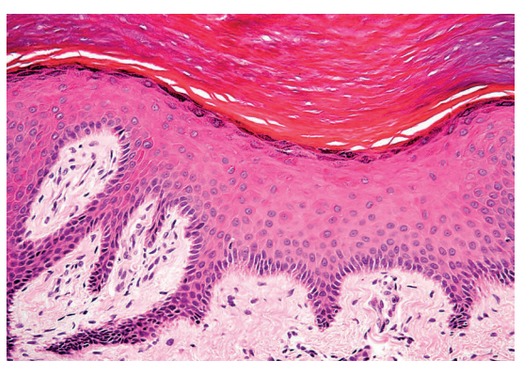
Further tightening is enabled from the inflammatory wound healing response which triggers new collagen synthesis. The fibrous septa, which separate the fat lobules in the subcutaneous layer, are also preferentially heated due to the higher impedance of that layer. This results in a contraction of the fatty layer tissue which is evident as an immediate tightening reaction to the treatment.

A prolonged wound-healing response lasting for more than three months may also occur, leading to dermal remodelling and the formation of new collagen fibre bundles. The ultimate result is an improvement in skin laxity and texture and an increase in dermal bulk. Wiley et al found around a 90% satisfaction rate with their patients at the three- and six-month follow-ups after RF treatments.

Clinical and histological studies have shown an increase in type I and type III collagen in addition to newly synthesised collagen.

Levels of collagen were observed to have further increased over a three month period which resulted in statistically significant improvements in skin tightening, skin texture and rhytides. Reports suggest that a low-energy, multi-pass, multi-treatment protocol results in consistently good results with minimal discomfort to the patients.

Another study using a fractional bi-polar RF unit showed both neocollagenesis and neoelastogenesis in addition to an increase in dermal cellularity and deposition of hyaluronic acid. This study also found a 28-fold increase in the level of the heat shock protein, HSP47.



The path of least resistance for RF current is through the stratum corneum to the epidermis, generating heat as it passes through

Heat shock proteins

Regardless of the method of heat generation in the dermis—by RF, lasers or IPLs—the heating process affects dermal collagen in at least two ways.

For dermal temperatures between 43–50°C, the heat generated within the dermis triggers a response from the heat shock proteins (HSP) resulting in molecular changes in the damaged collagen. HSPs reside within cells in the dermis and help to prevent irreversible cell damage under stressful conditions. They are responsible for the synthesis, transport and folding of proteins as part of a damage-control response to excess heat.

These changes include structural rearrangement of the collagen proteins through folding and unfolding activities resulting in contraction and thickening of the collagen. It has been shown that such thermally-damaged collagen can be completely replaced with new collagen through an active remodelling process mostly due to the collagen chaperone HSP47.

Many anecdotal reports discuss the 'painless' sensation during RF treatments. This indicates that the temperatures achieved in the dermis are probably below 40°C—the threshold temperature at which the pain nociceptors are activated.

Thermal pain is typically triggered between 40° and 45°C, so the clinical results from such low temperatures must be due to the HSP repair processes. However, HSP expression increases significantly at around 43°C, suggesting that a modest level of pain might lead to a better clinical outcome.

The low-energy, multi-pass and multi-treatment regime now appears to make more clinical sense since the accumulated thermal stimulation will result in further HSP expression. In particular, elevated levels of HSP47 result in the promotion of collagen synthesis, while recent research appears to indicate the role of HSP70 in determining those cells which are deemed irreversibly damaged.

Thermal denaturation

Below around 50°C, HSP expression dominates over collagen denaturation. However, above this temperature the denaturation process is too rapid for HSP repairs to be maintained and collagen breaks down more rapidly.

This is evident in treatments where higher energies are typically applied and where energy is applied directly into the dermal tissues via micro-needles.

For those cases where temperatures exceed 50°C, we can apply the Arrhenius Rate Equation. In such situations the temperature applied, coupled with the time for which it is applied, is critical in determining the amount of collagen denaturation, Ω:

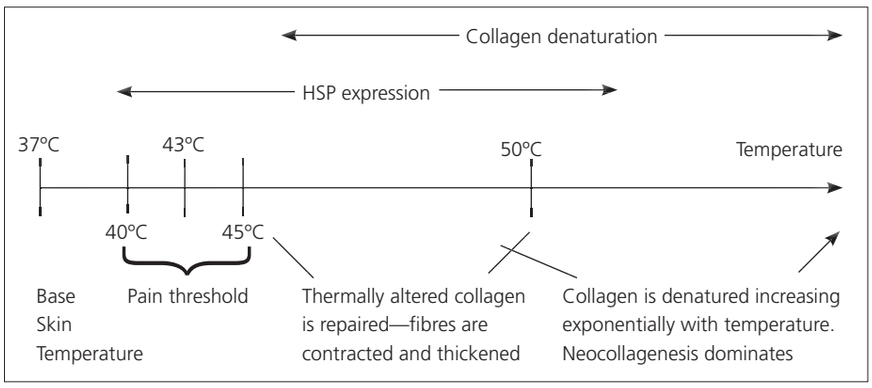
$$\Omega = A\delta t \exp(-E_a/RT)$$

where **A** is the frequency of decomposition of the molecules (or damage rate factor, s^{-1}), $\mathbf{E_a}$ is the activation energy per mole between the native and the denatured states of tissue (J/mole), **T** is the tissue temperature (in degrees Kelvin, K), **R** is the molar gas constant (8.314 J/mole K) and **δt** is the time for which the temperature T is maintained.

It is important to note that the amount of tissue damage, Ω, is linearly dependent on time but exponentially dependent on temperature (which is directly proportional to the absorbed energy).

Studies indicate that more readily observable results are achieved at higher temperatures. Berube et al found that the increase in collagen volume was almost three times greater at 75°C compared with 65°C. This is entirely in keeping with the above theory, since a small increase in temperature results in an exponential increase in tissue denaturation and consequently more neocollagenesis over time.

Therefore, the level of collagen damage is very sensitive to the local temperature. However, even with relatively low temperatures (<40°C) applied for sufficient periods of time, it is evident that an immediate contraction of collagen fibrils occurs, leading to significant improvements in the skin's textural appearance.



Graph demonstrating different temperatures triggering reactions at different rates.

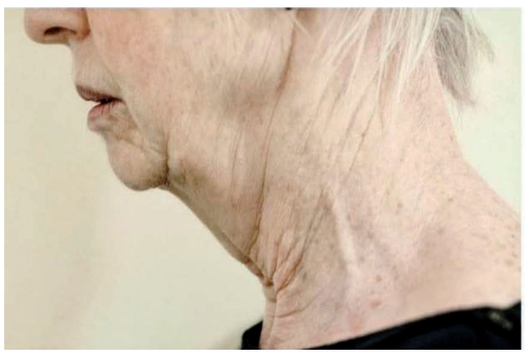
Activation zones

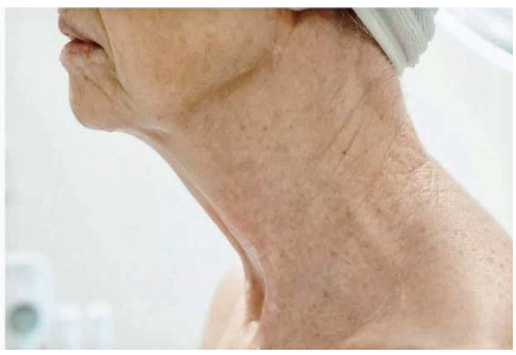
It is clear that the heating of skin induces a number of reactions, including HSP expression and tissue denaturation. These processes are triggered at different temperatures and result in various outcomes at various rates.

In addition to the wound-healing response and vasodilation, at least four heat-related processes are evident: immediate collagen fibril

Below: Results immediately following a ten minute RF session on the right hand side of the face—around the eye and forehead.

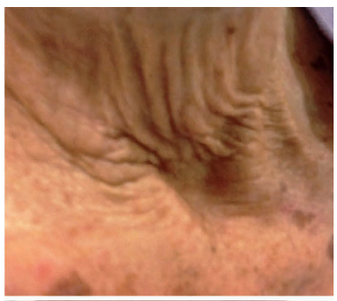
PHOTO CREDITS: Lynda V Price/XXY Photography

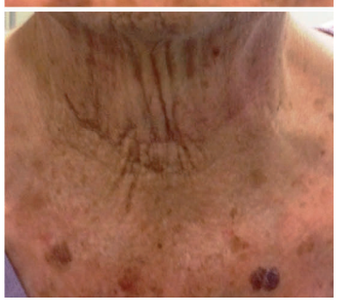




Left: Before and after one application of RF energy to a 68 year old female's neck

Below left: Results showing immediate improvement in the neck of an 89-year old female following one RF treatment.





contraction; HSP expression; collagen denaturation; and fibroblast stimulation

The rate of collagen denaturation depends exponentially on the temperature—for low temperatures, the rate is slow and the HSP expression dominates. As the temperature increases, the rate of denaturation becomes too fast for the HSP processes to repair the damage and the collagen breakdown process dominates.

Clinical results

Treatment was carried out using Omniface RF—a non-ablative, bipolar system and a multi-tip, fractional bi-polar system in one unit.

The author, Dr Murphy, received treatment on the non-ablative, non-fractional setting at 2MHz in a continuous mode at a power of 14W over a period of less than ten minutes (see image on opposite pag). A sweeping motion was employed on the skin surface to deliver current and heat the underlying tissues. No pain was felt during the procedure indicating relatively low temperatures (<40ºC). There were no visible signs of erythema or oedema, yet instantaneous skin tightening was evident around and above the right eye.

A 68 year old female patient received one session of non-fractional treatment to her neck. A continuous power of 22W at 2MHz was applied in a continuous sweeping motion over a 30 minute session. The immediate tightening of the dermal collagen was evident with a noticeable reduction in the appearance of the wrinkles.

While this is a relatively short-term improvement, the fibroblasts in the reticular dermis will also have been stimulated. This will result in neocollagenesis in the following weeks and months. Fibroblasts typically take around six weeks before reaching the peak of collagen synthesis but can continue this process for up to nine months post-treatment.

The neck of an 89 year old female patient was treated with a continuous 19W and 2MHz for 20 minutes. There was immediate improvement in the recessed area at the base of the neck, in addition to a significant improvement in the appearance of the deep wrinkles. Further treatments will improve the appearance over subsequent months.

RF energy may be applied to the skin resulting in instantaneous collagen shrinkage, collagen denaturation, neocollagenesis and dermal remodelling. At low energies the results are mainly due to HSP expression, while higher energies cause more thermal damage and tissue denaturation. However, good clinical results are obtainable using both processes with different levels of pain and outcomes.

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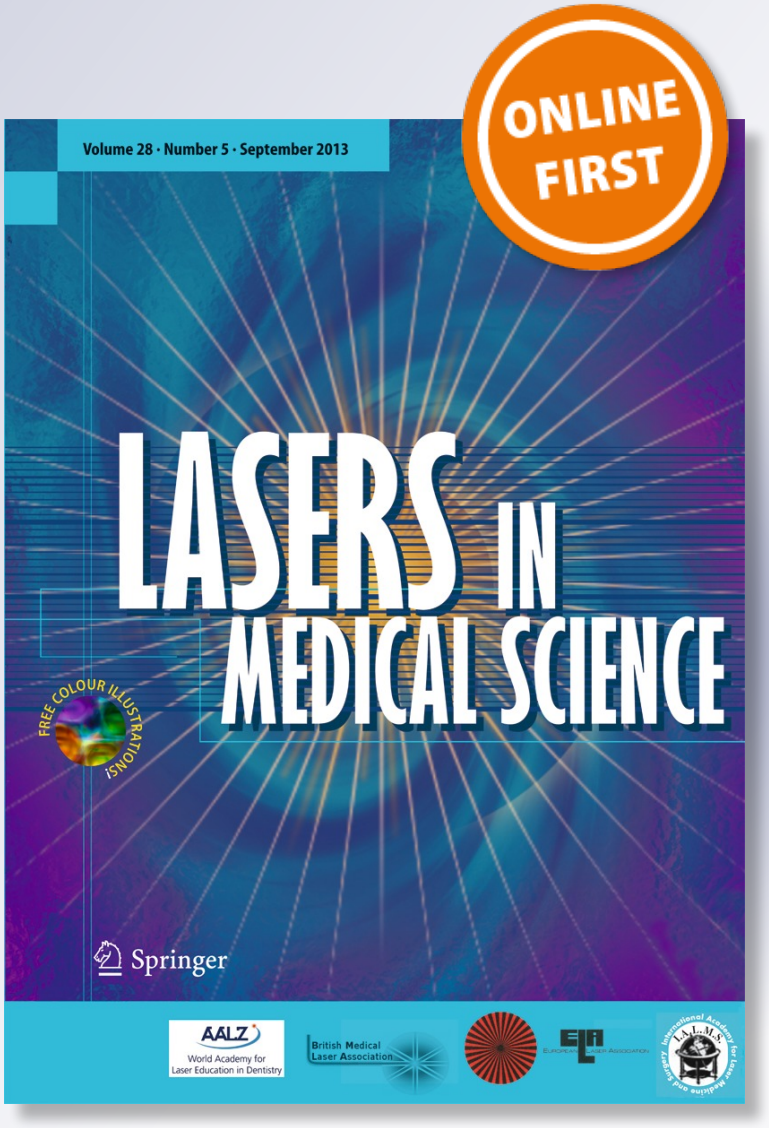

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ORIGINAL ARTICLE

Thermal relaxation times: an outdated concept in photothermal treatments

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Abstract Thermal relaxation times were introduced into modern skin-laser science with the inception of selective photothermolysis. As a result, laser pulsewidths were determined according to the thermal relaxation times of the tissue targets. The Arrhenius Damage Integral shows that this approach is incorrect. The important parameter is the time required to induce irreversible protein denaturation within the target. This time is determined by the tissue's intrinsic structure, not its physical dimensions. This report explains why thermal relaxation times should not be considered when treating many skin conditions with lasers or IPL systems.

Keywords Photothermal · Relaxation time · Arrhenius equation · Protein denaturation · Lasers · IPL · Vessels

Introduction

Selective photothermolysis (SPT) has been the cornerstone of many modern-day dermatology laser procedures since its inception in 1981 [1, 2]. This theory was constructed at a time when short-pulsed lasers were being developed for vascular conditions. Anderson and Parrish identified the problems with older technology and redefined the concept of acceptable clinical results following laser interventions.

A major part of SPT was the definition of thermal relaxation time (TRT). This was used to determine the maximum allowable pulsewidths to be used on blood vessels while minimising thermal injury to adjacent tissue. The TRT was defined as the time taken 'for the central temperature of a Gaussian temperature distribution with a width equal to the target's diameter to decrease by 50 %' and is calculated (in cylinders as a first approximation) as follows:

This should be 1/e = 36.8%

$$TRT = d^2/16\,\alpha \quad (1)$$

Where d is the target diameter (in millimetre) and α is the tissue diffusivity (in square millimetre per second). The theory of SPT proposes that minimal collateral thermal damage is achievable if the laser energy is delivered within this time.

Hence, a pulse of energy is applied to the skin surface with a duration calculated according to the diameter of the target tissue. When considering relaxation times, Anderson and Parrish were solely concerned with minimising collateral thermal damage to the dermis surrounding the target blood vessels.

This definition was extended by Altshuler et al. [3] in 2001 to include hair follicles, under the same principles as SPT, whereby target structures are denatured or destroyed by heat energy diffusing from adjacent light energy-absorbing chromophores in the hair shaft (absorber) rather than by direct absorption in the outer root sheet (target). To their surprise, they found experimentally that selective photothermal damage of hair follicles occurred even for radiant pulse durations five to seven times longer than the TRT of the hair follicle, which they could not explain. Haemoglobin and melanin are the light-absorbing targets in blood vessels and hair, respectively. Their temperatures become elevated and these heat sources conduct thermal energy to the target tissues—the vessel walls and hair germ cells [3]. The authors defined a new time—the 'thermal damage time' as the time when the outermost part of the target reaches the target damage temperature through heat diffusion from the heater (tissue), but this heat diffusion model

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does not explain why selective damage can occur even though the pulse duration is much longer than the TRT of the follicles.

Both reports determine 'appropriate' energy pulsewidths according to the relaxation (or damage) times of the targets, based on their diameters. Neither report discusses the requirement that tissues must be maintained at a particular temperature for a particular time. This is an intrinsic requirement to ensure complete and permanent destruction of the target cells.

The Arrhenius damage integral—application to tissue

There are at least two processes which occur during the irradiation of tissue. The first is the thermodynamic heating process which results in a local temperature rise. The second is a chemical process whereby the heated proteins denature resulting in a loss of their integrity.

Below boiling point, temperature-induced damage of tissue typically involves denaturation of the proteins which constitute the tissue. The rate of denaturation is a complicated function of temperature, local pressure, and other environmental parameters. Slow heating of proteins will cause denaturation at a lower temperature than rapid heating of the same proteins. The thermally induced denaturation of human cells starts at temperatures as low as approximately 43 °C [4]. This is due to the thermal rate constants governing the thermodynamic process. An approximation in calculating the amount of tissue damage may be found from the first-order Arrhenius rate theory model, as proposed by Henriques and Moritz [5, 6].

