

The Safety and Efficacy of Cosmetic Devices using Low Energy Photon Sources

Rebecca Elizabeth Whittall

Supervised by:

Professor John Rees – Ph.D. Director of
Studies

Professor Kelvin Donne – Ph.D. Lead
Supervisor

Dr. Tim Bashford – Ph.D. Second
Supervisor

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Declaration

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Abstract

This thesis describes the development of a bio-physical model which illustrates the volumetric heating effects of different intense pulsed light devices. The model is intended to objectively assess if the devices being investigated can successfully damage a human hair follicle without causing damage to its surrounding skin tissue.

The functions of human skin are discussed in depth, including how it is structured, and how it interacts with optical sources. Also discussed is how light and electromagnetic fields interact with biological media and the types of responses which are typically seen when skin interacts with these mediums.

The background and previous research of intense pulsed light devices is investigated and assessed. This highlights the lack of peer-reviewed research available about these devices, and other home-use light based devices. The limitations of the work which is available is also critically examined.

An experimental investigation is conducted to assess the parameters output by a selection of intense pulsed light devices available on the retail market, measuring the fluence, pulse durations, and spectral output of each device.

The experimental investigations provide the parameters which are used to develop a fully calibrated and validated computational model. The Monte Carlo numerical method is used to indicate the movement of photons from the light source to the hair follicle, then the Finite Difference method, is used to assess the thermal effect which could be caused to a hair follicle and its surrounding tissues.

The findings support the proposition that these types of light-based devices, when used correctly, are able to heat hair follicles without causing significant damage to the surrounding tissues. The computations suggest that the induced thermal damage to the hair follicle might be insufficient to reduce hair growth. The variability in safety mechanisms present in the devices may not be sufficient to mitigate misuse.

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Chapter 1 - Introduction

Introduction

The knowledge that light interacts with skin in a way which can be beneficial dates back to 4,000 B.C. At that time, individuals who were suffering with vitiligo would use sunlight to treat the patches of skin which needed re-pigmenting. The practice of using light in medicine continued through time – in the 19th century, sunlight was again used as a treatment for cutaneous tuberculosis [1].

In 1917, Albert Einstein published The Quantum Theory of Radiation, which contained the theory required to use light in a more concentrated form. Building upon this work, Townes & Schalow created the MASER (Microwave Amplification by Stimulated Emission of Radiation) in 1959, and the following year Dr. Maiman created the first laser (Light Amplification by Stimulated Emission of Radiation), a ruby laser. This led to the creation of further lasers, which allowed the use of light in a more precise manner with a monochromatic, coherent light source of a single wavelength [1]. Lasers are now used in a variety of practices, from use in the home for cosmetic purposes [2] to use in surgery, all of which intend to cause damage to one specific tissue without damaging tissues surrounding the target tissue [3].

The home-use laser market offers a wide range of devices to treat a variety of conditions [4], including Intense Pulsed Light (IPL) devices for hair removal, defined as light sources which produce a broadband spectrum of light rather than providing a single wavelength of light which typical laser-based light sources produce [3]. Home-use cosmetic devices represent 2% of the cosmetic market, with the United States taking the largest share of this portion of the market, though the popularity of these devices is growing throughout Europe.

This thesis intends to investigate how human tissue responds to typical commercial home-use IPL devices, specifically looking into their ability to successfully destroy hair without damaging the surrounding skin tissue as they claim to. It will also assess the safety of the devices, investigating the mechanisms which have been put into place to prevent misuse and injury.

1.2 Background

Home-use light and laser based devices are available for consumers to buy and use without any form of professional guidance, only offering a user manual to the buyer explaining how to use the device correctly. The devices are designed to treat a variety of cosmetic issues, including removing unwanted hair, inducing hair growth, acne, psoriasis and offering skin rejuvenation.

These devices are popular in the retail market as they offer a treatment which is not chemical-based in nature, however the results that manufacturers offer are not often backed up by scientific evidence. The small amount of scientific evidence which has been published regarding these devices has a number of limitations, including small sample sizes and only short term results, despite claims of long term results from the devices. As such little evidence is available, this means that should a consumer wish to ask for medical advice regarding the devices, medical professionals including GPs and dermatologists are unable to provide much information to the patient.

The safety of these devices has also been brought into question within the literature, questioning potential thermal and electrical damage to users, including damage to skin or ocular damage to the user or even others [5]. From studies which have been published about these devices, negative effects have included erythema and oedema, and some pain during use. More serious negative effects have included involve burns, blistering or crusting of the skin, potentially resulting in longer-term effects such as scarring or changes in pigmentation of the skin, however these effects are much less common [6]. If consumers use the product against guidelines, such as using a higher power setting on an inappropriate skin type, or using it on tattoos or moles, there is potential for burns on the skin [5].

Many IPL devices available to consumers do not provide the output parameters of their devices publically. Moreover, very little peer-reviewed data is available to offer scientific evidence to back up the claims made by the manufacturers about their device, and almost all of the peer-reviewed data which is available is now not up to date with the devices available on the current market. The research conducted as part of this thesis will provide scientific research which provides the output parameters of these devices, as well as the efficacy of the devices by using the measured outputs collected as part of the thesis along with a bio-physical computer models to assess the ability of the devices to sufficiently heat hair follicles in order to reduce hair growth. This model will also be able to determine if

the device is likely to overheat the hair follicles and potentially damage the surrounding tissues.

1.3 Research Aims

This project covers the principal technologies used for treatment of long-term hair removal. The fundamental research aims are:

1. To develop a bio-physical model of the volumetric heating effects of these different intense pulsed light devices.
2. To objectively assess if the various branded home-use IPL devices currently available on the market can successfully destroy the hair follicle without causing damage to the users' skin.

The subsidiary objectives of this project are:

- To undertake a systematic computational analysis of light-based medical devices for home-use treatment of hair removal.
- To undertake experimental measurements of key parameters of various home use devices for hair removal.

1.4 Contribution to Knowledge

This thesis has intends to provide the following contributions to knowledge:

1. To develop a bio-physical model to assess the safety and efficacy of current home-use IPL devices, calibrated for use with these devices on set skin tones and hair colours.
2. To produce a comprehensive list of dielectric properties of human skin when using frequencies between 200 kHz and 6MHz.

1.5 Research Methodology

In order to achieve the aims and objectives of this research, I will:

- Conduct a full literature review on all available home-use light devices. These include devices for hair removal, hair regrowth, skin rejuvenation, and other skin conditions.
- Undertake computational analyses on pulsed light systems for hair removal, using Monte-Carlo and Finite Difference methods. These results will be calibrated against experimental data. The results of the analysis will establish clear parameters for the optimal delivery of pulsed light-based sources.
- Measure the energy output, spectral output, pulse durations, and spectral distribution on various home-use devices for hair removal from well-known brands and apply the measured values in the calibrated computational model in order to analyse the therapeutic effect.

The various dimensions and outputs of brand name IPL devices will be measured within the University, using a small laboratory workspace. These devices will be purchased from retail outlets, or donated by the company supervisor. The following measurements will be taken using the equipment listed, as established by Town et al in a previous study [7].

- Fluence measured by an energy meter (Ophir LaserStar Power Energy Monitor, Ophir L40 (150) A-DB-SH-NS Absorber Head; Ophir Optronics Ltd., Jerusalem 91450, Israel).
- Pulse durations measured by a reversed biased photodiode acting as a light-dependant switch, with imagery captured by an oscilloscope using Fluke 196 Scopemeter and FlukeView version 4 software (Optimum Energy Products Ltd., Calgary T2-Z4M3, Canada).
- Spectral output measured by a HR2000+ spectrometer and Spectra Suite software (Ocean Optics, Dunedin, FL 34698, USA).

IPL devices aim to heat the hair follicle enough to cause permanent damage; in order to do this, the thermal relaxation time of the hair follicle, often somewhere between 25 and 55ms, must be the same or lower than the pulse duration emitted [8]. In order to assess if

the device can, in theory, heat the follicle effectively, TODDY, a custom 2 dimensional Monte-Carlo and Finite Difference Modelling system will be used to assess the thermal damage cause by the hair removal devices measured.

Chapter 2 - A Literature Review of Skin Structure and Physiology

Introduction

In this chapter, there will be an in depth discussion about the role of skin, how it is structured, and how it interacts with external and internal processes. This chapter will be split into two separate parts, discussing the skin and what functions it has, and then moving into some of the conditions and diseases which the skin can suffer from.

When discussing the structure and function of skin, each layer of human skin will be covered, giving detail about how each layer differs in its role within the skin and the outer body. How skin changes with age and certain external factors, such as UV exposure, will also be discussed in this section, as well as detailing the structure of hair follicles.

In the second part of this chapter, a selection of skin conditions and diseases will be discussed, describing the mechanisms behind how and why skin will change as a result of these issues. The skin diseases and conditions covered were chosen as they can be treated using home use light based devices or salon based radiofrequency devices.

This chapter is important for the thesis, as an understanding of the functions of skin and how it is structured is essential when building a computational model of the skin, and understanding how skin responds when interacting with light or electromagnetic fields.

2.1 The Structure and Function of Skin

The skin is the largest organ of the human body, constituting around 7% of a 70kg adult's body weight. It offers a barrier against potential harmful effects of our external environment. For example, melanin offers some protection against damage of DNA resulting from the harmful ultraviolet radiation from the sun, and defensins and cathelicidins - natural antibiotics derived from keratinocytes - provide a defence against fungi, bacteria, and viruses. It also stops the body from losing heat with a layer of subcutaneous fat, which also serves as cushioning from potential trauma to the body. The skin is made up of three layers – the epidermis, the dermis, and a layer of subcutaneous fat [9]. This section of this chapter will discuss each layer of the skin.

2.1.1 The Epidermis

The epidermis is made up of a differentiated, stratified, squamous epithelium. It has a varying thickness across the body ranging from 0.05mm to 0.1mm. The epidermis mostly consists of keratinocytes, comprising 95% of all cell types. The keratinocytes are pushed up from the epidermal basement membrane, passing through the five layers which form the epidermis, as shown in Figure 2.1 – the stratum corneum which is the surface layer. Below this is the stratum lucidum, followed by the stratum granulosum and the stratum spinosum, with the deepest layer being the stratum basale [10].

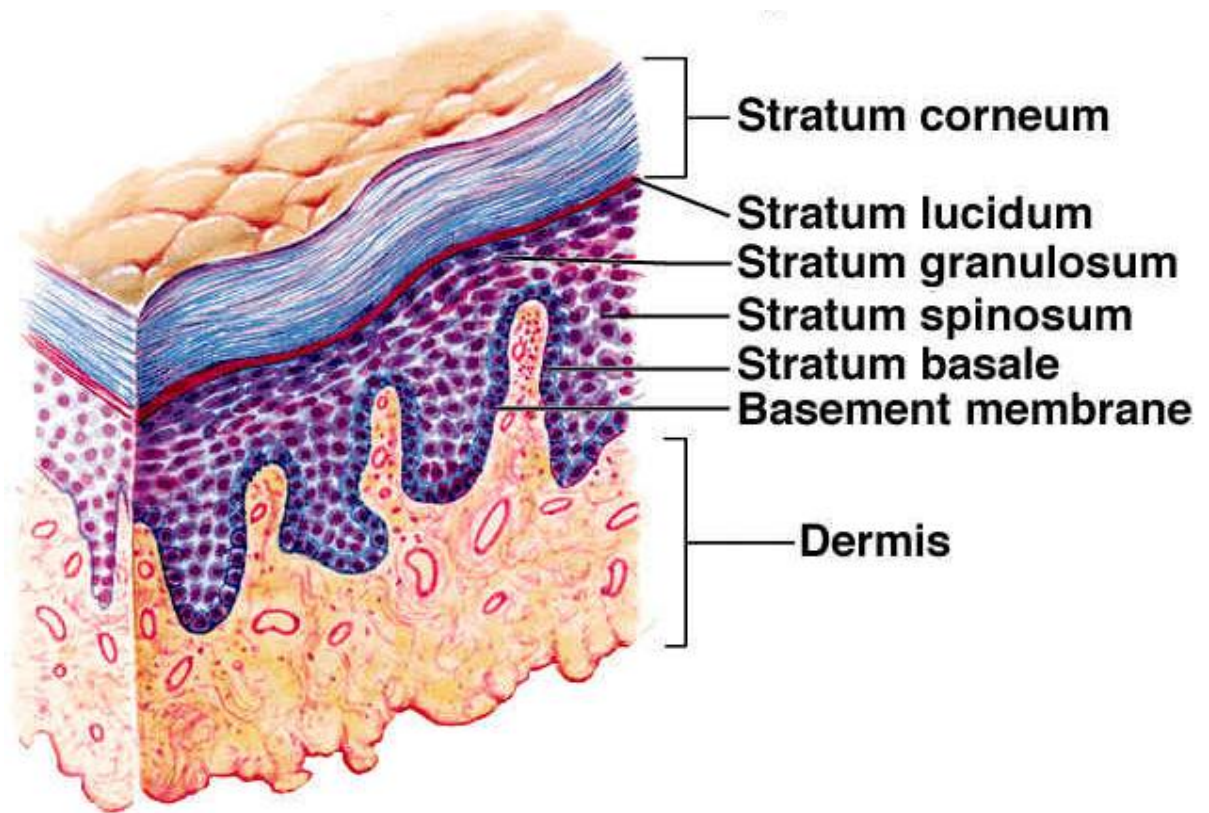


Figure 2.1 - The layers of the epidermis and the dermis [11].

The stratum basale is typically only one cell thick however this can be up to three cells thick in certain parts of the body, such as the soles of the feet, or as a result of disease. The keratinocytes which make up the epidermis are formed in this layer. The cells in the stratum basale are cube shaped, and are around 10–14 μm in diameter. They contain dark, large nuclei and compressed cytoplasm which contains ribosomes and groups of tonofilament. The types of cell include melanocytes, Langerhans cells, Merkel cells, as well as keratinic stem cells which create new cells, as well as keratinocyte cells which keep the epidermis attached to the basement membrane [10].

Above the stratum basale, the keratinocytes which have been pushed up from the basal layer grow to create the stratum spinosum. It consists of multiple layers of cells which contain keratin tonofilaments and connect both to each other and the stratum basale via desmosomes. These cells have a bigger cytoplasm than the cells in the stratum basale and contain various organelles and filaments. Due to the differences between the cells in the stratum basale and the stratum spinosum, it appears that the cells have developed as they moved up the epidermis. This suggests that the cells can change the expression of its genes despite mitosis having stopped. Intracellular granules which are around 100-300nm in

diameter are found in the cytosol of the outer cell layers, which indicates the beginning of the next layer, the stratum granulosum [10].

The stratum granulosum layer of the epidermis has granules of keratohyalin within its cells. These granules are larger than the ones found at the top of the stratum spinosum, and are oddly shaped and organised, at 2nm in length and arranged in rows or lattices in random parts of the stratum granulosum layer. It is thought that the granules later form the lipid membrane in the stratum corneum. The cells have again differentiated, however no new keratin is made in this layer [9].

The next layer, the stratum lucidum, is only present in the thickest parts of the skin, such as the soles of the feet and palms of the hands. It sits between the stratum granulosum and the surface layer, the stratum corneum. These cells are compact, and are considered to be transitional cells [10].

The final, surface layer of the epidermis is the stratum corneum, which is between 10 and 20µm thick. The cells, known as corneocytes, are now flattened and no longer have nuclei or cytoplasmic organelles. The cells are hexagonal and stacked on each other. The cell diameter is around 40µm, and the thickness around 0.5µm, varying depending on the site of the body. Each cell is made up of 70% keratins and 20% lipids. This layer regularly sheds its cells, and is completely renewed every two to three weeks [10].

The epidermis is the layer of skin in which melanin resides [12], however the amount of melanin varies throughout the layers of the epidermis, as well as from individual to individual [13] – studies have shown that melanin content between individuals can range from 17.9% to 72.3% [14]. Melanin is formed in melanocytes from tyrosine [12] - two types of melanin can be produced, eumelanin, which are brown or black in colour, or pheomelanin which is yellow or red in colour [15]. Most melanin and melanocytes are found in the stratum basale layer of the skin [16].

Melanin is one of the major factors which determine an individual's skin tone, along with haemoglobin and carotenoids. It is not just the presence of melanin which affects skin colour, but also the type of melanin present, its activity levels, as well as how it is stored and how it moves from melanosomes [14]. Melanin is typically found in melanosomes, which are spheroid shaped, and one of its important roles in the skin is to provide protection to the skin when it is exposed to ultraviolet (UV) radiation [12].

How melanin is distributed throughout the skin affects how effectively it can protect the skin from UV radiation, as well as other light sources [12]. The wavelengths of light which melanin absorbs is discussed in further detail later in the next chapter. Melanin is distributed from the basale layer of the skin via keratinocytes. During their transit via keratinocytes to the surface of the skin, the melanin will degenerate [14]. The activity of melanin can change depending on the external environment the skin is being exposed to. When the skin is exposed to UV radiation, melanosomes will move toward the surface of the skin via keratinocytes, and when it has reached the stratum corneum, all the melanosomes have degraded to melanin dust in light skin, but in darker skin some melanosomes will remain [12].

Melanin density changes depending on the part of the body being looked at – the palms of the hands and soles of the feet will typically see much less melanin, compared to skin on the torso [14]. However, accurately determining the amount of melanin in the skin is difficult, as results can be affected by how hydrated the skin is and other chromophores in the skin. Some studies suggests that the distribution of melanin varies between skin types, with melanin remaining in the lower skin layers for those with lighter skin, while in darker skin melanin can be found in the stratum corneum [13]. Other studies have shown that the melanosomes in darker skin are typically larger than those found in lighter skin [14].

Melanin density will also change as the skin ages intrinsically and extrinsically. A study by Gilchrest et al [17] took biopsies of skin which had been protected from the sun and had been exposed to the sun repeatedly over long periods of time from people of various ages. Their findings showed that the amount of melanocytes in decreased by 10% as the age of participants increased by each decade. They also showed that there were double the amount of melanocytes in skin which had been repeatedly exposed to sunlight compared to skin which had been protected from the sun.

2.1.2 The Dermis

The dermis, shown in Figure 2.2, is separated from the epidermis via a basal membrane, which has a diameter of approximately $2000\mu\text{m}$. This membrane consists of an intricate network of proteins and glycoproteins which begin in the basal keratinocytes and extend into the dermis. This membrane allows for cell movement between the two layers, and various macromolecules interact with it, including collagens and integrins [10].

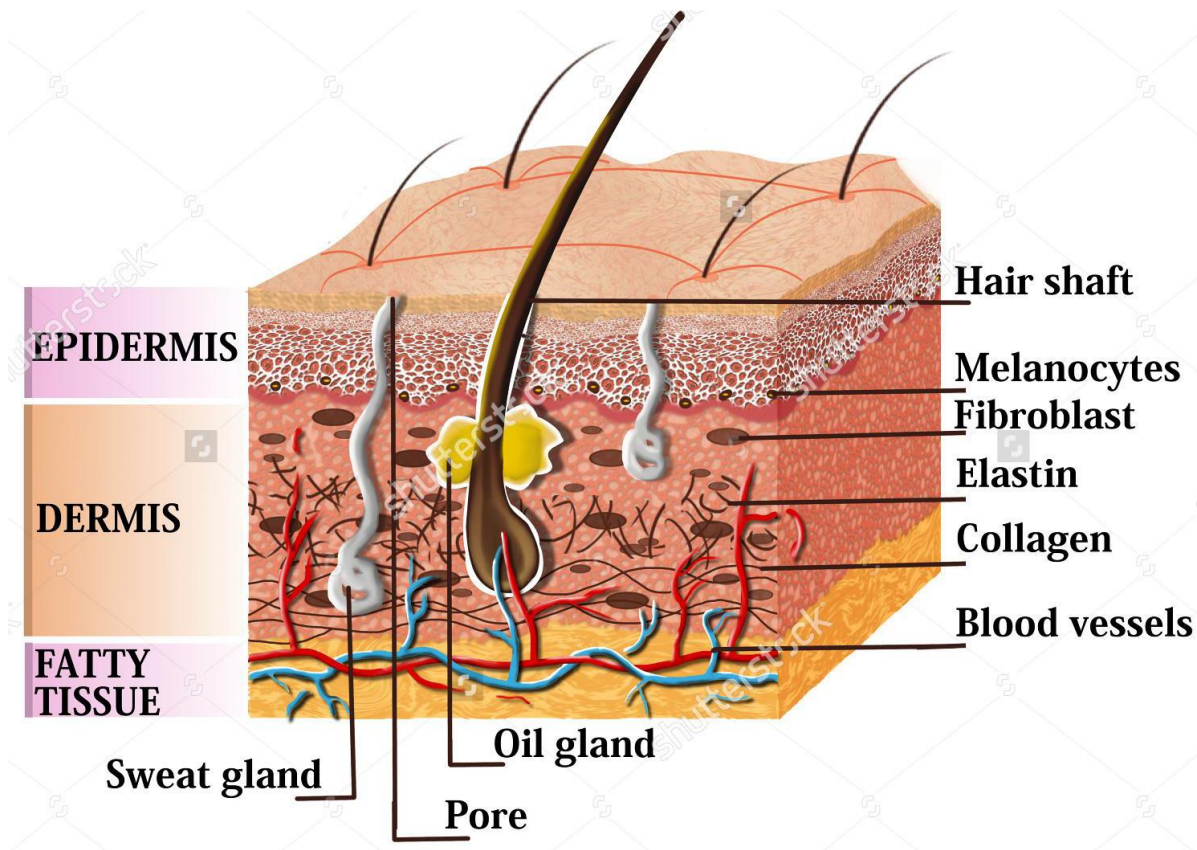


Figure 2.2 – The dermis [18].

The dermis is a network of proteins and polysaccharides which holds a large amount of water and adds flexibility to the skin, and is mostly made up of collagen and elastic tissue. The dermis offers nutrition to the epidermis, and helps regulate temperature and pain in the body. This layer can be anywhere between 0.5mm and 5mm thick, depending on its location on the body. There are fewer cells in the dermis compared to the epidermis - the cells are either fibroblasts and make up the connective tissue between proteins, mast cells which are part of the immune and inflammatory response in skin, or melanocytes which produce melanin [9].

2.1.3 Subcutaneous Fat

Below the dermis is a layer of subcutaneous fat, also known as the hypodermis, which is the deepest layer of the skin. It is connected to the dermis via collagen and elastin fibres, and also connects the skin to the muscle underneath. It is made up of 50% fat cells, as well as fibroblasts and macrophages [10].

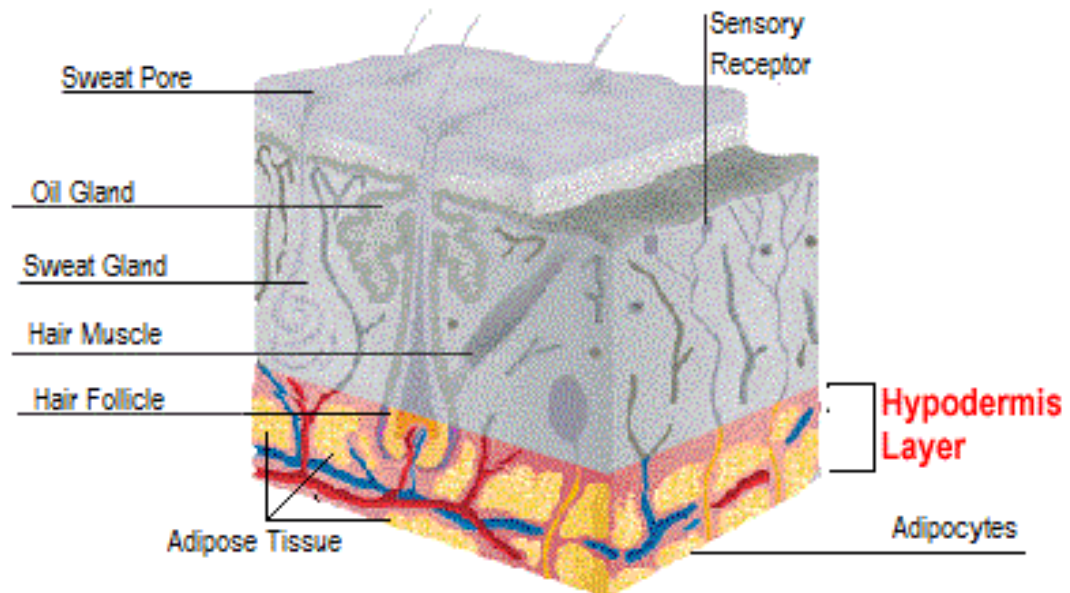


Figure 2.3 - The subcutaneous fat layer of skin [19].

Adipose, or fat, tissue was previously considered to be just an energy storage layer, with no other functions within the body [20]. However, recent research shows that it in fact provides vital functions within the body, with a large role in regulating metabolism of energy and hunger, by releasing the hormone leptin to the hypothalamus, and also have effects on tissue remodelling through providing signals for osteogenesis and angiogenesis. Adipose cells, or adipocytes, also release proteins related to inflammation and control of blood pressure. 80% of fat within the human body is located within the subcutaneous fat layer of the skin, which is shown in Figure 2.3, with the remaining 20% placed around the internal organs. Up to 12% of a healthy male's body weight is made up of fat, whereas fat can make up to 20% of body weight in a healthy female [21].

The development of mature adipocytes takes place in two stages, known as determination and differentiation. In the determination stage, stem cells differentiate into adipoblasts, which may then develop further into preadipocytes, which are unable to differentiate further into any cells except adipocytes. In the differentiation stage, dependent on the correct conditions, preadipocytes will become mature adipocytes. There are two forms of

adipose tissue, white and brown, shown in Figure 2.4. White adipose tissue provides energy storage to the body, while brown adipose tissue actually burns energy in response to body temperature dropping in order to prevent hyperthermia. Brown adipose tissue was once considered to be found exclusively in young children, however recent research has shown that active brown adipose tissue is present in adults [20].

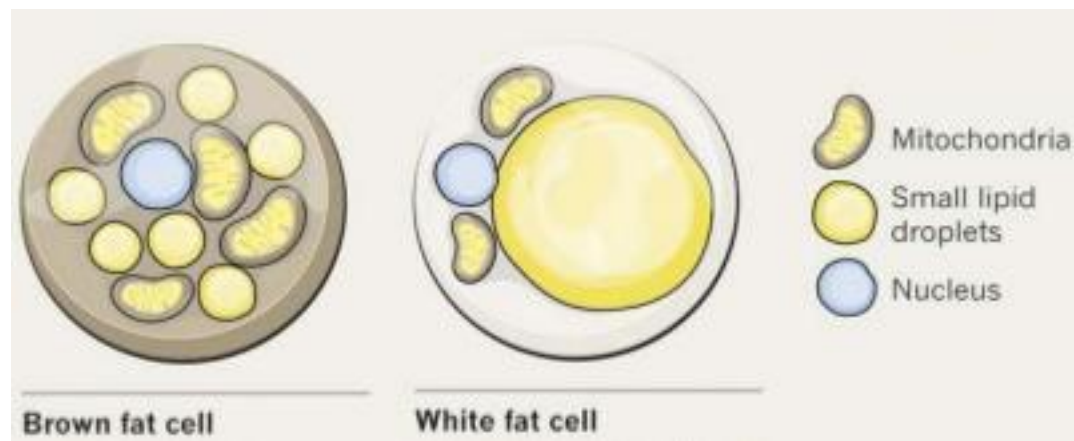


Figure 2.4 - Brown and white adipose tissue – brown adipose tissue will burn fat, while white adipose tissue stores fat [137].

Adipose tissue is incredibly flexible, and can expand and retract throughout a person's lifetime, depending on the intake and output of energy at any given time, as well as a response to disease. Adipose tissue can expand via two mechanisms, hypertrophy and hyperplasia. Hypertrophy is a change to the adipocytes themselves, causing them to increase in size, while hyperplasia involves a rise in the number of adipocytes which are developed from precursor cells, as adipocyte cells cannot multiply. Hyperplasia will typically take place as a response to the death of adipose cells [20].

Through the process of hypertrophy, adipose cells are able to hold lipids which are released if they are required by other organs for energy. In cases where an excessive amount of lipids are held by adipose tissues, this can cause problems in the body, especially if there are excessive lipids being held in the cells surrounding the internal organs, increasing the risk of developing cardiovascular problems, cancer, or resistance to insulin [20].

2.1.4 Skin Elasticity and Physical Signs of Ageing Skin

In the literature, the ability of skin to be both resilient and deformable is typically referred to as skin elasticity [22]. Skin elasticity is provided by various elements within the skin's structure – the epidermis and dermis are connected by the dermal-epidermal junction,

where the basal epidermal keratinocytes are connected to the basement membrane, which is made up of type IV collagen. Collagen VII fibrils and microfibril bundles connect the dermis to this basement membrane. These microfibril bundles are oxytalan fibres, and are part of the elastic fibre system within human skin [22].

There are various types of collagen found within tissue, with at least twelve of these found in the skin. Collagen makes up around 85% of the non-water weight of the dermis, and Collagen I & III are the dominant types found, and are dispersed among the dermis, and also found within the papillary and reticular dermis [22]. The dermal-epidermal basement membrane is mostly made up of type IV collagen [9]. Collagen polymerize to form fibrils and fibres, which are then arranged in bundles, which are generally either found parallel to the dermal-epidermal membrane, or are intra- or intermolecular cross-linked, giving the skin its flexibility and resilience, as well as its ability to interact with other parts of the basement membrane. Collagen VII is also found near the fibres on the dermal-epidermal membrane, and function to anchor the dermis to this membrane [22].

Certain types of collagen fibres are arranged in particular ways, and as a result are organised into different classes. Collagen types I, II, III, V and IX create large fibrils and as such are classed as fibril forming. Collagen type IV cross-links into the basement membrane, collagen type VI creates microfibrils and so are classed as microfibril forming, and type VII collagen creates securing fibrils. The remaining types of collagen (IX, XII, XIV, XIX, XX & XXI) are known as fibril-associated collagens with interrupted triple helices collagens, and are typically found within bigger collagen fibres as stabilizers within the structure [9].

The majority of the collagen found in the human dermis is type I collagen, making up around 80% of the total collagen found. It links with type II collagen to form large collagen fibres within the dermis. Type III collagen is the next most dominant type of collagen found in the dermis, constituting approximately 10% of the collagen found within the dermis. It is most abundant in the connective tissues, uterus, and gastro-intestinal tract of the human body. As previously stated, type IV collagen is found in the basement membrane in the dermal-epidermal junction, but it is also found within the vascular basement membranes; this collagen is particularly flexible in comparison to others due to the lack of interruption within its triple helical structure. Collagen V is found in most connective tissues, and contribute 5% of the total collagen within the dermis, often found at the surface of large collagen fibres, regulating their growth. Without the presence of this

collagen, collagen fibres will grow in irregular patterns. Finally, type VI collagen, a non-prevalent collagen within human skin, forms small microfibrils which secure the large type I & III collagen fibres and basement membrane collagen. The organisation of collagen fibres relies on cross-linking in order to keep its flexibility and strength. Once this has been achieved, the collagen fibres are fully matured and are stabilised, meaning they can exist without excessive degradation for long periods of time under normal circumstances [9].

