Quantifying the influence of the epidermal optical properties on laser treatment parameters

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ABSTRACT

Both the thickness and absorption coefficient of the epidermis influence the light transmission through skin. Different skin phototypes were modeled and show a more than 50% reduction in fluence rate for the darker skin phototypes at a depth of 200 μm into the skin.

Keywords: Medical optics and biotechnology; Light propagation in tissues

1. INTRODUCTION

Laser based treatment modalities offer patients a less invasive, often localised treatment method. This has advantages of faster healing times and fewer side effects from treatment. For most laser treatments though the target site is some distance into the skin so light needs to pass through some of the skin layers. The penetration depth of light in skin is determined by the total attenuation, constituted by the scattering and absorption coefficients of the tissue at the treatment wavelength. The absorption coefficient is a measure of the absorption (attenuation) of light through the medium (skin). Similarly the scattering coefficient is a measure of the scattering of light. Furthermore, the thickness of the epidermal layer in skin varies with location across the body. It stands to reason that a thicker epidermis will absorb more light than thinner epidermal layers. Hence in determining the fluence rate reaching a specific position (depth) in the skin, both the epidermal thickness and the absorption coefficient need to be taken into account. In vivo measurements to determine the fluence rate are not easy to implement. Computer modeling of the light interaction with the tissue is an alternative method that can be used to predict the fluence rate at any given depth in the tissue.

1.1 Human skin

Skin is generally described as consisting of three main layers. For this work we assume uniform layers as shown in Figure 1.

- The epidermis that is approximately 100 μm thick and is blood free. It is made of the stratum corneum and the living epidermis.
- The dermis that has blood vessels and is between 1 and 4 mm thick.
- The hypodermis which is a fatty layer consisting of subcutaneous fat and is between 1 and 6 mm thick.

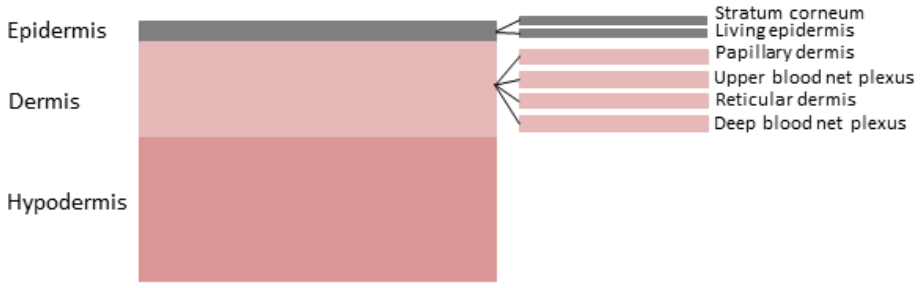

Figure 1: Structure of the human skin.

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The living epidermis, which is the layer of concern in this study, consists of keratinocytes, melanocytes and Langerhans cells. This is the layer that contains most of the skin pigmentation (i.e. melanin that is produced by the melanocytes)[1,2]. According to Kollias[1] melanin is the major absorbing chromophore in the visible range. The refractive index of the epidermis is close to that of water (nominally 1.33 in the visible wavelength range), therefore, only weak reflections is expected from the interface between the stratum corneum and the epidermis[1].

1.2 Melanin

Melanin in the skin is located in the melanosomes and consists of solid absorbing particles with a diameter between 20 and 40 nm. It is an optically dense material which absorbs light in the visible wavelength region. Melanin is not a single pigment, but consists of various chromophores each with their own optical and physical properties[3]. Both eumelanin and pheomelanin are forms of melanin that are synthesized within the melanosomes inside the melanocytes, located in the basal layer (or bottom layer) of the epidermis. Eumelanin is sulphur poor and results in a brown-black colour while pheomelanin is sulphur rich resulting in a yellowish-red colour. The typical extinction coefficients of the eumelanin and pheomelanin as a function of wavelength are shown in Figure 2.