For clarification, this model is based on the well-known physical processes where light energy (in joules) is absorbed by tissue chromophores which results in heat formation leading to local temperature increases (in degrees Celsius). Hence, increasing the incident radiant exposure (commonly known as 'fluence' or 'energy density') ultimately induces higher temperatures in tissues (for a given pulsewidth). In many cases, there is an almost linear relationship between the incident optical radiant exposure (in joules per square centimetre) and the local temperature rise (ΔT) under the assumption that non-linear processes, such as phase changes like vapourisation etc., are not taking place.

This model asserts that tissue damage can be expressed as a function of a chemical rate process where damage is proportional to the rate of denaturation of proteins, k. The amount of accumulated damage depends on the protein temperature, T, and the heating time, t.

The amount of tissue damage, Ω per unit time Δt, at any point can be calculated from the Arrhenius damage equation as follows:

$$\Omega/\Delta t = k(T) = A * exp(-E_a/RT) \quad (2)$$

which in the general case, with time dependent temperature, becomes:

$$\Omega(T,t) = \int_0^t k(T)\,d\tau = A\int_0^t \exp[-E_a/RT(\tau)]d\tau \quad (3)$$

Where 'Ω' is the total accumulated tissue damage, 't' is the total denaturation time (i.e. $T(\tau)\geq 43$ °C for $0\leq\tau\leq t$), 'A' is the frequency of decomposition of the molecules (or damage rate factor, s^{-1}), 'E_a' is the activation energy per mole between the native and the denatured states of tissue (in joules per mole), 'T' is the tissue temperature (in degrees Kelvin, K) and 'R' is the molar gas constant (8.314 J/mol K). This model is based on the tissue molecules absorbing an amount of energy reaching E_a followed by decomposition of the molecules (denaturation) at a rate determined by A. The terms E_a and A are generally known as the 'Arrhenius parameters'. Denaturation of the proteins cannot begin until the required denaturation temperature has been reached in the tissue, which is achieved when the appropriate amount of energy (the barrier energy E_a) has been delivered to the tissue. The value of E_a has been found to vary considerably between different tissue types.

There are several times which are important in this discussion (Fig. 1). The first is the duration of the radiant pulse of light energy—the pulsewidth, t_p. This time determines the overall energy input into the absorbing tissues. The second time is the total duration time of the denaturation process within the heated target tissue—'t' in Eq. 3. At slow heating rates with "steady-state" thermal conditions, t and t_p are approximately equal, and it is fairly straightforward to calculate the damage rate Ω versus time and temperature using the simplified 'linear' version of the Arrhenius equation, see Eq. 4 and Discussion below. However, in typical laser/intense pulsed light (IPL) treatments, the thermal process is highly dynamic and transient and the denaturation rate must be calculated with the general Arrhenius equation according to Eq. 3. In the general case, the total denaturation time t_{tden} corresponds to the time when the T>43 °C. If the peak temperature of the transient process is considerably higher than 43 °C, it may be appropriate to introduce the concept an effective denaturation time t_{eden} and corresponding effective (or 'threshold') temperature T_{eden} over which, say, 99 % of the denaturation takes place, see Fig. 1. As the denaturation rate accelerates exponentially with increasing temperature, the effective denaturation time can end up being much shorter than the total denaturation time, but still only leading to a 1 % error in the calculated value of the denaturation rate Ω. There exists no simple relationship between the thermal relaxation time t_{TRT} of a heated tissue structure and the effective denaturation time t_{eden} for transient heating processes.

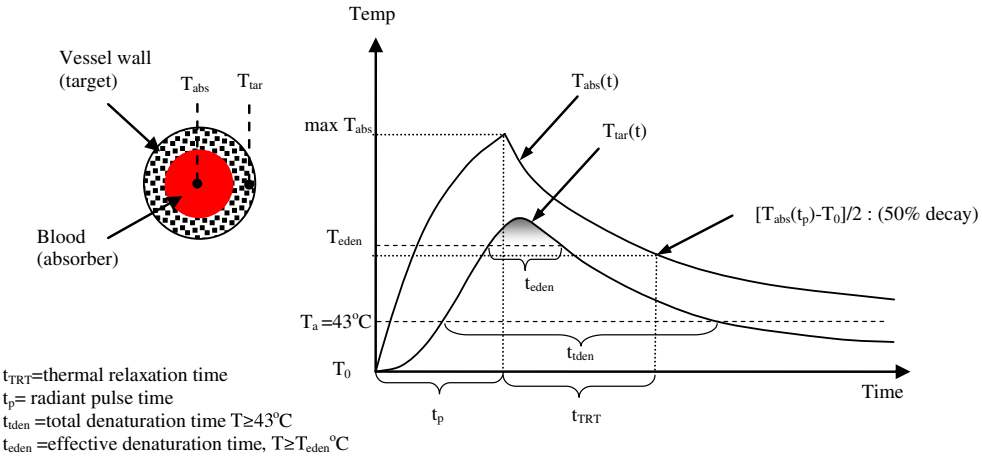

Fig. 1 Once T≥43 °C in the target tissue, the denaturation process starts up slowly and continues for the total denaturation time t_{tden}. However, the denaturation process accelerates exponentially with increasing temperature, and, therefore, it is useful to introduce the 'effective' denaturation temperature, T_{eden}, and corresponding time t_{eden} over which most of the denaturation takes place

In some applications (steady state), it may be appropriate to assume that the temperature is constant over the heating period Δt and the first order approximation of Eq. 3 becomes:

$$\Omega = A * \Delta t * exp(-E_a/RT) \quad (4)$$

This equation describes the rate of denaturation of the tissue as a linear function of time, Δt, and decomposition factor, A, and is exponentially dependent on the tissue temperature, T, and the activation energy, E_a.

The definition of Ω=1 is taken as being the threshold for irreversible protein denaturation [7], which corresponds to a quantity of 63.2 % cell damage. Hence, once 63.2 % of the cells in a target have been damaged irreversibly, that target is deemed to be incapable of protein re-naturation or regrowth. (Note: Δt is NOT necessarily equivalent to the pulsewidth of the light source in this discussion but is the minimum time that the temperature T is equal or greater than the 'threshold' denaturation temperature, T_a, necessary to ensure irreversible denaturation: Ω=1).

For example at T=60 °C, the required heating time is approximately Δt=1 s for human bulk skin, while the required heating time is around 33 ms at a constant temperature of T=70 °C, which is commonly accepted a 'standard' denaturation temperature in the literature for most tissue types.

However, the Arrhenius coefficients vary substantially between different types of tissues. The blood requires much longer heating time (or a higher temperature for a given heating time) to coagulate in comparison with bulk skin. For example, the required temperature for blood coagulation (Ω=1) is approximately 90.4 °C at Δt=33 ms, compared with 70 °C for bulk skin, and approximately 88 °C for arterial collagen (see Fig. 2).

Arterial collagen denatures at slightly lower temperatures than blood, for a given heating time, leading to a breakdown of the vessel walls before haemoglobin denaturation (Fig. 2).

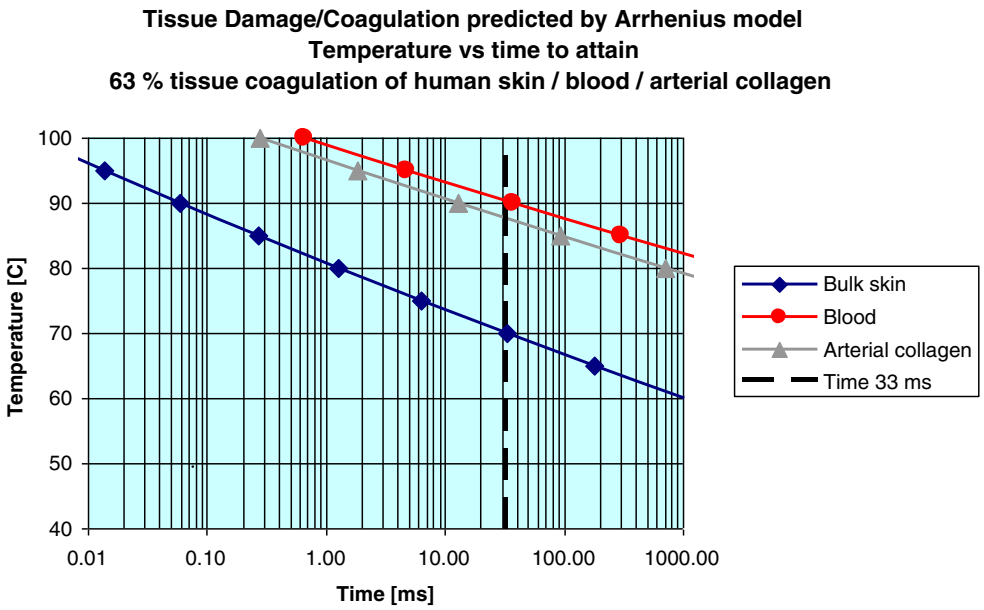

Fig. 2 Tissue denaturation temperature dependency versus time predicted by the Arrhenius model for bulk skin, blood and arterial collagen. Arrhenius coefficients used for bulk skin (Weaver [9]) $E_a=3.27\times10^5$ J/mol, $A=1.823\times10^{51}$ s^{-1}, and for blood (Lepock [9]) $E_a=4.55\times10^5$ J/mol, $A=7.6\times10^{66}$ s^{-1}, and for arterial collagen (Agah [10]) $E_a=4.3\times10^5$ J/mol, $A=5.6\times10^{63}$ s^{-1}

Longer pulsewidths clearly induce perivascular collagen injury [8] which appears to aid the overall result.

An Ω greater than 1 represents a greater percentage of damaged cells; Ω=2 is 86.5 % cell damage, while Ω=3 is 95.0 %. Hence an Ω greater than 1 is not undesirable. In a clinical setting, this can be achieved by either increasing the energy applied to the tissues or increasing the pulsewidths, or both.

Tissue denaturation time

The Arrhenius equation (Eq. 4) shows that the denaturation temperature, T, is closely linked to the denaturation time, Δt. In fact, the two parameters are tied—one cannot quote a denaturation temperature without quoting the associated time. One without the other is meaningless—they are an intrinsically coupled pair.

In a clinical setting, this means that merely achieving a desired temperature in a target tissue is not sufficient. That temperature must be maintained for a suitable time, Δt, to ensure irreversible denaturation of the tissue cells and, hence, a permanent clinical result.

This is contrary to the theory of SPT and relaxation times. In SPT, only the thermodynamic process is considered. The denaturation process is not considered, and hence the time which the tissue temperature is maintained is not indicated as important. Instead, the 'important' time is the thermal relaxation time, which is merely a function of the target's diameter and local thermal diffusivity. This relaxation time, which essentially describes the cooling time of an object, has no relation to the tissue's protein breakdown rate. Instead, the complete temporal, transient temperature history of the target tissue volume has to be considered and calculated using the general expression of the Arrhenius according to Eq. 3.

The thermal relaxation time does not consider the actual physical processes within the tissues. Hence, it cannot be used to determine the most appropriate 'heating time' necessary to achieve the desired result. The Arrhenius equation must be used for that purpose, since it links the tissue temperature and the protein destruction rate. In fact, the Arrhenius equation is the most important consideration for any photothermal process, regardless of the energy source (laser, IPL or RF). Note that the Arrhenius equation has no direct dependency on the physical size of the target tissue.

The peak temperature in any absorbing tissue depends on the rate of increase of temperature due to the incoming light energy, and the rate of decrease of temperature due to heat conduction from the tissue. Hence small targets, with inherently rapid heat loss, will not reach high temperatures unless the pulsewidth is very short ($t_p \leq TRT$), while larger targets will retain their heat energy for longer and subsequently achieve higher temperatures. As a consequence, larger targets will be more likely to achieve Δt and hence irreversible denaturation, given sufficient energy.

Laser treatment of blood vessels

Vessel diameters in PWS typically range from 10 to 300 μm [11] with a commensurate range of TRTs spanning three orders of magnitude from 0.057 to 51 ms (assuming a diffusivity of skin, α_s, of 0.114 mm^2/s). Pulsed dye lasers were used at the time of the formulation of the SPT theory to treat PWS with typical pulsewidths between 0.0003 and 0.36 ms.

Clinical researchers soon found the limitations of these devices with reports of 'resistant vessels' which did not respond to the treatment parameters available [12, 13]. Given the analysis above, this is not surprising. In arterial collagen, denaturation times less than 0.36 ms would require temperatures in excess of 99.4 °C to achieve irreversible thermal denaturation of the vessel walls; blood would require temperatures greater than 101 °C. Instead, the high peak powers of these short pulses typically result in short-lived temperatures at or above boiling point which can induce intravascular cavitation, with subsequent vessel wall rupture and purpura [8]. The early pulsed dye lasers simply could not denature arterial collagen or blood, since they were not capable of generating sufficiently long-lived temperatures in those tissues.

The smallest diameter targets which can be irreversibly denatured may be determined by the applying highest possible temperature in that target tissue, using Eq. 4. In arterial collagen, this is just below 100 °C which corresponds to a denaturation time of 0.296 ms. This time corresponds to the TRT of a vessel diameter of 25.5 μm, meaning that vessels below this diameter cannot be denatured by photothermal exposure.

Hence, it is impossible to destroy such small vessels using the photothermal process. They may only be destroyed by vapourising the vessel walls, but this is not guaranteed, since the vessels may retain the capacity to re-grow.

Consequently, results from the earliest pulsed dye lasers must have been entirely due to the physical destruction of the vessel walls rather than thermal denaturation, a photomechanical process similar to laser tattoo removal.

Modern pulsed dye lasers typically use pulsewidths between 1.5 and 10 ms. These corresponds to a denaturation temperature range of 90.7 to 95.7 °C. Assuming the output pulses are continuous, this range of pulsewidths should be able to denature vessels diameters up to approximately 150 μm, but not above. As with the above situation with small vessel diameters, a pulsewidth of 10 ms cannot denature vessels larger than 150 μm in diameter because of the lack of available time above the threshold temperature for denaturation to progress (see Fig. 2).

It is clear from this analysis that the energy pulsewidth must be calculated according to the absorber/target dimensions to ensure irreversible denaturation, with larger targets requiring longer pulsewidths.

Parlette [8] showed that longer pulses (40–60 ms) yielded better clinical results than shorter pulses (<20 ms) with less purpura and post-inflammatory hyperpigmentation in leg veins up to 1.6-mm diameter treated with an Nd:YAG laser at 1,064 nm. Their histological examination clearly showed contraction of the blood vessels with perivascular collagen damage. The longer pulsewidths resulted in 'better vessel clearance' which agrees with the above discussion that longer times are required to ensure irreversible denaturation. The histology did not reveal extensive damage in the surrounding dermis even though the pulsewidths were considerably longer than the TRTs of the smaller vessels.

Current IPL technology routinely uses pulsewidths from typically 5 ms up to 250 ms to successfully treat vascular conditions. There are several clinical reports where IPL systems have been compared with pulsed dye lasers in treatments of PWS, and in many cases, both clinical results and side effects are in favour of IPL sources [14, 15]. These pulsewidths correspond to a denaturation temperature range between 82.7 and 92.5 °C—a more gentle heating regime than with short pulsed lasers and which explains the lack of purpura with IPLs, since intravascular cavitation is avoided. Another benefit of using a 'long' pulsed light source is the reduced risk of adverse superficial skin burning in darker skin types if the light source is combined with a means for sufficient parallel skin cooling. Longer pulses allow excessive heat in epidermis to be drained by the heat sink during the pulse. The TRT of 80–100 μm thick epidermis is in the range of 5–10 ms which implies that parallel cooling of skin would be beneficial for pulsewidths longer than 10 ms.

The SPT theory suggests that such long pulsewidths, typically used in treatments with IPLs, should result in excessive collateral tissue damage, yet the clinical results show otherwise [16]. To take advantage of the Arrhenius equation, light-based therapies need to be able to induce constant temperature profiles in absorbing tissues. Such profiles would require complex pulse-forming systems to generate the necessary light pulse with the correct temporal profile.

Conclusion

Thermal relaxation times have been used to determine laser pulsewidths since the concept of SPT was introduced. However, the theory behind TRTs was solely concerned with the diffusion of heat energy from blood vessels into the surrounding dermis.

The Arrhenius equation shows, very clearly, that this is incorrect when considering the destruction of those target vessels. Irreversible denaturation of tissue is only possible when the required temperature is maintained for the required time. The cooling time of the target tissue is irrelevant with smaller vessel diameters when considering the target's destruction, but become more relevant as the diameters increase. In contrast, energy levels and pulsewidths should be calculated according to the tissue's intrinsic Arrhenius parameters to ensure irreversible denaturation, and hence successful clinical results.

In reality, the light-absorption profiles, tissue geometry, heat conduction from absorber to target tissues and the light device output temporal profiles all have an effect on this issue. Tissue denaturation will actually begin in the range from 60 to 80 °C, although little damage will occur within acceptable timescales. Clinical results are certainly achievable with current technologies in the range from 80 to 90 °C using properly controlled pulsewidths.

Ideally, technologies could be modified to deliver pulse energies and pulsewidths based on the Arrhenius equation to generate clinically useful temperature/time combinations in tissue which result in good clearance rates while minimising collateral damage.

A deeper analysis of this topic shows that the recommended pulse durations according to the original TRT concept are generally too short to achieve controlled and predictable clinical results. Very short pulse durations often lead to non-linear reactions such as tissue boiling and/or explosive responses that generally induce unexpected side effects and unpredictable clinical results.