Elastic fibres within the dermis has been suggested to have an important role in the resilience of skin tissue, and is an essential part of the connective tissues within the dermis, despite only providing up to 4% of the dry weight of the dermis in sun-protected adult skin. Elastic fibres are made up of various components, including elastin (a connective tissue protein which creates the core of the elastic fibres), microfibrils which contain multiple proteins, fibulins, microfibril-associated glycoproteins, and latent transforming growth factor-binding proteins. Elastic fibres are generally organised in the reticular dermis as part of a network structure, with each horizontal fibre topped with fibrils, often oxytalan fibres or cross-linked elastin, which extend vertically to the dermal-epidermal junction [22].

Elastin is created from a polypeptide known as “tropoelastin”, which is made up of around 700 amino acids. The microfibrils which are linked to elastin are shaped like tubes and have a diameter of around 12nm. These microfibrils are not directly associated with elastin and exist in various tissues without elastin – those which are associated with elastin contain certain types of proteins [9]. Fibroblasts in human skin are responsible for synthesising collagen within the dermal extracellular matrix. The dermal extracellular matrix dictates the structure within the dermis as well as how it changes as the skin ages [22]. Fibroblasts are also thought to be one of the main synthesizers of elastin within the dermis, as well as at least contributing to the origin of proteoglycan and glycosaminoglycan macromolecules [10].

Both collagen and elastic fibres are constructed to last for an extended period of time - the approximate half-life of types I & II collagen can vary between 15 and 95 years, and elastin fibres are the same as the lifetime of the individual, if not more [22]. Over time, collagens will naturally degrade and turnover, evidenced by the excretion of hydroxyproline by the collagen, which can be found in urine, and the proteins of elastic

fibres are at risk of being damaged as a result of cross-linking, the accumulation of fats or calciums, or from being changed over time by the residue of aspartic acid [22].

Like the rest of the human body, over time skin will ultimately age, an inevitable and complex process which results in cell death, and is marked by the redistribution of fat within skin, a decrease in the elasticity in the dermis, and a reduction in bone mass [23]. The physical signs of ageing in human skin includes changing in pigmentation, a lack of elasticity, wrinkling, and laxity, which are all a result of degradation in the structure and molecules within the skin [24]. Ageing within the epidermis is exhibited by being more susceptible to trauma, leading to more tears in the skin [25], whereas ageing in the dermis leads to skin losing its flexibility, elasticity, and its ability to respond to changes resulting from internal and external stressors [24].

There are two types of ageing which occur in skin: intrinsic, or chronological ageing, and extrinsic, caused by external factors such as long term exposure to ultraviolet radiation or smoking [22]. Both intrinsic and extrinsic ageing have similar features, including the reduction of water held by the epidermis, a loss in collagen fibres, and changes in pigmentation, however typically some of the physical expressions of ageing are more pronounced when resulting from extrinsic ageing, such as the lack of skin elasticity and deeper wrinkles [22], and extrinsic ageing will often accelerate the process of ageing in the skin [23]. The differences in the amount and structure of elastin and collagen between youthful skin, and both intrinsically and extrinsically aged skin are highlighted in Figure 2.5.

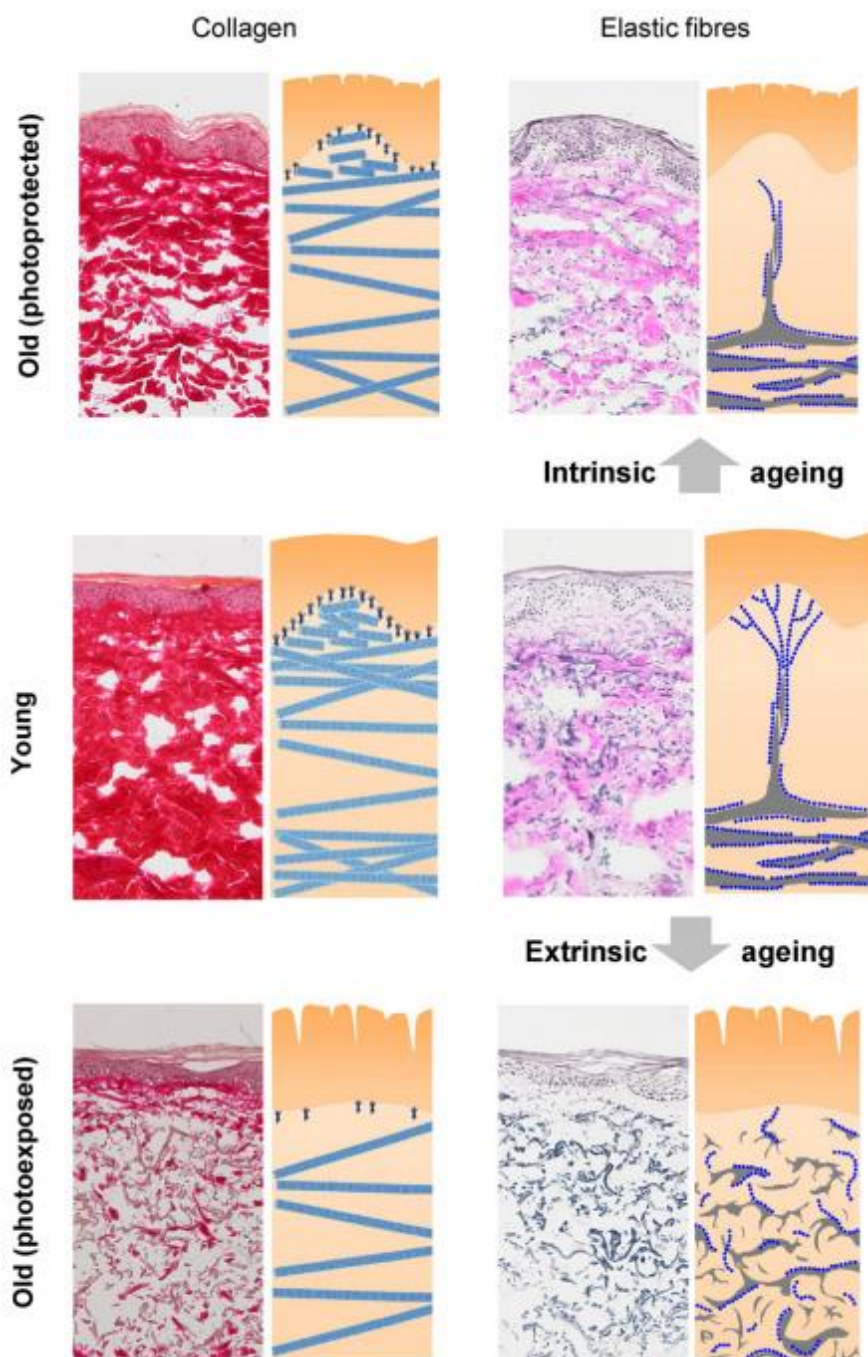


Figure 2.5 - The differences in collagen and elastin in young skin, intrinsically aged skin, and extrinsically aged skin [22].

The ageing of skin, particularly intrinsic ageing, has also been shown to affect the integrity of the epidermis, the structure and adhesion of keratinocytes, and stem cells. One of the important features of both types of skin ageing consists of changes in the structure and function in the dermal extracellular matrix, which is responsible for the communications between collagen, elastic fibres, and proteoglycans to keep the skin resilient, hydrated and flexible. These changes result in elastin, oxytalan fibres, and type I, III & IV collagens degrading [22]. There is also evidence to suggest that the ability of skin to detoxify free

radicals decreases with age. It is for this reason that in the 1950s, oxidative damage was believed to be the cause of ageing in human skin, and the number of free radicals in the skin increased, which could cause damage to nucleic acids, cell proteins, and lipids. It was also thought that increased amounts of nuclear DNA, the deletion of mitochondrial DNA, and incorrectly folded proteins led to the ageing of skin. It is now known that while these factors do contribute to ageing skin, they are not the only reason for it [9]. The immune response in ageing skin is also known to decrease, as well as its ability to repair injured cells, and these changes make the skin vulnerable to diseases [23].

Exposure to ultraviolet radiation such as sunlight leads to advanced ageing in skin, and is known as photoageing, the severity of which depends on the skin phototype of the individual and the length of their exposure over time. Chromophores in the skin such as nucleic acids and proteins absorb the ultraviolet light of the sun, ranging from 280nm to 400nm, with particularly strong absorption for ultraviolet B radiation with wavelengths of 280nm to 320nm. Exposure to these wavelengths results in DNA being damaged and repaired, leading to the damage of skin cells and tissue [23]. This type of UV exposure leads to fine lines and rhytids (wrinkles), as well as changes in the texture and colour of skin [26].

In skin which has been heavily exposed to sunlight, fibrillar type I & II collagens are lost from the dermis, type VII collagen is lost from the securing fibrils at the dermal-epidermal junction, and the elastic fibres proteins in the reticular dermis are disorganised and spread widely throughout the structure. Investigations into the pathological changes after exposure to ultraviolet radiation have shed light onto the mechanisms behind what leads to ageing in human skin - it has been discovered that the synthesis of certain enzymes which cause damage in the skin are initiated as a result of UV exposure, some of which are known as matrix metalloproteinases (MMPs), particularly MMPs 1, 3, and 9. MMP-1 is responsible for causing the initial degradation to type I & III collagens, which are then even further damaged by MMPs 3 & 9. There appears to be some genetic differences between individuals which governs the amount of activity the MMP-1 enzyme partakes in [22].

Research has suggested that when skin has been photoaged, the extracellular matrix releases MMPs, which have been found to have increased activity in photoaged skin, some of which have the ability to injure elastic fibres in the skin, and initiate damage to fibrillin-1 and fibulin-2 located at the dermal-epidermal junction. Naylor, Watson, and Sherratt [22] suggest that the proteins linked to elastic fibres in the skin can be directly damaged by UV

radiation. They showed that while collagen type I was not significantly affected by changes in skin resulting from ultraviolet exposure, fibrillin-rich microfibrils and the glycoprotein fibronectin, which has adhesive qualities, were heavily affected by exposure to ultraviolet exposure. Naylor, Watson, and Sherratt went onto suggest that this was due to differing amino acid structures – many of the proteins related to elastic fibres, except elastin, contain amino-acid based chromophores which strongly absorb UVB light, especially the fibrillins and fibulins [22].

The physical formation of wrinkles, or rhytids, is what is typically most often associated with skin ageing. Despite the focus of many anti-ageing products and surgeries being related to the removal, reduction, or prevention of wrinkles, the mechanism behind how they develop is currently unknown. While studies, like those mentioned previously, have shown that sun exposure can induce the synthesis of MMPs which leading to changes in the structure of the extracellular matrix are related to ageing skin [27], as well as the loss of certain types of collagens and other skin tissues, the link between these changes and wrinkles has yet to be shown experimentally, instead merely showing an inferred relationship between the two [22].

Lee et al [27] investigated the link between the degradation of the elastic fibre network and the formation of rhytids. In their study, they found that there was a distinct negative correlation between how severe rhytids were and the length, width, and number of oxytalan fibres as well as the size of the area they covered. They also found that the oxytalan fibres could be replenished, and repairs of elastic fibres were induced by topical retinoic acid. This was achieved due to the increase of fibrillin-1 mRNA expression and tropoelastin, and the decrease of MMP-12 expression. The application of topical retinoic acid for 24 weeks led to elastic fibres growth in photoaged skin, which correlated with a decrease in wrinkle severity. From these findings, it was concluded that damage to elastic fibres leads to rhytids in the skin. The mechanism behind the thermal degradation of collagen is discussed further in section 3.2 of this thesis.

Another sign of skin ageing includes skin becoming drier, partially a result of the reduction of the skin natural moisturization factor being reduced, resulting from a reduction in amino acids in the stratum corneum. There is also a reduction in the barrier lipid system, which is an organised structure of various lipids including ceramides and cholesterol, which can also lead to skin dryness. This reduction of barrier lipids is not as obvious, and has been experimentally demonstrated by destroying the barrier using either organic solvents, tape

stripping, or detergents – to mimic the actions of environmental damage - in both young and elderly participants, and showing that in elderly participants the recovery time is considerably longer in comparison to younger participants [28].

As a person ages, their infraorbital eyelids can become darker – this is known as infraorbital dark circle. While it can affect people with a large range of ages, all skin types and occurs in men and women, it is typically associated with ageing as it worsens with age due to the sagging of skin and changes in the distribution of subcutaneous fat. This can be caused by a multitude of factors including the skin of the lower eyelid on the orbicularis oculi muscle being thin and translucent, skin laxity and tear troughs causing darkening of the skin, and disproportionate amounts of pigmentation [29].

The skin over the orbicularis oculi muscle has very little subcutaneous fat, if any at all, and as a result the vasculature within the muscle or the subcutaneous vascular plexus may be visible through the skin. This can result in the infraorbital dark circles under the eyes. If the condition is caused by extra pigmentation, it may be a result of certain skin conditions, such as contact dermatitis leading to postinflammatory hyperpigmentation, or dermal melanocytosis involving multiple pigmented lesions under the eyes, and is a result of melanocytes located in the dermis. In the case of skin laxity and tear trough, this is directly related to ageing skin. As collagens and elastin in the tissue of the eyelids and periorbital skin degenerate, due to intrinsic and photo-ageing, the skin under the eyes begin to look darker, resulting in infraorbital dark circles. The tear trough, located near the centre of the inferior orbital rim, is subject to thinning subcutaneous fat as a person ages, which leads to the appearance of infraorbital dark circles [29].

While it is still unclear how the exact mechanism behind infraorbital dark circles in ageing works, it has been found that they are counteracted by the injection of fat between the muscle and skin of the lower eyelid. Based on this, Roh & Chung [29] hypothesise that one factor in infraorbital dark circle is due to changes in the muscle as well as the reduction of subcutaneous fat.

2.1.5 Hair Follicles

Hair serves multiple purposes to the human skin - it keeps it warm, and offers a layer of protection from the external environment, however the hair is constantly falling out and being replaced [30]. Across the whole surface of the skin, with the exception of the soles of the feet, palms of the hands, and the lips, hair follicles are present. Hair follicles are small

amounts of epithelium which contain a small papilla of dermis at the bottom. Above the papilla, there is a sebaceous gland attached to each follicle, which is generally between 200 and 2000um in diameter. Sebaceous glands secrete sebum containing wax, triglycerides and free fatty acids, which provides protection to the skin, and maintains a steady pH of around 5 [10]. In the mammary, axillary and genital areas of the body, the follicles are also linked to apocrine glands, a form of sweat gland which secretes a fatty fluid into the hair follicle and skin in response to emotional stressors. Between the hair follicle wall and the top of the dermis is smooth muscle known as the arrector pili which facilitates the hair standing on end [9].

A hair follicle is created via specialised dermal cells grouping beneath the epidermis, causing the above epithelial stem cells to grow downwards in order to create the hair follicle. The hair follicle takes the shape of a long cylinder which has the diameter of several cells. The internal layers of the cylinder differentiate to create the main hair shaft, and the inner root sheath which surrounds it. A collection of mesenchymal cells creates the dermal papilla, which is based at the bottom of the hair follicle within the hair bulb. As the bulb reaches the bottom of the dermis, the hair follicle becomes fully mature. The matrix cells then begin to divide in order to form the cells which become the hair [30].

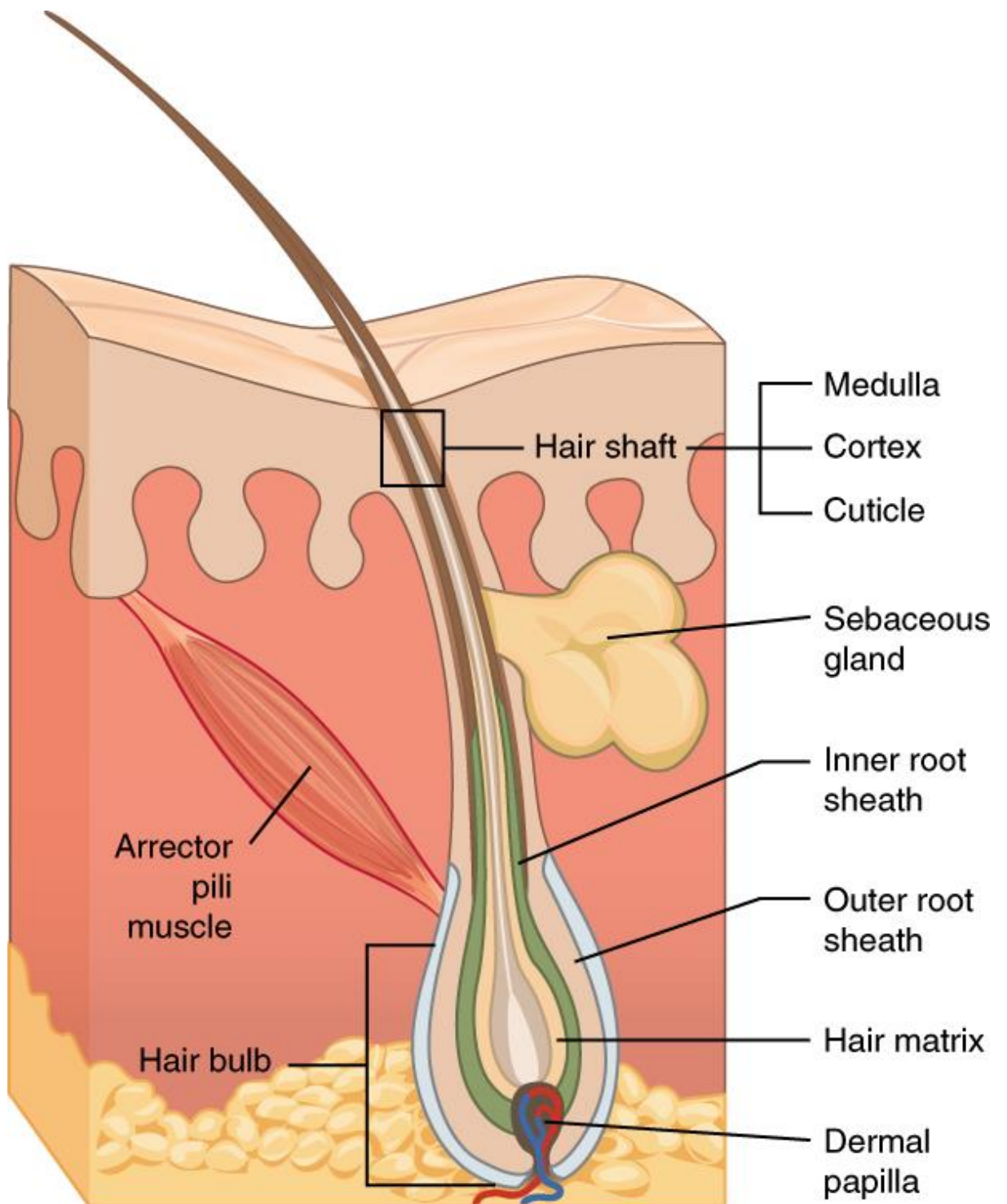


Figure 2.6 - The hair follicle [31].

There are various components of a hair follicle, as shown in Figure 2.6 – the matrix and outer root sheath make up the epithelial part of the follicle, while the dermal papilla and connective tissue sheath are the dermal parts [32].

The matrix cells, based at the bottom of the hair follicle produce the hair shaft itself. The main component of the hair shaft, known as the cortex, is made up of specific filaments

and proteins. There are melanocytes among the matrix cells which create the pigment for the hair. The matrix cells differentiate as they move up through the inner root sheath, which condenses them to create the shape of the hair [30]. The dermal papilla, based at the bottom of the follicle, is made up of fibroblasts and is believed to have a role in regulating the number of matrix cells within the follicle and therefore what size the hair will be [9].

The hair bulb contains a group of epithelial stem cells in the outer root sheath. These cells both live the longest and have the longest lasting cycles of all epithelial cells in the hair follicle. They offer a back-up to epidermal cells and the cells of the sebaceous gland. The outer-root sheath contains melanocytes, Merkel cells, and Langerhans' cells, which contain various keratins, growth receptors, cytokines and adhesion molecules. When the epidermis is injured or loses cells, these cells will move out of the hair follicle and replace the lost or injured cells [33].

Typically, hair grows between 300 μm to 400 μm per day. The growth of hair follicles follows a cyclical pattern, with three phases – anagen, the growth phase; catagen, the regression phase and telogen, the resting phase – a visual diagram of this cycle is given in Figure 2.7. The duration of these cycles vary between different parts of the body, with the hair of the scalp having a much longer cycle than hairs on the eyebrow [34].

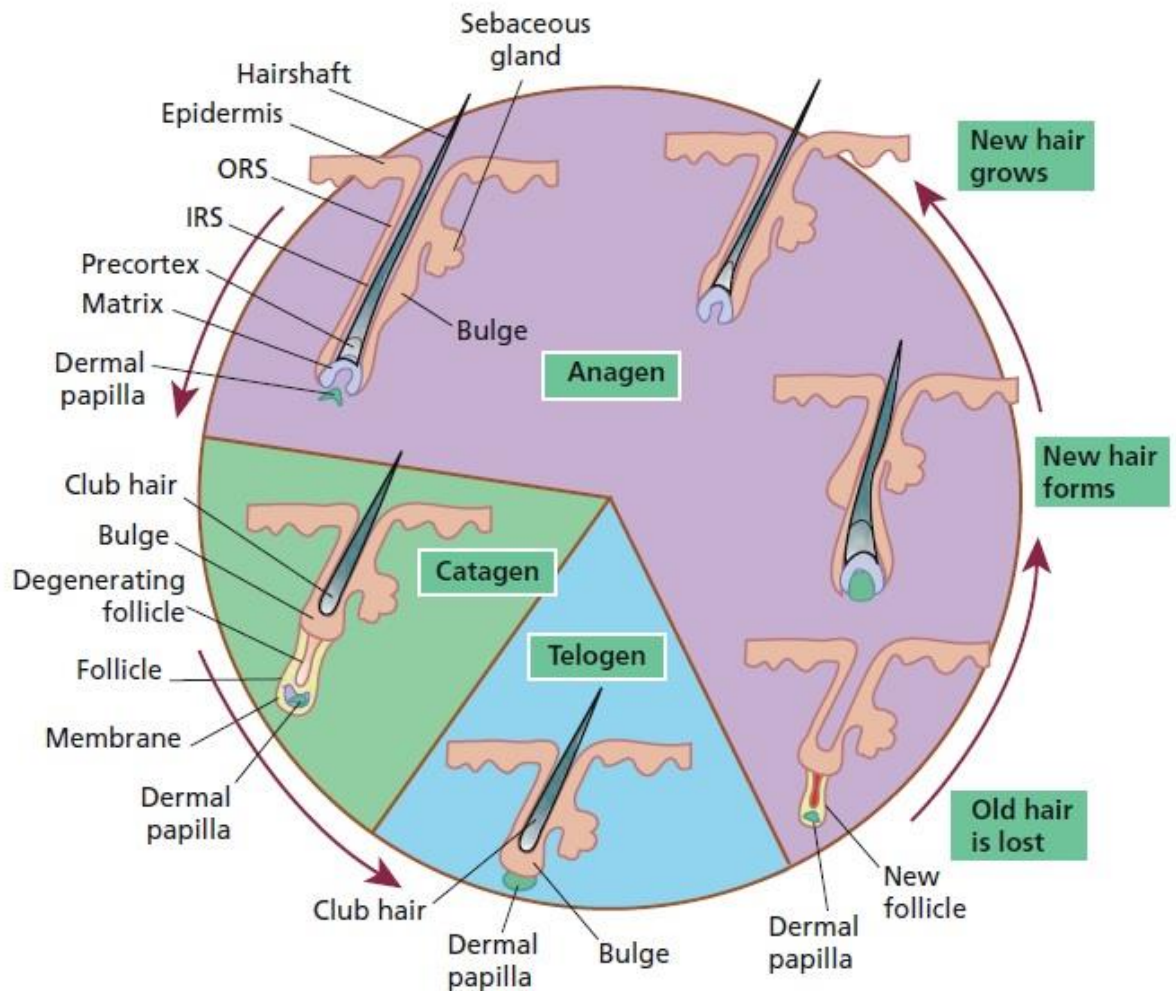


Figure 2.7 – The cycle of hair growth [9].

The anagen phase consists of the follicle creating the whole hair shaft. The cells created by the matrix cells move up through the hair shaft, each differentiating into cells from one of six layers of the inner root sheath and hair shaft. The hair shaft cells organelles are forced out of the cells and become compressed, and link with keratin filaments, which gives the hair shaft strength and flexibility. The inner root sheath uses keratin to become rigid in order to help guide and shape the hair shaft as it grows. The dead cells of the inner root sheath begin to degenerate as they get to the top of the hair follicle, and so the hair shaft is released to the skin's surface. The length of the hair is decided by how long the anagen phase lasts, which itself is decided by the matrix cells [30].

Between the anagen phase and the catagen phase, a small number of cells divide before differentiating. The lower number of matrix cells leads to the slowing growth of the inner root sheath and hair shaft, leading to the regressive phase of growth, catagen. By now, the cells in the hair shaft have stopped differentiating and the top seals into a club hair, which

moves up to the upper part of the hair follicle. The lower part of the follicle diminishes, and the epithelial strand forms. This strand links the dermal papilla to the upper hair follicle, and has been destroyed once the dermal papilla reaches the surrounding parts of the club hair in the upper follicle. Following the catagen phase is the telogen phase, where the follicle remains dormant [30].

When two dormant stem cells in the resting follicle are activated, the transition into the anagen phase begins. The stem cells generate daughter cells which will create the new hair follicle. The new follicle is created next to where the club hair is being held, which will later be shed during exogen. The bulge is created, and another layer is added to the stem cell supply [30].

2.2 Conditions & Diseases of the Skin & Hair

The previous section discussed the typical structure and function of healthy skin in considerable detail. The discussion will now move onto unhealthy skin, and a small number of the conditions and diseases which it can suffer from. The conditions and diseases discussed have been chosen as they can potentially be treated by home-use device laser or light treatments, or through salon-based radiofrequency treatments. Details of the above mentioned treatments for these conditions and diseases will be discussed in more detail later in the thesis.

There are various conditions and diseases of the skin which can cause both physical and psychological problems for an individual. Often, treatments involve medication or visits to a dermatologist, however some of these conditions can be treated at home using light or laser based devices, or in a salon using radiofrequency devices. This makes treatment less invasive, less expensive, and in the case of home-use devices, gives the patient the opportunity to conduct the treatment themselves in their own home at a time which suits them. The conditions which can be treated at home or in a salon will be briefly discussed in this section.

2.2.1 Cellulite

Cellulite, a term was initially coined in the 1850s in France, is a very common disorder which occurs in the adipose tissue of the skin of post-pubertal females. It causes a dimpled appearance in certain parts of the skin [21], often compared to orange peel. The structural differences between skin affected by cellulite and skin which is not affected by cellulite is shown in Figure 2.8. Cellulite can be clinically diagnosed, with 3 grades to separate the severity of each case of cellulite:

Grade I: Can see dimpling when skin is pinched, however otherwise it cannot be seen.

Grade II: Can see dimpling when patient is stood up, however not when they are lying down.

Grade III: Can see dimpling when patient is both stood up and lying down. [21]

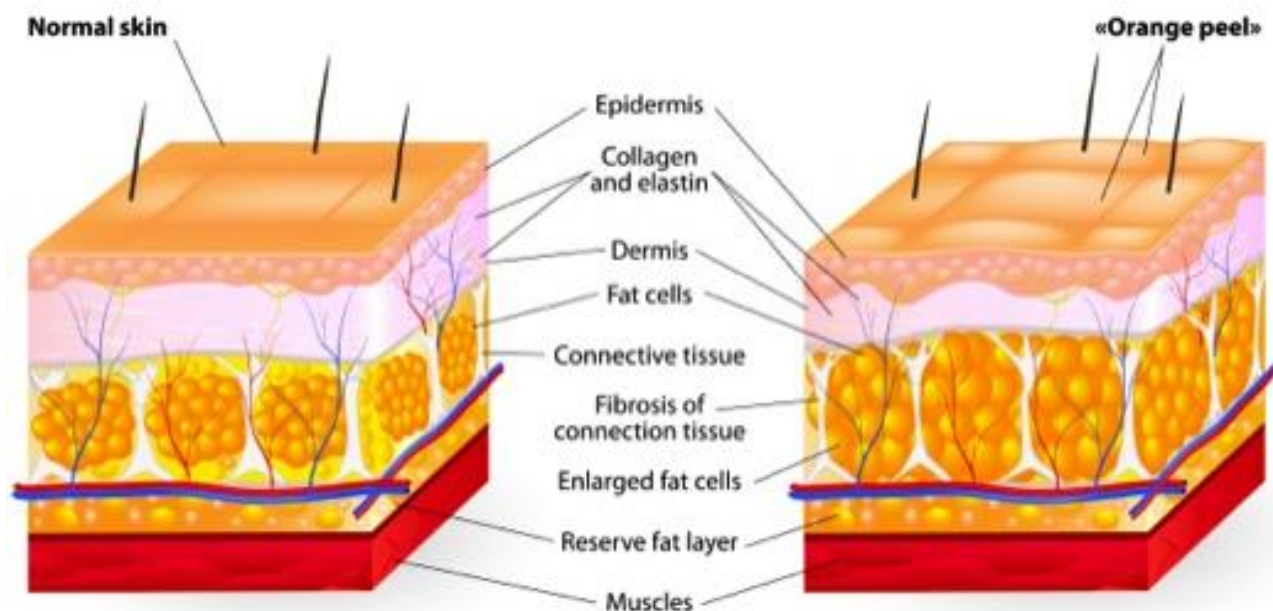


Figure 2.8 - Differences between skin unaffected by cellulite (left), and skin affected by cellulite (right) [35].

Cellulite is a metabolic disorder which typically affects the subcutaneous tissue of the limbs, abdomen and pelvic area. Research had yet to discover a definitive cause for cellulite [21]. One study by Rosenbaum et al [36] looking to investigate the cause of cellulite took samples from the thighs of both affected and unaffected males and females and took in vitro measurements of their subcutaneous fat tissue, and also in vivo measurements of tissue of the abdomen and thigh. Results showed that the adipose tissues of the sample affected by cellulite were displaced, pushing into the dermis. Samples also showed that the connective tissue layer between the dermis and subcutaneous fat layer was smooth in male subjects, but uneven in female subjects, and even more so in the samples affected by cellulite from females. These results suggests that the structure of the connective tissue layer in females can result in adipose tissue being pushed into the dermis, which leads to the appearance of cellulite.