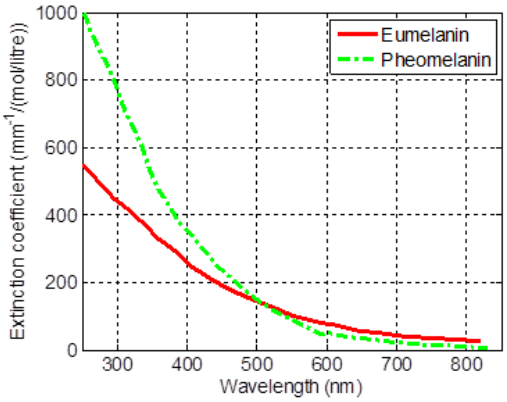

Figure 2: Extinction coefficient as a function of wavelength for both of eumelanin and pheomelanin (data from Jacques[4]**).**

Melanin in the epidermal layer is responsible for the skin colour or skin phototype of an individual and impacts on the optical properties of the skin. A higher absorption coefficient is associated with the darker skin phototypes. Darker coloured skins do not necessarily have more melanocytes than lighter coloured skins, but the melanocytes are more productive and produce more melanin. It is generally believed that one of the major functions of melanin pigmentation is to protect the skin from harmful ultraviolet radiation.

The range of absorption coefficients expected for typical South African skin phototypes (ranging from photo-sensitive light skin, phototype I on the Fitzpatrick scale, to the photo-insensitive darker skin phototype VI) was measured with a diffuse reflectance probe[5] and the typical trends as a function of wavelength is shown in Figure 3.

Skin damage has been reported during some laser treatments on darker skin tones, which seems counterproductive when used as a therapeutic aid. This necessitated the need to determine the effect of the optical properties of different skin phototypes on treatment parameters. The modelling work reported on in this paper aims to answer some of the questions that can bridge this gap.

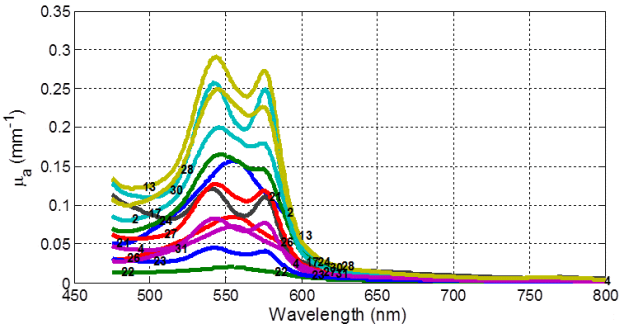

Figure 3(a): Absorption coefficient for the lighter skin tones.

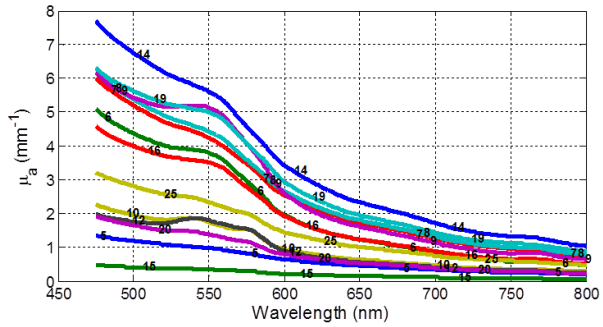

Figure 3(b): Absorption coefficient for the darker skin tones.

1.3 Photodynamic therapy

Photodynamic therapy (PDT), a potential treatment for skin cancer, was the application chosen to illustrate the influence of the epidermis on the fluence rate in skin. Skin cancer (consisting of basal cell carcinomas (BCC), squamous cell carcinomas (SCC) and malignant melanoma) is the most common type of cancer in the South Africa with about 20 000 reported cases each year[6]. Australia and South Africa have the highest incidence of skin cancer in the world[6,7]. Basal cell carcinoma accounts for more than 90 percent of all skin cancers. Squamous cell cancer is much less common than BCC but can be more aggressive than BCC and is also more likely to grow deep below the skin and spread to distant parts of the body. When SCC is identified early, there is nearly a 100 percent chance for cure[8].