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Q - switched laser removal of tattoos- A clinical and spectroscopic investigation of the mechanism

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ABSTRACT

The liquid phase spectra of tattoo pigments are shown to be unreliable as a basis for mechanistic deductions. The reflectance spectra of the solids from 2000 nm to 500 nm (5000 to 20000 cm^{-1}) are shown to accurately assess the relative loss of laser light for different pigments and to be useful in examining these to check for similarities in the pigments. The absorbance differences between the pigments are shown to be largely irrelevant in assessing the ease of tattoo removal by laser radiation of a variety of wavelengths. A multiphoton absorption mechanism with its concomitant shock wave is proposed to be responsible for the reduction of pigment particles to small sizes which the lymph system can remove. The different behaviour of blue and green tattoos, treated by Q-switched ruby and Nd:YAG lasers, is attributed to the particle aggregation size of the pigments in the tattoo.

Keywords : Tattoo, Clinical treatment of tattoos, Tattoo-pigments' spectroscopy, Pigment characterization, Nd:YAG laser, Ruby laser, Alexandrite laser, Multiphoton absorption, Shock waves

2. INTRODUCTION

The properties of laser light in biological applications can be efficiently exploited only if the mechanisms of the relevant processes are well understood [1-6]. Such mechanisms are not simple, since laser light of high intensity is frequently used (in terms of Joules per square centimetre-fluence or Watts per square centimetre-flux). Photophysical and photochemical processes resulting from this type of radiation differ markedly from those of low intensity radiation as obtained from even the most powerful lamps. The successful approach to the treatment of skin disorders or artificially induced skin discolouration as in tattoo engraving depends strongly on the mechanism of the transfer of energy from the laser beam to the relevant tissue or pigment[7-9]. When light is incident upon a medium such as skin with an embedded pigment, it is reflected partially at each mismatch of refractive index,i.e., at each material boundary. In the case of tattoos, this would be at the air/skin interface and at the tissue/pigment interface. Additionally, the light is partially scattered by inhomogeneities in the refractive index which in our example would principally be the transparent boundaries in the tissue. Finally, the light is absorbed partially by both the tissue and the pigment. Only this last process leads to energy transfer into the pigment particle, ultimately causing physical and chemical transformations. However the first two of these processes lead to loss of energy from the laser beam arriving at the target site and lead indirectly to effects on the perceived success of the clinical procedure. It is accordingly necessary to consider their contribution as well as the absorption process.

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Absorption as observed in a spectrometer (low light intensity conditions - ca 10^{15} photons cm^{-2} s^{-1}) results from the transfer of energy from the laser beam to excited states of the pigment molecules or ions. These may be electronic, vibrational excited states. Eventually, all of these excited states will either emit the radiation at longer wavelengths (fluorescence or phosphorescence) or they will convert the energy to heat and warm the sample. Fluorescence and phosphorescence are significant only for electronically excited states for which these may lead to substantial loss of energy being non-directional. We shall show that these effects are negligible. In a spectrometer, the heating effect is trivial. This is not so for laser experiments, however [8,9]. In laser work the light intensity is very high (ca 10^{28} photons cm^{-2} s^{-1}). If we consider the lifetime[10] of the relevant vibronic excited state as 10^{-11} s, and a molecule as 100^2 A in area (10^{-12} cm^2), it is clear that at low light intensities a given molecule interacts with 10^{15} x 10^{-12} x10^{-11} = 10^{-8} photons during the excited state's dephasing lifetime or possibly 10^{15} x 10^{-12} x10^{-9} = 10^{-6} photons in the electronic excited state's total lifetime of, typically, 1 ns. In practice this means that a molecule can only interact with one photon at a time under these conditions. However, at the high laser intensities a molecule can interact with 10^{28} x10^{-12} x10^{-11} = 10^{5} photons in the vibronic lifetime or 10^7 photons in the state's total lifetime. This process leads to multi - or multiple - photon absorption depending on whether the excited state has retained phase or not before the second photon interaction occurs. With reference to the present study, a Q-switched ruby laser, operating at 694 nm and a maximum energy density of 12 J cm^{-2} with a 25 ns pulse width, corresponds to $(hc/\lambda)^{-1}$x pulse energy / pulse duration = $(6.626 \times 10^{-34} \times 3 \times 10^{8} / 694 \times 10^{-9})^{-1}$ x12/(25×10^{-9}) = 1.67×10^{27} photons s^{-1}. If this laser pulse is applied to a 5 nm diameter spot, the laser flux becomes, $1.67 \times 10^{27} / (3.142 \times 0.25^2) 10^{28}$ photons cm^{-2} s^{-1}. Clearly this system, as used in clinical practice, is well within the multi - or multiple photon regime[11-13]. For convenience, we shall henceforth refer to this as the multiphoton regime and ignore the distinction between these in the interests of concise expression.

The relevance of the linear or low light intensity spectra to such a process is that an absorption is required to initiate this mechanism. Now all species absorb throughout the spectrum and so possess some residual absorption which will trigger multiphoton absorption[14] for any laser frequency if the laser flux is high enough. Multiphoton processes are enhanced if there is a really significant absorption at the laser wavelength as observed in a spectrophotometer. Nevertheless, the wavelength dependence of multiphoton processes is far less than that of single photon (low flux) processes as seen in a spectrophotometer. *Thus it is highly unlikely that spectrophotometric data will be a major determinant in the effectiveness of a given laser wavelength in the laser - tissue or laser - pigment interaction.*

When multiphoton absorption occurs, typical pigment ionisation energies of 10 eV (120 nm) can easily be reached (e.g. 6 photons of ruby laser light). The resultant electrons liberated from the pigment are accelerated by the electrical field (1.4×10^6 V cm^{-1}) of the intense light strongly absorbing the remainder of the 25 ns of the laser pulse (inverse Bremsstrahlung)[9,15] so that they are multiplied considerably by multiple collisions with adjacent molecules and produce a plasma even within picoseconds. The evolution of this plasma in time and space leads to light emission, spatial expansion and heating of the target area surface in tens of nanoseconds. The expansion of the plasma leads to a recoil momentum of the target resulting in a pressure wave travelling with supersonic velocity - i.e. a shock wave. Pressures of 10^3 atmospheres (10^4 p.s.i.) are estimated to be generated[16]. Clearly these lead to significant mechanical destruction of target pigments.

It is extremely difficult to obtain the absorption spectrum of a solid at UV/visible wavelengths because the extinction coefficient is so high. For example, a 10^{-5} molar solution can exhibit optical densi-

ties of 2 over a path length of 1 cm quite readily at the wavelength of maximum absorption (i.e. such a sample is transmitting 1% of the incident light). A solid of density 2 gm cm^{-3} and molecular weight of 300 (typical of a pigment) has an effective concentration of 2 x 1000 / 300 = 6.7 molar. This should have an optical density of 2 x 6.7 x 10^5 x 6 x 10^{-4} = 800 over the 6μm of a pigment particle diameter. No spectrometer could detect such a weak signal. Even an optical density of 8 is beyond commercially available machines. Thus, such particles are essentially 100% absorbing of the light falling on them *over a very wide range of wavelengths* providing that it is not reflected or scattered. Moreover, the light will be totally absorbed very near to the surface. This has important implications for the mechanism to be discussed later. Accordingly, we have resorted to diffuse reflectance spectroscopy which is a simple technique measuring a combination of scattered and reflected light i.e. measuring the loss of light available for the absorption process. This technique allows ready comparison of the spectroscopic behaviour of different laser frequencies across the spectrum. For the purposes of comparison with liquid phase absorption spectra *only* we present some of these reflectance spectra in the form (1-reflectance).

The general characteristics of pulsed lasers used in tattoo removal are shown in Table 1. Here it is clear that, while the maximum energy densities (fluences) for these lasers do not vary greatly, the flux can vary by five orders of magnitude. Phenomena related to the flux will thus vary greatly with laser type.

TABLE 1. General Characteristics of Lasers Used for Tattoo Removal

	Nd:YAG	Alexandrite	Ruby	Dye*
Wavelength	1064 nm	755 nm	694 nm	585 nm
Energy density (max)	8 J cm^{-2}	8 J cm^{-2}	12 J cm^{-2}	8 J cm^{-2}
Typical beam diam.	3 mm	3 mm	4 mm	5 mm
Beam cross section / cm^2	0.07	0.07	0.126	0.196
Pulse width	10 ns	100 ns	25 ns	450 μs
Flux/photons $cm^{-2} s^{-1}$	$6x10^{28}$	$4x10^{27}$	$1.3x10^{28}$	$2.7x10^{23}$

* inserted here for comparison. These have been suggested for tattoo removal in the past, but are not used much for this purpose currently.

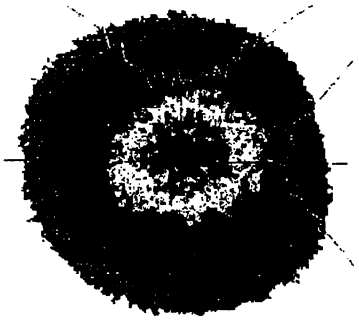

Fig. 1. The intensity profile of the Derma-Laser ruby laser. This closely approximates to the TEM_{00} profile. This was obtained with a Big Sky beam View Analyser, model BVA101 with a Cohu solid state camera No ER5002. Gaussian fit coefficients 0.9 horizontal and 0.93 vertical, diameters 2.86 mm horizontal and 2.79 vertical at 1/e points

TABLE 2. An analysis of the number, N, of treatment sessions needed for succesful removal of tattoos. Each session would consist of many laser pulses to a given site.

Laser type	Energy Density J / cm²	Pulse width /ns	Number of Sessions (N) Professional tattoos	Amateur tattoos	Reference
Ruby	6 -10	25	*13.1; 9.7; 9	*5.6; 2.5 ; 3	17
Ruby	6 - 8	40	6 -10	4 - 6	18
Nd: YAG (1064 nm)	8 -12	8	4 - 8	3 - 4	18
Nd: YAG (532nm)	(not quoted)	8	2 - 4	N/A	18
Ruby	8 - 10	28	**50% > Nd:YAG 42% = Nd: YAG best for greens	N/A	19
Nd: YAG (1064 nm)	10-14	8	8% > Nd:YAG	20% > Ruby	19
Nd: YAG (532 nm)	(not quotted, possibly 5)	8	very effective for red ink	N/A	19

* The data for 280 case studies. The first number is the mean, the second the standard deviation and the third the mode of the distribution.
** > means "better than with", = means "equally effective as".

Table 2 shows an analysis of the Number, N, of treatment sessions needed for successful removal of tattoos. Each session would consist of many laser pulses to a given site. Before analysing the clinical data, we should remember that the fluence and flux characteristics of a laser are not readily measured with any accuracy. The intensity of a laser can vary in an arbitrary manner across its diameter and so these characteristics represent an average over the laser beam cross section. If the distribution of intensity across the diameter is indeed arbitrary, this average is quite meaningless. For example, "hot spots" can readily arise, giving orders of magnitude more fluence and flux at such points than would be calculated from power meter data integrated across the full diameter. These can have a highly disproportionate effect on the decomposition mechanism initiated by such a laser. The only satisfactory route to meaningful measurements of fluence or flux is to ensure that the laser is operated with a well controlled and known intensity distribution across its diameter. The distribution of choice is usually Gaussian, being arranged by having the laser operate in TEM_{00}. It is possible to so design the cavity of a laser to produce a TEM_{00} profile [20], so that this is the simplest controlled distribution of intensity to obtain. However, energy is lost when the laser is operated in this manner and so some manufacturers will sacrifice this transverse mode quality for power. In these cases "hot spots" will undoubtedly occur and will appear randomly in position within the diameter and with time. The high quality TEM_{00} profile of the laser used in the first study[17] reported in

Table 2 is shown in Fig.1. *Without such control, comparisons of effects are unreliable.* From Table 2, it seems that the ruby laser (694 nm-red) is best for the removal of green tattoos, whereas the frequency doubled Nd:YAG (532 nm-green) is best for red ink. However, this experience contradicts the observations of the first study[17] of Table 2. *In this study, it was found that green tattoos were the most difficult of all colours to remove with the ruby laser.* Some red tattoos were removed as efficiently as e.g. blue, while others presented difficulties. This latter set of observations contradicts the simplest expectations based on considerations of low light intensity absorption spectroscopy which are that a green pigment should absorb red light and a red pigment should absorb green light. It must be remembered, of course, that for pigment mixtures metameric colour matching is possible when two colours appear the same to the eye, but differ markedly in spectral content (e.g. yellow + blue can appear the same as an appropriate mixture of green + red). Unfortunately, there can be no guarantees that tattooists will use single, pure pigments to obtain a given "red" or "green". Clearly, there is need for some simple spectroscopy to reveal the presence of such mixtures and to give an indication of the spectroscopic absorbance of a given pigment.

The purpose of the present paper is to demonstrate such a simple, reliable spectroscopy and to use it to examine the mechanism of laser induced tattoo removal based on the above clinical results.

3. MATERIALS AND METHODS

3.1. Spectroscopy

For the purpose of applying a tattoo, pigment particles of average diameter 6μm are taken up in liquids, typically proprietary mouthwash. We have found that this is not a solution, but is better described as a slurry. Indeed these pigments are essentially insoluble in any liquid, polar or non-polar. The larger particles soon precipitate, although the finer particles resist centrifuging, taking days to finally settle out. The pigments themselves are usually extremely bright and are often diluted with barium sulphate, calcium sulphate or titanium dioxide before use in tattoos. In both cases, it is clear that applying standard spectroscopic techniques to these inhomogeneous, time-varying samples presents great difficulties of interpretation and simple arguments based on the results of such studies will be unreliable.

The liquid phase "absorption" spectra were obtained on a Philips PU8720 UV/visible spectrometer using a 1 cm path length cell and freshly centrifuged preparations of pigment in mouthwash. The solid state reflectance spectra were obtained with a Spectratech diffuse reflectance attachment in Bomem DA3 Fourier transform spectrometer and referenced to filter paper (Whatman N° 1) which was found to have a flat response over the spectroscopic range of interest. The solid film was supported by the same filter paper and identical, highly reproducible, spectra were obtained irrespective of the thickness of the applied film. Solid state transmission spectra were obtained from pigment films sandwiched between two glass microscope slides in an IR Plan microscope attached to the Bomem DA3 instrument. Sites were selected where the solid film was essentially continuous and the film thickness was measured to be about 10 μm. Again, identical spectra were obtained irrespective of the site chosen in a given film. There was insufficient signal strength for this arrangement to be used to obtain the reflectance spectra. However, the percentage of light reflected in both systems is likely to be very similar, given the independence of the

spectra from film thickness in both cases. In order to check whether there was significant fluorescence present, fluorescence spectra were examined in a Perkin Elmer MPF 44 spectrofluorimeter over the complete range of excitation frequencies and no fluorescence was observed.

4. RESULTS

The interpretation of the results in a general sense, is not helped by the reticence of pigment suppliers to divulge the chemical nature of their pigments. These suppliers even refuse to acknowledge that they supply such pigments. Given the legal implications of any condition attributable to the pigments this reticence is understandable.

4.1. Identity of the Pigments

The pigments used in the current study were subjected to Energy Dispersive X-ray Fluorescence, EDXRF, analysis (Oxford-Tennelec Nucleus, Si/Li detector, 170 eV resolution at 5.9 ke V,^{109} Cd source) and Powder X-ray diffraction in order to acquire some knowledge of their chemical nature. It is out of the question to exactly identify these pigments, since they are undoubtedly mixtures and probably impure compounds. Nevertheless, these studies were quite revealing. The X-ray diffraction conclusively proved that the white pigment was titanium dioxide and that the blue was copper phthalocyanine .The green pigment seemed to be a mixture of TiO_2 and a copper compound, but with a high bromine content.

We deduce that this probably indicated the presence of a brominated copper phthalocyanine plus possibly other orange pigments. The yellow, orange and red pigments, which present similar reflectance spectra, are all heavily chlorinated pigments, the yellow and orange being diluted with calcium sulphate. Strangely, the light red pigment does not contain chlorine but is lightened by addition of the expected TiO_2. In fact the reflectance spectra, as used in this study, provide a simple and valuable diagnostic aid to determine whether pigment samples are of the same origin. The brown pigment was essentially two forms of titanium dioxide (anatase and rutile) together with some organic pigment.

4.2. Liquid phase spectra

Given the inhomogeneous nature of the liquid phase spectra in the visible wavelength range, these were not used as a basis for any deduction. They are shown with the accompanying solid phase spectra for comparison. In the case of the red pigment (Fig. 2) solid phase (1-reflectance) spectra and liquid phase "absorption" spectra yield similar results, but in the case of the blue and green pigments (Figs.3, 5 and 6) the liquid phase spectra show a broad structure which is quite different from that seen for the solid. The scattering properties of the solid particles suspended in the liquid will be quite different from those of a film of solid particles as found in a tattoo, so that such differences are not surprising. Accordingly, such spectra are considered to be quite useless in assessing the behaviour of the solid pigment to laser radiation.