While in the media cellulite tends to associated with obesity, cellulite can affect women of any weight. However, a high body fat percentage is considered to be a risk factor in the likelihood of developing cellulite; other risk factors include a decrease in circulation to cellulite prone areas, which can be caused by extended periods spent seated, and hormonal changes from pregnancy, as well as water retention [21].

Cellulite affects approximately 98% of women after they have experienced puberty, and is mostly seen in Caucasian women. It is less common in non-caucasian women, and very

rarely affects men. Even though cellulite is a cosmetic issue, and has no direct effect on physical health, many women will visit a dermatologist to see if it can be treated. The proposed treatments for cellulite are unreliable, with little scientific evidence to suggest that they offer a long-term solution, if any solution at all. Many treatments can provide some mild, short term change, though no single or combination of treatments has provided reliable results [21].

Invasive treatments for cellulite include liposuction, however as the adipose tissue causing cellulite protrudes into the dermis, the results may not be satisfactory, and negative effects of the treatment include possible necrosis. Somewhat reliable results have been seen with laser based techniques which aims to tighten skin as well as treat cellulite. Less invasive treatments include selective cryolysis, and radiofrequency, however more evidence is needed to provide evidence of efficacy of these treatments [21].

2.2.2 Acne Vulgaris

Acne vulgaris is a chronic disease which affects the pilosebaceous units in the skin. Acne is an incredibly common disease, affecting approximately 80-95% of the global population at some point in their lives [37], and is the reason behind 20% of all visits to a dermatologist [38]. Acne affects more than just the skin, with some patients reporting changes in their self-esteem, quality of life, and psychosocial development as a result of their skin disease [38]. Despite its prevalence, there are still many myths which surround acne, one of which being that it is a disease which only affects teenagers, when in fact, in the United States only 36.5% of those who suffer with acne are adolescents and 61.9% of sufferers are adults [37].

Acne is categorized by various factors, including increased production of sebum, proliferation of *Propionibacterium acnes* (*P.acnes*) in the pilosebaceous duct [37], as well as inflammatory pustules, papules and cysts, with the possibility of scarring [39]. Despite being a primary cause of acne, *P.acnes* is a naturally occurring bacteria which resides in the sebaceous glands of all people [38]. The process of acne forming in the skin is shown in Figure 2.9.

The first manifestation of acne is a comedo forming on the skin. A comedo is a plug in a follicle – it can be open, with a visible black tip on the skin, or closed where no black tip is visible. When it first begins to form, it is known as a microcomedo, and can eventually form into an inflamed papule or pustule if triggered by *P.acnes*. The development of a

comedo starts with defective desquamation of the lining of the follicle. When the epithelium sheds, it does so in sheets rather than smaller particles – this means it cannot be excreted through the follicular orifice, creating a plug (the comedo), and keratinous material builds up in the follicle as a result. These comedo will typically contain a vellus hair, and as time passes more hairs can grow within the comedo. What causes the initial defective desquamation within the follicle is not currently known. While microcomedos are not always visible, they can be extracted using cyanoacrylate glue – studies using this method have shown that there are many more of these on the skin of a person with acne compared to a person without acne [40].

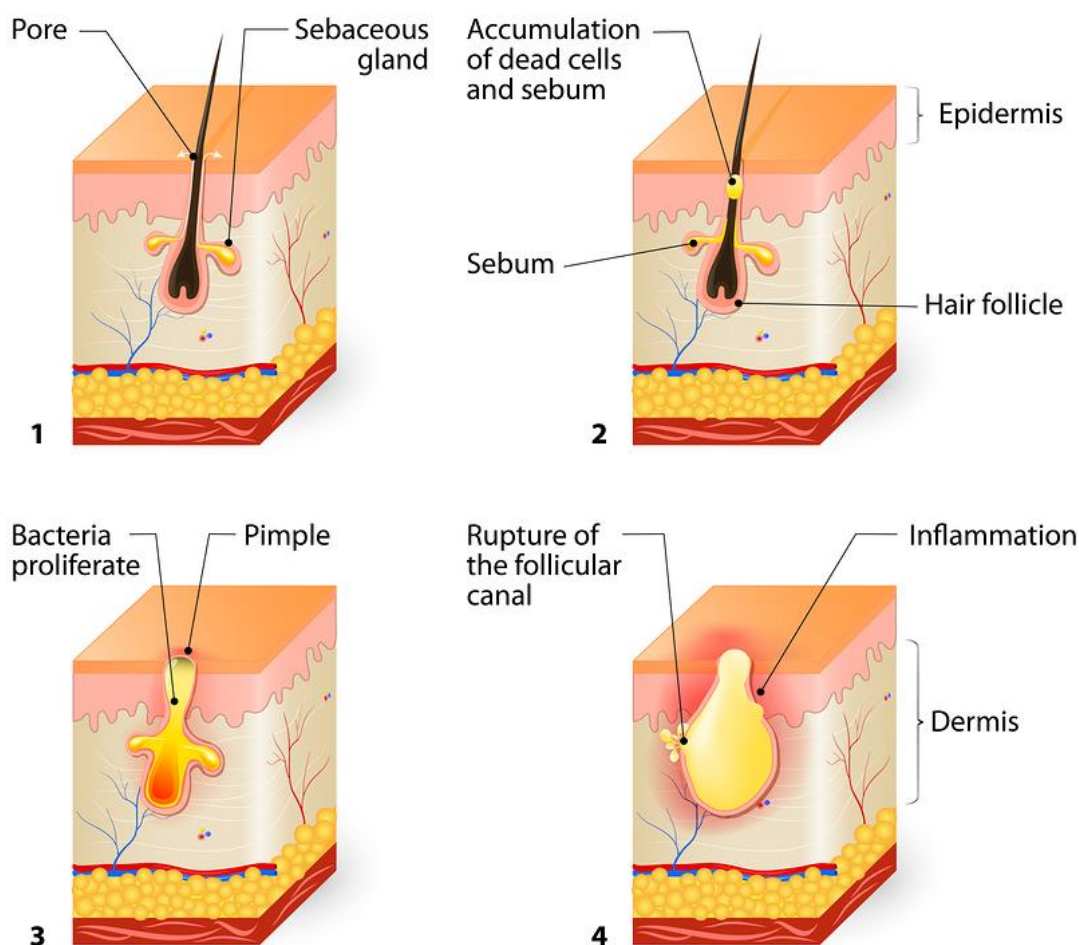


Figure 2.9 - How acne forms within the skin [41].

How inflammatory acne lesions are distributed is directly related to the population of *P.acnes* and how dispersed active sebaceous glands are across the skin. Typically, larger active sebaceous glands are found on the face, arms and the upper part of the torso, which is where acne lesions are most commonly found. When an individual reaches puberty, a lipid containing around 50% tryglyceride is found on the skin; this lipid encourages the

growth of bacteria, especially bacteria which can metabolize triglycerides – *P.acnes* is able to metabolize the glycerol portion of the triglycerides. When *P.acnes* begins to colonise in the follicle and begins to metabolize the glycerol, the follicle will release an extracellular lipase. This lipase metabolises the triglycerides into fatty acids, which will then remain in the sebum along with the glycerol – the amount of fatty acids in the sebum is relative to the population of *P.acnes* present in the follicle [40].

Acne lesions can take weeks before they are fully healed, and there is little information available about how this healing process occurs. A study by Kligman [42] investigated the development of acne from formation to fully healed lesions, and found that active granulomas formed during this process and that there was a later than expected response from lymphocytes. This may be due to *P.acnes* being difficult for lymphocytes to remove, with some studies showing that externally introduced *P.acnes* to skin will cause inflammation and can take weeks before until it is removed [40].

2.2.3 Psoriasis

Psoriasis is an autoimmune skin condition which causes inflammation and lesions known as plaques [43]. The chronic condition affects approximately 2% of the global population [44], and is identified by the extensive proliferation of keratinocytes, inflammation in the dermis and epidermis, and changes in keratinocyte differentiation [43]. There are 3 different types of psoriasis, however only plaque psoriasis will be relevant to the cosmetic treatments discussed in this thesis, as it is the form of psoriasis which can be treated using light and laser based home use devices.

Plaque psoriasis consists of scaly, red, hard lesions with very clear boundaries against the skin [45]. These plaques can range from tiny to very large lesions [44], which are typically located on the scalp or areas of skin over the joints, for example the elbows. The size of the plaques and whether they affect only one part of the body or multiple varies between people and over time, being affected by both genetics and the external environment, leading to different structures of the plaques and differences in how it develops [44], [45].

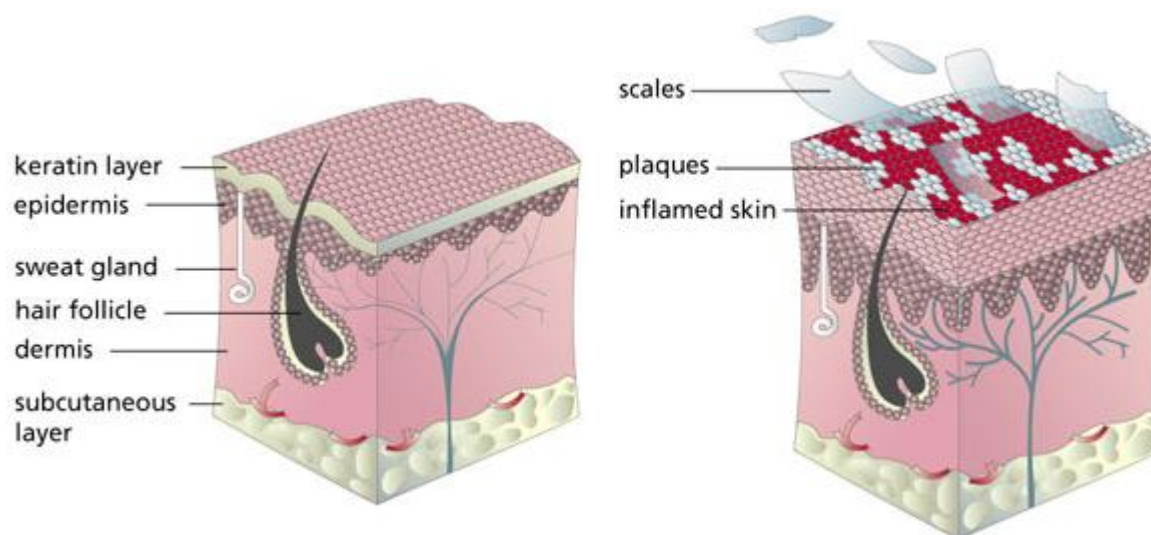


Figure 2.10 - Healthy skin (left) compared to skin with plaque psoriasis (right) [46].

While it is a normal process within skin for keratinocytes to divide and move up through the epidermis before reaching the keratin layer, this process would usually take approximately one month, whereas in those with plaque psoriasis, this process can take as a little as 5 days. There is excessive cell division in the epidermis, and the cells do not differentiate as much as they should. The plaques cause skin to thicken and the epidermal rete pegs to extend, result in the stratum granulosum being no longer present in the epidermis, cause new blood vessels to form from existing blood vessels in the dermis, inflammation in the epidermis and dermis, as well as irregular management of the neurotransmitters in the skin [45]. The structural changes which develop as a result of psoriasis are shown in Figure 2.10.

2.2.4 Herpes Labialis

Herpes labialis, otherwise known as cold sores or fever blisters, is one of the common infections across the globe. The infection causes a rash in both skin and the lips, as well as blisters, erythema, and a burning sensation in the infected area [47]. Herpes labialis is a result of the Herpes Simplex Virus (HSV) or the Human Herpes Virus (HHV-1). There are two forms of the virus – this thesis will be focusing on type 1, the cause of symptoms on the lips and face [48]. It is estimated that somewhere between 20% and 40% of the population suffer from herpes labialis [49], and when an individual contracts the virus, it will remain in the sensory nerve for the remainder of the person's lifespan [47]. While the infection does not cause any extensive damage, it can be cosmetically problematic due to the discomfort it causes during the active stage of the virus and the unpleasant aesthetic features of vesicles which form and then crust over [50]. Though the virus can be an issue

for immunocompromised patients, as the vesicles are more persistent and recurrences are difficult to control even with continuous treatment [48].

Then virus is transferred from person to person via the secretions of an infected individual - this may be through direct contact with an infected individual or coming into contact with moisture from the individual, such as from sharing a towel or glass. During this primary infection, the virus will travel to the ganglia of the initial infection site typically in the facial region, particularly the mucous membranes, for Type 1 HSV. If it replicates here, there is a chance the individual will suffer from recurrent infections; around 30% to 50% of people who contract the HSV-1 virus will experience reoccurring symptoms [48]. While it is unclear exactly what causes recurrence of the infection, the possible triggers which have been discovered appear to have an immunosuppressive component, such as experiencing a high temperature due to illness, infections in the upper respiratory tract, exposure to ultraviolet radiation, or a minor trauma, however in some cases, there is no apparent cause of the recurrence [50], [48].

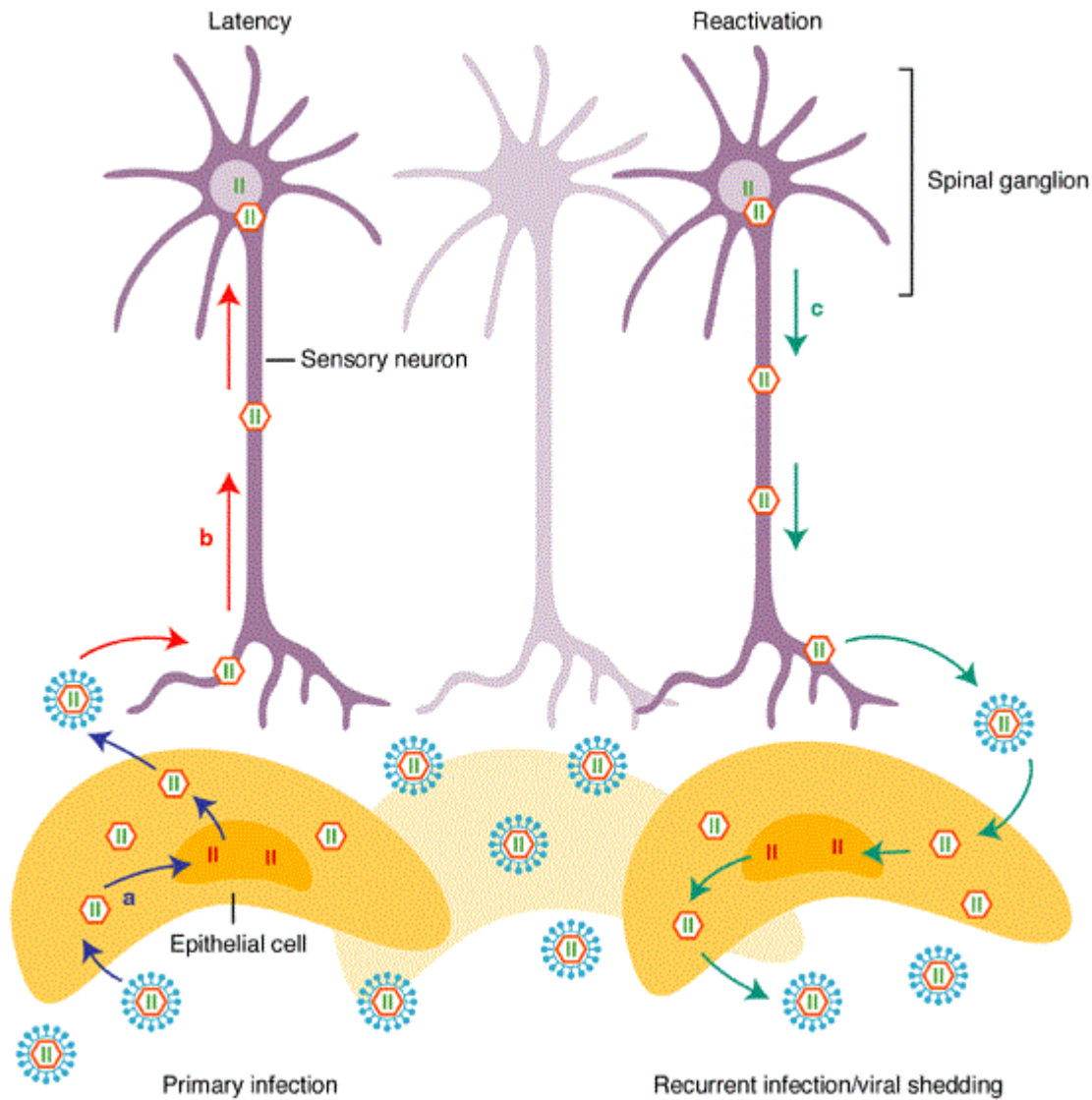


Figure 2.11 The life cycle of the Herpes Simplex Virus [51].

The development of the infection begins with ballooning degeneration of the infected epithelial cells, a result of the cytoplasm filling with fluid and causing the cells to swell. The inter- and intra-cellular oedema leads to the creation of intraepidermal vesicles (small sacs of fluid), and granulocytes enter the dermis, and from there the epidermis. The virus also causes changes in the nuclei of the cells during their development, and in the epithelium of the stratum corneum and cutaneous membranes large cells containing as many as 15 nuclei can be located [48]. Following this initial infection, the virus will travel to the cells of the sensory nerves, where it will remain dormant until it is triggered to cause infection again [50]. This cycle is highlighted in Figure 2.11

Any future reoccurrences of the infection will only affect the lips, or in young children the roof of the mouth, and will typically involve the development of multiple oral ulcers or

vesicles [50], preceded by a burning sensation and possibly swelling in the infected area. Approximately three to four days following the start of their formation, the vesicles will begin to crust over [49]. The reinfection begins with virus become active in the sensory ganglion again, causing infection in the cutaneous and mucous membranes. The virus multiplies in the cells of the ganglia, which then travel to the nerve terminals of the skin via neuron axons, and from here they are released into the cutaneous and mucous membranes [50].

2.2.5 Alopecia

Alopecia is a condition which leads to the loss of hair from any part of the body, and there are several forms of alopecia which can affect both men and women. Many treatments for alopecia are aimed at loss from the scalp, as this is often the most distressing location for hair loss – while the hair loss may be minor and easily covered by a change in hairstyle, more patterned loss of hair is more obvious to others and difficult to disguise. The reason behind this hair loss is can be due to abnormal hair growth cycles, or as a result of damage to the hair follicle itself. Which type of alopecia a patient has can often be identified based on how long loss has been occurring, the pattern in which hair is falling out or thinning, and if the hair appears to be breaking off or being shed from the root of the hair [52].

Alopecia areata is an autoimmune disease which affects up to 3.8% of the global population [53], affecting males and females equally, with typical sufferers' being children or young adults [52]. In 90% of cases the loss of hair is from the scalp [53]; the hair loss appears in patches which can be round, though may merge together, possibly leading to a complete loss of hair from the scalp [52]. When a scalp biopsy of someone with alopecia areata is taken, a peribulbar lymphocytic and eosinophilic infiltrate is typically found. When the case of alopecia areata is moderate, over 50% of the hair follicles are found to be in the catagen or telogen stage of growth – in more mild cases, there are more hairs in the telogen stage, whereas in moderate cases the number of hair follicles in the catagen stage increases [53]. Another form of alopecia is known as telogen effluvium, in which the hair follicle does not cycle correctly, which leads to losing hair in the telogen stage of growth. This can be due to anaemia, malnutrition, chronic illness, and as a side effect of certain medications [54], though the most common cause is stress, typically beginning approximately 3 months after a stressful event, and will last for months afterwards [52].

A form of alopecia caused by damaged hair follicles is cicatricial alopecia, with the follicle damage being caused by a condition, which also causes damage to the scalp. These

condition include infections, autoimmune diseases, scalp trauma, radiation therapy, and sarcoidosis. This causes both hair loss and plaques of erythema, which may also have scaling or pustules. Another similar type of alopecia is traumatic alopecia, where the hair follicles had been damaged as a result of cosmetic or chemical treatments to the hair. The individual may also be plucking the hair from the scalp themselves as a result of trichotillomania [52]. Alopecia can also be induced as a result of chemotherapy treatments – chemotherapy is aimed to destroy the rapidly dividing cancer cells, though cannot differentiate between these and the other cells which rapidly divide in the body including hair follicles. As a result, these cells are destroyed, resulting in the loss of hair after two weeks of treatments on average, and after a month or two of treatments, almost all hair is lost [54].

All of the forms of alopecia mentioned above currently cannot be treated using home-use laser and light based devices, and therefore no further detail on the mechanisms behind these forms of hair loss will be discussed in this thesis.

Androgenic alopecia, otherwise known as male or female pattern hair loss, is the most common form of hair loss, and affects 50% of men over 50, and 50% of women over 80 [55]. Hair loss can begin between the ages of 12 years of age and 40 years of age, however at first it is unlikely to be noticed by the individual. This form of hair loss is a result of the androgen dihydrotestosterone (DHT) being present in hair follicles [52].

Dihydrotestosterone creates a signal in the fibroblasts of the dermal papilla which causes changes in the dynamics of the metabolic and cellular activity in the follicle. This leads to a reduction in the division of cells in the epithelium of the follicle, resulting in the terminal hairs in the scalp shrinking [56]. With each following cycle, the hair shrinks further, eventually being replaced by vellus hairs with no pigmentation [52]. A visual representation of this mechanism is given in Figure 2.12. One of the mechanisms in bulge stem cells is also affected, which results in new anagen hair being unable to enter the follicle, which puts the new hair into the telogen stage of growth [56]. The underlying cause of the changes which leads to androgenetic alopecia is known to be genetic, though the exact genes which cause it are currently unknown [54].



Figure 2.12 - Proposed mechanism of dihydrotestosterone and its role in androgenetic alopecia [138].

While androgenetic alopecia is due to a product of the male hormone testosterone [56], females who suffer with the condition do not have more androgens in their body. They do have more of the enzyme 5- α reductase in their hair follicles, which is responsible for the conversion of testosterone into dihydrotestosterone, as well as increased androgen receptors, and a decreased amount of cytochrome P450, which is responsible for turning testosterone into estrogen [52].

Whether the changes caused by androgenetic alopecia can be reversed depends on the duration of the condition. As it is effectively only changes to the hair cycle, the hair cycle could be corrected, however if a person has been suffering with the condition for an extended period of time, there could be extensive damage to the hair follicle itself as a result of inflammation in the bulge part of the follicle, meaning that there may be no response to treatment [52].

2.3 Conclusion

At the conclusion of this chapter, a detailed description of the skin has been provided, giving explanation of the structure and role of various parts of the skin and some of its chromophores, as well as how the ageing process can affect skin. A small number of skin conditions and diseases have been described, explaining how they affect the skin, their proposed mechanisms and causes. This section will provide a basis of knowledge which

will be relevant throughout this thesis, as the interaction of skin with light and electromagnetic fields are discussed, various devices which are used in dermatology to treat skin and different afflictions, and the development of a biophysical computation model to predict the tissue response to a variety of devices are discussed.

Chapter 3 - Properties of Low Energy Electromagnetic Radiation and its Interaction with Tissue

Introduction

The section of the chapter will be focusing on light and electromagnetic fields, how they interact with biological media and the types of responses which are typically seen when skin interacts with these mediums.

There will be a brief discussion on the electromagnetic spectrum, followed by an in depth look at light tissue interaction, and how different characteristics of the skin affect skin responses to certain wavelengths of light. Following this, a more in depth description will be given to the three different forms of skin response, namely photochemical, photothermal, and photomechanical. The discussion will then move onto the types of Radiofrequency available, how skin responds when a closed loop electrical current is applied, and then dielectric properties of skin.

Finally, the chapter will describe how photons move through biological tissue, the different methods which describe this process. How heat is transferred throughout the skin will then be discussed, and different types of numerical and computational models which can be applied to predict how biological mediums will respond to different types of energy, concluding with the chosen programs which will be used during this thesis, and the method which the programs use.

3.1 The Electromagnetic Spectrum

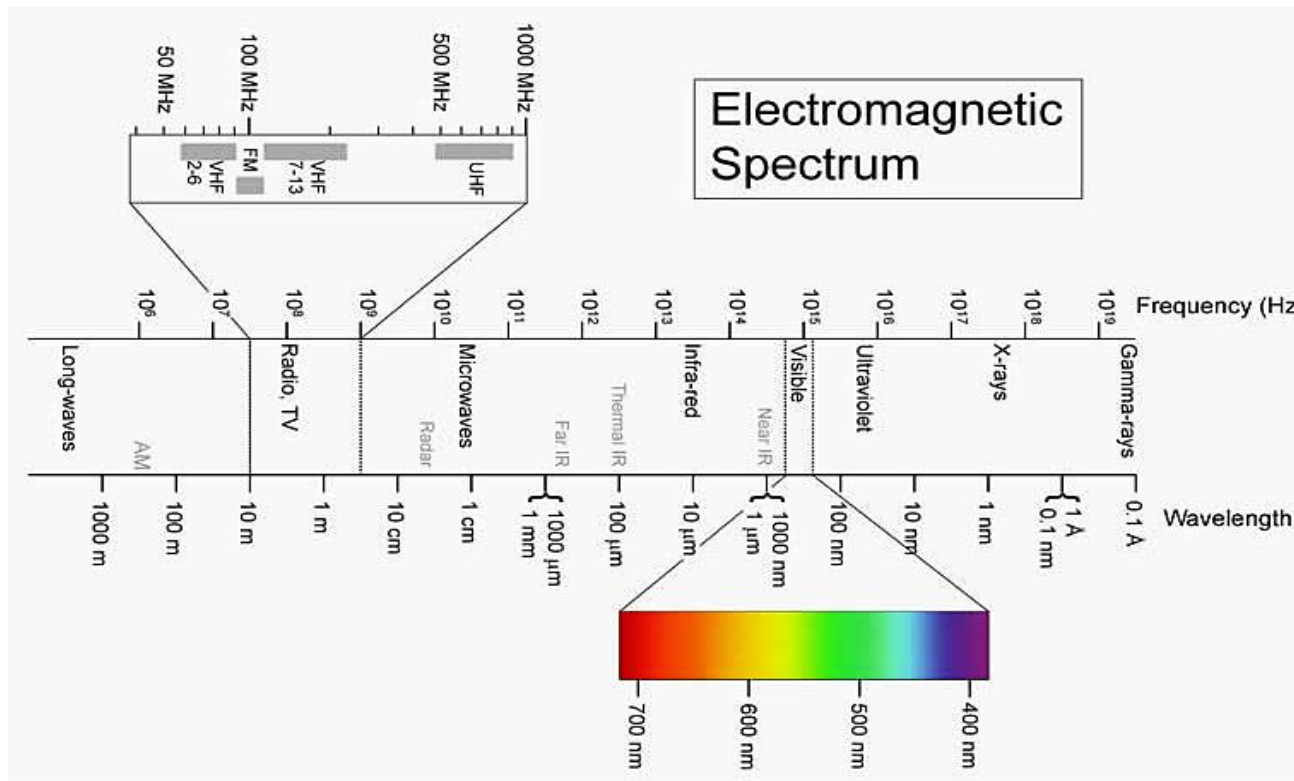


Figure 3.1 - Visual representation of the Electromagnetic spectrum, with visible light and radiofrequency highlighted [57].

The electromagnetic spectrum, as shown in Figure 3.1, encompasses all forms of electromagnetic energy. Visible light is a small part of the spectrum, ranging from approximately 400 nm to 700 nm, while ultraviolet (UV) is in the lower band of wavelengths, between 10 nm and 400 nm, and infrared is in the higher band, ranging between 700 nm to 1 mm. Radiofrequency takes up a larger portion of the electromagnetic spectrum, with one definition of the radiofrequency band ranging between 3 kHz and 300 GHz [57], however it is disputed. Both visible light and radiofrequency are talked about in further detail later in this chapter.

3.2 Light-Tissue Interaction

Light, a form of radiant energy, is made up of waves and photons. It is arranged into the electromagnetic spectrum based on its wavelength, which is categorised according to the distance between the troughs and crests of the light's waves. In the visible part of the electromagnetic spectrum, the wavelength is responsible for the colour of light [1]. The use of light to treat medical conditions is not a recent discovery. Dating from 4,000 B.C., light was used to treat individuals with vitiligo in order to re-pigment their skin, and by the 19th century, sunlight was used to treat cutaneous tuberculosis. More recently, in 1961 Dr. Leon Goldman used a ruby laser in medicine for the first time for the removal of tattoos and other pigmented lesions, which has resulted in him being described as the father of lasers in medicine [1]. Since then, there have been various applications of these lasers, including in surgery [3], and for the treatment of various conditions. Their use in dermatology includes removing unwanted hair, skin rejuvenation, and removing tattoos [2].

Lasers produced a single wavelength of monochromatic, coherent light [1]. Intense pulsed light (IPL) devices provide a broadband spectrum of light, rather than a single wavelength. The use of lasers in modern medicine aims to heat a specific tissue without causing widespread damage outside of the target [3]. They can provide continuous light, such as the CO₂ laser, delivering between 1 to 100 watts of power, with durations of 0.1 to 100 seconds, and in comparison, pulsed lasers provide pulse energies between 0.1 and 10 joules (J), with pulse durations between 100 femtoseconds to 500 microseconds. While pulsed lasers may not be very energetic, with 1 joule only heating 1 cc of water by 0.24°C, by condensing the energy into a very short pulse width create a powerful laser – for example, one joule in a nanosecond pulse gives a gigawatt of power. This relies on the product of power and duration being equal to the total pulse energy [58], as shown in Equation 1.1.

$$E_{pulse} = \int_{\sigma}^T P(t)dt$$

Equation 1.1

This effect can also be created by spatial confinement of laser light, such as laser light only being able to reach a superficial layer in skin as a result of scattering and absorption, creating the possibility of high energy densities being achieved. A one joule laser will only heat a 1cm² area, with light penetration of 1cm depth by 0.2°C, whereas if the light penetration depth is only 1µm, this leads to a temperature increase of 2,000°C [58].

When light interacts with tissue, it is either reflected, refracted, absorbed, or scattered. When photons reach the surface of tissue, 4% to 10% of the photons will be reflected, and the remaining 90% to 96% will be scattered or absorbed [59], with lighter skin reflecting more light than darker skin [60]. Absorption and scattering affect how light travels through tissue. Turbid tissues, tissues with inhomogeneities such as layers and macromolecules [61], cause absorption and scattering – an example of this is human skin tissue. As a result of scattering in turbid tissues, the light will remain in a superficial surface layer [58].

3.2.1 Scattering

Scattering is caused by inhomogeneities in the refractive index of tissue due to physical inhomogeneities in the skin, and is responsible for the propagation of photons in tissue. Scattering is either categorised as Rayleigh scattering, with small molecules or particles which are less than one-tenth of the wavelength and scattering is weak and near isotropic, or Mie scattering, with particles with dimensions similar to or larger than the wavelength, and scattering is stronger and more forward directed. Both Mie and Rayleigh scattering occurs in skin, however due to the size of the structures in skin and the wavelengths used in laser-tissue interaction Mie scattering is typically more dominant, however when longer wavelengths are used Rayleigh scattering dominates [59].