PDT is one of the newer cancer treatments[9,10]. PDT is a procedure in which a photosensitiser (PS) or drug is administered orally or topically to the patient and after the absorption of the PS in the cells, the tumour is irradiated with a light source (normally a laser) tuned to an absorption peak of the PS in the visible to near infrared region of the light spectrum. The formation of highly reactive singlet oxygen in the cells leads to cell death through apoptosis or necrosis[9,11,12]. Due to the short lifetime of the singlet oxygen in biological systems only molecules close to the PS are affected. The half-lifetime of singlet oxygen is less than 40 ns, and the radius of the action of singlet oxygen is in the order of 20 nm[13]. PDT is a localised treatment, having less of an adverse effect on the healthy cells not irradiated by the light source. PDT has been approved in a number of countries for selected cancers and drugs[10,14].

2. METHODOLOGY

2.1 Layered skin model

Raytracing software is commonly available and is mainly based on the Monte Carlo Multi-Layered (MCML) programs developed by Jacques[15]. These programs use the Monte Carlo raytracing techniques where 'photons' or 'rays' are traced through a medium with pre-defined absorption and scattering properties, until the photons are completely absorbed or leave the medium through the boundaries of the model.

The Advanced Systems Analysis Program (ASAP®) from Breault Research, a commercial software package, with the advantage of allowing the user to *easily make geometry changes to a tissue model*, was used for this work. ASAP was used to develop the computer model. The software is able to perform non-sequential ray tracing where rays (or photons) can interact with objects as they encounter them making use of Monte Carlo ray tracing principles. The rays are not restricted to the order in which the objects were defined in the model as is the case in sequential raytracing[16]. The model mimics the layered structure of skin consisting of a thin epidermal layer, a dermal layer and a "tumor" that was imbedded in the dermis (Figure 4). Each layer is described as a rectangular slab with known dimensions and known optical properties, i.e. absorption coefficient (μ_a), scattering coefficient (μ_s), anisotropy (g) and refractive index (n). Each layer is considered to be homogenous hence the same (averaged) optical properties apply everywhere in the layer. The model used for this work consisted of two layers (epidermis and dermis) with a skin tumor (SCC) embedded in the dermis. Three different epidermal thicknesses were used in the model to evaluate the influence of the epidermal thickness on the fluence rate loss during treatment.

During the propagation of a photon through the bulk media the following rules are followed:

- The path length (l) that photon undertakes between each interaction with the tissue (scattering or absorbing) is given by:

$$l = \frac{-\ln(\xi)}{(\mu_a + \mu_s)} \tag{1}$$

  with ξ a uniformly distributed random number between 0 and 1.

- A photon 'loses' part of its energy after each step by an amount of (1-albedo), where the scattering albedo is defined as:

$$albedo = \frac{\mu_s}{(\mu_a + \mu_s)} \tag{2}$$

ASAP implements a simplified model that uses the bulk absorption and scattering properties of the media in combination with the Henyey-Greenstein scattering profile or scattering phase function[17]. This phase function is a reasonable estimate of the forward scattering nature of biological media such as skin. Even though it not an exact representation of the forward scattering of the tissue, experiments showed that it is a good approximation that is practical to use[18]. One of the advantages of this phase function is that it only depends on one parameter, the anisotropy g[17]. The Henyey-Greenstein phase function, ρ, is given by:

$$\rho(\theta) = \frac{1}{4\pi} \frac{1 - g^2}{[1 + g^2 - 2g\cos(\theta)]^{3/2}} \tag{3}$$

The aim of the model was to be as uncomplicated as possible to evaluate the influence of specific parameters. In the development of the model only the essential skin layers were used, i.e. the epidermis and dermis and no hair or blood vessels were included. The main reason for the model development was to quantify the expected fluence rate losses in the tissue before reaching the treatment site, in this case the tumor. A schematic of the computer model is shown in Figure 4.