4.3. Solid State Reflectance Spectra

The reflectance spectra of the solid films may be classified into two groups. Pigments through the range from red to yellow and brown yield spectra similar to the red pigment as shown in Fig.4. The blue

and green pigments, however, show distinctive features in the infrared region (Fig.5). In Figs. 6 and 7, the solid phase spectra shown are calculated from 100% less the percentage of reflected light, scattered light and light transmitted by the sample. This is simply for the purpose of approximate comparison with the liquid phase spectra which are in the absorbance mode. Given the high extinction coefficient expected for such pigments, it is most likely that the observed transmitted light is transmitted indirectly by a series of reflections from particle facets in the thickness of the rather open film.

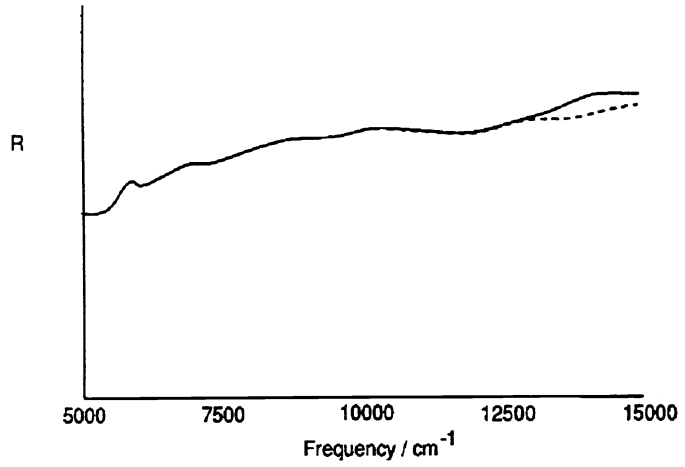

Fig. 2. Red pigment, solid line = (1-solid phase reflectance) spectrum, dotted line = liquid phase "absorbance" spectrum, (both in arbitrary units).

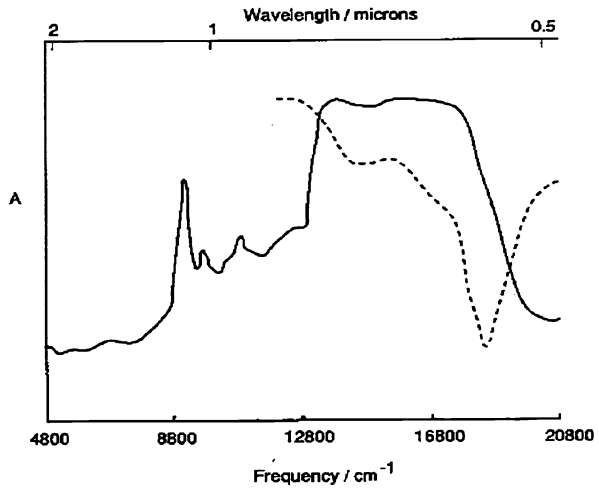

Fig. 3. Blue pigment, solid line = (1-solid phase reflectance) spectrum, dotted line = liquid phase "absorbance" spectrum, both in arbitrary units.

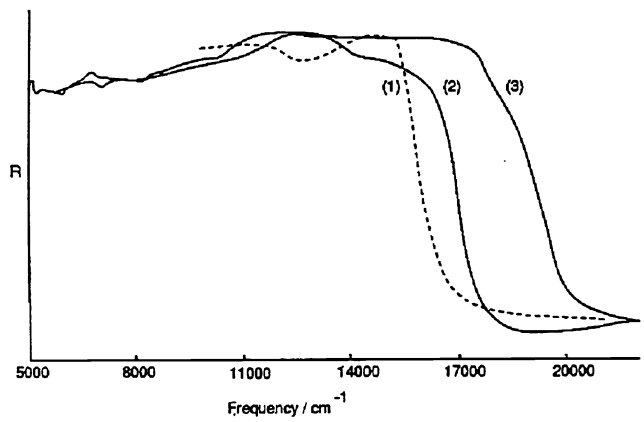

Fig. 4. Reflectance spectra of (1) = light red pigment, (2) = Red Pigment, (3) = yellow pigment, all in arbitrary units.

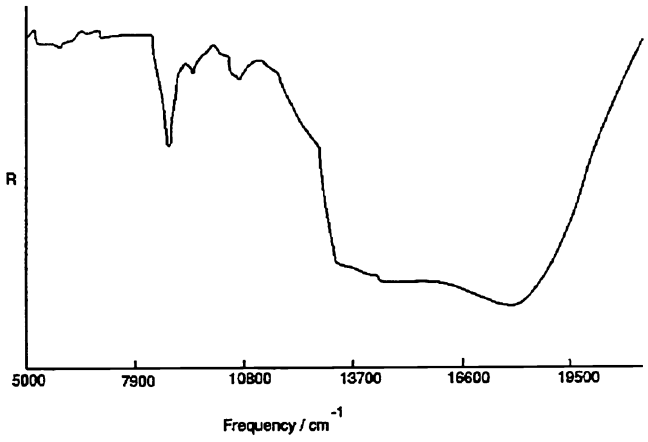

Fig. 5. Reflectance spectrum of blue pigment in arbitrary units.

In this case the transmitted light is simply the forward reflected light. There is little difference in the spectrum whether the transmitted component is included or not, although there is a slight red shift in the absorbance calculated by the former method and such a shift can only be due to a significant absorbance component affecting the transmitted light. The figures for absorbances estimated this way must be in arbitrary units, since the spectrometer will fail to collect all the scattered light by some degree which varies with each sample.

If we consider the reflectance spectra of the blue and green pigments in Fig. 7, remembering that these represent the light lost by reflection and backscattering, it is clear that the loss of light is low and similar for both pigments at the ruby laser wavelength. The units shown are exactly as produced by the spectrometer. However, differences in surface texture may change these by around 0.1 reflectance units. Thus the behaviour of these pigments to this laser should be similar. If these pigments behave differently, it is not, therefore, due to the spectroscopic characteristics of the compounds, but to some other factor. Given that the ionisation potential of these pigments will also be closely similar, the shock wave generation following multiphoton ionisation is expected to be similar. Closer investigation [21] of the two pigments reveals that the particle size distribution is different, however. The green pigment contains particles up to 200 μm diameter while the blue particles have a maximum diameter of 100 μm. Since the blue and green pigment spectra are similar in the ruby laser regime, however, the effect of the skin and the tissue/pigment interface as against the air/pigment interface will be common to both, we attribute the different behaviour of these two pigments to the ruby laser to this difference in particle size. In amateur tattoos the pigment

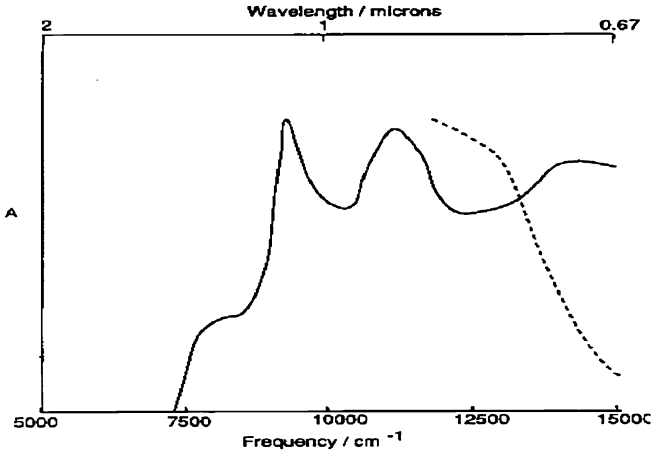

Fig. 6. Green pigment, solid line = (1-solid phase reflectance) spectrum, dotted line = liquid phase "absorbance" spectrum, both in arbitrary units.

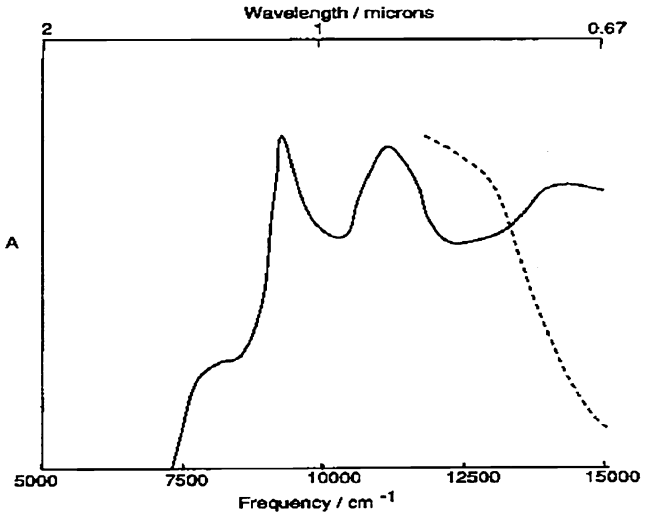

Fig. 7. Reflectance spectra of the blue (solid line) and green (dotted line) pigments referenced to an aluminum mirror. The vertical lines indicate laser wavelengths,

(a) = Nd:YAG, (b)=Alexandrite, (c)=ruby, (d)=frequency doubled Nd: YAG.

has been found to be largely extra-cellular located in "pools" in the mid to deep dermis. Professional tattoo work, however, lodges pigment both extra-and intra-cellularly, the latter being contained in the cytoplasm of macrophages. This is probably why professional tattoos are more difficult to remove [22,23]. Additionally, the green pigment is not a pure compound, but, as deduced above, probably contains a mixture of brominated copper phthalocyanine and other organic pigments. Unlike the pure, blue copper phthalocyanine, this mixture will not grind to such a fine powder, but will tend to form a "paste" and give the larger aggregates as observed.

Likewise, from fig. 7 it is clear that both alexandrite and ruby laser light are reflected similarly by these pigments and thus similar behaviour would be expected from low light intensity arguments. The alexandrite laser is found to be less effective[24] than the ruby[25], however, and this must therefore be due to the difference in flux (W cm^{-2}). Not only must the energy (J) be considered in such a comparison, but the pulse width and irradiated area are also vitally important, all these being involved in the calculation of the flux (see above). Multiphoton processes are flux driven not fluence driven, and so such a mechanism is most probably operating in the tattoo removal process as predicted from the calculations shown above.

5. DISCUSSION

"Absorbance" spectra of pigments slurried in liquid have been shown not to be true absorbance spectra for typical compounds and from their insolubility in essentially any solvent. It has also been shown above that the absorbances of all pigments throughout the visible spectrum may be considered to be extremely strong even at quite large wavelength separations from the centre of the transitions. These spectra are therefore disregarded as useful diagnostics either for the identification of pigments as similar or for predicting their spectroscopic behaviour in laser assisted tattoo removal.

Solid state spectra have been obtained by a simple diffuse reflectance technique and in transmission mode under a microscope. In the latter experiments, the "transmitted" light closely corresponds, spectroscopically, to reflected light. Additionally, there were no visible direct paths through the sample. It is therefore deduced that this "transmitted" light permeates the sample by multiple reflection in voids within the sample thickness and is not light remaining after true absorption. This is expected from the estimation of likely extinction coefficients for such materials.

Our interpretation of the reflectance experiments is that these give a reasonably accurate measure of the loss of light energy at the surface of the solid pigment. This measure will be valid both across the wavelength range and between different pigments, although in the latter case, sample preparation can lead to minor (<0.1 reflectance units) irreproducibilities. Given the enormous absorption coefficients in the visible spectrum expected for all these pigments from red through to blue and that their colour as perceived by the eye is directly related to their reflectance spectra as we obtain them, considerations of their colour in terms of their relative absorbance are certainly irrelevant. Of course, reflectance and absorbance are related, but the extremely high absorbance of all these solids at particle sizes representative of tattoo practice implies that they will differ in this respect less sharply, both as a function of wavelength and in their depth of surface penetration of the light, than would be expected. In all cases this will be extremely small, i.e., all light absorption of all colours of pigment will occur essentially within <1 μm of the surface. This process will, at sufficiently high *flux*, lead to multiphoton absorption, ionisation, plasma formation, followed by shock wave production and mechanical, pressure-wave-induced breakdown of the pigment

particle. The flash of light observed clinically is almost certainly indicative of emission of highly excited states in this plasma and not of a mechanism where such states are excited thermally. For the reasons given above, the wavelength dependence of this mechanism is much less sensitive than might be expected from the usual characteristics of absorption spectra of dyes.

In all experiments a comparatively fine dividing line exists between the onset of this mechanism for the pigment and the operation of this mechanism in the overlying tissues above the tattoo. If the flux is too high, the skin will be disrupted also. If the flux is too low, little or nothing will happen to the pigment or the skin. The alexandrite laser is less effective than the ruby quoted here, almost certainly because its pulse width is around 75-100 ns compared with the 25 ns of the ruby. For equal irradiated areas and pulse energies, this means that the alexandrite flux is 4 times less than that of the ruby.

Since this multiphoton mechanism is highly non-linearly dependent on the laser flux, the control of the laser beam intensity profile is of great importance. Failure to ensure such a stable profile will lead to random production of unusually high flux zones in the laser cross-section. These are very likely to initiate multiphoton processes in the skin and cause unwanted disruption, possibly leading to scarring. To minimise scarring, the flux on the beam axis must never exceed the value which allows multiphoton absorption to occur in the skin tissue. This can only be guaranteed if the laser operates in the TEM_{00} mode.

The mechanism explains also the vast superiority of the Q-switched laser over the cw laser. Multiphoton processes and their attendant shock wave cannot occur with cw radiation. Only truly thermal processes will occur, leading in effect to a burn in the traditional sense. The effect of the absorbance spectrum of the pigment will be greater in such a case, but the loss factors as measured by our reflectance spectra are still very relevant in assessing the differential effects of various lasers and pigments. The pigment will still be essentially totally absorbing at its surface.

In applications requiring the thermally induced coagulation of blood vessels, lasers with pulse lengths in the milliseconds regime are predicted to be best. This is because shock wave induced particle breakdown is not required in these cases. The heating of a blood vessel depends on the laser *flux* again, because now the temperature reached by the blood in the vessel depends on the fine energy balance[26] between the input laser flux and the thermal diffusivity of the vessel. This latter depends, amongst other parameters, upon the inverse of the square of the radius of the vessel. Thus, there will be a range of vessel diameters below which a given cw laser is ineffective, due to too rapid heat removal, and above which the temperature rise will be excessive, leading to unfortunate effects. In this context it should be noted that too high a repetition rate of the long laser pulses, applied to the same spot, will again lead to excessive temperature rise, because the thermal diffusivity of tissue (essentially that of water) is such that seconds must elapse before ambient temperature is reached (within 1%) in treated tissue. Being controlled by these kinetic factors, there is a great tendency for temperature to integrate with time if such long periods are not allowed. In the tattoo removal experiments all the applied energy is ultimately degraded to heat and, for the same reasons as just discussed, the Q-switched pulse repetition rate should not be much above 1 Hz at the same spot [27,28]. Indeed there is some evidence that patients treated with the higher repetition rate lasers do show more scarring than when low repetition rate systems are used.

6. ACKNOWLEDGMENTS

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CASE REPORTS

Q-switched Ruby Laser Treatment of Benign Pigmented Lesions in Chinese Skin

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CASE REPORTS

Q-switched Ruby Laser Treatment of Benign Pigmented Lesions in Chinese Skin

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Abstract

The Q-switched ruby laser has been demonstrated as an effective choice of treatment for a range of benign pigmented lesions. Its wavelength of 694 nm enables deep penetration of the skin allowing the treatment of both epidermal and dermal lesions. However, this wavelength is selectively absorbed by melanin thereby enabling efficient targeting of the lesion's melanocytes. By utilising a Q-switched pulsewidth of 25 nanoseconds, thermal conduction into surrounding tissues is minimised.

Lesions such as nevus of Ota, chloasma, lentigines and cafe au lait have been successfully treated with energy densities ranging from 6 to 12 J/cm^2. Four case histories are described in this report. The clinical evidence indicates that pigmented lesions in Chinese skin must be treated with energy densities higher than those used in Caucasian skin to minimise the incidence of hyper-pigmentation. Typically, lesions require a small number of treatments, usually within the range one to six, to effect complete removal. The technique is easy to apply, with no need for anaesthesia, in many cases.

Keywords: Laser-tissue interactions, Melanocyte, Photo-mechanical reaction, Selective absorption, Vacuolation

Introduction

The occurrence of pigmented lesions in Chinese skin is very common, as high as 80-90% for certain conditions in females. This appears to be due to a number of factors including sun-induced changes, skin composition and also possibly diet/cooking habits. A number of techniques have been used for many years to remove these lesions with varying degrees of success. The recent application of the Q-switched ruby laser has proven to be a major success with a range of lesion types.[1,2]

All lesions treated by any type of laser must be benign since it is impossible to know if any potentially malignant cells will remain following laser treatment. This, therefore, limits the types of lesions which may be treated by this method but these still represent a large number.

Many lasers are now being used to treat pigmented lesions of the skin. This is possible due to the broad absorption profile of melanin across the visible part of the spectrum, thereby allowing almost any visible laser to induce some kind of reaction within the melanocytes.[3] While some of these lasers possess suitable wavelengths, some of them are limited in their applicability and by their pulsewidths.[4] This topic will be discussed in more detail in a later section.