The direction of scattering is described by the anisotropy factor, g , which is valued between -1 and 1. When g is at -1, the scattering is entirely backward directed, when g is 0 this is considered isotropic, or completely randomised, scattering, and at 1, the scattering is purely forward directed [58]. The anisotropy factor is affected by wavelength; as wavelength increases, so does g [59]. In skin, the anisotropy factor can vary, typically around 0.8 in the lower end of the wavelength spectrum used in laser-based medicine, and as high as 0.99 in the higher end of the spectrum [62].

Whether photons are absorbed or scattered is determined by the absorption coefficient, μ_a , and the scattering coefficient, μ_s , both given in units of cm^{-1} [58].

Absorption coefficient	$\mu_a = \frac{1}{\text{Mean free path for absorption collisions}}$
------------------------	---

Scattering coefficient	$\mu_s = \frac{1}{\text{Mean free path for scattering collisions}}$
------------------------	---

The sum of the absorption coefficient, μ_a , and the scattering coefficient, μ_s , is the total attenuation coefficient, μ_t , shown in Equation 3.2

$$\mu_t = \mu_s + \mu_a$$

Equation 3.2

Scattering within skin is typically calculated based on probability using a phase function for each photon interaction with skin. The phase function for scattering is shown in Equation 3.3.

$$= p(s, s')$$

Equation 3.3

This shows the probability density function of a photon moving from its current direction (s) into another direction (s') [63]. If there is an equal probability that the photon could move in any direction, isotropic scattering will occur [58], and for slightly forward scattering to occur, Rayleigh must be dominant [62]. The photon movement in human skin tissue can be described using the Henyey-Greenstein phase function, as shown in Equation 3.4 [64].

$$p(\theta) = \frac{1}{4\pi} \frac{1 - g^2}{(1 + g^2 - 2g \cos(\theta))^{3/2}}.$$

Equation 3.4

This is typically used to describe light transport in biological tissue, as well as other mediums, as it gives a reasonable representation of how photons from visible wavelengths scatter – the scattering is not entirely forward directed as Mie scattering would describe, however is strongly forward [62].

The anisotropy factor, g , is able to describe the probability density function of the Henyey-Greenstein phase function, which is normalised to an area of 1. The phase function is able to estimate the probability of scattering at numerous g values, and those between $-180^\circ \leq$

$\theta \leq +180^\circ$ are shown in Figure 3.2. Figure 3.3 demonstrates the Henyey-Greenstien phase function when g is at 0, 0.4 and 0.6 [65]. When g is almost at the value 1, then the phase function is approximately $\theta=0$, and when g has a value of 0, all scattering angles θ have a constant value of $1/4\pi$ [62].

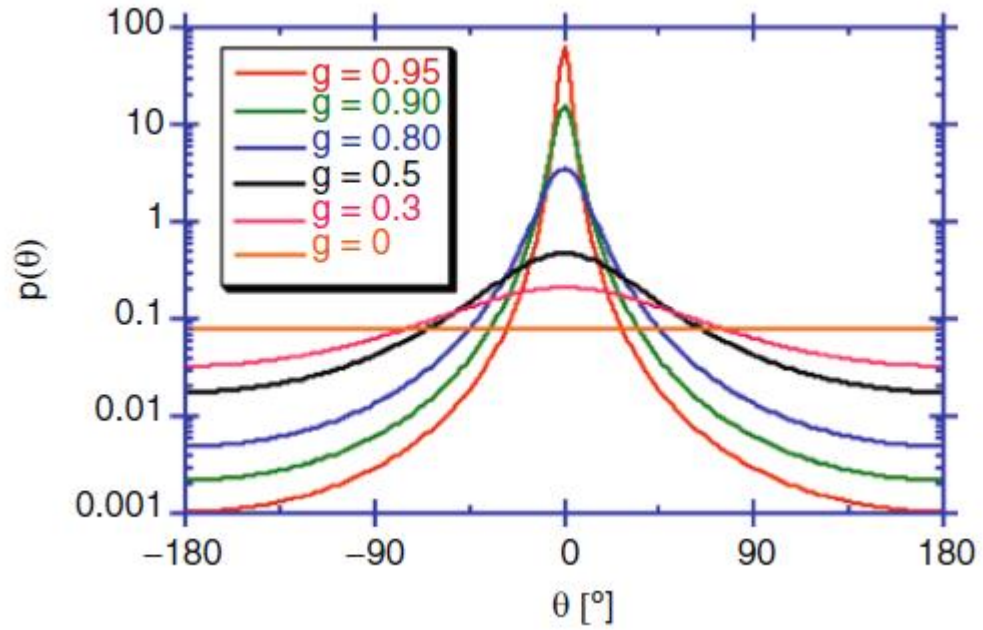


Figure 3.2 - Henyey-Greenstien phase function probability of scattering for various g values [62]

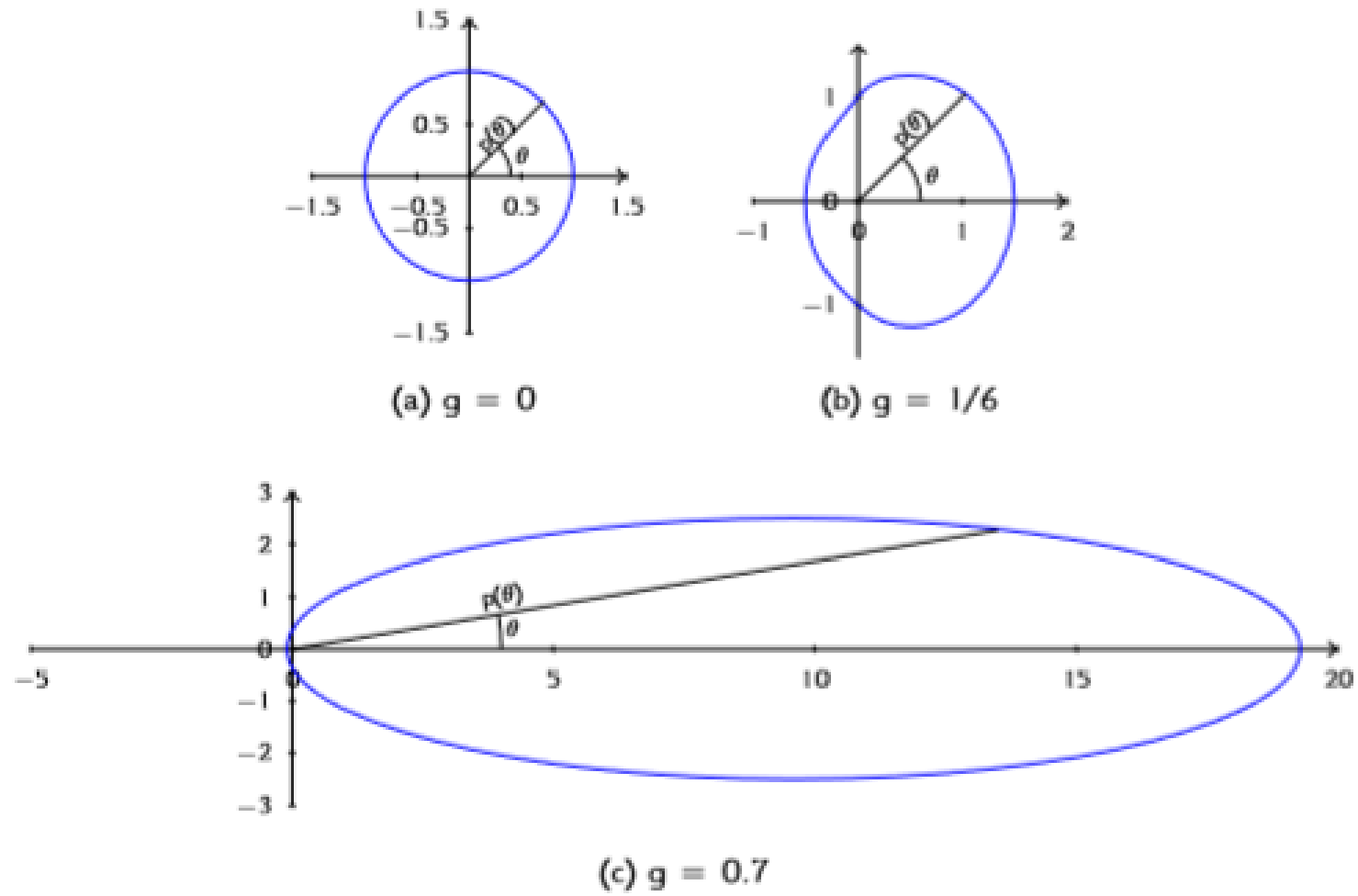


Figure 3.3 - Henyey-Greenstien phase function when g is at 0, $1/6$ and 0.7 [66].

3.2.2 Absorption

In order for laser light to have an effect on biological tissue, it must be absorbed. The absorption of photons into tissue transforms the radiant light energy into another form of energy such as heat [1]. This change in leads to a photothermal, photochemical, or photomechanical response in the skin – these responses are discussed later in this chapter. Photons are absorbed in skin by chromophores; this occurs when the radiation from light causes excitation in the molecular chromophores. The major naturally occurring absorbing chromophores in skin are melanin, water, haemoglobin, and proteins, and their absorption at different wavelengths are shown in Figure 3.4. Artificial chromophores can also be used to absorb photons, such as ink, or dyes [2]. Many of the natural chromophores are confined into a single layer, for example melanin is typically only found in the epidermis, in the stratum basali [67], and haemoglobin is typically found in the dermis. Different parts of the skin absorb different wavelengths of light, and whether a chromophore absorbs light energy depends of the wavelength of light. Melanin absorbs wavelengths of light between 250nm and 1200nm, with higher absorption in the UV range due to its role in the skin to provide protection from UV damage. Melanin is responsible for almost all of the absorption in the epidermis, and wavelengths longer than 1100nm are mostly unaffected by melanin. However the amount of melanin varies hugely between individuals, meaning that the levels of absorption also vary – in lighter skin, there is generally more melanin granules but less overall melanin than in darker skin tones [59].

In the dermis, absorption is affected by haemoglobin – the wavelengths at which haemoglobin peaks depend on whether it has been oxygenised or not. Oxyhaemoglobin has the highest absorption rates at 420nm and 577nm, whereas haemoglobin has its highest absorption rate at 560nm. Wavelengths longer than 600nm are relatively unaffected by haemoglobin. Absorption by water in the skin is mostly for wavelengths below 200nm and above 1200nm, and has no effect on absorption in the visible part of the spectrum [63].

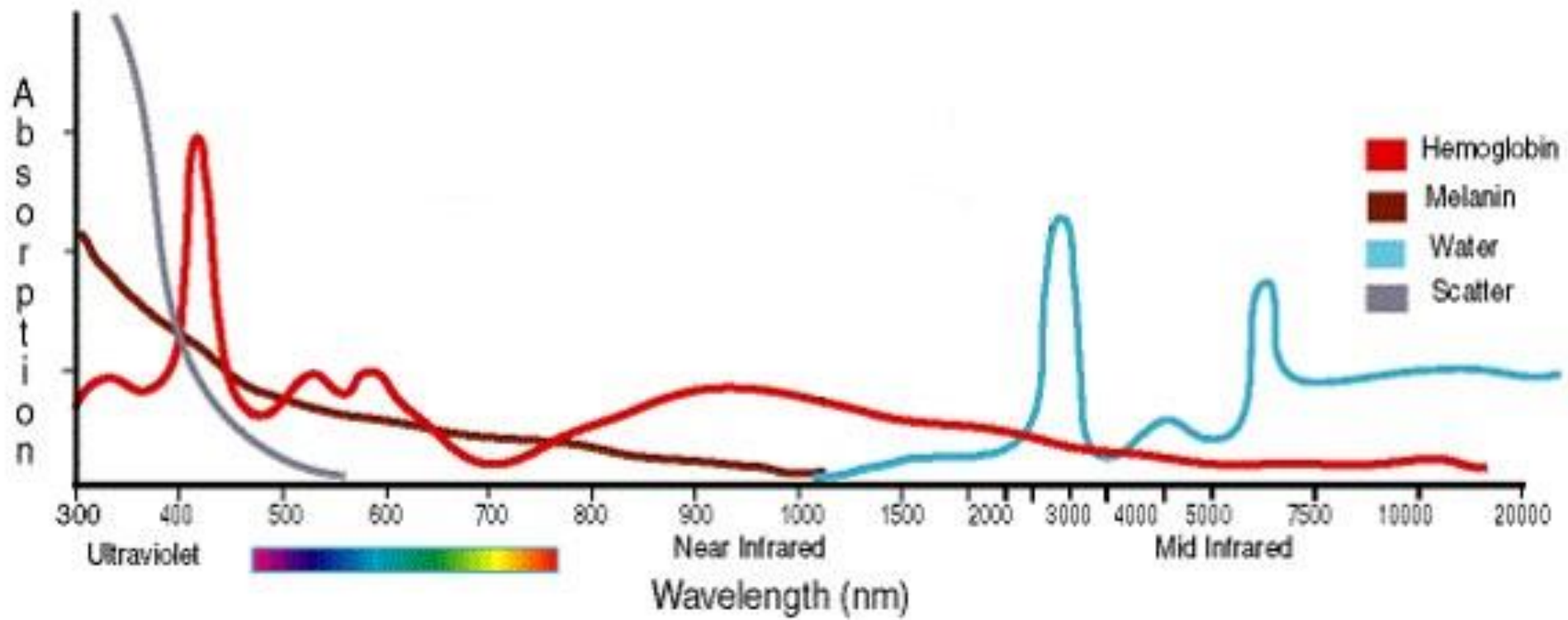


Figure 3.4 - Absorption of chromophores in human skin at different wavelengths of light [68].

3.2 Laser-Tissue Interaction Mechanisms

When laser light is absorbed by tissue, the way in which skin responds is split into three separate classes. Photochemical is the first class, and involves biostimulation of the skin and a form of photoradiation. The second class is photothermal, whereby photon energy is converted into heat energy. How the skin reacts to photothermal interaction depends on the temperature the skin is heated to. The third and final class is photomechanical, and this involves the interaction leading to the induction of stress on the skin, and causing breakages in the structures and bonds within the molecules of the skin [58], [69].

Interactions are partly categorised by the speed in response by the tissue, and healing can be immediate, delayed, or long term. They can be further categorised by which level of tissue is affected, such as the tissue or organ as a whole, the cells, or the organelles [58]. How tissue responds to laser light can be a direct response to both the wavelength of the light, the target chromophore, the power of the laser, and the duration of the laser interaction [70] – the type of interaction which occurs based on the duration of interaction and intensity of the laser is demonstrated in **Error! Reference source not found..**

A brief discussion of these types of laser-tissue interactions are given here, with a focus on photochemical and photothermal interactions, as these are the responses seen when using home-use light-based devices and salon-based radiofrequency devices.

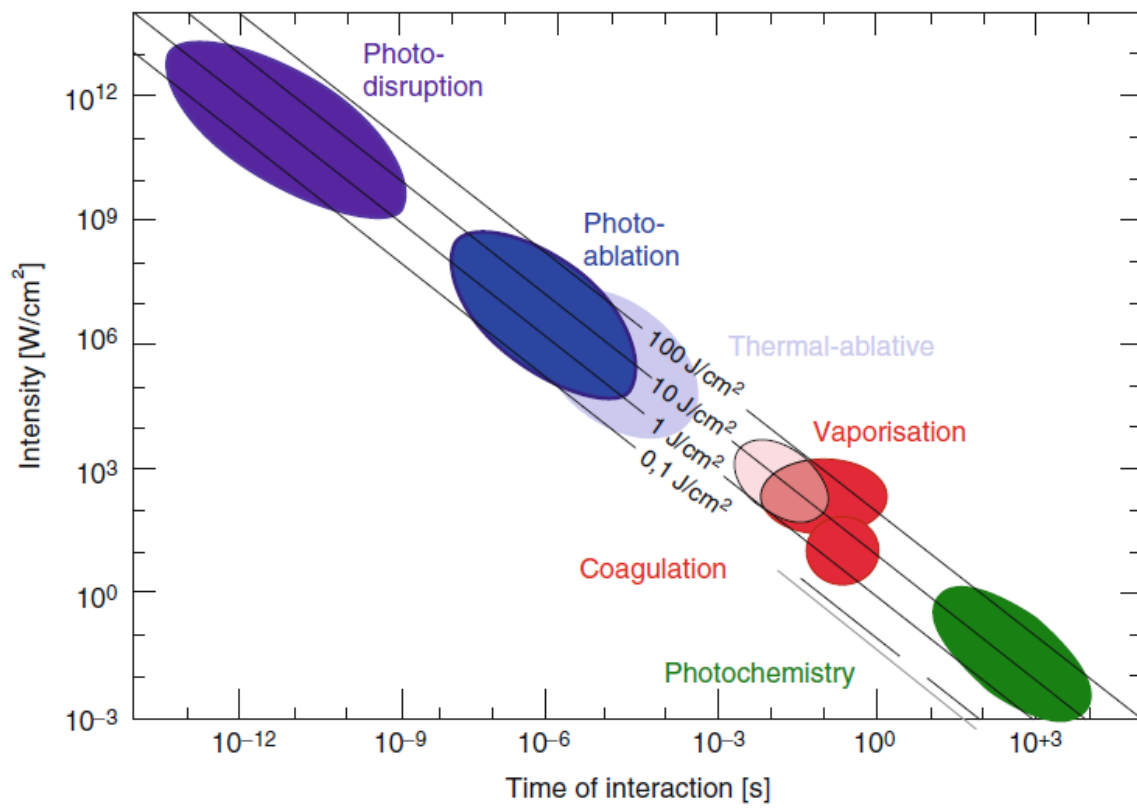


Figure 3.5 - Skin response to different classes of laser-tissue interaction based in duration and intensity of the laser interaction [62].

3.2.1 Photochemical

Photochemistry is a highly important process which occurs all the time, with examples including plants photosynthesizing sunlight to produce oxygen and enabling vision in certain animals [69]. The type of photochemical response in skin is dependent on the wavelength of light used, and the chromophores which interact with the photons, as a change in wavelength will lead to a different response in the skin [67].

Photodynamic Therapy

An example of a photochemical reaction would be photodynamic therapy (PDT). PDT is a type of photochemical reaction which uses a photosensitiser (PS), oxygen, and a light source [71]. It is used in various applications, including as a cancer treatment and in dermatology. PDT is used for the destruction of specific tissues or cells, typically cancer cells, while not causing damage to surrounding tissues [71]. This is achieved by applying a photosensitising agent topically, locally or systemically to a lesion, before applying a light source of a specific wavelength, typically in the visible or infrared range, to interact with the PS while oxygen is present. A suitable PS is required in order for PDT to have the desired effect, and the ideal PS will be chemically pure, accumulate quickly in targeted tissue following application, and clear from non-targeted tissue swiftly, its peak absorption would be at an optimal tissue depth, it would have the ability to produce a large number of reactive oxygen species and have a lack of toxicity [72].

A light source emitting an appropriate wavelength causes the PS to become excited, leading to the transfer of energy from the PS to the oxygen molecules – this process leads to the formation of a singlet state oxygen [71]. The singlet oxygen, which has a lifespan of nanoseconds, will either emit its energy in the form of fluorescence, convert it into heat, or become a triplet state as a result of intersystem crossing – this state has a smaller amount of energy than the singlet state, however it lives for microseconds rather than nanoseconds [61]. The triplet state will then react in one of two ways, named type 1 and type 2. Type 1 results in the formation of radical ions following interaction with a substance such as the cell membrane, whereas type 2 leads to the production of singlet oxygen due to direct interactions with molecular oxygen. Both of these types of reaction can happen at the same time, and both lead to the production of reactive oxygen species which are toxic, and are responsible for the destruction of cells [61], [73]. This process is demonstrated in Figure 3.6. The death of cells as a result of PDT is a result of one of two processes, identified via the various changes taking place in the dying cell. The first is apoptosis, in which the cell

will play an active role in its destruction, and no inflammatory response is induced. The second is necrosis, when the cell is destroyed by cytotoxic agents and an inflammatory response is triggered – in this pathway, the cell plays no role in its own destruction [72].

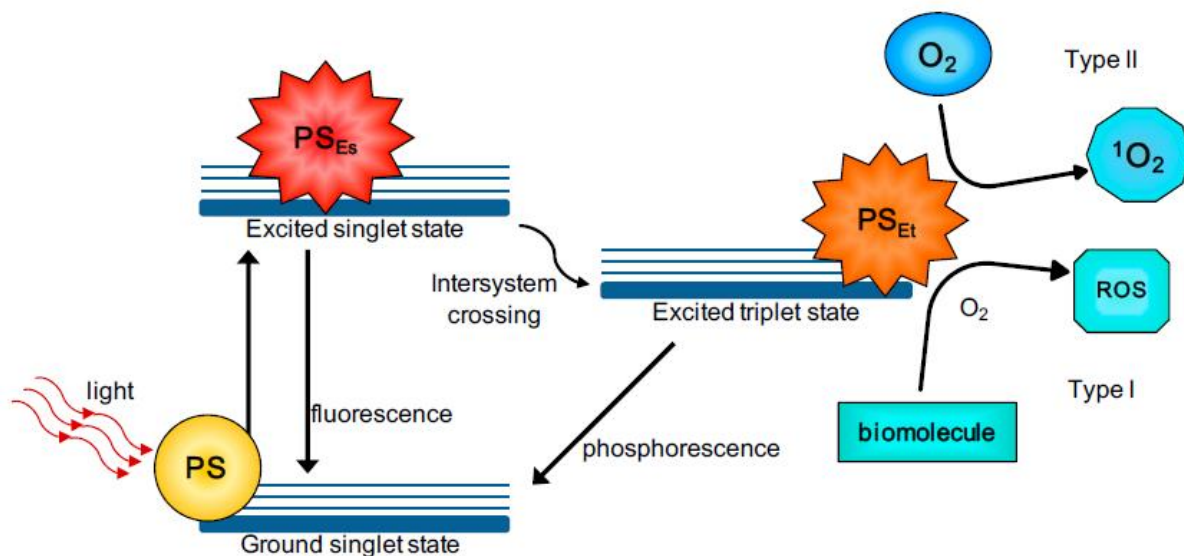


Figure 3.6 - The mechanism behind PDT, and how this leads to the formation of radical ions and reactive oxygen species [74].

The use of PDT in dermatology is a relatively recent technique – it was first used in the 1990s, when aminolevulinic acid (ALA) and methyl aminolevulinic acid (MAL) were used in conjunction with a broad-spectrum red light was used to treat non-melanoma skin cancer [71]. Now, PDT has become more popular in dermatology and skin surgery, used to treat acne vulgaris, skin rejuvenation, actinic keratosis, among other disorders and other cosmetic skin conditions [75]. When using 5-ALA as a photosensitizer, it is metabolised to protoporphyrin IX (PpIX). PpIX can absorb a wide range of wavelengths in the visible light spectrum, typically between 400nm and 800nm. When the PpIX has been activated by a light source, singlet oxygen is produced – the actions of the singlet oxygen is dependent on where the 5-ALA has accumulated, which is often in the keratinocytes and pilosebaceous units.

The effectiveness of PDT when used to treat infections has been known for some time – how well PDT works depends on whether the bacteria being treated was gram positive or gram negative due to their different structures. In gram positive bacteria, a porous layer surrounds the cytoplasmic membrane, whereas in gram negative bacteria has a non-porous cell wall, therefore effective treatment required the PS to be absorbed into gram negative bacteria whereas the PS molecules can simply bind to gram positive bacteria with no need

to penetrate the bacteria [73]. *Propionibacterium acnes* (*P.acnes*), a naturally occurring bacteria found in the sebaceous glands of human skin which has a major role in the development of acne vulgaris [38], is a gram positive bacteria which PDT has been found to effectively treat, offering a treatment which is not an antibiotic or another drug [76].

The use of topical-PDT in the treatment of acne vulgaris has been found to be effective when using a range of light sources, including red light at 630nm [77], blue light, green light, yellow light and IPL sources [78], and photosensitizers, but the success is determined by how much PpIX is produced following the penetration of ALA into the skin, specifically the sebaceous glands [77].

The PDT effect on *P.acnes* can be induced naturally via ultraviolet radiation through sunlight, having been observed to improve the lesions caused by acne vulgaris [79]. In this situation, the proliferated *P.acnes* in the sebaceous glands results in the production of both PpIX and Coproporphyrin III. When activated by the UV radiation of sunlight in the presence of oxygen, this leads to the *P.acnes* bacteria being destroyed, and as a result the lesions caused by the bacteria are cleared. While this method is effective, UV light is known to cause harmful effects following long term exposure, therefore this cannot be used to effectively treat acne [79]. PpIX and Coproporphyrin III have absorption peaks in the near UV range, but also in the Soret band at 415nm, and in the red light range at 630nm; as a result, light sources which produce red, blue, or a combination of the two, devices have been produced to treat acne vulgaris [78].

Devices in the home-use sector to treat acne typically utilise blue light to treat acne, using a similar mechanism seen in PDT, which is demonstrated in Figure 3.7. This approach does not require the use of photosensitizers, and is much less harmful than ultraviolet radiation [76]. Ashkenazi et al. [80] discovered that 5-ALA is not required in order for *P.acnes* to produce a sufficient amount of coproporphyrin to result in the death of *P.acnes* following exposure to blue light at wavelengths between 407nm and 420nm. The mechanism behind this approach, known as blue light therapy, is not as well understood as PDT however it is hypothesised that the porphyrins in the sebaceous glands are excited by the blue light, and the photons absorbed leads to the transfer of energy, resulting in the productions of cytotoxic ROS such as singlet oxygen, which then go on to destroy the *P.acnes* bacteria - much like in the case of PDT, blue light therapy appears to be dependent on oxygen [76].

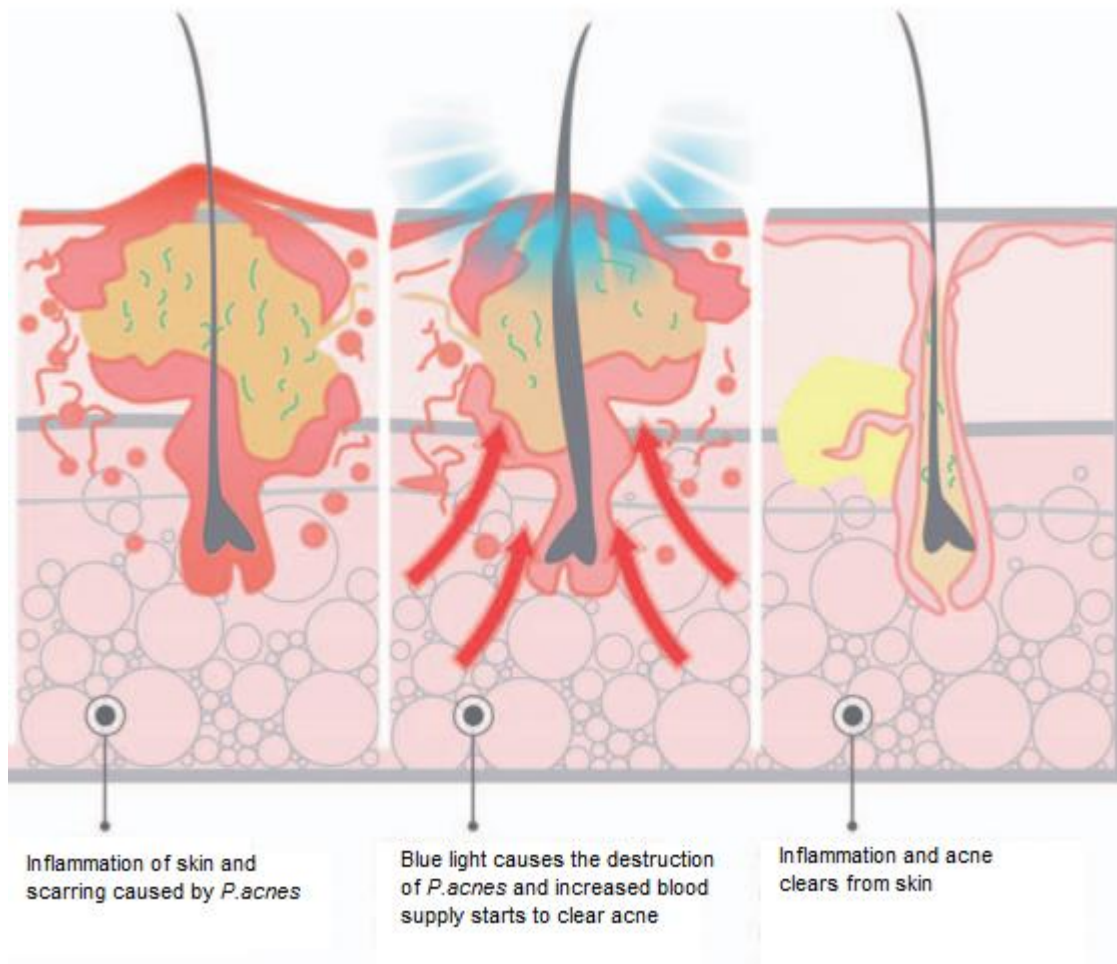


Figure 3.7 - A proposed mechanism of action behind blue light therapy for acne – image has been amended [81].

3.2.2 Photothermal

Unlike photochemical reactions, the response in skin to photothermal interaction is will typically be incredibly similar no matter the wavelength used [67]. Instead, the extent and effects of thermal injury depend on the temperature reached, the duration of exposure, and the mechanical stress experienced by the tissue during heating. The amount of heat and how quickly this is applied, as well as the targeted tissue and its surrounding tissues, that will determine the thermal response at micro and macroscopic levels [3].

An Arrhenius plot, shown in Figure 3.8, can demonstrate the effect which temperature and length of temperature exposure has on the rate of destruction in biological tissue [82] – in order to do this, the rate of thermal damage in time is plotted against the temperature of the skin. In human skin, the Arrhenius plots, the breakpoint – the point at which irreversible thermal damage to proteins and enzymes occur – is at approximately 44°C, and the rate at which thermal damage occurs almost doubles at each single degree rise in temperature above the breakpoint of the plot. The plot for human skin also has shallow curves suggesting longer times are needed in order to cause damage to its cells, indicating the level of thermotolerance human skin has [83].

The Arrhenius damage integral, shown in Equation 3.5, is used to approximate the amount of damage to tissue caused by changes in temperature. This can be done using the Arrhenius Damage Integral, given below. If the calculated response is more than or equal to 1, this indicates the tissue has been irreversibly damaged by the temperature [84].

$$Arr(r, z, t) = \int_0^{t_f} A \exp \left[-\frac{\Delta E}{RT(r, z, t)} \right] dt$$

Equation 3.5 – Arrhenius damage intergral.