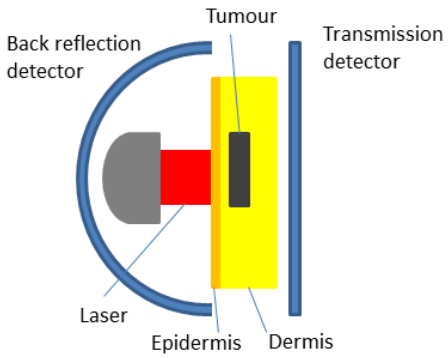

Figure 4: Schematic of the computer model.

The major contributions to the loss of fluence rate through the tissue are the absorption in the epidermis and the scattering of the light. Scattering of light leads to an increase in the spot size and as such reduces the 'power density' or fluence rate deeper in the skin. Consequently, the loss in laser light intensity due to absorption depends on both the absorption coefficient and the path length through the medium (in this case the epidermis). As such the epidermal thickness is an important parameter.

A laser beam (wavelength 676 nm) with a beam diameter of 12 mm and an output power of 50 mW was modeled and traced through the layered skin. Such a laser was used in some of the *in vitro* cell work that led to the defining of the laser dose parameters[19]. Two evaluation detectors were used to evaluate the back scattered light and the light transmitted through the model to ensure that no photons are unaccounted for. The model was validated against physical phantoms and actual measurements performed with an integrating sphere as described elsewhere[20]. Due to the thin epidermal layer,

the evaluation slice thickness was reduced to 0.01 mm. The number of slices in depth (Z-direction) was varied to keep the slice thickness constant.

At present there is no easy way to measure the epidermal thickness *in vivo*, therefore the data published by Whitton[21] was used. It is the most comprehensive work on epidermal thicknesses that could be found. Only areas of the skin that are usually exposed to sunlight were selected because that would be the areas most prone to skin cancer. In those areas the published values of the epidermal thickness varies from 39 μm on the cheek to 85 μm on the back of the hand. For easier comparisons, the epidermal thickness in the model was varied between 40 and 90 μm.

2.2 Epidermal absorption coefficient

For the application of the computer model to the South African environment, it was important to determine the range of epidermal absorption coefficients that will typically be found in clinical settings. A calibrated diffuse reflectance probe system was used in the measurements on 30 South African volunteers to determine the absorption coefficient of different skin phototypes[5]. The results indicated that the epidermal absorption coefficient varies from as low as 0.002 mm^{-1} to more than 3 mm^{-1}.

The input parameters to the computer model are shown in Table 1. The optical properties have been published by Salomatina[22].The value of g was constant at 0.8 (using the data from Salomatina[22]).

Table 1: Geometrical dimensions for the planar surfaces and optical properties of the different layers in the skin model.

Layer	Width (mm)	Start position (mm)	Thickness (mm)	μ_a (mm^{-1})	μ_s (mm^{-1})	μ_s' (mm^{-1})
Epidermis	40	0	0.04-0.09	0.002-3	22.4	4.48
Dermis	40	0.04-0.09	3	0.15	13.9	2.78
Tumor (SCC)	10	0.2	2	0.11	8.55	1.71

3. RESULTS AND DISCUSSIONS

For ease of comparison, all the evaluations are reported at a depth of 200 μm into the model (just before the tumour). The fraction of the light that reached the tumor is reported in Table 2 for the different epidermal thicknesses and absorption coefficients. The laser beam diameter expanded from 1.2 cm to 1.3 cm at the tumor depth (200 μm into the model). For the application of the model in a clinical setting, the fluence rate reaching the tumour site is important. The treatment light dose is normally specified in J/cm^2 which allows optimising of the contribution of the laser power (normally a continuous wave laser or light source) as well as the treatment time. Apart from the absorption taking place in the skin, the light distribution also changes from the original beam profile due to the scattering in the skin, leading to a larger beam diameter.