Unlike vascular lesions which require a photo-thermal reaction to induce necrosis, pigmented lesions are thought to require a combination of both a photo-thermal and a photo-mechanical process. The latter reaction induces the formation of a pressure- or shock-wave at the surface of the melanin granules within the melanosomes causing these to fracture. This results in the melanocyte becoming dysfunctional while leaving the surrounding compliant tissue relatively undamaged. A little thermal coagulation may occur in the immediate vicinity of the melanocyte but this does not usually lead to gross skin damage. The process is similar to that in the treatment of tattoos by this laser.[5]

CHOICE OF LASER PARAMETERS

Most of the melanin in normal skin resides in the thin basal layer at the dermal-epidermal junction. In pigmented lesions, however, this is not the case since the large amounts of melanin may be found throughout the epidermis or dermis, depending on the type of lesion. The nevus of Ota typically contains melanin through the depth of the dermis whereas cafe au lait lesions are generally located only in the epidermis. This distinction is very important when considering laser treatment of these lesions since not all lasers are capable

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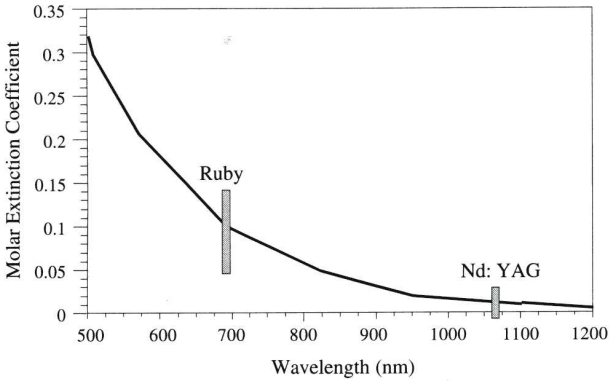


Fig. 1. Melanin extinction profile showing the ruby and Nd:YAG wavelength positions. Note that the ruby laser energy is absorbed approximately 3.6 times more efficiently than Nd:YAG energy.

of doing so. The reason for this lies in the melanin absorption profile (Fig. 1).

CHOICE OF WAVELENGTH

Melanin absorbs light across the whole of the visible spectrum, from 400 nm (blue light) to 700 nm (red light). However, this absorption decreases as the wavelength increases which has an important effect on the way in which laser light interacts with the skin. In addition, the epidermis and dermis possess absorption and scattering characteristics which are also dependent on the wavelength of the incoming light.[6-8] The combined effect of these processes is clearly demonstrated when laser light is used to treat lesions of the skin.

Much work has been done with the treatment of vascular lesions by lasers.[9,10] The results of this work have yielded a reasonable understanding of the laser-tissue interaction for a number of laser types. These include the argon, pulsed and continuous dye and the copper vapour lasers. Theoretical studies have revealed the importance in choosing the 'correct' laser parameters when considering treatments such as the wavelength, pulsewidth and spot size.[11,12] Using the knowledge built on the treatment of vascular lesions, the same theories may be applied to the laser treatment of pigmented lesions.

The choice of wavelength has two major implications. The first of these is directly related to Figure 1 in that the amount of absorption of laser energy is determined by the wavelength. Therefore, more light energy at 500 nm will be absorbed compared with light at 600 nm at some particular depth. At first this may seem to favour the shorter wavelengths for this application but at this point the second implication comes into account. Due to the general absorption and scattering processes within the skin, as a whole, red light can penetrate deeper into the skin than blue light. Therefore, the initial choice of a blue laser output is no longer so attractive since this would only allow an effective treatment of the more superficial lesions but not the deeper, dermal lesions.

Hence, a wavelength which allows deep penetration of the skin coupled with sufficient absorption by the melanin is required to maximise the range of lesions which may be treated.

CHOICE OF PULSEWIDTH

The next parameter to consider is the laser pulsewidth. This dictates how quickly or slowly the laser energy is absorbed by the melanin. A slow absorption (i.e. a long pulse) will allow any heat build-up to conduct into surrounding tissues which may result in unwanted thermal damage. Such damage may lead to fibrosis and scar tissue formation. Obviously these need to be avoided and so a suitably short pulse should be used. A short pulse will cause the laser energy to be absorbed relatively quickly by the melanin thereby reducing the likelihood of thermal conduction.

By using a Q-switched laser output, the pulsewidth can be reduced to tens of nanoseconds (1 nanosecond = 10^{-9} s). Such short pulsewidths result in minimal conduction within the skin which in turn results in very rapid localised temperature increases. The temperatures attained may be several hundred or even thousand degrees Celsius at the surface of the absorbing chromophore, in this case the melanin granule. However, these temperature gradients exist for very short timescales and they collapse to induce localised shockwaves. As these shockwaves propagate outwards from the chromophore, they cause any nearby brittle tissues to fragment while leaving compliant tissue unaffected. This process is known as a photo-mechanical reaction.

Some of the absorbed energy causes local tissue water to evaporate causing the creation of steam pockets around the melanocytes. This is evident immediately following irradiation of the lesion as a white patch approximately the same size as the laser spot. This process is initially a photo-thermal reaction leading to a mechanical response.

It is thought that a combination of the above processes may be required to induce clearance of a pigmented lesion.

CHOICE OF SPOT SIZE

Computer modelling of the effect of laser beam diameter in the interaction processes within the skin has revealed that even this parameter must be considered carefully.[13] These researchers have shown that the skin attenuates small laser beam diameters (around <0.5 mm) more efficiently than larger diameters. This is due to increased scattering effects in skin which are more prevalent with small beam diameters. The result of this effect means that less energy will penetrate the skin when small beam diameters are used. Hence some

lasers which may have suitable wavelengths might not be able to treat deep lesions if only a small spot diameter is available.

Other factors which will determine the outcome of any treatment will generally be attributable to the physical make-up of the lesion, in particular its depth and thickness. However, these parameters may not be influenced by the clinician whereas the choice of the above laser parameters may be.

Materials and Methods

A Derma-Lase DLR-1 ruby laser was used in this study in the Mainz Body Clinic, Taipei. Its wavelength of 694 nm and pulsewidth of 25 ns comply well with the above requirements. A spot size of 5 mm at the patient surface was used for each treatment, again complying with the above requirements. Laser pulses were placed contiguously on the lesion with a slight overlap of around 0.5 mm. This overlapping procedure did not appear to cause any problems either during or after the treatment. Safety goggles were worn by all personnel, including the patient, in the treatment room at all times when the laser was active. This is very important since eye damage can occur even with a small amount of reflected laser energy if goggles are not worn.

The patients were selected according to lesion type. Only those patients with benign lesions were treated. All patients with any possibility of malignancy were directed to alternative treatments. The lesion types treated included nevus of Ota, cafe au lait, chloasma, epidermal melanosis and lentigines.

An immediate whitening reaction occurred in all patients following irradiation which corresponded to steam vacuolation within the epidermis. Occasional surface pinprick haemorrhaging and/or sub-surface bruising occurred in a small number of patients, particularly those with darker lesions, although these usually cleared within three days. This is thought to be caused by the photo-mechanical shockwave inducing some superficial capillaries to fracture due to their proximity to melanocytes. However purpura, as observed following pulsed dye laser treatment of vascular lesions, was not evident in any case. The standard weal and flare response usually occurs within minutes of the treatment.

Treatment energy densities generally started in new patients at 6 J/cm^2. If no whitening reaction was observed, the energy density was increased by approximately 1 J/cm^2 increments until whitening did occur. Generally lighter lesions required energy densities in the range of 6-9 J/cm^2 while darker lesions needed up to 12 J/cm^2 to induce the desired endpoint.

No anaesthesia was used since the treatment is not considered painful by patients. It is typically described as a sensation similar to an elastic band being snapped against the skin.

Results

CASE 1

Figures 2(a) and 2(b) show a young (20 years old) female patient with a cafe au lait lesion before and after treatment with the ruby laser. An energy density of 6 J/cm^2 was applied in two sessions lasting approximately 20 min each. The sessions were six weeks apart. An immediate whitening response occurred which lasted for a few seconds. The result shown was photographed after the second treatment.

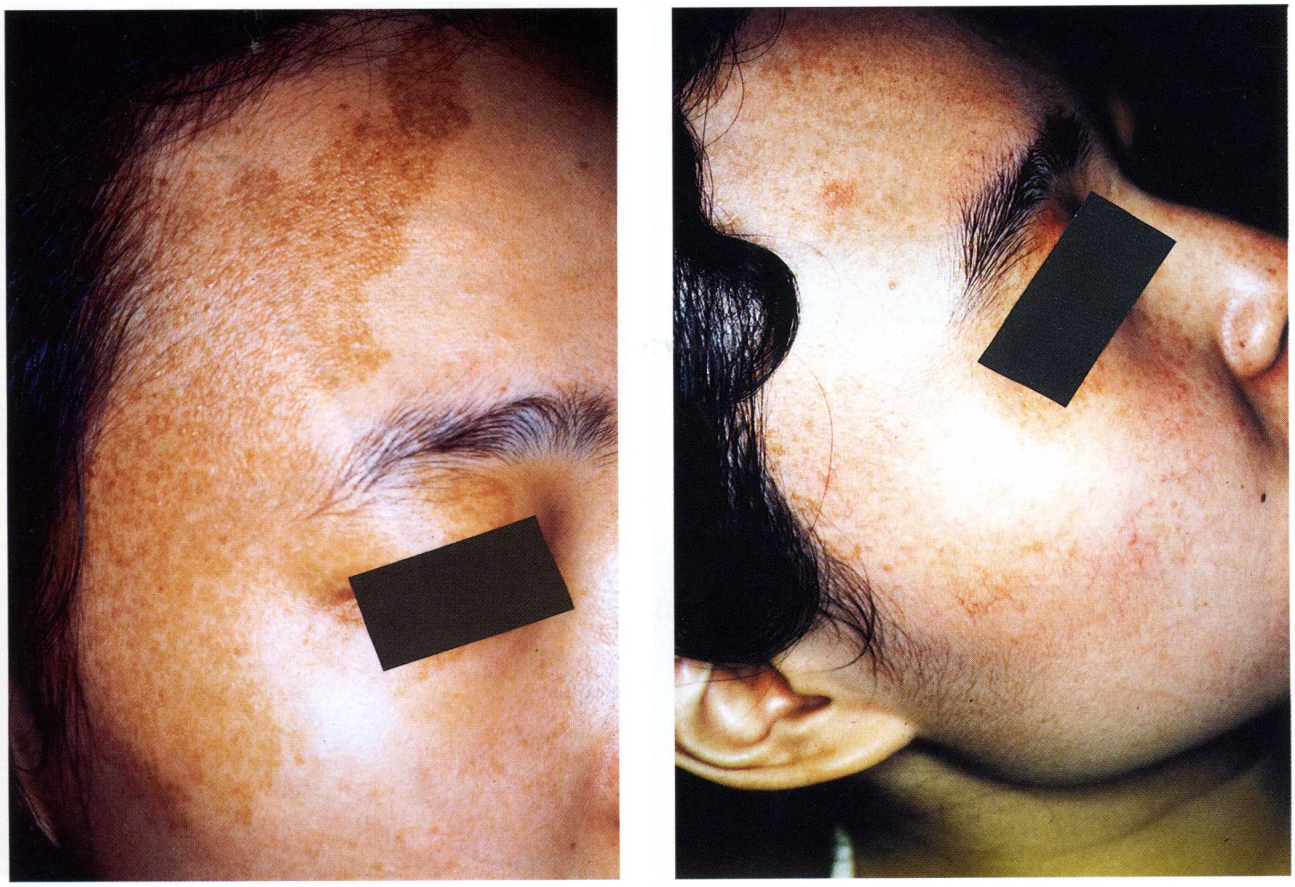
Most of the lesion has disappeared following these treatments although the patient will probably undergo one further treatment. The area immediately around the eye was not treated due to the lack of the specialised eye safety shields. The skin texture and tone was not affected by the treatments although some slight hypo-pigmentation was evident. The lesion has not yet recurred but the patient is still under observation.

CASE 2

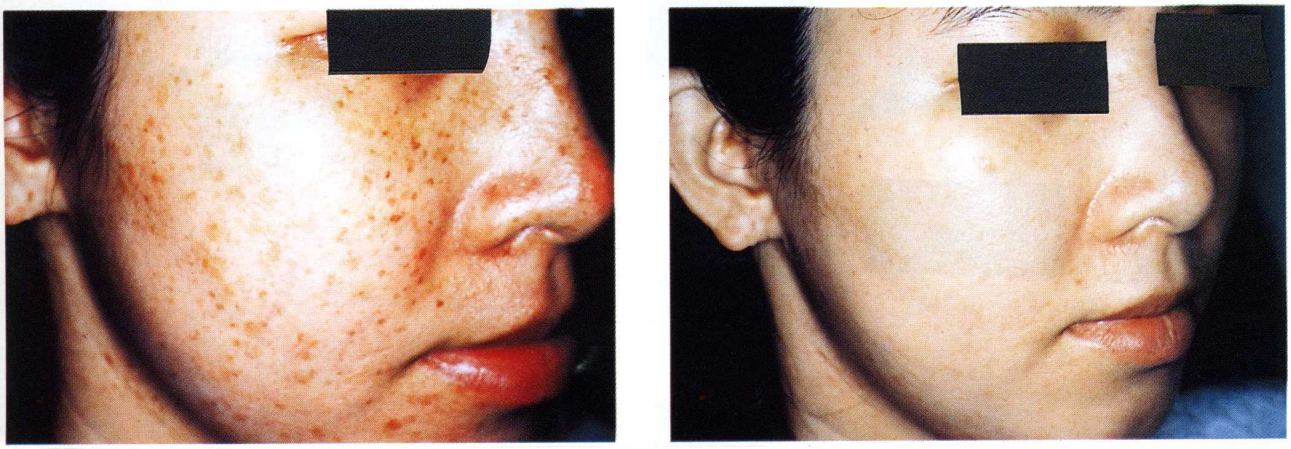
Another female patient (33 years old) presented with freckles with verruca planus (Fig. 3(a)). She was treated at 7, 9 and 10 J/cm^2 over three consecutive treatment sessions. The first two of these sessions were partial area treatments and were carried out over two days. The third session occurred nine days after the second session. Once again, an immediate whitening reaction was observed following irradiation. Two weeks later, the treated area appeared to be free of most of the lesion again with some slight hypo-pigmentation (Fig. 3(b)). This patient is currently under observation as there is some evidence of recurrence in some areas.

CASE 3

The female patient (48 years old) in Figure 4(a) presented with chloasma and lentigines on her left cheek. It was decided to compare the effects of the ruby laser against conventional treatment methods. Part of the lesion was treated with the laser while the remainder received chemical treatment via Retin-A, corticosteroids and hydro-quinone. After only one treatment at 5 and 7 J/cm^2 by laser, the lesion appeared to clear completely. Similarly the chemical treatment resolved the lesion. However, the patient was subsequently exposed to sunlight which resulted in a surprising reaction. The area treated by the chemical method began to show signs of recurrence while the laser-treated area did not. The follow-up photograph of the laser-treated area (Fig. 4(b)) was taken three months following treatment and shows no signs of recurrence. She is still under observation for any further indications of recurrence.



Figs. 2(a)(b). Female patient with cafe au lait before (left) and after (right) two treatments. An energy density of 6 J/cm² was applied during the treatment.



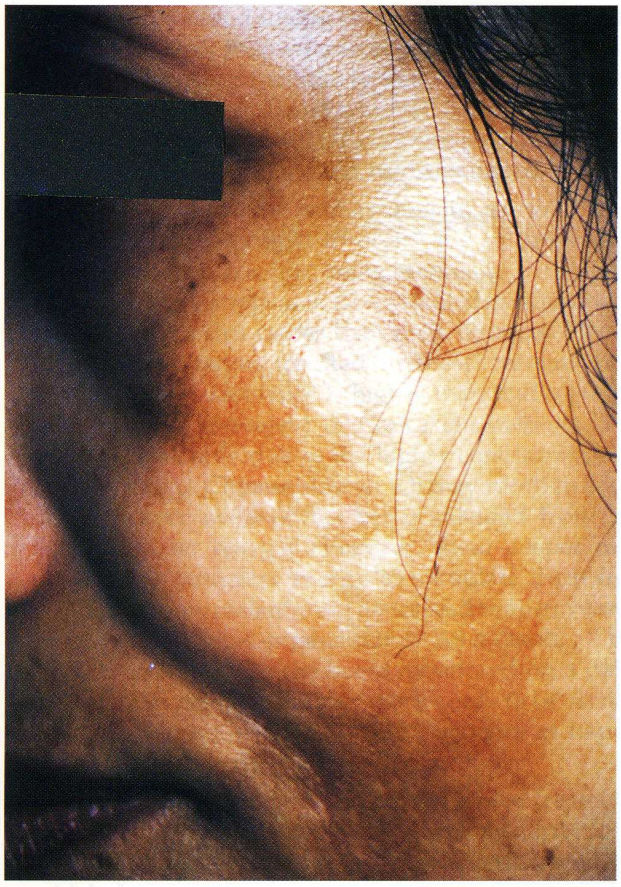
Figs. 3(a)(b). Female patient presenting with freckles with verruca planus (left). These required the range 7 to 10 J/cm² to effect clearance (right). However, some recurrence has been observed.