In Equation 3.5, $R = 8.3143$, the gas constant in $\text{mol}\cdot\text{K}$, ΔE = activation energy in J/mol , A = pre-exponential factor, in $1/\text{s}$, $T(r, z, t)$ = temperature at the point considered, $[0, t_f]$ = time interval considered, and t_f = time of the end of the analysis.

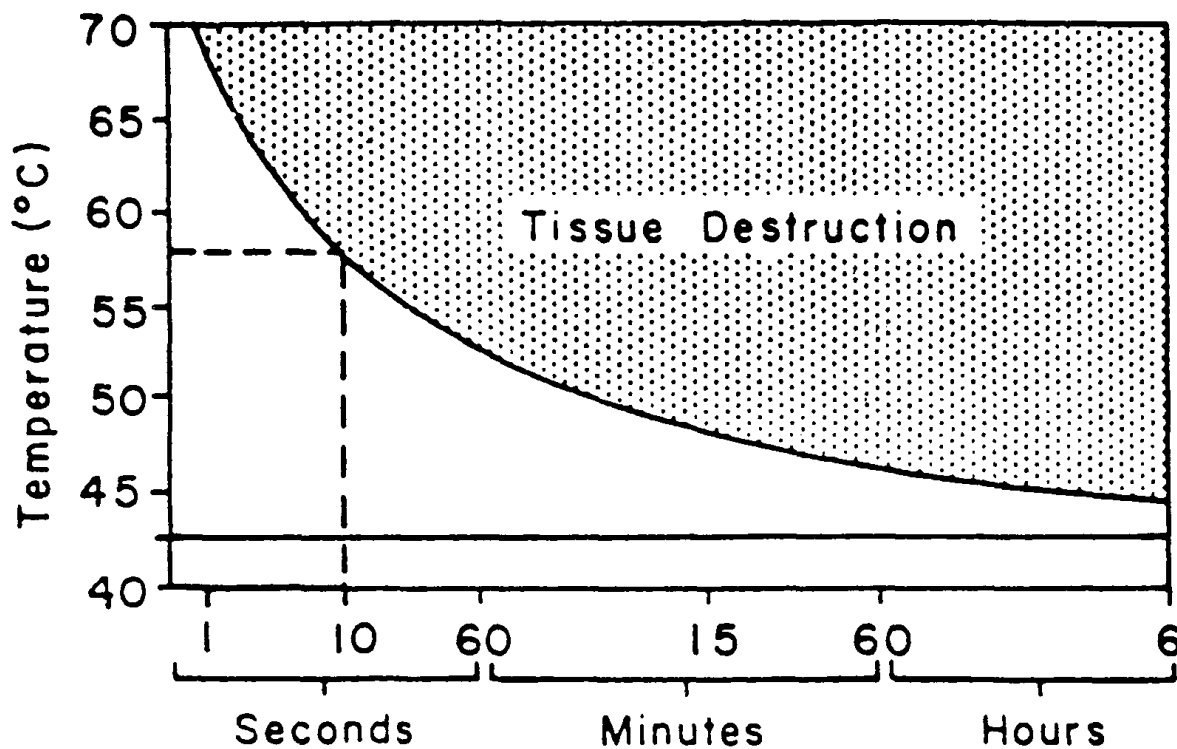


Figure 3.8 - The temperature of skin and duration of increased temperature required to cause irreversible tissue damage [69].

When the temperature of skin is slightly elevated, up to 44°C, it can take up to 24 hours before necrosis sets. In this time, the heat causes denaturation of proteins and irreversible damage within cells affecting metabolic machinery, ultimately resulting in cell death – this is known as hyperthermia. In contrast, photocoagulation occurs when there is a short exposure to a high temperature, where the results are immediately visible, and is much more obvious than hyperthermia [58]. Between 44°C and 51°C, the amount of time required for causing thermal damage double with every degree increase. Above 51°C, only very short exposures will cause destruction of the epidermis, but as the temperature increases the rate at which injury occurs begins to slow [85]. Exposure to temperatures between 60°C and 70°C cause structural proteins such as collagen to denature. When reaching temperatures between 70°C and 80°C nucleic acids begin to denature and membranes become more permeable, between 80°C and 100°C protein denaturation may result in coagulation, and above 100°C tissue water is vaporised, rapid volume expansion occurs and there is carbonisation of dry mass. The highest temperature is typically used for the ablation of tissue [70].

Selective Photothermolysis

An example of photothermal reaction in skin is Selective Photothermolysis, a theory proposed by Anderson & Parrish [70], in which they theorised that by using a brief pulse

of radiation of a specific chosen range of wavelengths for targeting a single pigmented chromophore, you can selectively heat the pigmented structure to the point of denaturation. This offers an alternative to microbeam based technology, but without the risk of causing damage to other tissues surrounding the target. Selective Photothermolysis can be used to target a number of different tissue structures, assuming that a wavelength can be chosen which will be strongly absorbed by the target but not by its surrounding tissue. When the radiation is absorbed by the pigmented target, the radiation will be converted to heat, causing the temperature of the structure to rise to a sufficient heat which causes irreversible damage to the structure. After the pulse, the heat will slowly diffuse from the structure to the surrounding tissues, however these will only be warmed via thermal diffusion, and will not reach a sufficient heat to cause significant damage. A potential target chromophore for selective photothermolysis is melanin within the matrix cells of a hair follicle. The matrix cells are endogenously pigmented, therefore there is no need to dye any tissue in order for selective photothermolysis to occur. The pulse of radiation must be shorter than the thermal relaxation time of the pigmented structure, in this case the melanin, and the wavelength range chosen must be strongly absorbed by the melanin but weakly absorbed by the surrounding tissues; the wavelength will also determine how far the radiation will penetrate into the skin.

This theory was added to by Altshuler et al two decades later, in a paper titled 'The Extended Theory of Photothermolysis' [2]. They argued that Selective Photothermolysis could only occur in structures which allowed for uniform absorption, therefore in cases where a structure is only partially pigmented, or not pigmented at all, the brief pulse of radiation recommended by selective photothermolysis will not be sufficient to cause the intended irreversible damage to the targeted structure. They suggest that by using a longer radiation pulse which is almost equal to or exceeds the thermal relaxation time of the structure but does not exceed the thermal damage time, which is often much longer than the thermal reaction time. The thermal damage time is described as the amount of time required to heat the structure sufficiently to cause irreversible damage to it but not to any surrounding tissues; the desired temperature will be above that required to denature the proteins of the targeted structure, but not enough to cause vapour bubbles to form (100°C). In order to achieve this, the pulse must have enough power to heat the structure but also limited in order to avoid vaporisation, and therefore the pulse of radiation must be long enough to allow for sufficient heating of nearby, unpigmented structures via thermal diffusion. As the targeted structure is being heated via thermal diffusion rather than

directly from the radiation pulse, the size and shape of the structure is now an important factor which must be considered, as it will affect the efficiency with which the heat diffuses to the targeted structure. The shape of the pulse of radiation is also an important factor which would not be considered in the original hypothesis for selective photothermolysis.

One example of where this extended version of photothermolysis is useful would be to offer a more permanent solution to hair removal than the original selective photothermolysis theory could, where the stem cells are selectively destroyed. Stem cells in the hair follicle contain no pigment which would absorb the wavelength range typically used in hair removal (600nm to 1200nm). Therefore, the hair shaft which contains large amounts of melanin would be heated using a pulsewidth which was similar in duration to the thermal damage time of the hair shaft, which could be ten times the thermal relaxation time of the follicle itself, and with a shape which initially shows an intense peak of power, before sloping off. Following the pulse of radiation to the hair shaft, the heat will diffuse across to the unpigmented stem cells, sufficiently heating them to cause irreversible damage, but sparing the other surrounding tissues [2].

3.2.3 Photomechanical

Photomechanical responses in skin are a result of the generation of stress from laser interactions. The stress on the skin can lead to the irreversible deformation of skin at macroscopic or microscopic levels. Examples of photomechanical damage to skin can be seen in ablative laser treatments, where a short pulse delivers a very high amount of power [58].

When the ablation of skin occurs, the skin temperature is very suddenly increased, which leads to thermoelastic expansion of the tissue. Other causes of thermoelastic expansion of tissue include rapid phase changes in skin, including water in the tissue being rapidly vaporised, or the sudden removal of an ablative mass leading to recoil. The stress waves which have been generated will spread from the target heating area to surrounding tissues. These stress waves can cause changes and breakages in the structure of tissue and at cellular levels [58].

3.3 Electromagnetic Field Interactions with Tissue

Radiofrequency (RF) has a multitude of uses throughout various disciplines and mediums, and many of us use it in our day to day lives, including during the use of wireless internet, microwaves and TV broadcasting. The various services that RF contributes to is due to the wide range of frequencies within the RF band [86]. Its exact definition of the RF band range is disputed, with many arguing it lies between 30 kHz to 300 MHz, however the Institute of Electrical and Electronics Engineers Inc. defines a wider band of 3kHz to 300 GHz [57]. Typically, the use of RF in medicine and aesthetics operates on frequencies between 200 kHz and 6 MHz, however in some cases frequencies of up to 40 MHz are used [87]. The first use of RF in medicine was for electrocautery in the 1920s [88], and now has a much wider reach across medicine, being used in the treatment of sleep disorders, pain, and tumours, cardiology, and aesthetic applications [89], [90].

3.3.1 RF-Tissue Interactions

RF is a form of electromagnetic wave which uses an electric current rather than light [88]. Due to the wavelengths utilised by radiofrequency devices, the alternating current is safe to apply directly to human skin. When the frequency is above 100 kHz, the effect of the electrical current on muscles and nerves decreases, meaning that the device can induce thermal effects without adverse effects [87]. When electromagnetic waves transition through tissue, they are not absorbed by chromophores or diffracted, and therefore travel through mostly uninterrupted, but do lose energy as they move further through the tissue [91]. For this reason, RF is unaffected by melanin, so can be used by a person with any skin type, unlike laser based treatments which can only be used by specific skin types in order to achieve the desired effects, or avoid adverse ones [91]. RF can have both ablative and non-ablative applications in medicine [87], however this thesis will be focusing on the non-ablative application of RF in the treatment of skin laxity and cellulite.

When transforming electromagnetic energy into heat, the electric field will change the polarity regularly. These changes lead to heating of the molecules within the medium where the electric field has been applied – when a medium can be heating in this way, it can be described as a lossy material, and an example of a lossy material is biological tissue. Heat generation within a lossy material are the sum of the square of the electric field, the dielectric loss factor of the material being heated, and how often the polarity of the electric field is being alternated.

In order to describe the mechanism behind the heating experienced by a lossy material interacting with an electric field, the constitutive heating equation is given in the more manageable sequential form rather than in a coupled form, as per Equation 3.6.

$$P_{av} = \frac{1}{2} \text{Re} \int \int_s (\bar{\mathbf{E}} \times \bar{\mathbf{H}}^*) \cdot d\bar{\mathbf{s}}$$

Equation 3.6

In Equation 3.6, P is the flow of energy, S is the surface, ds is the elemental area vector, vector E is the electric field and vector H is the magnetic field at a specific time, and * represents the complex conjugate. To calculate P, the Poynting vector is included over S with ds.

The surface integral must be amended to the volume integral, and therefore the Divergence Theorem is introduced, as shown in Equation 3.7.

$$P_{av} = \frac{1}{2} \text{Re} \int \int \int_v \text{Div}(\bar{\mathbf{E}} \times \bar{\mathbf{H}}^*) \cdot d\mathbf{v}$$

Equation 3.7

In Equation 3.7, V represents the volume which is in with S, while dv is the elemental volume. A vector identity can now be added to the equation, shown in Equation 3.8.

$$\text{Div}(\bar{\mathbf{E}} \times \bar{\mathbf{H}}^*) = \bar{\mathbf{H}}^* \cdot \text{Curl}(\bar{\mathbf{E}}) - \bar{\mathbf{E}} \cdot \text{Curl}(\bar{\mathbf{H}}^*)$$

Equation 3.8

Maxwell's equations are able to express the initial term on the right side of the equation with reference to the intensity of H, resulting in Equation 3.9.

$$\bar{\mathbf{H}}^* \cdot (\text{Curl} \bar{\mathbf{E}}) = -j\omega\mu_o\mu' \bar{\mathbf{H}}^* \cdot \bar{\mathbf{H}}$$

Equation 3.9

In Equation 3.9, j serves as the square root of -1, ω represents the angular frequency, permeability of free space is shown as μ_o , while the relative permeability of the medium is μ' .

Maxwell's equations are also able to express the second part of the previously mentioned equation for lossy dielectric mediums, as shown in Equation 3.10.

$$\bar{E} \cdot \text{Curl} (\bar{H}^*) = +j \omega \epsilon_o \epsilon^* \bar{E} \cdot \bar{E}^*$$

Equation 3.10

In Equation 3.10, ϵ_o represents the permittivity of free space. The relative permittivity of the lossy dielectric material in its complex form is given in Equation 3.11.

$$\epsilon^* = \epsilon' + j\epsilon''$$

Equation 3.11

By combining Equations 3.10 and 3.11, you are left with Equation 3.12.

$$\bar{E} \cdot \text{Curl} (\bar{H}^*) = -\omega \epsilon_o \epsilon'' \bar{E} \cdot \bar{E}^* + j\omega \epsilon_o \epsilon' \bar{E} \cdot \bar{E}^*$$

Equation 3.12

This now allows the following amendment to the right side of equation 3.12, shown in Equation 3.13.

$$\bar{H}^* \cdot \text{Curl} (\bar{E}) - \bar{E} \cdot \text{Curl} (\bar{H}^*) = \omega \epsilon_o \epsilon'' \bar{E} \cdot \bar{E}^* - j\omega (\epsilon_o \epsilon' \bar{E} \cdot \bar{E}^* + \mu_o \mu' \bar{H}^* \cdot \bar{H})$$

Equation 3.13

As $\bar{E} \cdot \bar{E}^*$ and $\bar{H} \cdot \bar{H}^*$ are actual quantities, the initial constitutive heating equation is now transformed into Equation 3.14.

$$P_{av} = \frac{1}{2} \int \int \int_v (\omega \epsilon_o \epsilon'' \bar{E} \cdot \bar{E}^*) dv$$

$$P_{av} = \frac{1}{2} \omega \varepsilon_o \varepsilon'' \int \int \int_v (\bar{E} \cdot \bar{E}^*) dv = \frac{1}{2} \omega \varepsilon_o \varepsilon'' |\bar{E}|^2$$

Equation 3.14

The above equation represents the generation of heat within the medium, and is able to combine the electromagnetics which explain heating via RF and the heat flow issue. To calculate the flow of energy within a medium, Laplace's equation, given in Equation 3.15, must be solved.

$$\text{Div } \varepsilon_o \varepsilon \text{ Grad } V = 0$$

Equation 3.15

In Equation 3.15, V is the electrostatic potential. The relative permittivity of the material is described in Equation 3.16.

$$\varepsilon = \varepsilon' - j\varepsilon''$$

Equation 3.16

The electric field between the electrodes of the RF device can be calculated using the electrostatic potential's negative gradient, if there is a fixed value for permittivity and a set voltage from the electrodes, as shown in Equation 3.17.

$$\bar{E} = - \text{Grad } (V)$$

Equation 3.17

In Equation 3.17 describing the relative permittivity, the complex permittivity depends on the frequency which can be calculated using the loss tangent and values of ε' using Equation 3.18.

$$\tan \delta = \frac{\varepsilon''}{\varepsilon'}$$

Equation 3.18

The RF field can be estimated using a computational model of the quasi-static electric field which is created between the RF devices electrodes. When compared to the electrode size, the size of the wavelength of the RF in the range relevant to this thesis, 500kHz and 40 MHz, is much larger. As a result, wave propagation does not need to be taken into account. Due to this, the heating rate of the alternating electric field can be calculated using the expanded constitutive heating equation given above.

The frequency of the electric field is determined by the size of the wavelength in comparison to the size of the electrodes. Due to this, the most logical choice for solving the electric field analysis would be an electrostatic one. This will include the loss tangent, conductivity and variance of the permittivity by temperature in the medium. The electrostatic solution can solve the problem by changing between the electrostatic and the heat flow problem over time [92]. The heat source term for RF heating is the given in Equation 3.19.

$$Q_{rf} = \pi f \varepsilon_o \varepsilon \left| E(x, y, z) \right|^2$$

Equation 3.19

Creating heat in biological tissue using an alternating current, such as RF, is affected by a multitude of factors, and involves a number of complicated mechanisms. For the current, the frequency and amplitude of the current can affect the thermal effects it will have on tissue, while the water and electrolyte content, temperature, and other variable features of the tissue itself will also lead to variations on the thermal effect of the RF [90].

A RF device will release charged particles to the tissue which it is in contact with. As the tissue is closed, these particles create a current. The tissue will resist the current, and this resistance is known as impedance. When the current is impeded, the interaction creates heat, leading to thermal reactions in the tissue [88]. The amount of heat created depends on the current used and the amount of time it has been applied for.

How the energy from the RF device is transferred into the tissue can be accomplished via three mechanisms, all of which involve the charged particles in the tissue and the electromagnetic field of the RF device. The first mechanism is a change within the electric dipoles of the molecules which are part of the tissue – this creates heat due to the energy required to move the molecules. The second is the production of dipole moments caused by the polarisation of these molecules, which again creates heat due to the movement of molecule. The third is the movement of electrons and ions in the tissue which are responsible for conduction in the tissue, which creates heat as the transmission charges collide with particles [86].

The energy which an RF device produces has two forms - peak and average power. How quickly a target tissue is heated is affected by the average power, while how the heat affects the target tissue is dependent on the peak power. In a similar vein to laser heating, the density of the power will affect the thermal effect the RF has on skin. The same amount of power can have drastically different effects when applied to different amount of tissue. When high power is applied to a bulk of tissue, this will simply warm the tissue or potentially caused coagulation, however when that same amount of power is condensed via a needle-sized electrode, ablation of the tissue will occur [87]. A critical parameter of RF devices is its pulse duration. As with laser based therapy, pulse duration has a significant effect on the thermal reaction in the tissues, and how heat disperses from the target tissue to surrounding tissues [87].

How energy is delivered by a RF device can be in various modes suited to treat certain issues or geometries of tissue, including continuous wave, burst, or pulse. Each of these

modes has a different application of power of the device. For treatments where the initial power of the current is important, instead of the continuous power of the device, such as causing coagulation in blood vessels, burst mode should be used. If the RF is being used for ablation and the pulse duration should not exceed the thermal relaxation time of the target tissue, then pulsed mode is the ideal choice. For both pulsed and burst modes, the average power can be calculated taking the power delivered and dividing it by the amount of time the RF device was applied for. If the target tissue is a large area which needs to be heated slowly, such as subcutaneous fat or collagen in the dermis, continuous wave mode (CW mode) is the best suited option. In CW mode, the peak and average powers are equal [87]. The mode of RF devices that will be discussed and utilised in this thesis is CW mode.

3.3.2 RF in Dermatology

The use of RF in dermatology was initially approved by the Food and Drug Administration (FDA) in 2002 for the treatment of facial wrinkles, and by 2006 the FDA extended its use for skin treatments across the rest of the body [88], [91]. RF works by penetrating deeply into the dermis or subcutaneous tissue and heating the tissue, without damaging the epidermis or other surrounding structures. The size of the wavelength allows this action to occur, as it means the RF cannot heat just small areas of tissue, or be as targeted as is experienced with selective photothermolysis [87]. The heating effect created by the RF can lead to collagen contraction in the skin when treating skin laxity [87], and leads to lipolysis and reducing the size of the fat cells when treating cellulite [93]. RF is the ideal tool for these treatments as it is able to penetrate deeply enough into the skin, somewhere between three to six millimetres, to cause significant thermal damage to the dermis and subcutaneous tissue, a depth which laser light typically cannot easily reach without ablation or other invasive techniques [87].

The treatment of skin laxity in the face and neck, a result of ageing and exposure to UV rays, was initially something which could only be successfully achieved by surgical means, however RF offers a non-surgical option which gives consumers the option of a treatment which is faster and has little to no downtime. The downside is much more subtle results, with the need for more than one treatment, and possibly maintenance treatments to ensure the results do not fade [89]. Shin and Kim [91] found that RF treatment had the best results on patients who had only recently started showing signs of ageing, and the rhytids were only of mild to moderate severity. Those with more pronounced rhytids and signs of ageing did not benefit from RF treatments as much as the younger patients, and required further invasive treatments or if they wished to have just non-invasive treatments, a combination of the RF treatments with another non-invasive treatment such as laser treatments or botulinum toxin would have been required.

Many of the current available treatments for cellulite lack much scientific basis, with much of the justification for the effects of the treatments being based on anecdotal evidence or subjective patient reviews. Another option for patients suffering with cellulite is liposuction, however this treatment is both invasive and expensive, and the possibility of negative side effects [93].

Types of RF Devices

RF devices can be unipolar, monopolar, bipolar, and tripolar – in medicine, monopolar and bipolar are often used [87]. These terms related to how the electric current is applied to tissue via electrodes. Monopolar consists of a single electrode and a back plate, bipolar has two electrodes, and so on [90]. The type of electrode utilised by the RF device affects the penetration depth the energy can reach within tissue [87]. Belenky, Margulis, Elman, Bar-Yosef, & Paun [86] argue that despite the claims that multipolar such as tripolar and octapolar RF devices exist, these are all just different forms of monopolar or bipolar devices – for example, a tripolar device consists of a monopolar electrode and a bipolar electrode, or creating a variation of this using a negatively charged electrode and two positively charged electrodes, which is essentially just two bipolar systems combined into one. The focus of this thesis is on the use of monopolar and bipolar applications.

Monopolar RF Devices

A monopolar RF device consists of a single negatively charged electrode, and a bigger positively charged grounding pad which is placed away from the area which is being treated – for example, if the face is being treated, the grounding pad may be placed on the shoulder [86]. Monopolar devices are typically used in the treatment of rhytids, however have also been used for cellulite, acne and the scarring it can cause [88].

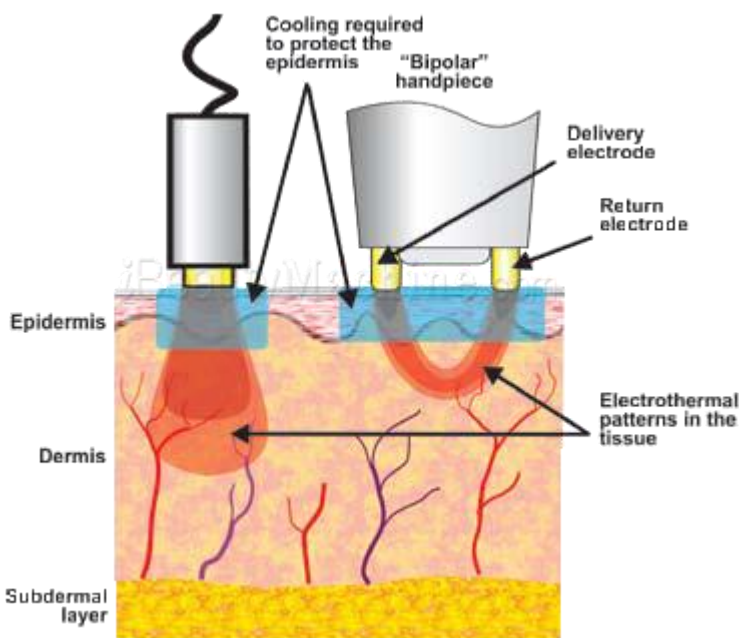


Figure 3.9- Monopolar radiofrequency device vs bipolar radiofrequency device [139].

How much heat is created by a monopolar RF device is dependent on the size of the electrode, how it is shaped, and where it is placed in comparison to the grounding pad, unless the grounding pad is considerably bigger than the electrode and placed at a significant distance from the electrode. As the current from the active electrode travels through tissue towards the grounding pad, the current will become weaker, and once it has travelled through a distance of the skin which is equivalent to the size of the electrode, it will no longer significantly heat the tissue. The energy created will convert to heat at the point of contact with tissue, and will only be able to penetrate to a depth equal to half the size of the electrode being used [87]. When a monopolar device is used, a cooling gel or spray may be used due to the concentrated electrical current generated at the point of contact between the electrode and skin in order to avoid causing damage to the epidermis [88].

The energy which monopolar RF creates is spread across the skin evenly via a process termed as capacitive coupling. Capacitive coupling allows an elevated temperature which can be controlled at a set distance from the electrode, for example in the dermis. When the skin is heated by the monopolar RF device, the cooling agent creates a reverse thermal gradient, keeping the epidermis at a non-damaging temperature while volumetrically heating the dermis to temperatures up to 75°C, causing breakages in the bonds of collagen triple helixes in the target area, and partially denaturing the collagen. As a result of this denaturing process, the collagen fibrils will then thicken and tighten, possibly leading to a similar response by the collagen framework. Following this, the body's immune response can lead to further contraction of the collagen and the creation of new collagen, known as neocollagenesis. The thermal effects can extend to the subcutaneous fat layer of the skin, heating the fibrous septa, which leads to shrinkage of the subcutaneous layer. This, along with the contraction in the collagen framework, can result in an immediate visible effect to skin [89], [88].

There are advantages and disadvantages to the use of monopolar RF devices in dermatology. Advantages include that a very specific target area can be heated without damage to surrounding tissues, consistent effects to the skin adjacent to the electrode, and a larger penetration depth than offered by other electrode-based RF devices [87], as shown in Figure 3.9. However monopolar RF is painful for patients, therefore in order to make the treatment tolerable, the power of the device must be reduced, meaning that effects of the

treatment are more subtle, and may take more than one treatment to reach the desired effect [88].

Bipolar RF Devices

Bipolar RF devices use two electrodes which produce equal amounts of energy to heat tissue, both of which are applied directly to the area being treated and are a set distance apart – there is no need for a cooling mechanism as with monopolar RF [87].

Bipolar RF devices are used for the treatment of rhytids, skin laxity, cellulite, as well as skin lesions, hair removal, acne and the scarring it can cause [88]. As the energy generated by the RF device travel through tissue, the tissue resists the current, creating heat. This heat causes the same effect seen in monopolar RF device, with the contraction of collagen and its framework, the shrinkage of fibrous septa in the dermis, and the immune system responding to damage in the tissue [88].

The penetration depth of bipolar RF devices is considerably less than that of monopolar RF devices. The energy created circulates between the two electrodes, and the current is only able to penetrate into the tissue at approximately half of the distance between the electrodes. This feature does make the bipolar RF device more tolerable with regard to pain, and makes it easier to manage where the current is travelling within tissue [88].

Bipolar RF devices can be combined with other technologies in order to enhance the effects caused by the heating of tissue. This includes a combination treatment including RF and light sources such as LED; this pairing is known as Electro-optical synergy (ELOS). The light source of ELOS reduces impedance in the tissue via selective photothermolysis to increase the penetration of the RF energy. Bipolar RF devices may also be paired with a vacuum system called Function aspiration controlled electrothermal stimulation (FACES). This system creates a fold in the skin of a set depth meaning that the electrical current can penetrate deeper into the tissue, and the electrode can be positioned directly onto the skin with fewer potential heterogeneities between the electrode and skin. Both of these combination techniques allow for lower levels of energy to be used by the RF system, meaning less incidence of pain and side effects, and also leads to better results, as both systems allow more direct treatment, since ELOS reduces impedance prior to the electrical current being applied, and FACES folding the skin to allow for deeper penetration [88].

Some of the advantages and disadvantages of using bipolar RF have already been discussed, including the reduced penetration depth, but decreased pain for patients and ease of control over where the current travels in tissue. One disadvantage of the bipolar RF device which has not been discussed is that due to most of the heat being centralised at the electrode, this can lead to potential hot spots, which can result in adverse thermal effects. Another advantage which was not mentioned is that bipolar RF devices are able to heat larger amounts of tissue consistently than monopolar is able to [87].

3.3.3 Physiological Consequences of Radiofrequency Treatment

The mechanism behind how RF devices improve skin laxity is well understood, however this is not the case for cellulite. Please see the beginning of this chapter for further detail about the structure of skin and subcutaneous fat, including ageing skin and cellulite.

As described above, the heat of RF devices penetrates into the skin at a depth which laser light cannot reach without invasive treatments [87]. By heating the dermis, RF devices are able to denature collagen, leading to the retraction of tissue which has started to become lax [88]. There is no set temperature which the dermis must be heated to in order to see results, as time is an equally important variable, and instead a range between 45°C and 65°C is suggested. As the temperature is lowered by 5°C within this range, the amount of time needed to achieve the same effect is increased by 10, for example if it takes 2 seconds to achieve results with an RF device at 60°C, it would take 20 seconds to get the same result at 55°C [89].

This process begins by deconstructing the collagen proteins by breaking intra-molecular hydrogen bonds within it the triple helix [94]. This transforms the collagen into a form similar to gel, shrinking the collagen, however this does not result in entirely liquid collagen, as the heat stable bonds are unaffected by the RF-induced changes [90]. The heat also affects the fibroblasts, initiating the synthesis of new collagen molecules, which results in a change in the structure of the tissue [88], becoming tighter with an increase in the amount of collagen within the skin due to neocollagenesis [94]. Following the initial heat damage, it can take up to six months to see the complete results of RF. For the first month, collagen is repaired, after 3 months, the epidermis may enlarge, and rete ridges are formed; for up to six months after treatment, further neocollagenesis takes place [89]. This process is demonstrated in Figure 3.10.

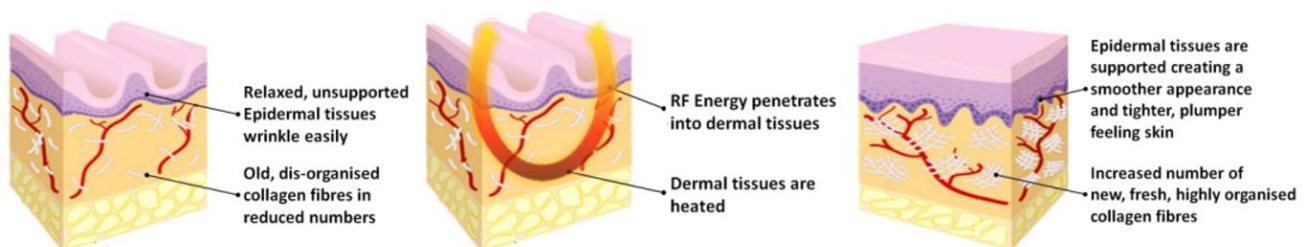


Figure 3.10 - How radiofrequency treatments affect the skin [95].