In this model the initial laser beam diameter was 1.2 cm and the power 50 mW resulting in a fluence rate of 44.2 mW/cm^2. A laser treatment dose of 4.5 J/cm^2 at a wavelength of 676 nm is a typical parameter established for effectively killing SCC with Photosense® (a commercial Photosensitizer) in a research laboratory setting in a Petri dish[19]. For a fixed laser power of 50 mW and no losses, the cells need to be illuminated for 102 s with the laser. The fraction of the light that is absorbed in the outer skin layers is an important parameter and must be taken into account when calculating the laser dose delivered onto the skin. In the model, the beam spread (due to scattering) to about 1.3 cm at a depth of 200 μm with a reduced fluence rate of 38 mW/cm^2. In Table 2, this loss in combination with the loss due to absorption, are used to determine the treatment time required if the laser output power stays constant at 50 mW.

For the lighter skins (low μ_a values) typically up to skin phototype III, the transmitted power is nearly constant (about 50% of the initial power). In the darker skin (higher μ_a values) much less power reaches the tumour, only about 30% of the initial fluence rate. This significantly affects the optimal treatment parameters for the different skin phototypes and may require adjustment in treatment time for the darker skins (more than 50% longer).

Table 2: Fraction of power reaching the tumor at a depth of 200 μm into the skin and the resulting treatment time to deliver a light dose of 4.5 J/cm^2 onto the tumor.

Epidermal thickness (mm)	**0.04**			**0.06**			**0.09**		
μ_a **(mm^{-1})**	0.002	1	3	0.002	1	3	0.002	1	3
Power fraction transmitted to tumor	0.54	0.48	0.40	0.54	0.46	0.36	0.54	0.41	0.29
Required treatment time (s)	222	250	300	222	260	333	222	292	413

Both the epidermal thickness and μ_a determine the fluence rate reaching the tumour. In a clinical setting the absorption coefficient can be measured non-invasively before the treatment commences. A diffuse reflectance probe[5] can be used for these measurements. Specific procedures to maximise the accuracy of the probe are still under investigation. The μ_a for most of the lighter skin phototypes (I-III on the Fitzpatrick scale) is below 0.05 mm^{-1}.

The non-invasive measurement of the epidermal thickness is more problematic and does not fall within the scope of this paper. The tumor depth used is an assumption for illustrative purposes. The tumor position can be moved as required by the application.

4. CONCLUSIONS

The major advantage of the computer model was that the extent of the absorption effect could be quantified. Use of the model allows the clinician to compensate for the absorption and establish safe and effective treatment power and times before treatment commences. When comparing treatment time between skin of phototype I and VI, and keeping the fluence rate constant at 44.2 mW/cm^2, the treatment time is increased from 222 s (phototype I) to 413 s (phototype VI), an increase of more than 50 %.

Both the thickness of the epidermis and the absorption coefficient of the epidermis are important parameters in PDT treatment planning for embedded tumours. An increase in the epidermal thickness results in increased absorption of light in the epidermis. For the absorption coefficients evaluated, the ratio in the absorption between the thinner (40 μm) and thicker (90 μm) epidermal layers stays nearly constant. For the parameters used in this work, the effect of the absorption coefficient in the epidermis (due to the skin phototype) is more important than the effect of the epidermal thickness. The analysis for this work was aimed at typical sun exposed areas of the skin where the incidence of skin cancer is more likely. Other areas of the skin may have thicker epidermal layers which will affect the results. In future work the effect of a non-planar epidermal surface should be investigated as this may potentially have an influence on the backscattered light from the epidermis due to the higher differences between the index of refraction for the two media.

In most PDT applications there is a minimum fluence rate required to activate the PS and a maximum beyond which healthy cells will be adversely affected. Within this range, the power of the laser can be adjusted to compensate for light absorbed before reaching the tumour. According to the ANSI laser safety standard[23], the safe power density for skin at 676 nm is 200 mW/cm^2. When nearing this skin damage threshold, the safer option will be to adjust the irradiation time to result in the required dose instead of increasing the laser power. This irradiation time, for the data used in this work, needs to be increased from 222 s for the lightest skin to 413 s for the darkest skin.

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