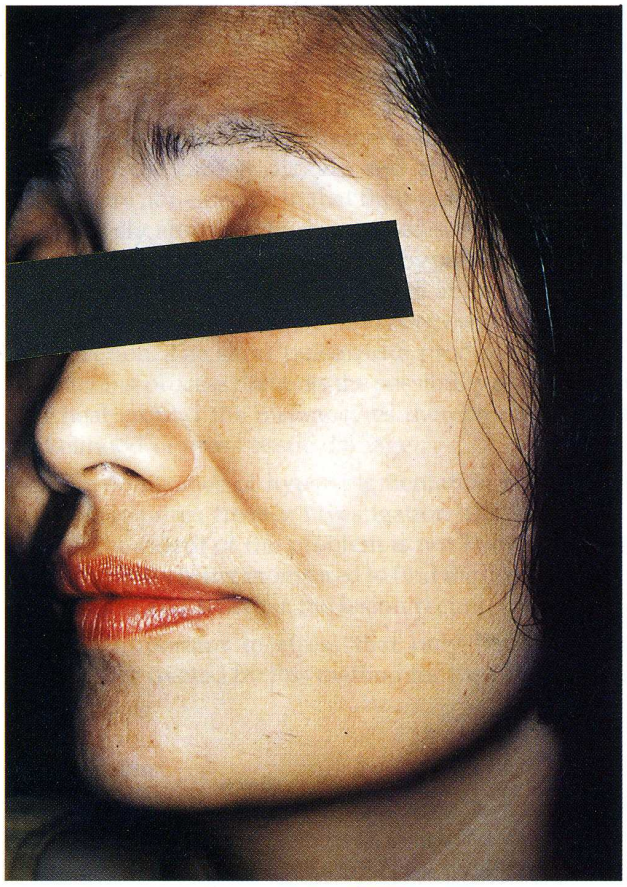
CASE 4

This male patient (39 years old) presented with a nevus of Ota (Fig. 5(a)) for treatment. The final result was obtained after six treatments with energy densities in the range 10 to 12 J/cm² with intervals of one to three weeks between treatments. The top layer of skin formed a scab after the first treatment which flaked off after around six days (Fig. 5(b)). No recurrence of the lesion has been observed to date.

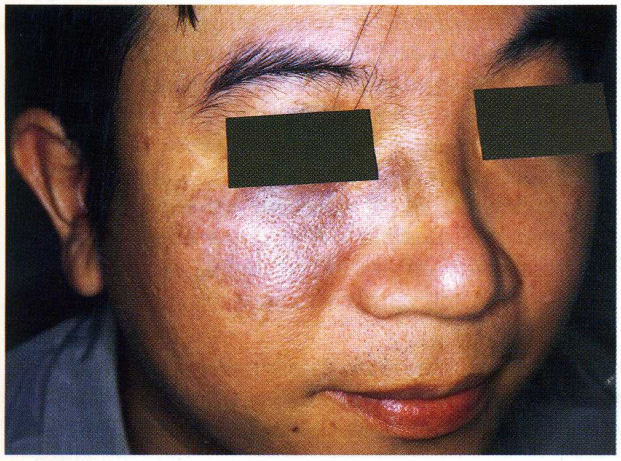
Discussion

In general, superficial lesions were treated within a range of energy densities from 6 to 9 J/cm² while the deeper lesions required up to 12 J/cm² to effect removal.





Figs. 4(a)(b). This patient required treatment for chloasma and lentigines (left). Using energy densities of 5 and 7 J/cm², the lesion was effectively cleared after only one treatment (right).



Figs. 5(a)(b). Male patient with nevus of Ota. Six treatments were required with energy densities between 10 and 12 J/cm².

No lesions were treated above this energy density. It was found that superficial and lighter-coloured lesions typically required fewer treatments than the deeper, darker variety. Some lesions, such as lentigines and the lighter cafe au laits, required only one or two treatments at intervals ranging from one to four weeks. Deep lesions like nevus of Ota needed more treatment sessions

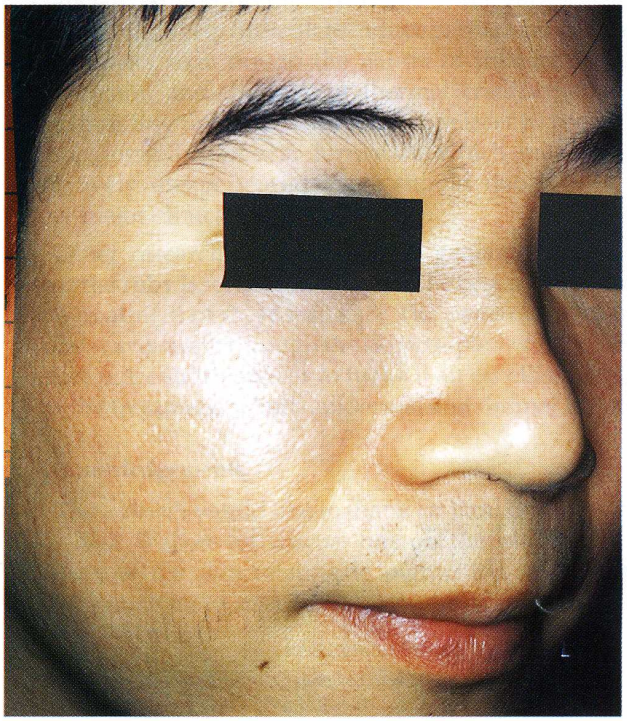


Fig. 5(b).

although this varied among patients. Scabbing occurred in some patients following irradiation. Unfortunately, some patients, particularly female, disliked the appearance of the scab and removed it themselves. It is felt that this removal has had a detrimental effect on the overall treatment and should be discouraged.

Hyper-pigmentation was evident in up to 25% of patients. This is thought to occur due to lower than required energy densities being applied to the lesions. These treatments appear to have resulted in stimulation of the melanocytes rather than their necrosis. Hence, hyper-pigmentation resulted in these patients post treatment. This incidence is higher than that reported following the treatment of Caucasian patients. The reason is probably due to the higher concentration of melanocytes in Chinese skin which may result in some of the deeper melanocytes being shielded from the incoming laser energy. However, these deeper cells may absorb sufficient energy to stimulate them into producing more melanin and hence lead to an increased probability of hyper-pigmentation. As a result, all the patients in this study are being monitored on a daily basis, where possible. Further work needs to be carried out to determine why the higher incidence of hyper-pigmentation occurs in this patient group.

The clinical results indicate that effective treatment may be achieved by the use of the Q-switched ruby laser without inducing scarring. Two unwanted side effects which have been observed are hypo- and hyper-pigmentation although the former of these was found to be transient in nature. Hyper-pigmentation appeared within days of the treatment and in some cases remained for a few months. Other researchers have indicated that this can persist for up to 12 months post treatment but that, in most cases, it disappears naturally. A suggested method for prevention of hyper-pigmentation involves the application of hydro-quinone on the lesion up to two weeks in advance of treatment. By blocking the enzymes involved in the production of melanin, it is thought that treatment-induced hyper-pigmentation may be avoidable. At the time of writing, this theory had not been tested.

Another side effect which occurred in a small number of patients was the appearance of telangiectatic vessels in the vicinity of the treated lesion. These were small and generally faded naturally over the course of two to four weeks. They generally appeared after any scabs had been removed. Interestingly there was a strong correlation between the appearance of these vessels and the subsequent appearance of hyper-pigmentation. If the vessels did not appear, hyper-pigmentation did not usually follow. This was particularly evident in lesions on the cheek and chin, however, hyper-pigmentation was never observed on the forehead. The reason for the appearance of these vessels is not yet fully understood.

The ruby laser appears to offer an excellent treatment modality for benign pigmented lesions, particularly in Chinese skin which is more prone to scar tissue formation than Caucasian skin. This fact negates the use of any laser which induces a photo-thermal reaction in the skin such as the carbon dioxide and argon lasers. These lasers are non-specific in that their wavelengths are not selectively absorbed by pigmented tissue whereas the ruby wavelength is well absorbed by melanin. However, the dermis is relatively transparent at this wavelength which allows penetration of the energy with little dermal absorption. The short pulsewidth produced by the Q-switching process prevents the possibility of conduction of heat around the melanocytes thereby reducing the likelihood of gross tissue damage.

The occurrence of hyper-pigmentation is a problem which requires further investigation although at this time, the extent of the problem is not known. Patients are currently being monitored to find the duration of the condition and whether the lesion recurs.

It is important to stress that only benign lesions should be treated by this method for the reasons given previously.

Conclusion

Further clinical studies are needed to quantify the numbers of treatments necessary and the most suitable energy density for each lesion type. However, as with tattoos and vascular lesions, there is a degree of variability between patients which cannot be predicted by the clinician. An important advantage of the ruby laser is that it is relatively difficult to induce permanent damage to patients' skin due to the nature of the laser-tissue interaction and the lack of thermal conduction into surrounding tissues. Hence it is a safe laser to use with little possibility of scar formation which means that relatively inexperienced users should not encounter any major clinical problems.

Other researchers seem to be in general agreement that the ruby laser currently offers the best modality for the treatment of these lesions.[1,2] The penetration of the ruby wavelength through the skin coupled with its very short pulsewidth appear to make it an excellent choice for the treatment of both epidermal and dermal lesions.

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Treatment of portwine stains using the pulsed dye laser

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SUMMARY. **Five years of clinical experience of the treatment of portwine stains using the flashlamp-pumped dye laser is presented.**

The dye laser, when turned to a wavelength of 577 nanometres with a short pulsewidth of the order of 340 microseconds, may be used to target selectively the dilated vasculature constituting the lesion.

Patients with ages ranging from 5–45 years were treated under general anaesthetic using a computer controlled scanning system developed by the authors.

Several repeat treatments were found to be necessary. Results are presented ranging from total eradication of the lesion to marginal lightening only. No scarring of the treated sites was evident.

In recent years, many workers have described the application of laser technology to the treatment of portwine stains. Lasers have been used to target specifically the oxy-haemoglobin encapsulated within the dilated vasculature constituting the lesion. In this context, continuous wave argon and dye lasers, in addition to pulsed dye and copper vapour lasers, have received attention.

Laser treatment of portwine stains dates to first reports by Apfelberg *et al.* (1976) who described the application of the argon laser to the management of vascular lesions. A later report, by Dixon *et al.* (1984), detailed a study of 146 patients using the argon laser. Results demonstrated a higher incidence of scarring of 40% among young patients, compared to a 20% incidence of scarring in adult patients.

The argon laser wavelength of 514 nm does not coincide precisely with the absorption maxima of the targeted oxy-haemoglobin. Three such absorption maxima exist, at 418 nm, 542 nm and 577 nm. Highest blood absorption is exhibited at 418 nm, a wavelength at which the melanin in the epidermis displays significant absorption. Competitive epidermal absorption decreases through the visible region to the 577 nm wavelength, which has consequently been the subject of more recent study.

The identification of the optimal 577 nm wavelength was accompanied by studies of the effect of the exposure duration on the efficacy of treatment. Anderson and Parrish (1981) described the requirement for the impartation of the energy within the thermal retention time constant of the targeted vasculature. These parallel studies prompted the development of the flashlamp-pumped tunable dye laser. The use of a short-pulse (0.3 microseconds) dye laser was first described by Greenwald *et al.* (1981). In that study, and later reports by Tan *et al.* (1984), the ability of the laser to produce purpura was noted, although neither group of workers was able to report favourable response to treatment.

An explanation for the lack of efficacy was advanced by Hulsbergen-Henning *et al.* (1984) who demonstrated the effects of the short pulse dye laser to include locally specific microvaporisation and mechanical damage to the vasculature. They showed that these processes constituted reversible damage mechanisms.

These findings prompted the redevelopment of a longer pulsewidth dye laser, thought more likely to induce coagulation and shrinkage of the targeted vasculature as a result of limited conduction of heat during the 340 microseconds pulsewidth, and this pulsewidth was thought more closely to approximate the thermal retention time constant of the targeted vasculature.

The efficacy of the longer pulse dye laser has been documented by Garden *et al.* (1988) who found, by direct comparison, a higher incidence of lesion lightening among patients treated with the longer pulse laser. This study documents the findings from a 5-year clinical trial of the use of the long pulse flashlamp-pumped dye laser. The treatments are based on extensive theoretical modelling of the interaction process (Miller *et al.*, 1991), and use a novel scanning system developed by the authors.

Materials and methods

A flashlamp-pumped dye laser (Candela Corporation, US) was used in these trials. This laser emitted pulse energies of up to 5J with pulsewidth of 340 microseconds. The laser was sited remotely from the treatment area, energy being delivered by means of a 1 mm diameter optical fibre. The laser light was launched into the fibre using a 5 cm focal length lens and was collected at the distal end by means of a 1.8 cm focal length lens contained in the endpiece.

A computer controlled scanning assembly designed by the authors controlled the movement of the endpiece over the area to be treated. A mechanical

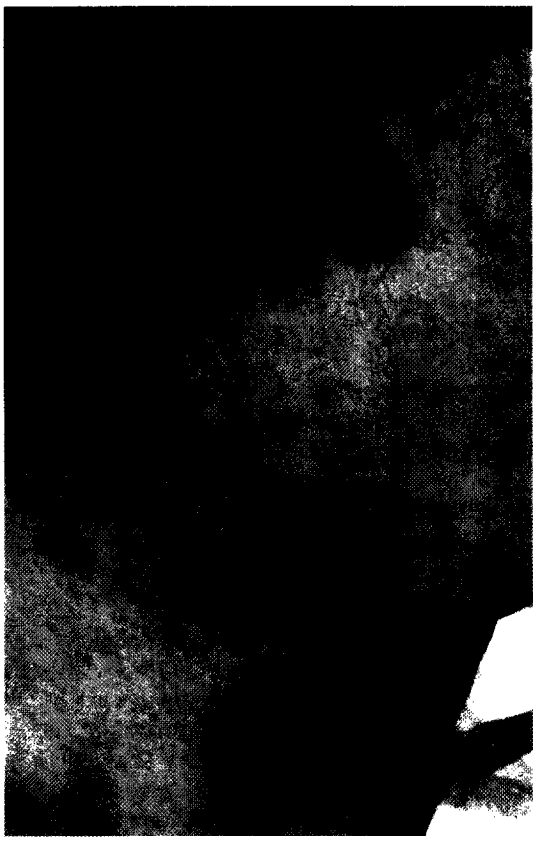

Fig. 1

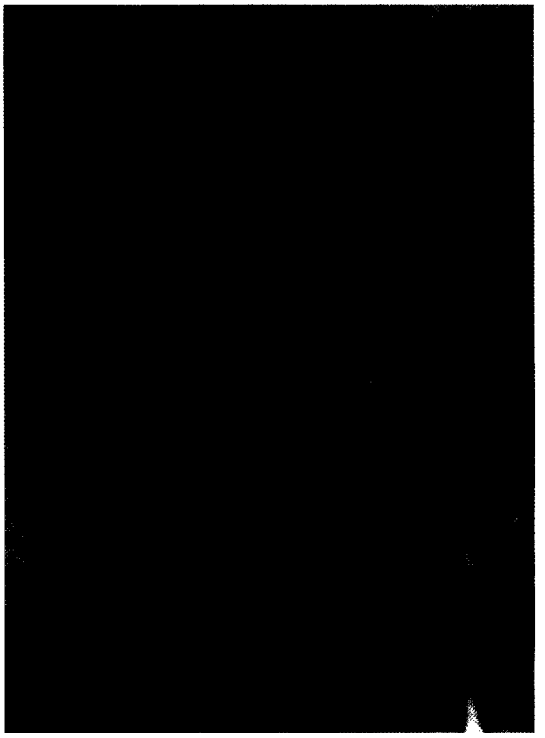

Fig. 2

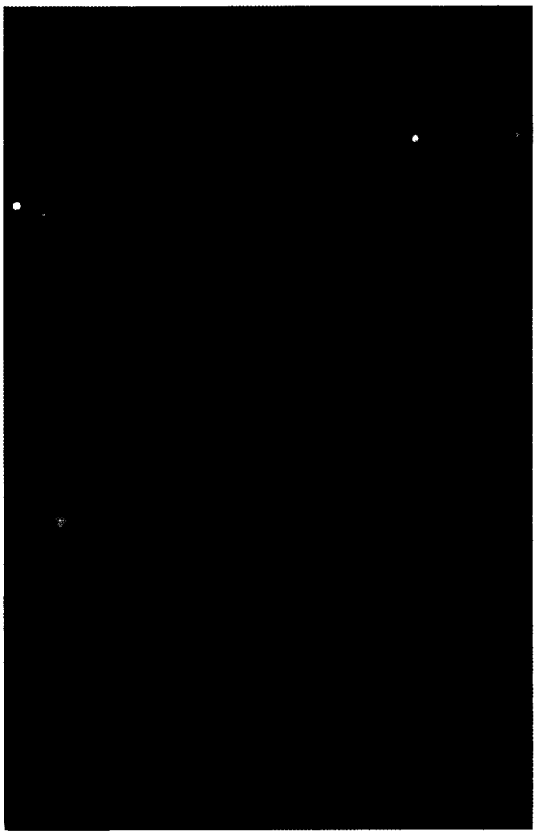

Fig. 3

Fig. 4

Figure 1—Lesions on the neck before treatment. **Figure 2**—Lesions after application of 4 full area treatments. **Figure 3**—Faint facial lesion before treatment. **Figure 4**—Lesion after application of 3 full area treatments.

scanning rig manoeuvred the endpiece in two dimensions via stepper motors interfaced to the computer by an Amplicon PC14 (a card and associated circuitry). The software was written in Turbo Pascal 5.5. This was flexible to allow various parameters, such as spot size, distance and delay between spots to be input at the start of treatment. The spot diameter used in this study was 3 mm.