RF devices are able to heat large volumes of tissue, including the adipose tissue in the subcutaneous fat layer of skin. When this tissue is heated, it is reported to increase the

microcirculation of blood, increasing the flow of blood to the adipose tissue. The increased blood flow results in increased metabolism. This creates homogeneity within the subcutaneous fat layer, and improving its elasticity. Due to the increased elasticity, the fat layer becomes smoother, therefore leading to a change in the appearance and texture of the skin in the target area [86], as shown in Figure 3.11.

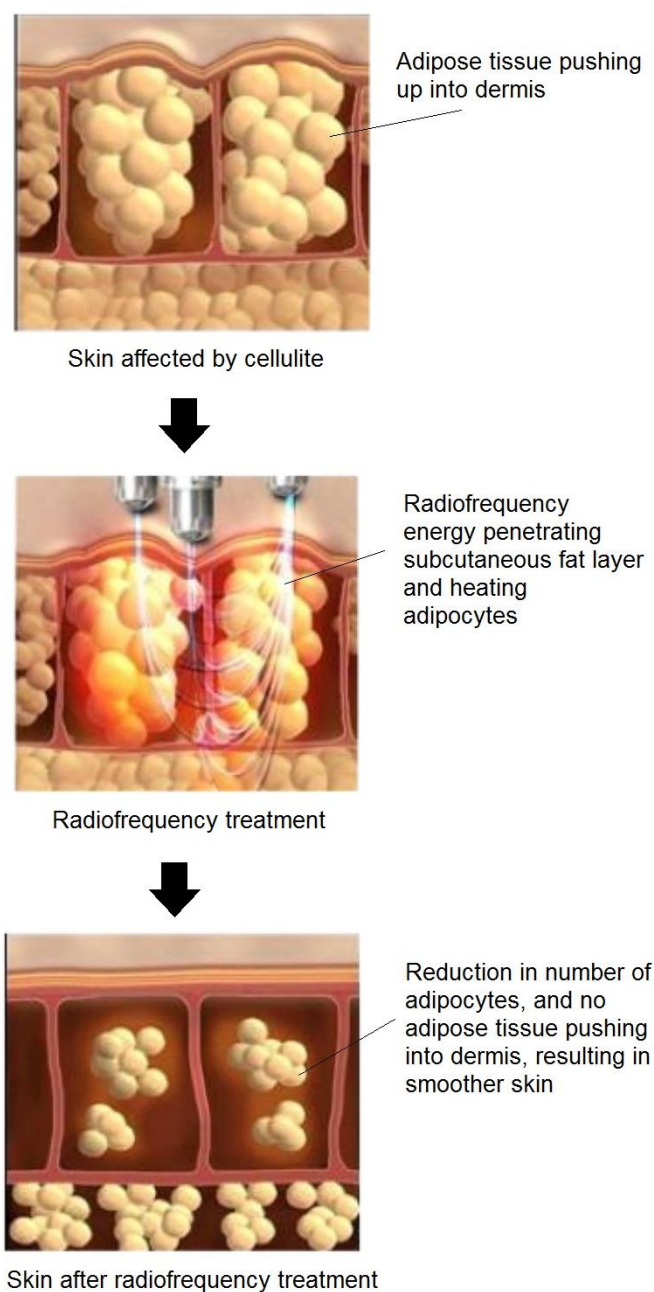


Figure 3.11 - Suggested mechanism of action for the treatment of cellulite via radiofrequency [96].

Safety Mechanisms

The energy produced by an RF devices travels through human tissue in a closed loop in order to stop the risk of electrocution. As RF devices operate at relatively high frequencies

of above 100 kHz, the stimulating effect which electricity has on nerves and muscles decreases. The combination of these two characteristics of RF allows electricity to be applied to skin in a safe manner [87]. Despite these characteristics, further safety mechanisms are put in place to ensure the safety of the user. The first of these include a monitoring system which continuously checks current and voltage being output by the device, meaning the temperature of the tissue being treated can be monitored also, a factor which affects the impedance of the tissue. The skin surface temperature can also be monitored using the electrodes when they are in contact with the skin – this ensures that there is no damage caused to the epidermis. Devices are often also equipped with systems which can detect if the electrode and skin are not coupling well, and amend outputs to fix this issue. This system is dependent on the closed loop characteristic, and therefore is unique to this type of treatment, since light based treatments do not have the means to conduct this type of monitoring [87].

Unlike light-based treatments, RF is suitable for all skin types, however there are still restrictions to who can safely be treated using RF. Due to the nature of how RF devices work, anyone who has a medical device such as a pacemaker fitted cannot be treated using RF. Caution must also be exercised when the person being treated experiences recurring infections as a result of the herpes simplex virus or are undergoing radioactive therapies [91].

As with light-based treatments, there are also safety concerns related to potential adverse effects related to thermal damage to the skin. One of the advantages of RF treatments is that it can heat the dermis without causing any damage to the epidermis, if used correctly – this means there is a smaller chance of adverse effects in comparison to more invasive treatments which can cause extensive damage to the epidermis as part of the procedure [88], [91]. The effects of heat on skin by an RF device, like light-based heating, causes damage according to the Arrhenius Damage Integral, explained earlier in this chapter. Like other non-invasive procedures, RF treatments can lead to short-term side effects which can be expected by the user, such as oedema, bruising, focal depressions, and sometimes arcing injuries, including potential small burns to the skin as a result of electrodes not being in constant, direct contact with the skin.

There are multitude of reasons why RF may lead to negative thermal effects, for example, as a result of the person applying the electrodes. If this is done improperly, and electrodes are kept in one place on the skin for too long, a hotspot may be created, leading to

unwanted thermal damage. The ideal parameters for RF treatment vary between patients and between the targeted tissues, therefore if the incorrect parameters are chosen, it can lead to undesired effects on the target and its surrounding tissues [87]. If the temperature of the skin is too high as a result of the described misuse of the device, there is a possibility that the patient may experience hyperpigmentation or hypopigmentation in the area treated [89]; this effect is typically seen in patients with darker skin, as oedema can stimulate melanocytes in the tissue [87].

If a nonablative RF device is used appropriately and correctly, then it can be considered a safe procedure which is tolerable for most patients [88]. Many adverse effects can be prevented by careful selection of parameters and temperature depending on the patient being treated, and opting for multiple, less intense sessions, rather than one aggressive treatment. Typically, the results seen from these devices are subtle, and therefore patients should be made aware that they should not expect similar effects as those experienced by patients who have undergone surgical treatments. It does however have advantages over surgical treatments, despite RF's more modest results, with a lower rate of side effects, and much less downtime expected – many patients can be treated in under one hour and have very little downtime [88].

3.4 Dielectric Properties

Almost all materials have electrical properties, and these properties can either be conducting or insulating. When electricity is applied to a conductive material, the charges within the conductor have freedom to move. This freedom means that the charges will move within the conductor until the electrical field in the conductor reaches zero. However, when electricity is applied to an insulating material, the charge are fixed into position, therefore there is no change to the net migration of charge [97].

3.4.1 Dielectric Properties & Displacement Currents

Dielectric was initially used by Whewell in 1798, and it describes a property which is neither a conductor nor insulator. Typically, a dielectric material will have little to no conductivity, and is not simply an insulator as they can be polarised, and the ability to hold electrical charge [98]. The electrons within a dielectric material are fixed in place to atoms, and do not have the ability to move freely. As the electrons are not able to move within the dielectric material, charge is transferred via a displacement current [99].

A displacement current isn't actually a current – instead, it describes how charges change when current cannot flow, such as in an insulator [98]. This is achieved through changing the electric field, or imposing one upon the dielectric material. In the dielectric material, the electrons of each atom will pull towards the electrons of the electrical field, while the nucleus will be pushed in the opposite direction. As a result, each atom is partially negative and partially positive – these charged atoms are known as dipoles [99]. A displacement current can be described using Equation 3.20 [100].

$$I_d = \int_S \mathbf{J}_d \cdot d\mathbf{s} = \int_S \frac{\partial \mathbf{D}}{\partial t} \cdot d\mathbf{s}$$

Equation 3.20

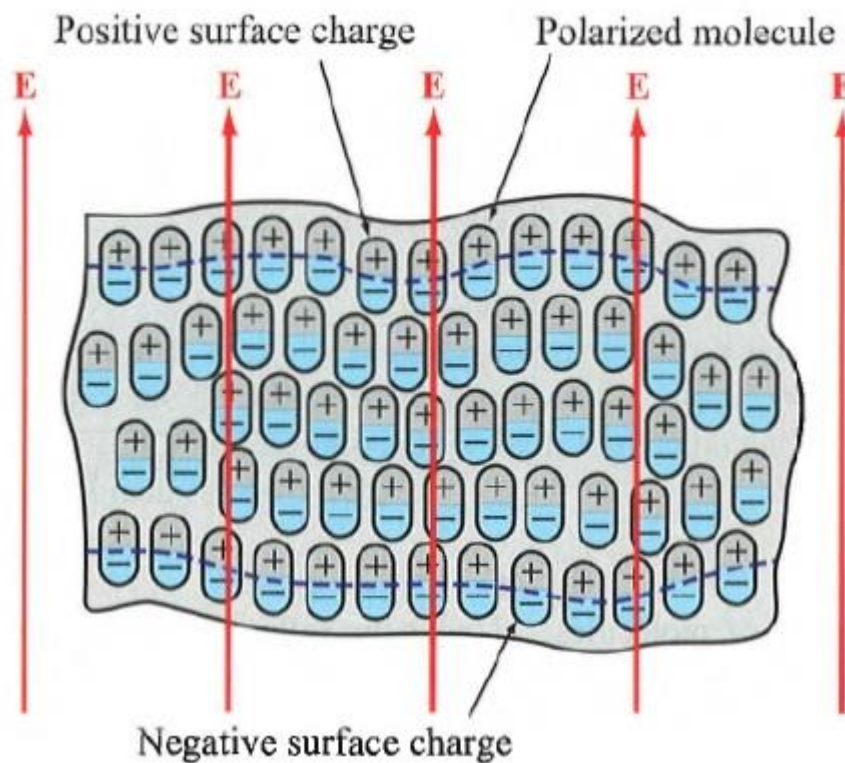


Figure 3.12 - A polarised dielectric material [99].

The dipoles will then orientate themselves linearly in accordance with the electrical field, creating a polarisation field, which is demonstrated in Figure 3.12. The polarisation field which has been created is typically directed in the opposite direction to the electric field, and is also smaller than the electric field. The direction of the polarisation field depends on the properties of the dielectric material. If the dielectric material is linear, the polarisation field will be proportional to the electric field, however if the dielectric material is isotropic, the polarisation field will be in the same direction as the electric field [98].

Biological tissue is both a conductor and an insulator. The dipoles within tissue are fixed, therefore acting as insulating features, though there are also charges present which have some freedom to move within the tissue. The heterogeneous nature of biological tissues can lead to charges being caught between the layers of skin, therefore when an electric field is applied, the tissue can behave as a large dipole, due to the movement of cations and anions and separation of charges within the tissue [97].

The permittivity of a material, such as biological tissue, is defined as the measurement of how its dipoles move or the charges are stored when an external field is applied. A material's conductivity is defined as the measurement of its capacity for the charge to move through the tissue when an electric field is applied. As the frequency of the electrical

charge increases, the displacement current will also increase, assuming the conductivity and permittivity remain the same. Though in biological tissue, conductivity and permittivity will vary depending on the frequency of the current applied – this variation is known as dispersion [97].

As the frequency applied to biological tissue increases, the permittivity of this tissue will decrease. The decrease will occur in three parts, called α , β , and γ dispersions. Dispersion in this context is defined as how electrical properties of the tissue change depending on the dielectric losses caused by electric dipoles relaxing, and will have a relaxation time [101]. As the frequency applied increases, the ability of the dipoles to adapt to changes in the field decreases, which charge carriers are less likely to be caught between the layers of skin, meaning permittivity decreases while the conductivity will increase [97].

3.4.2 Dielectric Properties of Biological Tissues

The electrical properties of biological tissues have been investigated for a long time. In the 18th Century, Galvani noticed that electrical sparks caused stimulation of muscles during ex vivo studies he was conducting, which led to the use of electricity as a treatment for some diseases and as a therapeutic tool. Despite this knowledge, electricity was not used in diagnostics until the late 1800s [102]. The dielectric properties of tissue can be defined as how the relative permittivity and conductivity of the tissue changes with varying frequency. This is not straightforward to measure, as a number of variables can lead to inconsistencies in measurements, including the polarisation of the electrodes [101].

The dielectric properties of tissues and how electrical energy is dispersed into tissue can be affected by a number of factors, including the type and temperature of tissue being treated, the frequency being applied to the tissue, the placement of the electrodes on skin, the electrolytes in skin, and the geometry of the tissue itself [101], [103].

As an important capacitor for the body, skin has incredibly varied dielectric properties, and due to the heterogeneous nature of skin, it can cause problems with collecting dielectric measurements, and measuring its impedance or calculation of the total body water. The varying condition of the skin itself can affect dielectric properties, including its temperature, amount of sweat being produced, its hydration levels and amount of electrolytes, if it is diseased, and the blood flow to the skin [104].

The type of tissue and its geometry are major factors in the dielectric properties of skin – the inhomogeneous structure means inhomogeneous properties [97]. It can cause changes to the depth which can be treated by RF, its conductivity, and the distribution of energy through the tissue. There are three main characteristics of skin which have the most influence over its dielectric properties; the part of the body being treated, the layers of the skin, and the moisture content of the skin [87], [103] [97].

The thickness of skin being treated, and which part of the body is being treated, will cause changes in the dielectric properties being observed. For example, there is lower conductivity in areas with bone, such as the forehead when treating skin laxity, as bone has very low conductivity [87]. There is also considerably less blood flow in these areas, and therefore there is less conductivity in these areas [86]. This means that energy being applied in areas over bone will have much less depth of penetration in comparison to areas with much more tissue before reaching the bone, such as in the thigh region when treating cellulite. This means when treating these areas, different parameters for the RF device must be used [87].

As briefly mentioned above, the electrical conductivity of skin is affected by the blood content in the tissue and general hydration levels of the skin. The higher the content of water in the tissue, the more conductive the tissue is likely to be [105]. Sweat ducts can also effect dielectric properties - the palms of the hand and soles of the feet have low impedance as there are a considerable number of sweat ducts in these areas [101]. The water content of skin can cause a complete change to its dielectric properties, and due to this it is the only tissue where separate measurements have been taken for when skin is both dry and moist. When applying an electrode, by using a moisturising agent such as a gel, it can allow for better coupling with the skin. Tests were conducted in vivo on tissue which was dry and on tissue which had saline applied, with RF currents with frequencies between 100 Hz and 100 MHz. Results showed that dispersion was 5 times higher in moistened skin compared to dry skin. Raicu et al [106] suggested that their results showed that the moisture allowed an increase in penetration depth due to reducing the effects which the heterogeneous layers of the skin had upon the impedance [105]. As the water content in skin can also vary between layers of skin, the geometry of skin has a large effect on its dielectric properties also [103].

As explained in the previous chapter, the skin has a layered structure, with the epidermis as an outer layer, the dermis below the epidermis, and the bottom layer of subcutaneous fat.

The dermis, with varying thicknesses between 1 mm and 4 mm, has higher electrical conductivities than the two layers which surround it. Both the water content in these layers as well as their thicknesses can affect the dielectric properties, as well as the penetration depth [103]. Typically, in the top layer of the epidermis which has an approximate total thickness of $80\mu\text{m}$ (Sandby-Moller, Poulsen, & Wulf 2003), the stratum corneum which is approximately $10\mu\text{m}$ to $40\mu\text{m}$ thick, the water content is below 20%, then increases to between 70% and 80% in the remainder of the epidermis and the dermis. The stratum corneum contributes a vital part of what makes up the dielectric properties of skin. Despite its small size, it has a high impedance, meaning it can be difficult for electrical energy to pass through this layer in comparison to the dermis [97]. The water content then drops again down to 10% in the subcutaneous fat layer, where the thickness can vary to a few millimetres to several centimetres. As a result, it is more difficult to cause heating in the adipose tissue in the subcutaneous layer compared to the collagen in the dermis [103].

The anatomy of the skin is a factor in the skin's impedance, along with its reactance, resistance and phase angle. Impedance is defined as the resistance of skin to electrical currents [87], and the skin's impedance levels can be affected by the frequency of the current being applied. Impedance is made up of resistance, repelling the current flow applied to the skin, and reactance, which opposes change to the voltage of the tissue using an inductor or capacitor [102]. When the frequency of the current applied is low, the impedance is high and so the current cannot be carried through cells and tissue interfaces, and must be done so via electrolytes and fluids – in this context, the impedance is entirely resistive, with no reactance. When the frequency is higher, the impedance is low enough to allow the current to flow through cells and tissues – in this context, the reactance is considerably higher, whereas reactance plays less of a role [102]. Typically, cosmetic RF treatments which range between 200 KHz and 1 MHz, the skin will behave in a resistive manner [87]. Temperature is also an important factor in the impedance of the skin. Gudivaka, Schoeller & Kushner [104] conducted a study investigating the change in impedance between frequencies of 5 kHz and 500 kHz with varying temperature. Their results showed that as temperature decreased, impedance increased across all frequencies. This was also the case when the electrode was placed either distally or proximally, however the results were not as marked when the electrodes were in a proximal position.

Dielectric properties of skin can be incredibly varied between different frequencies, especially for frequencies below 1 kHz and between 10 kHz to 100 MHz. For frequencies above this range, the dielectric properties in skin will be dependent on the water and fluid content of the tissue, and the ions present within the fluids [101]. Measuring the dielectric properties of skin when current frequencies between 10 Hz to 10 MHz are applied is not a simple task, as a multitude of factors can lead to inconclusive or incorrect readings [107]. Within the range of 20 kHz and 20 MHz, dispersions will be seen in the proteins of the skin, though the intensity of these dispersions will depend on the size of the protein, as the effect is weaker on smaller proteins at the higher end of the frequency range [101]. As frequency increases, impedance has been shown to decrease, with studies finding that the stratum corneum provides 50% of the skin's impedance at 10 kHz whereas this drops to 10% of the total impedance at 100 kHz [97].

The amount of data available for conductivity and permittivity for skin in the academic literature is scarce, especially for frequencies below 1 MHz. For the data which is available, few papers differentiate between the epidermis and dermis, and almost none state how dielectric properties change between the stratum corneum and the rest of the epidermis. Some data is available for moistened skin, though other available data does not state if the skin is dry or moistened. When compiling a comprehensive list of dielectric properties from the available data, non-human tissue was excluded, and the frequency range between 200 kHz and 6 MHz was focused on. Dielectric properties for wet skin, dry skin, and fat were collected, and are provided in Table 1, Table 2, and

Table 3.

Frequency	Conductivity (S/m)	4CC Conductivity	Conductivity Data	Conductivity Literature	Permittivity	4CC Permittivity	Permittivity Data	Permittivity Literature
200 kHz	0.13	0.13	0.13	-	11428.57	8250	10000	-
	1233	-	-	-	10940	-	-	-
300 kHz	0.16	0.15	0.15	-	7250	6000	8000	-
400 kHz	0.18	0.17	0.19	-	5875	4500	6500	-
500 kHz	0.212	0.19	0.21	-	4500	3750	5000	-
600 kHz	0.225	0.2	0.225	-	3750	3000	4000	-
	2242	-	-	-	-	-	-	-
700 kHz	0.25	0.21	0.235	-	3250	2500	3250	-
800 kHz	0.262	0.215	0.275	-	2850	2250	3000	-
900 kHz	0.275	0.22	0.29	-	2300	2000	Not clear	-
1 MHz	0.287	0.225	0.3	0.55	2500	1850	Not clear	1625
	2638	-	-	-	-	-	-	-
1.5 MHz	0.25	0.25	0.25	-	2150	1500	2500	-
	2212	-	-	-	-	-	-	-
2 MHz	0.287	0.275	0.3	-	1625	900	1500	-
	2638	-	-	-	1325	-	-	-
2.5 MHz	0.437	0.285	0.31	-	1187	800	1125	-
	3438	-	-	-	948.2	-	-	-
3 MHz	0.45	0.3	0.325	-	975	700	950	-
	-	-	-	-	858.1	-	-	-
3.5 MHz	0.465	0.31	0.35	-	900	575	850	-
	3261	-	-	-	631.7	-	-	-
4 MHz	0.475	0.315	0.375	-	650	490	700	-
	3742	-	-	-	544	-	-	-
4.5 MHz	0.487	0.32	0.39	-	600	450	600	-
5 MHz	0.495	0.325	0.4	-	525	400	550	-
	3742	-	-	-	441.4	-	-	-

5.5 MHz	0.5	0.33	0.4	-	475	370	500	-
6 MHz	0.515	0.34	0.4	-	425	225	400	-
	-	-	-	-	363.8	-	-	-

Table 1 - Dielectric Properties of wet skin. Data taken from [107] (in red) and [105] (in blue). 4CC refers to the 4-Cole-Cole method used in [107].

Frequency	Conductivity (S/m)	4CC Conductivity	Conductivity Data	Conductivity Literature	Permittivity	4CC Permittivity	Permittivity Data	Permittivity Literature
200 kHz	0.00175	0.0011	0.0017	-	900	1000	900	-
	1233	-	-	-	10940	-	-	-
300 kHz	0.00275	0.002	0.0028	-	895	990	900	1125
	0.01	-	-	-	1500	-	-	-
400 kHz	0.0036	0.0031	0.004	-	875	985	900	-
500 kHz	0.005	0.0042	0.0047	-	860	985	900	-
600 kHz	0.006	0.0065	0.0065	-	850	980	890	-
	2242	-	-	-	3511	-	-	-
700 kHz	0.0075	0.0075	0.0075	-	825	980	850	-
800 kHz	0.0085	0.009	0.009	-	800	975	825	-
900 kHz	0.01	0.01	0.01	-	790	975	810	-
1 MHz	0.0125	0.012	0.012	0.02	780	975	800	400
	0.02	-	-	0.025	450	-	-	950
	0.025	-	-	-	1000	-	-	-
	2683	-	-	-	-	-	-	-
1.5 MHz	0.02	0.019	0.025	-	750	950	775	-
	2212	-	-	-	2130	-	-	-
2 MHz	0.029	0.04	0.029	-	700	900	700	-
	2683	-	-	-	1325	-	-	-
2.5 MHz	0.0385	0.05	0.04	-	675	800	682	-
	3438	-	-	-	948.2	-	-	-
3 MHz	0.0533	0.065	0.05	-	625	750	650	-
	-	-	-	-	858.1	-	-	-
3.5 MHz	0.065	0.075	0.06	-	600	725	600	-
	3261	-	-	-	631.7	-	-	-
4 MHz	0.075	0.085	0.07	-	575	700	575	-
	3742	-	-	-	544	-	-	-

4.5 MHz	0.085	0.095	0.085	-	550	650	550	-
5 MHz	0.095	0.11	0.09	-	500	600	500	-
	3742	-	-	-	441.4	-	-	-
5.5 MHz	0.1	0.0125	0.1	-	475	550	475	-
6 MHz	0.125	0.14	0.12	-	425	525	450	-
	-	-	-	-	-	-	363.8	-

Table 2 - Dielectric Properties of dry skin. Data taken from [107] (in red) and [105] (in blue).

Frequency	Conductivity (S/m)	4CC Conductivity	Conductivity Data	Conductivity Literature	Permittivity	4CC Permittivity	Permittivity Data	Permittivity Literature
200 kHz	0.025417	0.0225	0.025	-	55	57	Unclear	-
300 kHz	0.02558835	0.02286667	0.0252	0.0225	42	47	45	125
	0.020823	-	-	-	-	-	-	-
400 kHz	0.0257597	0.02323334	0.0254	-	38	40	38	-
500 kHz	0.02593105	0.02360001	0.0256	-	32	35	32.5	-
600 kHz	0.0261024	0.02396668	0.0258	-	30	32.5	30	-
700 kHz	0.02627375	0.02433335	0.026	-	28	30	29	-
800 kHz	0.0264451	0.02470002	0.0262	-	27	29	29	-
900 kHz	0.02661645	0.02506669	0.0264	-	26	29	29	-
1 MHz	0.0267878	0.02543336	0.0266	0.025	25	27	26.5	17.5
	-	-	-	0.025	-	-	-	27
	-	-	-	0.035	-	-	-	35
	-	-	-	0.175	-	-	-	275
1.5 MHz	0.02695915	0.02580003	0.0268	-	22	25	22	-
2 MHz	0.0271305	0.0261667	0.027	-	20	22.5	20	-
2.5 MHz	0.02730185	0.02653337	0.0272	-	19.75	21.5	19	-
3 MHz	0.0274732	0.02690004	0.0274	-	19.25	21	18.5	-
3.5 MHz	0.02764455	0.02726671	0.0276	-	19	20.5	18	-
4 MHz	0.0278159	0.02763338	0.0278	0.018	18.5	20	17.8	10
	0.298908	-	-	0.07	-	-	-	50
4.5 MHz	0.02798725	0.02800005	0.028	-	18.2	19	17.6	-
5 MHz	0.0281586	0.0282835	0.0282835	-	18	19.5	17.4	-
5.5 MHz	0.02832995	0.02864175	0.02864175	-	17.8	18	17	-
6 MHz	0.0285013	0.029	0.029	-	17.5	17	16.5	-

Table 3 - Dielectric Properties of fat. Data taken from [107] (in red).

3.5 Photon Movement in Biological Tissue

There have been various models designed to describe the passage of photons through biological tissues. These explanations can be split into analytical and numerical methods. In this section, a selection of these explanations will be discussed.

The Boltzmann Transport Theory, otherwise known as the Radiative Transport Equation, was used to describe mathematically the movement of a photon in turbid tissue. The equation for the radiative transport equation was initially used by Chandrasekhar, and is shown in Equation 3.21 [108].

$$\frac{dL(\mathbf{r}, \hat{\mathbf{s}})}{ds} = -(\mu_t)L(\mathbf{r}, \hat{\mathbf{s}}) + \frac{\mu_t}{4\pi} \int_{4\pi} p(\hat{\mathbf{s}}, \hat{\mathbf{s}}') L(\mathbf{r}, \hat{\mathbf{s}}') d\omega'$$

Equation 3.21

In Equation 3.21 ω is the solid angle, $L(\mathbf{r}, \mathbf{s})$ is the radiance which is confined within the solid angle, s is the direction in which the radiance is moving, and $\mathbf{r}$ is the position vector

The first part of this equations represents the loss of radiance as a result of absorption and scattering, while the second represents the increase in radiance due to due to scattering from all other directions (s'). The radiance is held in the solid angle, while the probability function for scattering is represented by $p(s, s')$, and μ_a and μ_s represent the amount of photons which have been scattered and absorbed. The solid angle integration of the phase function is described by the following equation:

$$\int_{4\pi} p(\hat{\mathbf{s}}, \hat{\mathbf{s}}') d\omega = 4\pi \frac{\mu_s}{\mu_t}$$

Equation 3.22

The integrated radiance at the solid angle represents an important part of the laser-tissue photothermal process.

The Boltzmann Transport equation is applicable in situations where absorption and scattering is somewhat balanced, similar to biological tissue. This mathematical equation is rigorous but is generally suited to only one dimensional models of light-tissue interaction.

A solution can only be derived in simple one dimensional geometries, typically using the Kubelka-Munk method, however as the skin is not a homogenous, simple geometry this method will not be discussed further. As there is no solution in more complex geometries, the distribution of light of a specific wavelength in the radiative transport equation can be calculated using numerical methods. These numerical methods include the Lambert Beer law, which is applied when absorption is heavily dominant over scattering, whereas when scattering strongly dominates absorption, the Diffusion Theory can be applied. When there is no dominance of scattering or absorption, the radiative transport theory can be solved numerically on a computer, with two examples being the discrete ordinate or S_n method and the Monte-Carlo method.

These simple analytical methods will now be briefly described, followed by the numerical methods with an emphasis on the Monte-Carlo method, as this will be the method used later in the thesis when creating a computation model for Intense Pulsed Light home-use devices and the company radiofrequency device.

3.5.1 Simple Analytical Methods

Lambert-Beer Law

In mediums where absorption is heavily dominant over scattering, the Lambert-Beer Law can be used to measure light transport. There are two equations for the Lambert-Beer law, one for one dimensional geometries, and one for two dimensional geometries. As the profile of a laser beam requires a two dimensional geometry, this is the equation which will be given in Equation 3.23 and will be discussed.

$$I(z, r) = I_0 e^{\left(\frac{-2r^2}{w^2} - (\mu_a + \mu_s)z\right)}$$

Equation 3.23

In Equation 3.23 (z,r) is the irradiance at a specific point, and w is the radius of the laser beam

This is most suitable to situations where light travels through a homogenous medium with high absorption rates, and low rates of scattering, and can be used in one- and two-dimensional models. As per **Error! Reference source not found.**, this law describes the attenuation curve which occurs when absorption is much stronger than scattering. Examples of this would be with wavelengths below 300nm and above 1500nm, but is generally inaccurate within the scope for laser therapeutics [63].

Diffusion Approximation Theory

When scattering is much stronger than absorption, the appropriate method to describe the transport of photons in such a medium is the Diffusion Approximation Theory. The propagation of light is assessed based on the photon density gradient within the medium. Typically, for two and three dimensional geometries, this must be solved via a numerical code.

$$L(r,s) = \frac{1}{4\pi} \int_{4\pi} L(r,s) d\omega + \frac{3}{4\pi} \int_{4\pi} L(r,s) s \cdot s d\omega$$

Equation 3.24

In Equation 3.24, the first part of the right hand shows the isotropic scattering, and the second part represents the forward peak compensation.

This is most appropriate to use in highly scattering tissue over highly absorbing, and for tissues with simple geometries without boundaries. It has been shown to give unreliable results at borders and boundaries of layers, and therefore would not be suitable for use in modelling many light-tissue interactions in skin.