The system could be run in several modes. In the "outline" procedure, the surround of the stain to be treated was traced using the keyboard arrow keys. This moved the endpiece, which was followed on the skin surface by the movement of the visible He/Ne aiming beam. The computer mapped the area thus delineated and upon instruction the laser energy was deposited in continuous, hexagonally placed shots. The system was also used in a "manual" mode where the clinician simply moved the endpiece to the desired position with the arrow keys and pressed the designated key to fire the laser. This facility allowed small areas to be treated. The entire scanning rig could be tilted to cope with the contours of the face. This scanning system permitted the contiguous or overlapped placement of the laser spots over the lesion in a precise manner.

The laser pulse energy was measured by use of Scientech model 365 energy indicator with a black body response, giving +3% accuracy.

Subjects

128 treatments were administered to 25 patients over a 5-year period. During this period, technical difficulties with the laser resulted in less than 1–2 years operational time. In addition, due to the need for general anaesthesia, these sessions had to be incorporated in the hospital theatre list. The accommodation was for three patients to be treated per week. The patient age ranged from 5–45 years, with 20% in the < 12 year category, 56% in the 12–25 year category and 24% over 25 years old. Lesion type, sited on the head and neck regions, ranged from pale pink and flat to deep red and nodular.

Methods

Patients were photographed and placed under general anaesthesia to ensure a stable and immobile target site. Choice of laser energy was determined corresponding to the onset of immediate purpura followed by a delayed purpuric reaction, usually evident within several minutes. These observations have been linked to the induction of both coagulation and vaporisation of blood vessels below the treated site (Garden *et al.*, 1988). These requirements dictated the use of an energy density of 8–10 Jcm^{-2} on the skin, with a pulsewidth of 340 microseconds.

Patients were recalled at intervals of 4 weeks if possible, although many of the patients were treated at less regular intervals. Several repeat exposures were found to be necessary in all cases. The laser spots were scanned over the lesion under computer control over a grid within the area of the lesion. The spots were slightly overlapped to minimise inter-spot spacings corresponding to untreated areas.

Results

Clinical response was recorded after each exposure. The desired reaction included immediate, followed by further delayed, purpura sometimes lasting several days. Erythema was evident following treatment. Hypo-pigmentation, which did not persist, was evident among several patients.

The treatment response of a 19-year-old female patient is illustrated in Figures 1 and 2. The lesions were treated on 4 occasions with a mean spacing between treatments of 8 weeks.

The response of a 24-year-old female patient is shown in Figures 3 and 4. Here, a total of 3 treatments were administered.

The partial treatment of a 45-year-old female patient is shown in Figures 5 and 6. Here, the automatic scanning system was used to administer 2 treatments. The treated area, corresponding to the lightened scanning grid area, can be clearly seen in Figure 6.

The treatment of a 5-year-old male patient is shown in Figures 7 and 8. Two treatments were administered uniformly over the entire lesion.

Figures 9 and 10 illustrate the treatment of a 7-year-old female patient. Two treatments were administered uniformly over the affected sites.

Figures 11 and 12 illustrate the treatment of a 21-year-old female patient. The grid pattern associated with the use of the automatic scanning systems is apparent in Figure 12 which illustrates the appearance after 4 treatments had been administered.

The above results document the response of 6 of the 25 patients treated. Of the remainder, 5 patients displayed greater than 50% lesional lightening after 2–6 treatments, 3 patients exhibited between 25% and 50% lesional lightening after 1–6 treatments, while the remainder (11) demonstrated less than 25% lesional lightening after 1–6 treatments. One of these latter cases was a child of 9 years who had a very dark (although smooth) stain covering more than 50% of one side of the body, who exhibited less than 10% lesional lightening after 5 treatments. Excluding this case, the average lesional lightening for the under 12 year-old age group was 52% for 1–6 treatments. 45% of patients displayed in excess of 50% fading after a mean of 3.9 treatments, while a further 25% displayed 25–50% fading after a mean of 3.8 treatments. The remaining 14% displayed less than 25% fading after a mean of 4.33 treatments. 2 patients, both of age 45 years, presenting deep red lesions, displayed in excess of 50% lightening after only 2 treatments. Most of the patients are continuing to undergo treatment.

Discussion

The progressive ectasia of portwine stains has been noted (Barsky *et al.*, 1990) from infancy onwards. It has been suggested also that younger patients, presenting faint pink lesions, respond more favourably to

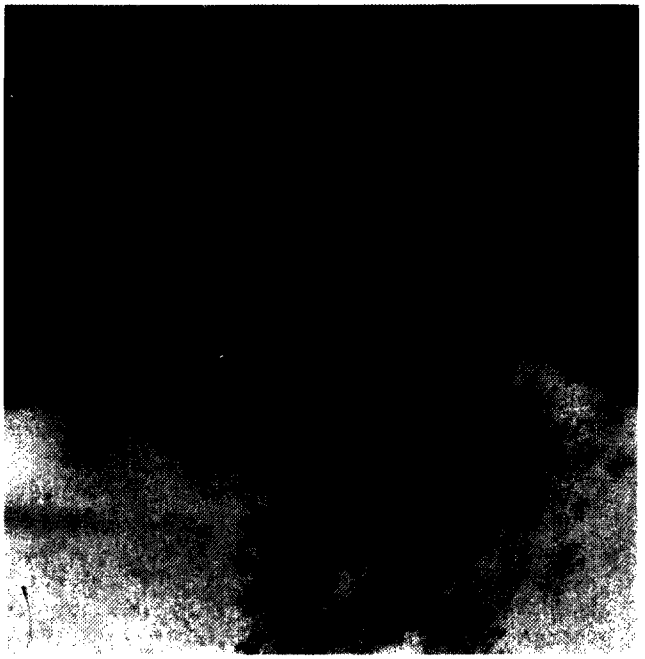

Fig. 5

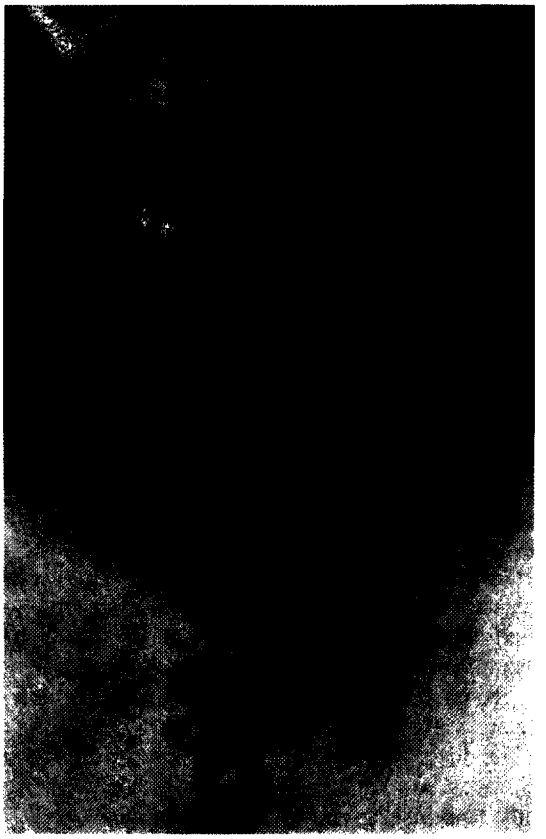

Fig. 6

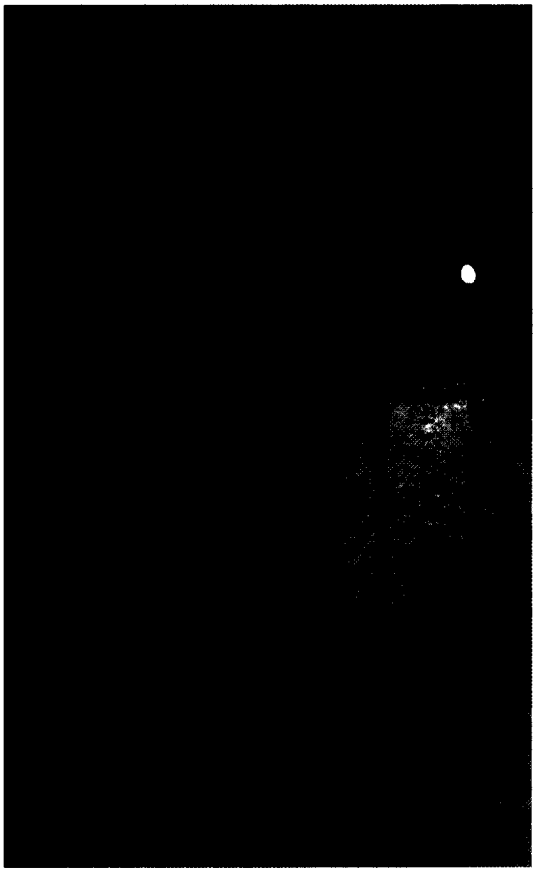

Fig. 7

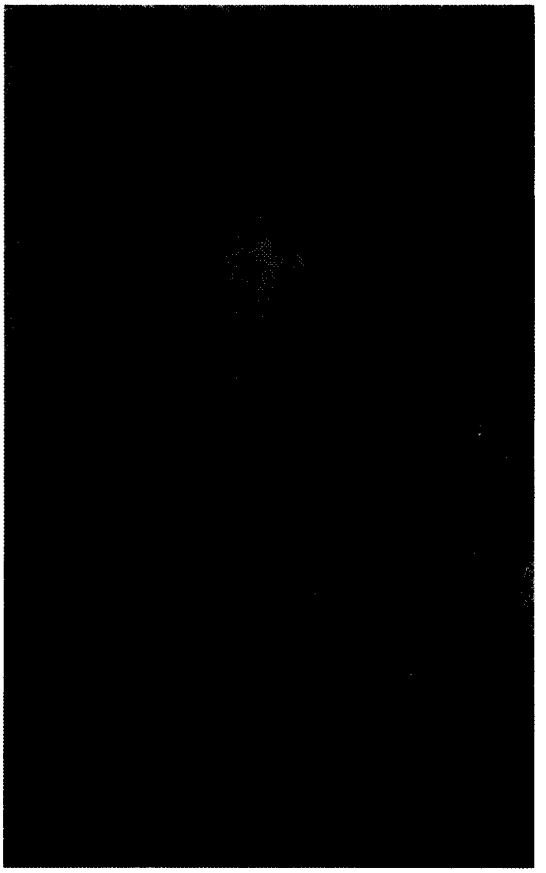

Fig. 8

Figure 5—Dark mature lesion before treatment. **Figure 6**—Lesion after application of 2 partial area treatments. **Figure 7**—Faint facial lesion before treatment. **Figure 8**—Lesion after application of 2 treatments.

Fig. 9

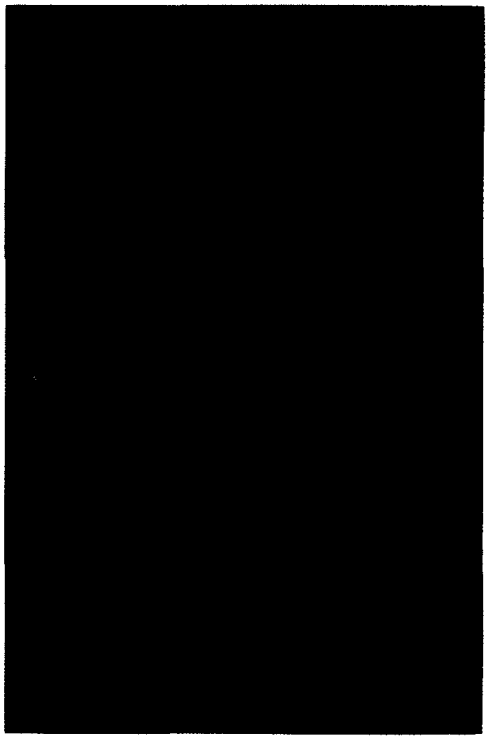

Fig. 10

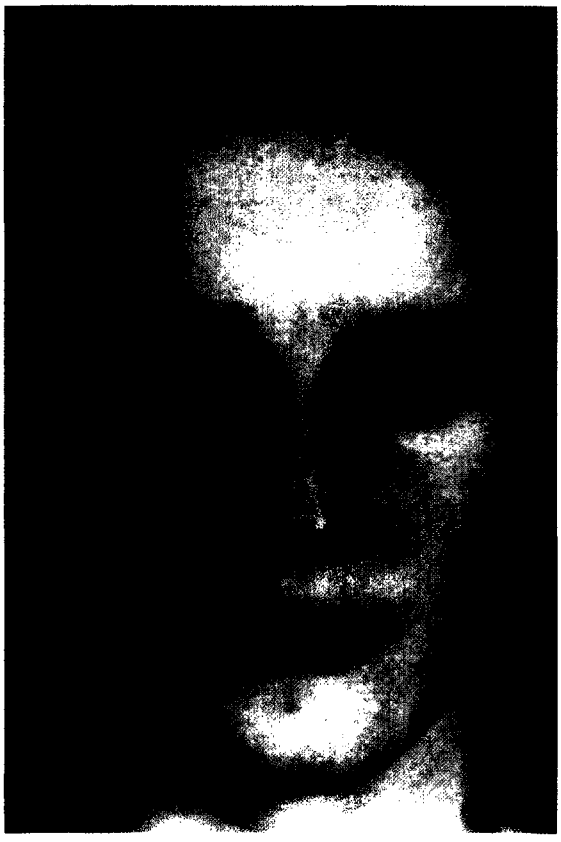

Fig. 11

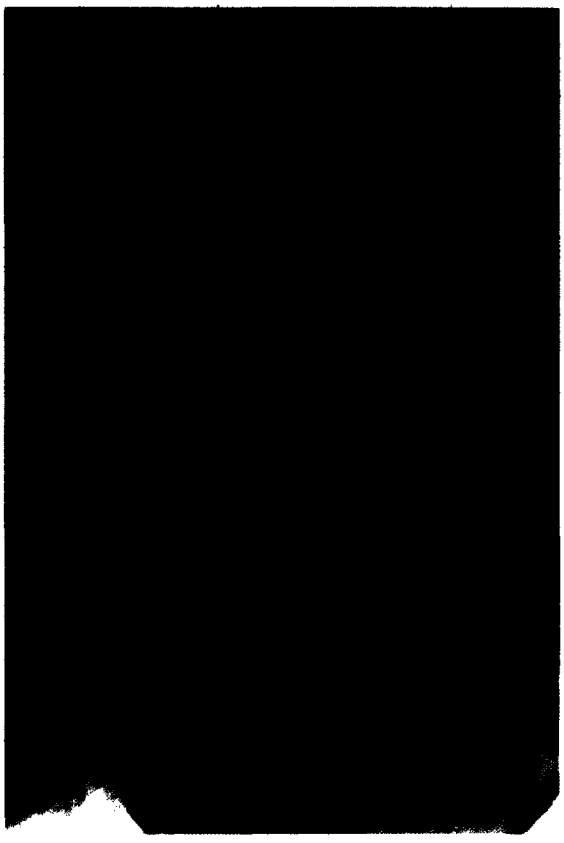

Fig. 12

Figure 9—Facial lesions before treatment. **Figure 10**—Lesions after application of 2 treatments. **Figure 11**—Facial lesions before treatment. **Figure 12**—Lesion after application of 4 treatments.

treatment (Garden *et al.*, 1988; Tan et al., 1989). Tan *et al.* (1989) reported that lesions overlying bony prominences responded more rapidly to treatment.

In this study, repeat applications were found to be necessary in all instances. This may be a consequence of the distribution of the vessels within the dermis. Although most vessels are found in the sub-papillary plexus, they may shadow deeper vessels extending to a full depth in excess of 1 mm (McLeod, 1984).

Response did not correlate well with age of patient or location of lesion. The youngest patients did not typically display the optimum response to treatment. These findings are not entirely in agreement with those reported by Tan *et al.* (1989), who described a lower required number of treatment sessions among the youngest children with the lightest lesions.

It was found that an inter-treatment spacing of 4 weeks was preferred, where possible. On each occasion, the entire area should be treated. Failure to treat portions of the lesion may permit regrowth of the dilated vasculature from neighbouring untreated sites. Equally, lengthy inter-treatment delays may permit a feeding from deep vasculature. This was suspected in the case of a 19-year-old male patient treated at mean intervals of 25 weeks who displayed a darkening of the treated area as a result of vascular regrowth.

The automatic scanning system designed by the authors ensured a very precise and uniform coverage with no untreated gaps in the stain. The scanning system allowed the laser to be used to its full potential without the additional need for the variance of applications from clinician to clinician to be taken into account.

It has been difficult to correlate response to nature of lesion as histology has not generally been available. A means of non-invasive monitoring would be highly desirable, enabling correlation of effect with the nature of the vasculature structures. In particular, a knowledge of depth, distribution and ectasia would be of relevance.