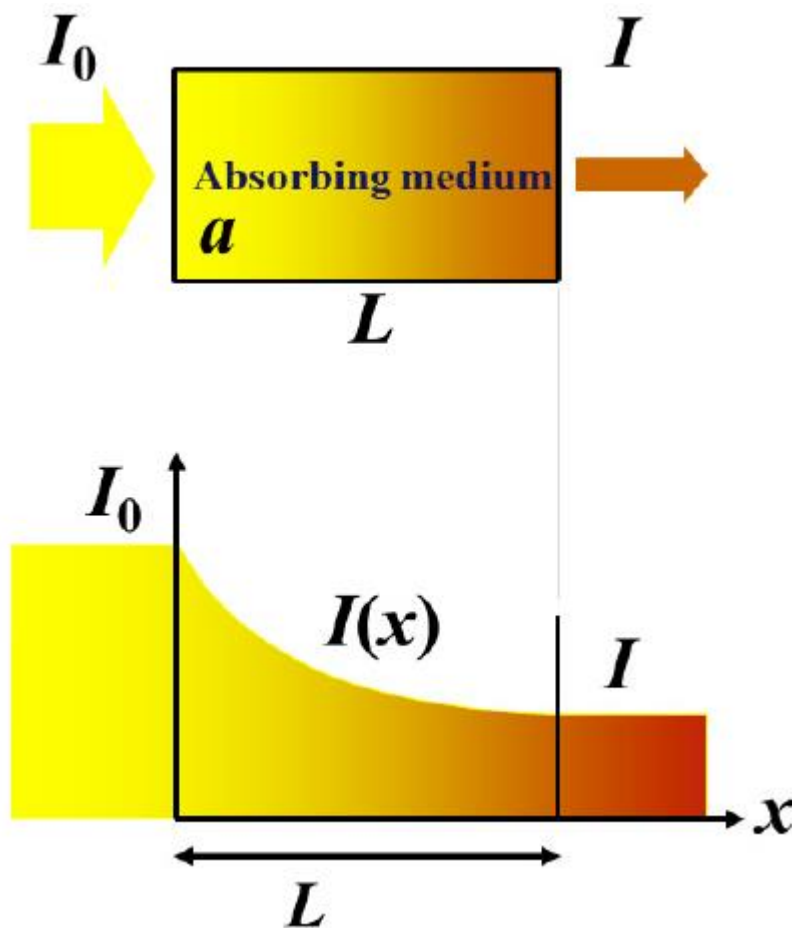


Figure 3.13 - The absorption of light as it travels through a medium according to Lambert-Beer Law [109].

3.5.2 Numerical Methods

Discrete Ordinate Method

One numerical method for modelling a photons' movement through a medium is the Discrete Ordinate Method, also known as the S_n method. This method is most appropriate when presenting tissue as a plane parallel medium and the light is a plane wave. This method involves transforming the radiative transport equation into a matrix differential equation. It can be solved using computer programs which will determine the scattering angle and radiance in the target area, which produces the pattern of light. An example of this, which is given in Equation 3.25, would be Lengendre polynomial expansion of scattering phase function:

$$\frac{\partial}{\partial \tau} \begin{bmatrix} I_1 \\ I_2 \\ - \\ - \\ I_n \end{bmatrix} + \begin{bmatrix} S_{11} S_{12} \cdots \\ S_{21} S_{22} \cdots \\ - \\ - \\ S_{n1} S_{n2} \cdots \end{bmatrix} \begin{bmatrix} I_1 \\ I_2 \\ - \\ - \\ I_n \end{bmatrix} = \begin{bmatrix} B_1 \\ B_2 \\ - \\ - \\ B_n \end{bmatrix} e^{(-t)}$$

Equation 3.25

In Equation 3.25, τ is the optical depth.

As the method cannot be applied accurately for a forward directed phase function, it is not suitable for use when investigating laser-tissue interactions in human skin.

Monte Carlo Method

Another model which aims to describe the movement of photons in tissue is the Monte Carlo Model, a computational method which follows the path of each proton when entering tissue and states the likelihood of the proton being absorbed, scattered or reflected. It is based on work conducted on neutron transport in nuclear reactors by Cashwell & Everett [110], who used a weighting method which was later used by Wilson & Adam in simulations of laser-tissue interactions. It imitates photon transport by calculating each individual photons history by probability of the multiple interactions which could occur. The Monte Carlo method allows for complicated mediums to be modelled in a relatively simple manner, with more accuracy than other options near boundaries. The model takes a

lot of time to run due to the individual photon runs it has to make – while the number of photons can be reduced, this reduces the accuracy of results [63].

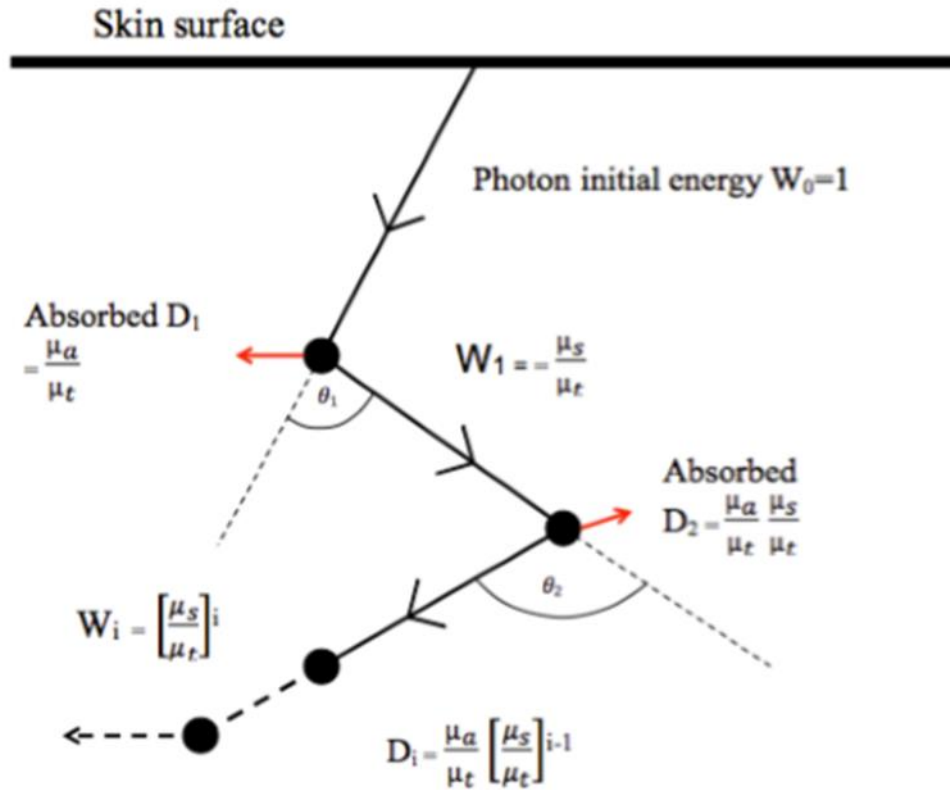


Figure 3.14 - Illustration of the movement of photons in human skin according to the weighting method [66].

A basic description of how Monte Carlo simulations work will be given here. A specific weight is given to each photon in the simulation, and depending on if the simulation is for a collimated beam of laser light or diffuse irradiance, the photon will be launched downwards or a random direction will be chosen based on all directions the photon could travel in. The photon has a specific step size which is also randomly chosen. The direction in which the photon travels after it has been launch will be determined on scattering angles which is based on the Henyey-Greenstein function, discussed earlier in this chapter. When the photon completes its “step”, the photon may be absorbed, scattered, or both. If the photon is just scattered, it takes another step. If the photon is absorbed, no energy is lost and no further steps are made. In a situation where it is both absorbed and scattered, at each step the photon takes, a little energy is lost before it takes its next step, and when it

reaches the next step, a little energy is lost for absorption and so on, until the photon has lost all of its energy. When the photon runs out of energy, another photon is released, and the process begins again. This is the weighting method, mentioned in the previous paragraph, and this method of photon movement is dependent on the tissue properties, and is illustrated in Figure 3.14. Typically, this method has been found to have better accuracy than when the photon is simply absorbed or scattered, and also requires fewer photons input to receive valid results.

A Monte Carlo method is suitable for modelling the interaction of light and tissue in human skin as due to the probabilistic nature of the method, when enough simulations of the photon movement into skin are completed, it can give a valid representation of photon movement in human tissue, rather than directly solving the radiative transport equation. This thesis will involve the use of a Monte-Carlo program named TODDY, which uses the weighting method described above in its simulations.

3.6 Thermal Heat Transfer in Biological Tissue

Detailed models of how heat travels through biological tissues have been created, some of which are used in order to enhance the efficiency of the use of lasers in surgery and cosmetic treatments. How quickly heat is transferred within biological media will be affected by the structure of the tissues. The heat of transfer between the boundaries of various parts of tissues is continuous, and heat balance can be reached if the rate of heat gained and heat lost is the same. If these are out of balance, the extra heat is either stored leading to an increase in local temperature, or removed leading to a reduction in the local temperature. The heat balance can be affected by how quickly heat is deposited into the tissue, the tissue it is being deposited into and its function and organisation, and the boundaries of the tissue.

3.6.1 Basic Principles of Heat Transfer

Calculating the change in temperature in skin is not a straightforward task, as there are three thermal transfer mechanisms are involved, along with metabolic activity and blood perfusion, and all of these should be included in the solution. The three mechanisms – conduction, convection and radiation [111] – will be further described in this section.

Conduction

The transfer of thermal energy as a result of a temperature gradient via a solid or liquid channel is known as conduction of heat. This mechanism of heat transfer occurs with systems which are in direct contact, and takes place within the atoms and molecules of the medium, rather than required movement on a larger scale. In solids, this occurs via the vibration of lattices and the movement of electrons within the solid, whereas within liquids which are not moving, the vibrations, rotations and translational movement of molecules lead to collisions which result in heat transfer between areas with higher temperatures to those of lower temperatures. This type of heat transference is determined by Fourier's law of heat conduction, given in Equation 3.26, which can determine heat conduction at a specific point (r) [112].

$$\frac{1}{\alpha} \frac{\partial T(r, t)}{\partial t} = \nabla^2 T(r, t) + \frac{H}{k}$$

Equation 3.26

In this equation H is the heat source or sink term, in W.m^{-3} . This is determined during the radiative transport problem in tissue, and will affect the local temperature changes. α is the

thermal diffusivity of the tissue's thermal properties, in $\text{m}^2.\text{s}^{-1}$, determined by Equation 3.27.

$$\alpha = \frac{k}{\rho C}$$

Equation 3.27

The thermal conductivity is a function of the microscopic structure, and typically reliant on temperature, with values higher in solids but lower in gases. Heat conduction is usually the basis for mathematical models which calculate the transient and steady state temperature changes as a result of laser irradiation [112]. This type of heat transfer in the skin would typically occur between layer of the epidermis, and between the dermis and the blood vessels within it.

Convection

The transfer of heat via a liquid as a result of movement of the entirety of the fluid is known as convection. This mechanism is important when assessing the transfer of thermal energy between a moving fluid and a solid, such as between blood and skin, and is relevant in the mechanisms behind photodynamic therapy, and thermal energy transfer following laser irradiation. When convection occurs, there are four mechanisms which take place simultaneously. These are heat being conducted from the surface of the solid to the particles of the fluid directly adjacent to it. The energy which has been conducted to the fluid particles is absorbed and stored, resulting in an increase in the energy of the particles; these particles then move to areas with lower temperatures, and as a result mix with particles there and transfer some of the energy which has been stored and the movement of the fluid as a whole resulting in the transport of energy. Convection can be conducted in two forms, free or forced. Forced convection is the movement of fluid caused by an external force such as a fan or pump, for example how blood is pumped around the body via the heart. In comparison, free or natural convection is the movement of fluid as a result of differences in density of the fluid, which cause changes in the fluid temperature. This type of thermal transfer occurs when vapour is emitted from irradiated tissue.

When modelling for thermal transfer via convection, the boundary layer between the fluid and a solid surface must be considered – Newton's law for free and forced convection

calculates the heat flow (f) between a large volume of fluid and a solid boundary, as demonstrated in Equation 3.28.

$$f = h(T_2 - T_1)$$

Equation 3.28

Here, the temperatures of the solid and fluids are represented by T_1 & T_2 , while h is the proportionality constant, which represents the convective heat transfer coefficient, and is a higher value when calculating forced convection in comparison to free convection.

When modelling heat convection in biological tissues, the effect of blood flow and supply to tissue must be considered, as it is an important factor to the body's thermoregulatory system. The heterogeneity of these tissues which contain aspects which can affect thermal transfer, such as the cells and blood vessels which may be not be organised in a predictable manner makes the task incredibly complex and challenging. This is complicated further by the fact that blood flow will change depending on which part of the body the tissue is located and the time. Typically, Fick's principle is used to calculate the effect of blood flow in biological tissue, shown in Equation 3.29. The principle states that "the amount of substance taken up by an organ (or control volume) per unit time is equal to arterial level of substance minus the venous level times the rate of blood flow."

$$q_b = \rho_b c_b w_b (T_{art} - T_{ven}) [W]$$

Equation 3.29

In Equation 3.29, w_b represents the tissue average volumetric blood perfusion rate. T_{ven} is the venous blood temperature as it leaves the tissue and is a function of the tissue temperature at the point of exit. Heat transfer from blood vessels is a better way of cooling a specific area in comparison to convection.

Radiation

The transfer of thermal energy via radiation is conducted between two systems with different temperatures which are not in contact. A medium is not required for this form of heat transfer as it is conducted through electromagnetic waves between the wavelength

bands of 0.1 μm and 10 μm . Any heat emitted by a body via radiation is lost from the energy of the body from which it is emitted. A perfect example of a radiating body is known as a blackbody, which emits the maximum amount of energy possible for any wavelength appropriate to the temperature of the blackbody. The blackbody will also not reflect any energy, and will only absorb it. The emissions of a blackbody are explained by Planck's law, as shown in Equation 3.30.

$$W_b(\lambda, T) = K_1 \lambda^{-5} / [\exp(k_2 / \lambda T) - 1] \quad [\text{W}/\text{m}^2 \cdot \mu\text{m}] \quad []$$

Equation 3.30

λ represents the wavelength and T represents the absolute temperature. The value of K_1 is $3.743 \times 10^8 [\text{W} \cdot (\mu\text{m})^4/\text{m}^2]$, and the value of K_2 is $1.4387 \times 10^4 [\mu\text{m} \cdot \text{K}]$. To calculate the total energy emitted by a blackbody, E_b , can be determined by integrating $W_b(\lambda, T)$ across the whole emission spectrum, which is calculated by the Stefan-Boltzmann law, shown in Equation 3.31.

$$E_b = \int_0^\infty W_b(\lambda, T) d\lambda = \sigma T^4$$

Equation 3.31

The Stefan-Boltzmann constant is $\sigma = 5.67 \times 10^{-8} [\text{W}/\text{m}^2 \cdot \text{K}^4]$. However, bodies which actually emit radiation will not be as productive as a blackbody, emitting much less energy. A non-blackbody will only have monochromatic emissive power, $W(\lambda, T)$, which offers very little in comparison to the emissive power of the blackbody $W_b(\lambda, T)$, as demonstrated in Equation 3.32.

$$W(\lambda, T) = \epsilon_\lambda W_b(\lambda, T)$$

Equation 3.32

In this equation, $\epsilon_\lambda \leq 1.0$ represents the thermal emissions of the actual body. When an emitter is imperfect, the radiation wavelength has no effect on the thermal emissivity of the body, and is known as a grey body, with its emissive power defined in Equation 3.33.

$$E(T) = \epsilon \sigma T^4$$

Equation 3.33

In Equation 3.33, ϵ is split across the spectrum for thermal radiation, weighted by the power distribution of the monochromatic emissions $W_b(\lambda, T)$. The grey body has a high rate of thermal energy radiation at 97%, similar to the human body which is also efficient in its emissions of thermal energy [112]. Typically in skin, radiation has an effect at the stratum corneum, but has little effect on heat transfer on chromophores deeper in the skin.

3.6.2 Calculating Thermal Transfer

When creating a mathematical model of thermal transfer within biological tissues, there are various factors which must be considered. This includes the structure of the tissue, how much heat the tissue can hold, the physical characteristic of the tissues, especially those relating to heat, such as how temperature and heat transfer changes depending on time and the location of the tissue, its conductivity, and the density of the tissue. One of fundamental parts of every thermal model is the principle of the conservation of energy within tissue volumes. Equation 3.34 demonstrates the energy balances which is used as a control volume:

$$\dot{Q}_{gain} = \dot{Q}_{storage} + \dot{Q}_{loss} + W$$

Equation 3.34

$\dot{Q}_{gain}$ is the rate of heat which has been gained, e.g. via laser irradiation. $\dot{Q}_{storage}$ represents the heat which is stored within the tissues and fluids of the body. $\dot{Q}_{loss}$ is the amount of heat lost from the tissues via conduction and convection or exchange with the external environment and W represents how much work is performed by the tissue itself; however this typically has little influence on the heat transfer within tissues as a result of laser irradiation.

The bioheat transfer equation, shown in Equation 3.35, introduced by Pennes in 1948 is the standard form of energy balance, and is used in models depicting laser-tissue interactions.

$$\rho C \frac{\partial T(r, t)}{\partial t} = \nabla(k \nabla T(r, t)) + Q_b + Q_m + Q_{\text{ext}}$$

Equation 3.35

In Equation 3.35, ρ represents the product of density in kg.m^{-3} , c represents specific heat of tissue in $\text{J.kg}^{-1}.\text{K}^{-1}$, k is the thermal conductivity in $\text{W.m}^{-1}.\text{K}^{-1}$, Q_b is the volumetric blood perfusion rate, Q_m is the metabolic heat production rate, and Q_{ext} is the external heating, or sink term, rate.

When solving the bioheat transfer equation, the temperature of the entire tissue must be known, and relevant boundary conditions must be used in order to account for the loss of heat via convection and the evaporation of water on the surface level. The boundary conditions usually required for the solution of the bioheat transfer equation are a constant surface temperature of each boundary, known as the prescribed temperature, and a constant rate of heat transfer across each boundary, known as the prescribed heat exchange. This may be more complex in situations where tissue is being ablated, or if the boundary is between two solid forms which are not completely in contact. If the parameters used when solving the equation are dimensionless, it can make the solution considerably less complex by reducing it into a few tables, meaning that if you subsequently solve for a different tissue or condition, there is no need to solve the equation again. The bioheat transfer equation does not take into account the body's thermoregulatory functions or thermal cautery caused by laser irradiation as it focuses on the immediate effects of thermal energy transfer.

When creating a mathematical model for laser-tissue interaction, there are three main factors which must be considered. The first is the how the laser irradiation has been dispensed across the tissue is. Then the resultant change in temperature following laser irradiation is calculated using the bioheat transfer equation. Following this, the thermal damage the laser irradiation has led to can be approximated based on how the temperature has changed across the tissue and how quickly this occur – this can be done using the Arrhenius Damage Integral, which was described in chapter 3.

The Arrhenius damage integral is used to approximate the amount of damage to tissue caused by changes in temperature. If the calculated response is more than or equal to 1, this indicates the tissue has been irreversibly damaged by the temperature [84].

3.6.1 Numerical & Computational Modelling Heat Transfer in Biological Mediums

Various models have been developed to attempt to accurately represent heat transfer in laser-tissue interactions, taking into account the previously mentioned factors. There are two different numerical solutions the model is based on – the Finite Element Method and the Finite Difference Method.

Finite Element Method

The Finite Element method is based on the diffusion equation, and splits the area being assessed into separate elements. Using the elements, the solution is calculated using polynomials, which are put into a separate equation, which creates an overall equation which can be solved. This is incredibly complex, and it is appropriate for complicated and heterogeneous mediums. However many packages which offer a Finite Element Method program are difficult to amend to work with something outside of its set application, making it unsuitable for use in this thesis.

Finite Difference Method

The Finite Difference Method uses the differential diffusion equation, but replaces the derivatives based on the Taylor series equation, meaning forward, backward and central differences can become equations which may be solved assuming the initial and boundary conditions are known. Two forms of this method are available, the explicit and implicit method. The explicit method calculates the temperature at each point in time of a specific area based on known temperatures at different times. It takes a long computational time to calculate due to the small differences in time at each step. The implicit method calculates the temperature of a specific area at a chosen time based on the known temperature of nearby areas at the same time. This method can take a lot of time to calculate computationally for multidimensional models.

The implicit finite difference method and explicit finite difference method can be combined into one, which is called the Alternating Direction Implicit (ADI) method. This method involves one derivative being calculated implicitly while the others are calculated explicitly. This is more complex to calculate than the implicit method, but it reduces the amount of computational time taken without becoming unstable. This can be done due to implicitly expressing derivatives of one space direction while explicitly expressing other directions. This creates a set of equations which can be displayed in matrix form, as shown in Equation 3.36.

$$A \cdot X = Y$$

Equation 3.36

In Equation 3.36, X & Y are vectors, and A is a tridiagonal matrix

When the rows of the matrix have been calculated, the direction is altered due to changing the implicit angle. The final space is expressed explicitly and two other implicitly, meaning the equation can ultimately be solved.

This method will be used with the results from the Monte Carlo program TODDY when assessing the potential heat changes in skin when using a variety of home use IPL devices for hair removal.

Conclusion

This chapter has given an in depth overview of how light and electromagnetic fields interact with biological tissues, how photons behave in tissue, and the types of tissue responses which are typically seen during laser interactions with skin.

Furthermore, the types of non-ablative radiofrequency available in salons were discussed due to the later focus of the thesis being on a salon based RF device, as were the typical response seen in skin when they are treated by non-ablative RF devices. Following this, the dielectric properties of skin were considered, and a table of dielectric properties for skin and fat were provided, based on work by Gabriel et al [107], [105].

The discussion then moved onto the movement of photons in biological tissues, and the different methods which are used to calculate how photons are likely to transport through skin, including analytical and numerical methods. Of particular importance was the Monte Carlo method, as this is the chosen method to computationally assess photon movement when an IPL is applied to skin later in the thesis. The chosen program is named TODDY.

Finally, an overview of thermal heat transfer in biological tissues was given, along with a selection of numerical and computational methods to calculate this. A brief overview of the Finite Element and Difference methods were discussed. The ADI method, a form of Finite Difference method, is the chosen methods to assess heat transfer in this thesis - the ADI method will assess if the chosen IPL devices are theoretically capable of sufficiently heating hair follicles to lead to hair reduction, without damaging surrounding structures,

while the boundary element method will be used to assess if the chosen radiofrequency device can effectively heat collagen or subcutaneous fat to treat skin laxity and cellulite.

The next chapter will be a market review, assessing the available scientific literature for home-use devices and salon-based radiofrequency devices. The purpose of this is to see how many peer reviewed articles are available for these products, if they have been independently assessed, and to identify any gaps in the literature.

Chapter 4 - A Literature Review of Home-Use Intense Pulsed Laser Devices

Introduction

Home use light and laser based devices are products which consumers can buy to use in their own home without professional guidance. There are a number of home-use devices available on the market. The most popular is those for hair removal – these consist of Intense Pulsed Light (IPL) devices or diode lasers. Other home-use devices include blue light therapy for acne, LED treatment for hair loss, psoriasis and skin rejuvenation, and some of the newer devices include tattoo removal or vaginal rejuvenation.

These types of devices are very profitable, earning \$1.9 billion worldwide in 2015, an 11% growth in comparison to the previous year. However, Home-Use Devices only represent 2% of the total cosmetics market, valued at \$181 billion, and therefore there is much more room for growth in this sector. Currently, these devices are most popular in the US, which represents 37% of the home-use market, followed by Asia comprising 36% of the market. 19% of the market is covered by Europe, and the remaining 8% is covered by the rest of the world.

Despite the devices popularity in the retail and cosmetic market, very little scientific evidence has been published regarding these devices. Therefore there is not much work available demonstrating that these devices can perform to the same standard as the manufacturers claim. The evidence which has been published, there are a number of limitations to the research, which predominantly has small sample sizes with results only demonstrated in the short term.

Similarly, there is a lack of scientific evidence available for radiofrequency use in salons. Many published works are written from a marketing standpoint rather than from a scientific one, with little explanation for the choice of parameters chosen.

In this chapter, the limited work which has already been published of various home-use IPL devices will be reviewed and discussed. Please note that the devices which are named in this chapter, as they have been named in their publications, do not necessarily reflect the devices which will be assessed in chapters 5 and 6.

4.1 Literature Review

In many cultures across the world people wish to remove their unwanted hair for cosmetic purposes [5], with the professional hair removal business earning approximately US \$244 million per year [113]. Typically, methods for hair removal involve waxing, shaving, plucking, and electrolysis, however these are only short-term solutions and are time consuming partially due to how often they need to be repeated [5]. In 2013, the American Society for Aesthetic and Plastic Surgery (ASAPS) reported laser and light-based hair removal as one of the most popular in-office treatments (4). A more long-term solution to hair removal is offered by professional laser and light-based treatments, taking a new approach to hair removal i.e. rather than removing the hair, these devices aim to destroy the hair follicle itself [114]. These treatments have recently become more popular [5]; in 2013, the American Society for Aesthetic and Plastic Surgery reported that one of the most popular treatments conducted in office settings was for hair reduction [4].

A wide range of home-use laser and IPL hair removal devices is available to consumers, which can make it difficult to decide which product is best suited to the individual's needs [4]. This is further complicated by the fact that many of these domestic energy based devices (EBDs) do not have published clinical reports or scientific data evidencing that the devices perform as they claim [114]. Of the literature which is available, many of the studies conducted do not provide rigorous clinical evidence [4], and only give short term results, with very few studies offering outcomes beyond six months' post-treatment [113]. The lack of peer-reviewed information also means that in many cases, medical professionals such as dermatologists and GP's are unaware of the home-use devices and may not be able to provide the information that a patient requests [113].

The potential safety issues which may be raised by home-use devices include their electrical safety and potential risks to the user from thermal injury [5], [114]. Human safety is a priority, as lasers and IPL devices for hair removal could result in accidental skin or ocular damage to the user and possibly others [5]. Studies have shown that the generally observed negative effects of these devices include pain during use, erythema and oedema. The less common, more serious adverse effects can involve burns, blistering or crusting of the skin which could lead to scarring and pigmentation changes [6]. If the product is used incorrectly, for example use on a skin type outside of the safe range, on tattoos, or on moles, this can lead to burns [5]. Manufacturers have reduced potential occurrences of adverse effects by placing warning labels over switches, placing pin codes to activate devices in the instruction

manual, and secure mechanical and electrical safety systems. As with all optical energy devices, there is also a risk of temporary or permanent ocular damage, especially if the eye is exposed to laser or IPL [6], [114]. This damage can lead to blind spots or glaucoma, and if the wavelengths of light are below 400 nm or above 750 nm, the user could suffer corneal damage or cataracts [113].

As the home-use devices usually have significantly lower fluences than their professional counterparts, it is believed that the number of potential side effects is reduced [6]. However, many devices are still fitted with safety features in order to further minimise the risks of the device accidentally or intentionally injuring a user. These design features include filters which cut off hazardous wavelengths below 450 nm [114] and mechanical sensors to ensure the device is in full contact with the skin [5], both in order to reduce the risk of ocular damage to the user, as well as sensors which detect the skin tone of the user to decrease the likelihood of burns. These devices also come with user manuals, which detail the precautions which should be followed in order to use the product correctly, however, it is not certain that the consumer will read this [113].

The consumers who will receive optimum results from home-use laser and IPL devices are those with pale skin, no hormonal imbalances and have thick, dark terminal hairs [6]. Devices which have been Food and Drug Administration (FDA)-cleared for sale offer “permanent hair reduction”, meaning that they do not permanently remove all hair in the treatment area [4]; often, only 15% to 30% of hair follicles of treated hairs are permanently reduced. This most probably is achieved by destroying the cells in the germinative layer of the hair follicle bulge [5]. When using laser or IPL devices, ideally the highest fluence which does not result in adverse effects should be used [6] as it has been shown that a fluence of only 5 J/cm² can be used to stop hair regrowth, whereas fluences below 5 J/cm² will only delay regrowth [113].

Professional laser and IPL devices have a wavelength range between 500 nm to 1100 nm, being in the red or infrared part of the wavelength spectrum [6]. IPL devices mostly use a xenon polychromatic broadband flashlamp which creates light which operates in this wavelength band [5], whereas home-use laser devices are pulsed diode lasers with a nominal wavelength range of 800 nm to 810 nm [113]. The energy distribution from an IPL can be through either ‘free discharge’, which is a fixed pulse duration with a non-fixed amount of energy, or ‘partial discharge’, which provides a set energy output which is determined based

on the chromophore it is targeting [4]. Research has found that the fluence and wavelengths which IPLs operate at are inconsistent between pulses, meaning that resulting clinical efficacy can be variable [5].

4.1.1 Tria Laser (Tria Beauty Inc, Dublin, CA, USA)

The Tria Laser is a home-use hand-held pulsed diode hair removal laser. According to the manufacturer, the laser produces a wavelength of 810 nm, has high, medium, and low energy settings, with fluences of 22 J/cm², 17.5 J/cm² and 13 J/cm² respectively, and has a recommended retail price (RRP) of £299 [115]. The pulse durations are between 300 ms and 600 ms, with a spot size diameter of 1 cm. It is classified as a Class I laser by the manufacturer, therefore being considered eye-safe by the FDA [116]. In our literature search, we found two peer-reviewed papers assessing the efficacy of the Tria laser.

One study on the Tria Hair Removal Laser home-use laser was intended to assess the safety and efficacy of the product on suitable hair colour and Fitzpatrick skin types, but also the safety of the device on non-suitable hair colour and Fitzpatrick skin types. For the suitable user group of 70 with skin types I-IV and dark brown or black hair, three treatments over 9 weeks were self-administered, and had follow-up appointments for 12 months after the final treatment. For the non-suitable user group of 44 with skin types V-VI, or light coloured hair, received one single laser pulse by a member of staff at the highest fluence setting. The hair reduction in the appropriate user group peaked at an average of 69.8% compared to baseline 3 weeks after the second treatment, and remained significant at 32.7% compared to baseline 12 months after the third treatment [116]. Another controlled study by Wheeland in 2012 [117] used the Tria Laser on the lower leg of 13 subjects who received 8 monthly treatments, with follow up appointments up to 12 months after the final treatment. At the highest fluence, there was an average hair reduction of 73% compared to baseline one month after the final treatment when the highest setting of the laser was used, and 47% when using the lowest setting. 12 months after the final treatments, an average hair reduction of 62% was recorded compared to baseline using the highest fluence, and 44% at the lowest fluence [117].

The side effects of the Tria Laser in one study for appropriate users were mainly erythema in 33% of subjects, however, other self-reported adverse effects included skin abrasion, a burning sensation in the treatment area and one case of folliculitis, with only 3 subjects reporting more than one adverse effect of the treatment. 42% of subjects described the pain during application of the laser as slight, and only 1 subject dropped out of the study due to

pain [116]. A later study on just appropriate users also found that mild erythema occurred in all subjects who used the highest setting and almost half of those who used the medium setting. 8% of patients who used the highest setting also experienced mild oedema [117].

In a group of inappropriate users, the adverse effects noted included blisters in 26.2% of subjects, which one healed left minor hypopigmentation, hyperpigmentation, or induration in the area of the laser treatment. All subjects in this group found the application of the laser somewhat painful, with only 26% of subjects reporting their pain as slight, while 17% considered it to be severe [116]. Another study had one participant of 13 subjects who met the criteria for safe usage of the laser drop out due to pain [117].

With regard to safety features, one study gave subjects the opportunity to decide if they would be a suitable user for the laser, based on the packaging and instruction manual alone, and found 18% of those who were not suitable, stated they would be a suitable user for the laser [116]. While this is not large percentage, it does show that these products may be used innocently by those with a skin type or hair colour which is not suitable and safety features on the device itself could ensure inappropriate usage.