Although a significant lightening of colour has been demonstrated, it is felt that the inflexibility of this type of laser to respond to different target requirements may preclude its further widespread use. In particular, the pulsewidth may not be modified to correspond to the thermal requirements of the targeted vessels. In this regard, it is felt that lasers such as the copper vapour laser may supersede the use of the dye laser as they continue to demonstrate extended modes of operation. In particular, the variable laser parameters available and ever increasing power capabilities offer a flexibility not associated with the dye laser. Candela is currently marketing a dye laser with a 585 nm wavelength. Mathematical modelling carried out at the Bioengineering Unit, Glasgow, predicts that much higher fluences are necessary to produce purpuric reactions with this wavelength. This work will be considered in more detail in a later paper.

Acknowledgements

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Q-switched ruby laser treatment of tattoos; a 9-year experience

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Summary—Nine years of clinical experience of the application of the Q-switched ruby laser to the removal of tattoos is presented. This laser achieves optimal removal of blue/black amateur tattoos by its selective interaction with the dermal suspensions of pigment which constitute the tattoos. The scarfree cosmesis thus achieved is a considerable improvement on non-specific laser techniques whereby the laser is absorbed to a comparable degree in both pigmented and non-pigmented tissue. Long-term results are analysed and it is noted that a variety of professional tattoos may also respond to treatment. The mechanisms and appearance are discussed and correlated with short-term healing processes.

It is found that power densities in the range 1200–2800 GW/m^2 are most suitable. Appropriate dosimetry can be witnessed by the appearance of opaque intradermal vacuoles corresponding to the vapourisation of the tissue water surrounding the pigment suspensions.

Treatment by Q-switched ruby laser offers a viable scar-free option for a wide range of dark tattoos, leading to a more acceptable clinical outcome in most cases than other current therapies.

A number of laser therapy techniques have been proposed for the removal of unwanted tattoos. Many of these induce localised burning of the tissue by an unselective targeting of the tattooed site (Reid and Muller, 1978). Carbon dioxide, argon and Nd:Yag lasers have all been used in this application. While offering to many of those inflicted a desirable option, the cosmesis is generally unacceptable, with scarring resulting in many cases.

An alternative technique targets the pigment as a chromophore within the translucent dermis. This requires a judicious choice of wavelength and pulse width to ensure selective absorption of the optical radiation and confinement of the thermal energy by the targeted pigment.

In order that competitive absorption by the epidermal melanin be minimised, a wavelength towards the red end of the visible spectrum is desirable. This precludes the removal of red pigments by direct selective absorption, although other mechanisms can be invoked. Consequently, earlier reports describe only the removal of blue/black tattoos (Goldman, 1967; Reid *et al.*, 1983).

While appropriate choice of wavelength ensures optimal absorption within target structures, laser exposure duration dictates the extent of the local confinement of the heating effect produced. Subsequent damage may then be of a thermal or mechanical nature. If the energy is delivered in a time less than the "cooling time" of the optical target, conduction is minimised and local temperature rise is higher. This may lead to an explosive reaction.

A mechanical process is thought appropriate to the disturbance of the enclosed pigment suspensions whereas thermal damage, commonly associated with the application of a continuous wave emission, would tend to produce shrinkage of the surrounding dermis, with no obvious beneficial pigment dispersal. Indeed, the encapsulation might be reinforced.

For selective effect on tattoo ink, and subsequent tissue repair, it is vital that the wavelength and pulse width are appropriate to the induction of selective absorption, followed by minimal conduction, leading to localised mechanical interaction. The ruby laser in Q-switched mode offers such a modality. Prior studies (Reid *et al.*, 1983) have investigated the treatment of black tattoos using this laser. When Q-switched, a maximum energy of 3J in a 30ns pulse may be attained. This pulse width is within the thermal retention time of even the smallest pigment clusters which constitute the tattoo and hence will induce minimal thermal damage to the surrounding tissue. Excellent results

have been reported in the treatment of blue/black tattoos, although multiple exposures have been found to be necessary in many cases (Reid *et al.*, 1983).

This study collates a 9-year experience of the treatment of tattoos using the Q-switched ruby laser. Clarifications of mechanisms and damage thresholds are presented and new observations concerning the response of multi-coloured tattoos discussed.

Materials and methods

A Q-switched scientific ruby laser (manufactured by JK Lasers) was used in these trials. Q-switching provides a means by which nanosecond-domain pulses of high individual energies may be produced from certain host materials.

This produced pulse energies of up to 3J with pulse widths of 30ns, at a wavelength of 694nm. An articulated arm was used to deliver the high peak powers to the treatment site. This arm used prisms to deflect the beam through a plano-convex focusing lens to a spot size of 5 mm incident on the skin. The pulse energy passing through this 5 mm aperture was measured using a Scientech model 365 energy indicator with a black body response. The pulse-to-pulse stability of the laser was 10%.

Subjects

Over a 6-year period, following the *in vitro* trials (Ritchie, 1982), 418 patients were treated (Tables 1 and 2). All were fair Caucasians with no known history of cutaneous disease. Of these, a total of 341 had amateur or self-inflicted tattoos while 75 had professionally-applied tattoos. A range of tattoo sites was treated, including arms, neck, head and chest.

Methods

A local anaesthetic (1.0% lignocaine) was injected subcutaneously to all patients prior to exposure. The laser pulses were then manually directed onto the skin by means of the articulated arm and overlapping 5 mm exposures induced at intervals of several seconds.

In each patient an energy was found corresponding to the onset of whitening. Earlier studies had linked this with the formation of vacuoles in the dermis due to the production of steam (Ritchie, 1982). Patients were recalled at intervals of 3–4 weeks for additional exposures, this having been previously identified (Reid *et al.*, 1983) as the minimum period for effective fading of the whitening. A number of exposures of the same treatment site was found to be necessary in all cases. Biopsies were obtained in a number of patients and long-term dermal/epidermal response monitored (Newstead, 1988).

Table 1 Patient results, amateur tattoos (December, 1989)

No. of tattoos treated	341	(100%)
No. of completed treatments (< 10% pigment remaining)	191	(56%)
Mean no. of treatments required	4.92	
Standard deviation	2.4	
No. of ongoing treatments	118	(35%)
No. with < 50% pigment remaining	50	
No. with > 50% pigment remaining	68	
Mean no. of treatments	3.5	
No. of discontinued treatments	32	(9%)
Reason for discontinuation:		
Inconvenience (*e.g.* travel)	21	
Medical advice (*e.g.* hyperpigmentation)	11	

Results

Clinical response was recorded after exposure and prior to each repeat treatment. Most subjects experienced a pinprick sensation when the threshold was reached, accompanied by a blanching of

Table 2 Patient results, professional tattoos (December 1989)

No. of tattoos treated	77	(100%)
No. of ongoing treatments	68	(91%)
No. of completed treatments	2	
No. with 50%–80% pigment removal	16	
Mean number of treatments	4.56	
No. with 0–50% pigment removal	52	
Mean number of treatments	2.4	
No. of discontinued treatments	7	(9%)
Reason for discontinuation:		
Inconvenience (travel)	4	
Medical advice (*e.g.* hyperpigmentation)	3	

the pigmented site. This blanching persisted for a period of several hours after treatment. In addition, a number of patients experienced hypo- or hyperpigmentation of the treated site, which was recorded on their subsequent visit.

The treatment of 418 tattoos is recorded. The mean duration of laser treatment was approximately 12 minutes. Both amateur, or "self-inflicted", and professionally-applied tattoos were treated although the treatment of many more amateur than professional tattoos was attempted in the earlier stages of the study. Consequently the number of "completed" professional tattoos at the time of writing is substantially less.

The results documenting the treatment of 341 amateur tattoos are presented in Table 1. Treatment is judged to be complete if less than 10% of the pigment remains. Treatments are then terminated. A good result is related to the subjective identification of 50–90% removal of pigment, following which repeat irradiations may be administered in order to complete the course of treatments.

The spread around the mean of 4.92 shown in Table 1 is large, with requirements varying from 2 to 12 treatments to effect removal. Such a removal is associated with a normal, scar-free cosmesis (Figs 1 and 2).

The statistics relating to ongoing treatments identify the achievement of a "good" result in 50 of the 188 patients after a mean number of 3.5 treatments. Such patients might reasonably be expected to progress to completion after a mean additional 1.42 treatments.

A number of patients (9%) discontinued during treatment for personal reasons or due to the onset of a degree of hyperpigmentation at the treatment site. Subsequent to the induction of hyperpigmentation, treatment was discontinued pending the results of histological and cytogenic studies (Ritchie, 1982). Occurrence of mild hypopigmentation was common although difficult to quantify due to the fair skins of many of the subjects originating from the West of Scotland.

A total of 77 professionally-applied tattoos was treated in addition to the 341 amateur tattoos. Histologically such tattoos are similar (Figs 3 and 4), consisting of collagen-enclosed dermal capsules, although professional tattoo pigment is generally more evenly distributed to a higher density.

All of the professional tattoos treated were principally blue/black although many contained traces of brighter colours. These additional colours were not irradiated directly. The treatment of professional tattoos was a more recent development from the earlier trials of amateur tattoos; consequently, of the 77 treated, 68 were still undergoing treatment at the time of writing, only two having had 100% pigment removal.

Of the ongoing treatments of the professional tattoos, a "good" result has been achieved in 16 of the tattoos, having had a mean of 4.56 treatments. This compares with the two completed professional tattoos having had 6 and 7 treatments respectively (Figs 5 and 6). The remaining 52 tattoos were insufficiently far advanced in their course of treatments to exhibit greater than 50% fading, having had a mean of only 2.4 treatments. A small proportion (approximatley 9%) of patients were forced to discontinue treatment for personal or medical reasons.

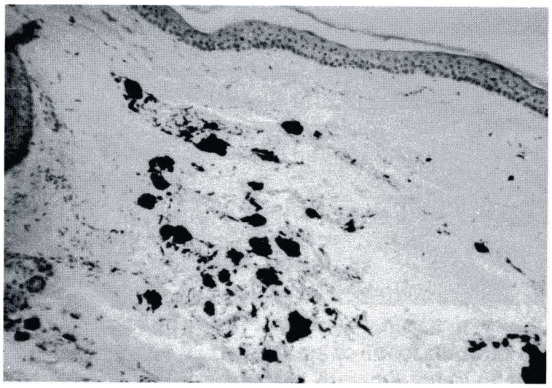

Fig. 3

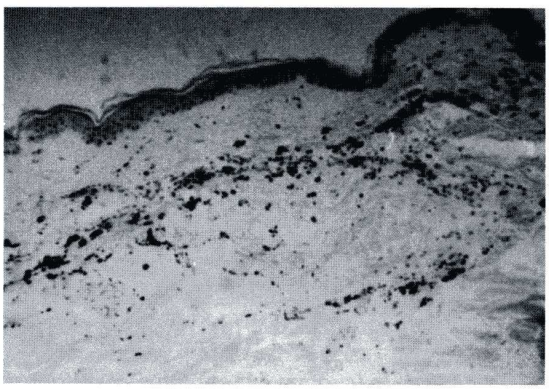

Fig. 4

Figure 3—Histological section of amateur tattoo. The irregular size and distribution of the pigment clusters can be clearly seen (× 150). **Figure 4**—Histological section of professional tattoo (unstained) (× 100).

Many of the dark professional tattoos had areas of red and green pigment which, although not irradiated directly, were found to fade considerably in response to the treatment of neighbouring sites (Figs 7 and 8).

Discussion

Pigment removal occurs as a two-stage process. In stage one, large temperature gradients are induced in the vicinity of the pigment clusters, leading to an explosive interaction which breaks apart the clusters. In stage two, physiological defence mechanisms are subsequently invoked to dispose of the debris.

The 694nm wavelength emitted is highly absorbed by the dark dermal pigment suspensions while the short pulse width of energy, within the thermal retention time constant of the clusters, is effectively retained by the target site. A rapid increase in temperature is then achieved which causes disruption of the collagen-enclosed pigment particles by vapourisation of the surrounding tissue water. Calculations show that carbon dioxide may also be produced (Ritchie, 1982) following a reaction with the carbon-based pigment. Evidence suggests that physical expansion of the site produces rupture of the collagen matrix followed by a shock wave. Fragmentation of the rigid pigment particles then occurs as a result of interaction with the shock wave. The smaller remaining pigment clusters may then be removed through the process of phagocytosis, whereby macrophage activity transports the scattered pigment away from the site of suspension. During this 1 to 3-week period any localised damage associated with the rupture of the collagen is repaired.

A number of repeat treatments is found necessary to remove the remaining pigment completely (Tables 1 and 2). This is a consequence of the scattered nature of the pigment suspension within the dermis whereby a non-uniform depth distribution ensures a partial shadowing of the deeper clusters by the superficial "layers". The repeat treatments are optimally spaced by the "healing" period of the dermal matrix (1–3 weeks), while the skin physiology is allowed to return to normal.

The results (Tables 1 and 2) suggest a mean requirement of 4.92 treatments to effect removal of an amateur tattoo, while the ongoing study of the removal of professionally-applied pigment would seem to entail an additional requirement of 1–2 sessions. These observations may be related to the density of pigment being higher in the case of professional tattoos than that found in the "typical" amateur tattoo. The nature of the chemical compound may also be of importance and is presently under study.

A number of the treated sites (approximately 3%) exhibited signs of hyperpigmentation (Fig. 9) and treatment was discontinued, although normal skin appearance resumed after several weeks. Hypopigmentation, associated with the removal of melanin from the epidermis above the treated site, was more commonly observed in highly tanned patients and was found to persist for a number of weeks. Such subjects were cautioned to avoid direct exposure to sunlight while the whitened appearance remained (4–8 weeks).

A long-term study (Newstead, 1988) found no evidence of mutagenicity associated with any of these observations. In none of the patients followed were instances of atrophic or hypertrophic scarring observed.

Several of the professional tattoos which were treated contained red and green colouration which was observed to fade substantially during the course of treatments, although not directly irradiated. Such colouration only faded when a surrounding area of dark pigmentation was treated. The subsequently enhanced phagocytotic response which appeared to be produced had affected both treated and untreated sites to a similar extent, leading to a fading of colours which might otherwise not have been expected to respond to treatment on account of their low absorption at the laser wavelength of 694nm.

In summary, both amateur and professional tattoos responded favourably to treatment by Q-switched ruby laser. This laser, when traced over dark pigmented areas, induced a gradual fading in the irradiated site, accompanied by an additional fading of any surrounding lighter pigment.

Major technical advances have recently been made in the laser and delivery equipment, facilitating its use clinically and minimising inconvenience to the patient. These advances include the development of an articulated delivery system enabling highly efficient and reliable coupling of the laser energy onto the treatment site. Large areas may then be treated within a small time period. Thus, Q-switched ruby laser treatment has been shown to be eminently suited to the removal of dark amateur tattoos. In addition, present studies strongly indicate the efficacy of this technique for the removal of dark tattoos of the professional variety.

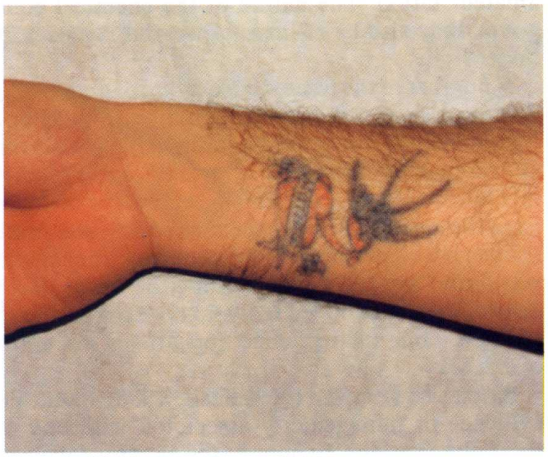

Fig. 7

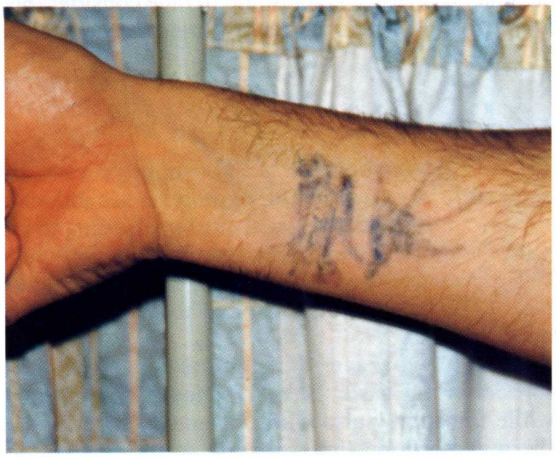

Fig. 8

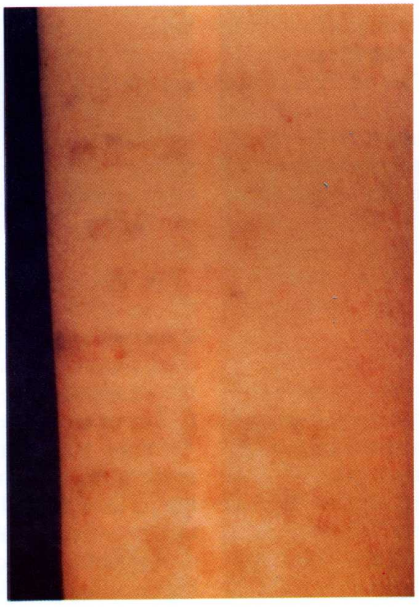

Fig. 9

Figure 7—Professional tattoo containing red pigment, before treatment. **Figure 8**—Professional tattoo during treatment (after four exposures). **Figure 9**—Hyperpigmentation following treatment of amateur tattoo.

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