4.1.2 P+G Diode Laser Prototype (Braun AG, Kronberg, Germany)

A randomised controlled trial was conducted using an 810 nm diode laser prototype produced by Braun AG to assess hair reduction, thickness and colour changes following treatment. The laser has a 100 ms pulse duration with a 1.5 cm² spot size and energy outputs of either 5 J/cm² or 6.4 J/cm². 36 healthy females with Fitzpatrick skin types I-IV took part and received either no treatment or 8 weekly self-administered treatments on the axillae. The results found that after 8 weeks of usage, the average hair reduction was 59% and remained as such for 1 week after the final treatment. However, 1 month after the final treatment, the hair counts had returned to baseline numbers and by the 2 and 3 month follow ups, hair growth was on average 29% higher than it had been at baseline. Similarly, with hair thickness, this reduced by an average of 38% compared to baseline up to one week after the final treatment, and increased by 7% compared to baseline 3 months after the last treatment. Hair colour had reduced by 5% one month after the final treatment, but had returned to baseline by the 3 month follow up [118].

With respect to side effects, the study found that 40% of subjects experienced mild transient erythema, 28% found the laser treatment to be uncomfortable and 25% felt a burning

sensation during and shortly following treatments [118]. This particular study shows that when home-use treatments are not maintained, the results are not permanent and hair growth can often return to the same patterns as prior to treatments, or as with this study, hair growth may exceed what it had been prior to treatment.

4.1.3 iPulse Personal (CyDen Ltd, Swansea, UK)

The iPulse Personal was a home use IPL system offering permanent hair reduction. It emits wavelengths between 530 and 1200nm, with fluences between 7 and 11 J/cm², distributing energy evenly. The pulse durations are between 15 and 60ms with 6 second intervals between pulses, and the device has a spot size of 3cm². The device requires the use of a clear ultrasound gel which it comes supplied with [119], [120].

In a controlled clinical study of the iPulse Personal device, ten subjects with Fitzpatrick skin types III to IV had their axillae treated weekly for four weeks. Hair counts were taken at baseline, at the final treatment, then at 2 weeks and at six months following the final treatment. The results showed a peak reduction of 92% compared to baseline two weeks following the final treatment, and an 87% reduction 6 months following the final treatment, with an overall average hair reduction of 70% [120]. In a similar study, 29 subjects with Fitzpatrick skin types I-III took part in 3 weekly treatments with the iPulse Personal in a clinical setting, with photos taken at each treatment and at one month and 6 months following the final treatment. At one month post-treatment, the overall average hair reduction compared to baseline was 47%, and was significant in all but four subjects. Results in the 6 month follow up photos showed an average hair reduction of 41% compared to baseline, and 84% of subjects had significant hair reduction in the treatment areas. However, some subjects reported an increase in the number of hairs in the treatment areas after the initial treatments, with a total of four participants showing an increased hair count at 6 months after the final treatment [119].

Some side effects have been reported in the studies on the iPulse Personal. The study conducted by Trelles et al. [120] noted that subjects felt a small amount of pain during treatment, comparing it to a flick by a rubber band. They also stated that subjects experienced perifollicular oedema and reactive erythema. Another study had subjects report pain on a scale of 0-10, and found the average score was between 1.5 and 1.7, but one patient recorded their pain as 8 during one treatment, and one rated their pain as between 6 and 7 at each of

their treatments. The same study only noted mild erythema as a side effect during treatments [119].

The safety features of the iPulse Personal include four contact points around the window of the device to ensure that the device is in full contact with the skin before it can be fired [119]. The device also comes with a skin tone chart for consumers to check their Fitzpatrick skin type, to ensure their skin type is suitable for the device, along with user manuals which contain instructions for use and warning labels, advising users of the danger of using the device incorrectly. The iPulse Personal has also been confirmed as eye-safe according to the British Standards for protection against intense light sources used on humans and animals for cosmetic and medical applications [119].

It is worth noting that the iPulse Personal is not the latest model for iPulse, and the current systems, the SmoothSkin Bare & Gold, do not have the same specifications, however there are currently no peer-reviewed studies available for the latest devices.

4.1.4 Spa Touch, (Radiancey Corp., Orangburg, NY, USA)

The Spa Touch is a hair removal IPL home-use device developed by the Radiancey Corporation [121]. The device emits wavelengths between 400 and 1200nm, however the majority of light is between a spectrum of 550 and 800nm. The fluence of the device is up to 10 J/cm², has a pulse duration of 35ms, and has a spot size of 2.2 x 5.5 cm² [121].

A clinical study investigating the effectiveness and safety of the device enrolled 67 subjects with Fitzpatrick skin types I-IV. The patients were given a user manual, shown an instructional video, then shown how to use the device by the investigator before being asked to self-apply the device on two pre-decided treatment sites, and then asked to do the same at a follow up appointment 4 weeks later. Photographs were taken at baseline, at the second treatment, then at 2 and 12 weeks following the final treatment. An independent blinded reviewer assessed the photographs. Results showed a peak average hair reduction of 44.4% compared to baseline 2 weeks after the final treatment, and this dropped to 32.3% 12 weeks following the final treatment [121].

The side effects noted during the clinical studies found that erythema was frequent side effect, with 44% of subjects experiencing it after the second treatment. This was followed by oedema, experienced by 15.5% of subjects after the first treatment. 3 cases of crusting

and of blistering were reported during the experiment, as well as 13 cases of hyperpigmentation and 5 cases of hypopigmentation. All of these side effects had cleared by the final follow up visit, 12 weeks following the final treatment [121].

Contact switches are incorporated onto the device as a safety feature in order to make sure the device is only used when in contact with the user's skin. While this prevents potential damage to the eyes when used correctly, it is still possible that a consumer could attempt to use the device on the eyebrow, and flash the light onto the eye [121].

4.1.5 Silk'n™, (Homeskinovations, Kfar, Saba, Israel)

The Silk'n home-use IPL device emits wavelengths of light between 475 to 1200 nm, has a fluence of up to 5 J/cm², a spot size of 2 x 3 cm (6 cm²), 5 energy settings and an interval of 3.5 seconds between pulses [122], [123]. There have been multiple clinical studies conducted on this device, with four peer-reviewed articles available, which is high in comparison to many other IPL and laser devices currently on the market.

In a randomised, blinded study, 34 subjects received three treatments at 2 week intervals, and a follow up appointment 3 months after the final treatment, with photographs taken at baseline and each appointment. Each treatment area had 50% receive IPL treatment, and 50% remain untreated as a control. The hair counts were conducted by a blinded observer. 2 weeks following the second treatment, the treatment side had an average hair reduction of 84% compared to baseline, and the untreated side had no significant reduction. They found that 3 months following the final treatment, the overall average hair reduction was 84% compared to baseline (4). In another study, 20 subjects with Fitzpatrick skin types I-IV received 6 bi-weekly treatments over 16 weeks. The energy level of the device was determined by skin type, with types I-II receiving the highest level, and type IV receiving the lowest. The treatment areas were photographed at baseline, then at 4 weeks and at 12 weeks following the final treatment. Results showed an average hair reduction of 78% compared to baseline one month after the final treatment, and an average of 72% reduction three months after the final treatment [124].

A smaller study found lower reduction rates; 10 patients with Fitzpatrick skin types I-IV were recruited, receiving 4 to 6 bi-weekly treatments, with the energy levels ranging between 2 and 5, depending on the subject's skin type. There was a 15% overlap between treatments, and one or two passes of the IPL were conducted. Subjects also attending follow-up

appointments at 4 and 12 weeks after the final treatment. Hair counts showed that the average hair reduction compared to baseline was 36.2% at 4 weeks after the final treatment, and only 10.1% at 12 weeks, which was not a statistically significant reduction [123]. However, a slightly larger study of 20 subjects with Fitzpatrick skin types I-IV were asked to conduct 3 self-administered treatments to non-facial areas at 2 week intervals with better long-term results. Photographs were taken at baseline, and at 1, 3, and 6 months after the final treatment. There was a significant reduction in hair growth in all treatment areas compared to an untreated control site, however at one month post treatment, the average reduction was 73.5% on the leg compared to 59% on the arm and 47.8% at axillary or inguinal areas. This pattern continued at 3 and 6 months after the final treatment, with a 61% and 53.6% reduction on the legs compared to 57.8% and 53.6% on the arms, 42.3% & 37.8% on the axillae, and 40.4% & 38.2% on the inguinal regions. There was an overall reduction of 43% six months after the final treatment on all treatment areas, with results suggesting the results are not just short term, as only 10-20% of hair regrew between one month post-treatment and 6 months post-treatment [124].

Side effects were noted in most of these studies; the three studies which did record side effects, all noted that most patients experienced mild erythema. One study [124] noted it in all patients, whereas Alster & Tanzi [124] only found that it occurred in 25% of patients. Oedema was also noted in two studies, one just stated that it occurred within 10 minutes of application of the IPL [122], and the other stated that it occurred in 25% of patients [124]. Mulholland reported in his study that some patients experienced a small amount of discomfort when the IPL was being used [122].

Elm et al [123] hypothesised that as the device allows for control of the energy output, and that the optical energy is low, use of the IPL at home will be safe, even on unsuitable skin types, and effective. In their small-scale study, this seemed to be the case for users with skin types I-IV, however no subjects had a skin type outside of this range. The device is fitted with a sensor which detects the skin tone of the user, and will not fire on an unsuitable skin type [124]. Another safety feature is a sensor which ensures the device is in full contact with the skin before it can be used, meaning that it cannot be accidentally flashed into the user's or others eyes [125]. Alster & Tanzi also showed in their study that the device can be used easily and appropriately by their subjects without any help from the investigator [124].

In 2015, a study was conducted on a more recently released device, the Silk'n Glide. This is a hand-held IPL device, designed so that the user can manoeuvre the device in a similar way to when using a razor, in order to make treatment faster than with the traditional stamp method. It provides an energy output of up to 5 J/cm² and emits lights between wavelengths of 475 and 1200nm. Fifteen subjects with Fitzpatrick skin types I-IV took part in a clinical trial for unwanted facial hair. Each participant had 6 bi-weekly supervised self-administered treatments, then attended two follow-up appointments at one and three months after the final treatment. The treatments were applied to the face below the cheekbone, and energy settings were decided based on skin type and reactions to test pulses [126].

Results showed that one month after the final treatment, there was an average decrease in hair counts of 83.3%, which dropped to 78.1% three months after the final treatment. An overall significant decrease in the number of hairs compared to baseline throughout the study. The only side effects noted in the study was mild perifollicular erythema and oedema, which occurred in all subjects and cleared within one day of treatment [126].

4.1.6 Me (Syneron Medical Ltd., Yokneam, Israel)

The me system is a combination system that uses both IPL and Radiofrequency technology for hair removal. The device emits wavelengths between 550 to 1,200 nm, with a fluence between 2-4 J/cm², and a Radiofrequency pulse at the same time at 6.78 MHz with 2W of power. The pulse duration is 6 ms, and the repetition rate ranges from 0.5 Hz at 4 J/cm² to 1 Hz at 2 J/cm² [127].

A study of 94 subjects investigated the ability of the me device to reduce hair counts on all Fitzpatrick skin types; 85% of subjects had skin types I-IV, and 15% had skin types V-VI. Each subject had 7 weekly self-administered treatments of 3-4 passes in 2 treatment areas, and an additional 3 monthly treatments in one of the treatment areas. The energy setting was decided by the subject; if they found the higher setting bearable, this was used, but if not, a lower setting was used. In total, 334 non-facial and 15 facial areas were treated, and hair counts were conducted by independent third party evaluators [127].

One month following the initial treatments, hair counts had reduced by 54.1% on the non-maintenance side and 56.5% on the maintenance side of the leg treatment areas on average compared to baseline. At 3 months following the initial treatments, hair reduction was at 58% for the maintenance side, but 43% on the non-maintenance side. Overall, at least a 40%

reduction of hair compared to baseline was seen at all post-treatment visits for both the maintenance and non-maintenance sides, and there was a significant difference between maintenance and non-maintenance sides at 3 months post initial treatments [127].

With regard to adverse effects, the study found that a small number of subjects found the treatment painful, with 10% reporting mild pain and 4% reporting moderate pain, and 86% of patients reported no pain. Two subjects, with skin types III and V, considered their axillae treatments to be severely painful. In 4.6% of subjects, transient erythema was noted, 1% experienced oedema, 1% reported pruritus, and one subject reported mild blistering in the axillae due to the treatment. It is worth noting that these skin reactions only developed in 1% of all individual treatments [127].

4.2 Discussion

Home-use hair removal devices are sold to consumers with the promise of safe, long term hair reduction. Unfortunately, there is comparatively little peer-reviewed, scientific evidence for the claims many of these devices make. Manufacturers who undertake clinical testing for CE certification and FDA pre-marketing approval may not wish to share proprietary clinical results and safety testing publically. This makes it difficult for buyers to decide which product is best for their needs, and challenging for medical professionals to give appropriate advice when unsure patients ask about the devices. Data from peer-reviewed publications on the efficacy of the various at-home devices are sparse, limited primarily to industry-sponsored uncontrolled trials with small sample sizes and a lack of long-term follow-up.

Of the 14 studies reviewed, IPL for hair removal has the most published data. Although the literature shows modest results for home-use IPL, small sample sizes and short follow-up periods limit detailed analysis of studies. Most studies evaluated short-term hair reduction up to 3 and 6 months following light exposure at different body sites. Hair reduction percentages ranged from 6% to 72% after repetitive treatments. The most frequently reported side-effect was erythema, but oedema, blistering, crusting and pigment changes were also reported. No ocular damage and paradoxical hair growth have been reported in any of the studies reviewed.

Patients may present to a dermatologist after already having tried these devices because of complications from incorrect use or because they are unhappy with results because of unrealistic expectations or misinformation about the product's efficacy.

This literature review only gathered 14 peer-reviewed articles, which covered just six different devices, many of which are now out of date or unavailable on the market. Results were varied, with the highest overall clearance rate compared to baseline at 92% (iPulse, IPL) [119], whereas the lowest was only 36.2% (Silk'n, IPL) [123]. In comparison, the highest clearance for the long term results was 84% (Silk'n, IPL) [124], 3 months after the final treatment, and the lowest was no clearance at all (P&G, Diode Laser) [118]. The Silk'n device providing the lowest overall hair clearance in one study and the highest long term clearance in another highlights that there is considerable variance between studies, even if the device is the same.

The studies conducted on home-use devices differ considerably with regard to the parameters of the research itself. For example, many studies are described having long

term results, however what is considered “long-term” changes - most studies only follow up to 3 months post-treatment, some up to 6 months post-treatment, and one followed up for 12 months post-treatment. The number of subjects also varies, with two studies only conducted on 10 subjects, and one looking at a total of 94 subjects. The treatment areas of the investigations also differ, with some studies only looking at one specific area of unwanted hair, for example, the axillae, and some looking at various sites. Alster & Tanzi’s [124] study looked at various sites, and showed that there is a significant difference between treatments sites, with a 73.5% reduction on the leg compared to a reduction of just 47.8% at axillary or inguinal areas. Without a standardised procedure for scientifically testing these products, it is incredibly difficult to compare devices, especially considering that the same product can be tested in diverse studies with considerably different results.

The side effects found in the studies were relatively similar for all devices, with most reporting erythema and oedema in some, if not all patients. Other side effects noted included some pain when the treatment was applied, but in many cases the pain was mild, and there were only a handful of cases where a subject withdrew from a study due to pain. The studies on diode lasers found there were a small number of cases where skin abrasions occurred when used incorrectly, and subjects reported a burning sensation during treatment. Research on IPL treatments found a small number of cases where blistering, crusting, hyperpigmentation, or hypopigmentation occurred. All side effects recorded in the studies were considered to have been cleared by the end of the follow up appointments.

Almost all studies only investigated the side effects on subjects who were considered to appropriate users of the device being tested, however Wheeland (9) showed when asking patients to decide, based on the information that the packaging and instruction manual of a device, whether the product was suitable for them, 18% of those who would not be considered a suitable user said they were. This emphasises the need to ensure home-use devices cannot cause severe or permanent damage to a user who applies the device incorrectly. This study found a higher incidence of side effects in users who were considered inappropriate for treatment, including, blistering, hyperpigmentation, hypopigmentation, and every subject reported some degree of pain during treatment. All of these side effects had cleared by the end of the study. While it is important to be aware of the consequences of inappropriate usage of these devices, many devices available now incorporate an in-built skin tone meter meaning that the device cannot fire if the skin tone of the user is not appropriate.

Many of these investigations intend to show that the devices can be used safely at home. The devices themselves have various safety features, including mechanisms to ensure the device cannot be used if it is not in full contact with the skin, skin tone meters as mentioned above, along with appropriate instructions and warnings on the packaging and instruction manuals. However, in some studies, the treatment is conducted or overseen by the investigator, meaning that the subjects can ask questions, be shown how to use the device correctly or stopped before using the device incorrectly. This does not reflect the environment in which a consumer will use the device, where an expert is not available to offer assistance if it is needed. No study mentioned how safe the device is with respect to eye safety, beyond stating that the device met eye safety standards.

Consumer comfort is overlooked in almost all peer reviewed clinical studies, with many only focusing on whether the device being assessed causes enough pain to withdraw from the study. One study compared the E-One IPL to hot wax methods over a 35-week period on 63 persons with Fitzpatrick skin types I-V [128]. Each person had one axillae treated with the IPL device, and the other with hot wax, and one of the intended aims was to see which of the two methods were the most tolerable. They clinically assessed any erythema, oedema and desquamation which occurred in the treatment areas using a 4-grade scale from 0 (no appearance) to 3 (severe). Their findings showed that patients found the IPL system to be far more tolerable than the more traditionally used method of hot wax. Investigating the comfort of consumers using IPL systems compared to their typical hair removal regimen is an area which has limited information, and further research into this area would be valuable.

Philips performed an in vitro study on cultured hair follicles for device optimisation. In the study, they took biopsies from the lower leg of 12 female subjects who had received a single 15 ms pulse from a 9 J/cm² fluence device just before the biopsy was taken, 3-days after, or 7-days after, as well as in vitro models from the scalps of Caucasian women undergoing facelift surgery. The findings showed that hair which had been treated by the IPL responded in four ways. The main response, observed in 61% of hair follicles, showed that after 1 day in culture the melanocytes had moved upwards and away from the dermal papilla. After 3-days, the hair shaft had moved further upwards, and the hair fibre had decreased in length while the dermal papilla had shrunk. The second response occurring in 14% of hair follicles was similar to the first, and a thickened epithelial column between the fibre base and melanin zone also developed after 4 days. In 11% of hair follicles, melanin clumped together in the hair shaft, and the fibre stayed close to the dermal papilla. Finally,

in 7% of hair follicles, which were of Fitzpatrick skin type IV, there was only a small retraction of the melanin, and some isolated melanocytes near the dermal papilla. This in vitro study provided important information about how hair follicles respond to IPL treatment, clearly showing the effects of light treatment compared to control samples. While the paper references clinical data collected on Philips devices, no clinical data has been published in peer review journals by Philips [129].

4.5 Conclusion

There is no published data on the prevalence of use of energy-based optical devices beyond industry market research reports. FDA pre-market approval as medical devices and the classification in the European Union of all laser and intense light source devices, including domestic appliances as medical devices, will eventually ensure a high level of consumer safety.

A rapidly increasing volume of safety and efficacy studies in peer-reviewed literature indicates that the majority of energy-based optical devices are safe for use by the consumer. Controlled trials comparing devices would be helpful to substantiate the efficacy and to better predict the incidence of adverse events associated with home use cosmetic devices.

The authors conclude that efficacy studies should be independently assessed over a twelve month period at minimum. Studies should incorporate multiple cohorts of statistically significant sizes covering various device outputs on various body locations.

Overall, the studies reviewed suggest the devices are for the most part effective, and do not pose any serious safety concerns to consumers when used correctly. The differences between the limited studies that have been conducted highlighted in this literature review for home- use device demonstrates a weakness in published clinical efficacy compared to professional light based laser and IPL systems.

The market for home use hair removal devices is likely to expand in the coming years, as suggested by Kline research. As such evidence of device efficacy and safety is paramount to a sustainable future.

Chapter 5 - Experimental Results of Intense Pulsed Light Devices

Introduction

Following the literature review of home-use Intense Pulse Devices, the next stage of the research involved conducting an experimental investigation into the parameters output by a selection of IPL devices available on the retail market in the United Kingdom. Some devices were donated by the company supervisor, while others were purchased through the university from retail outlets. All devices were new and had not been opened or used. This chapter will demonstrate and discuss the measurements gathered.

5.1 Devices and Methods

The various dimensions and outputs of brand name IPL devices will be measured within the University, using a small laboratory workspace. To measure the fluence of the devices, an energy meter (Ophir LaserStar Power Energy Monitor, Ophir L40 (150) A-DB-SH-NS Absorber Head; Ophir Optronics Ltd., Jerusalem 91450, Israel) was used. To measure the pulse durations, a reversed biased photodiode acting as a light-dependant switch was used, and it was captured as an oscilloscope image using a Fluke 196 Scopemeter and FlukeView version 4 software (Optimum Energy Products Ltd., Calgary T2-Z4M3, Canada). To measure the spectral output, a HR2000+ spectrometer and Spectra Suite software (Ocean Optics, Dunedin, FL 34698, USA) was used. The dimensions of the glass transmissions block were taken manually, using a digital calliper. This method of measurement was chosen based on previous work conducted by Town & Ash in 2009 [130].

Information about the devices used are given below.

Device 1, by Manufacturer A, is an intense pulsed light device which is suitable for use on Fitzpatrick skin types I-V. It contains a skin tone sensor, which will determine which of the 10 power levels will be used when it is in contact with skin. There is a gentle mode function, which can reduce the power suggested for the skin tone if required. There is an activation button, which must be pressed in order for the device to begin flashing. Either stamp mode or glide mode can be used – if the consumer holds the activation button down, they can move the device along their skin and the device will continually flash; if they just press and release, it will only flash once.

The safety mechanisms which ensure the device does not flash if it is not in contact with skin was overridden using copper tape, as demonstrated in Figure 5.1, however mimicking

different skin tones proved difficult, therefore using masking tape and the gentle mode, measurements could only be taken at full power (setting 10) and gentle mode (setting 6).

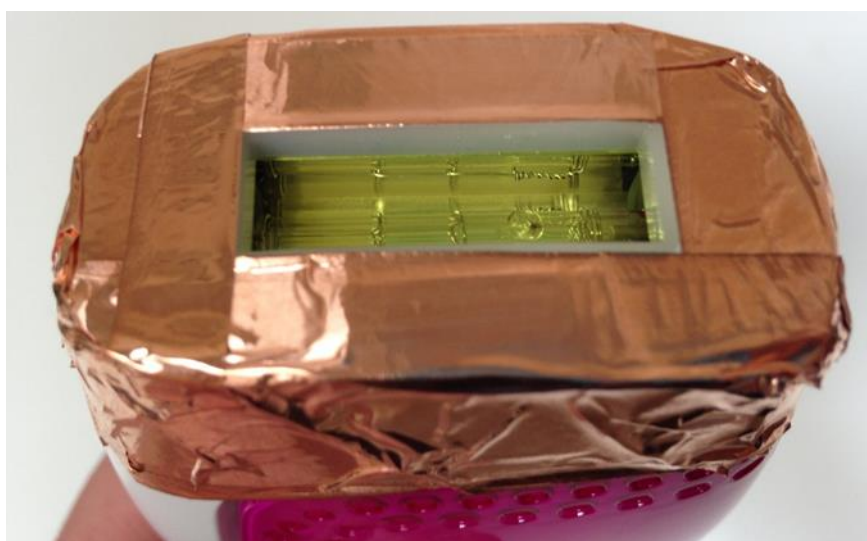


Figure 5.1 - Copper tape was used to override the safety mechanisms for many of the IPL devices.

Device 2 is also by manufacturer A. The device is an intense pulsed light device which is suitable for use on Fitzpatrick skin types I-V. It also contains an automatic skin tone sensor, and activation button. There is no indication on the device what power the device is being used, and no gentle mode. As with device 1, either stamp or glide mode can be used. The safety mechanisms were overridden using copper tape however with no gauge for the power mode, we were able to get readings at only full power using masking tape.

Device 3 is incredibly similar to device 1, under manufacturer B, with the same suitable skin types, power levels, skin tone sensor, stamp, glide and gentle modes, and safety mechanisms. Again, only measurements could only be taken at full power (10), a mid-power level (6), and at a low power (2).

Device 4 was created by manufacturer C, and is an IPL device suitable for use on skin types I-IV. It includes attachments for use on the face and for the bikini area. The device is equipped with a skin tone sensor which ensures that the device is in contact with skin before it can be used, and that it is not used on a skin tone which is not suitable. There are 5 energy settings, which are determined by the user. There is an activation button on the body of the device which can be pressed when the device is ready for use. There is a glide and stamp function on the device. The safety mechanisms were overridden using copper tape and masking tape, so measurements at all energy levels were taken.

Device 5 was also created by manufacturer C, and is an IPL device suitable for use on skin types I-IV. The device, like device 4, also contains a skin tone sensor, activation button, and 5 energy settings which can be chosen by the user. The safety mechanisms were overridden using copper tape and masking tape, so measurements at all energy levels were taken.

Device 6 is an IPL device developed by manufacturer D, suitable for use on skin tones I-V. The device has 5 treatment levels, the use of which is determined by the consumer using a button on the front of the device. The device has a mechanical push switch to activate, with no safety mechanisms stopping a consumer from flashing the device when it is not in contact with skin. It is intended to be used in glide mode and therefore when the push switch, located around the treatment window as shown in Figure 5.2, is pushed against the skin, it will automatically flash continuously until the switch is no longer activated. As there were no safety mechanisms to override, measurements were taken without the use of copper tape for all five levels of power.



Figure 5.2 - Device 6 only had a large mechanical push switch to activate the flashes. This could easily be overridden when not in contact with the skin by manually pushing on the switch.

Device 7 was developed by manufacturer E, suitable for use on skin types I-IV. It has 5 levels of power, which can be determined by the user on the main body of the device. The device comes with 3 attachments for different uses – for hair on the body, one for the face, and one for the bikini area. A skin tone sensor is given on the main body of the device, which is provided by the user via a thumb or fingerprint, and is required to switch on the device. The hand piece is then used to apply the device to the skin, and has an activation button which the user can press when they are ready for the device to flash. There are small mechanical push switches on each side of treatment window to indicate when the device is in contact with skin. As the safety mechanisms just included a push switch and external

skin tone sensor, measurements at all 5 levels of power were taken without the use of copper tape.

Device 8 is an IPL device by manufacturer F suitable for use on skin tones I-V. The device has 5 energy settings, which can be chosen by the user on the main body of the device. The device cannot be used if it is not in complete contact with the skin. It comes with an attachment to be used for facial treatments. It is designed to be used in glide mode, however can also use a stamp mode. The safety mechanisms were overridden using copper tape and masking tape, and measurements for all 5 levels of power were taken.

Device 9 was developed by manufacturer G which is suitable for use on skin tone I-V. It has 5 levels of power which can be determined by the user using a button on the device itself. It has a skin tone sensor built in. There is a button which the user has to press to begin flashes, and if the device is in contact with skin and the skin tone is appropriate for the power chosen, it will begin flashing. It is intended to be use in glide mode, holding down the activation button as it is moved along the skin, however stamping mode can also be used. The safety mechanisms were overridden using copper tape and masking tape, and measurements for all 5 levels of power were taken.

Device 10 is by manufacturer C, and is an IPL device suitable for use on skin types I-IV. It includes attachments for use on the face, the bikini area, and the underarms. Like devices 4 and 5, also contains a skin tone sensor, activation button, and 5 energy settings which can be chosen by the user. There is a glide and stamp function on the device. It was not possible using the methods at the disposal of the researcher to override the safety mechanisms used by the device, despite the device being in full working order.

Device 11 is an IPL device developed by manufacturer H which is suitable for use on skin tones I-VI. It has 5 levels of power, which can be chosen by the user on the front of the device. Eye goggles were provided in the packaging, and it is recommended that the user wears these while using the product. The device can only be used when in direct contact with the skin, and the activation button, on the main body of the device, has been pushed by the user. Glide mode can be selected by the user and is recommended for use on the body, while stamp mode is recommended for use on the face. It was not possible using the methods at the disposal of the researcher to override the safety mechanisms used by the device, despite the device being in full working order, and therefore no measurements were taken.

A summary table of all the gathered results along with the claimed outputs from the device manufacturers are given in Table 4, and are further discussed throughout this chapter.

Device	Spot size				Stated Fluence Range Ø J/cm²	Measured Fluence Range Ø J/cm²			Pulse Duration		Wavelength (Cut off Filters)					
	Stated cm²	Measured cm²							Stated msec	Measured msec	Stated nm			Measured nm		
Device 1 Full Power	3.0	3.0			Max: 6	6.80			2.6	2.4	N/A			>500		
Device 1 Gentle Mode	3.0	3.0			Max: 6	5.79			2.6	2.2	N/A			>500		
Device 2 Setting 1	3.0	2.61			Max: 3	4.14			1	0.9	N/A			>500		
Device 3 Full Power	3.0	3.0			Max: 6	7.09			2.6	1.8	N/A			>500		
Device 3 Mid Power	3.0	3.0			Max: 6	6.02			2.6	1.85	N/A			>500		
Device 3 Low Power	3.0	3.0			Max: 6	3.56			2.6	1.6	N/A			>500		
Device 4 Setting 1	N/A	No Adapter	Facial Adapter	Bikini Adapter	N/A	No Adapter	Facial Adapter	Bikini Adapter	N/A	0.75	No Adapter	Facial Adapter	Bikini Adapter	No Adapter	Facial Adapter	Bikini Adapter
		3.9	2	2		2.67	2.75	2.78			>530	>600	>530	>575	>585	>585
Device 4 Setting 2	N/A	3.9	2	2	N/A	3.37	3.52	3.25	N/A	0.925	>530	>600	>530	>575	>585	>585
Device 4 Setting 3	N/A	3.9	2	2	N/A	4.15	4.27	4.24	N/A	0.875	>530	>600	>530	>575	>585	>585
Device 4 Setting 4	N/A	3.9	2	2	N/A	4.99	5	4.86	N/A	0.975	>530	>600	>530	>575	>585	>585
Device 4 Setting 5	N/A	3.9	2	2	N/A	5.65	4.98	5.67	N/A	0.9	>530	>600	>530	>575	>585	>585
Device 5 Setting 1	N/A	3.00			Max: 1.92 +/- 0.43	2.31			Single Pulse – 0.8 +/-0.2	1.2	>530			>525		
Device 5 Setting 2	N/A	3.00			Max: 2.56 +/- 0.43	2.99			Single Pulse – 0.8 +/-0.2	1	>530			>525		

Device 5 Setting 3	N/A	3.00			Max: 3.41 +/- 0.43	3.98			Single Pulse – 0.8 +/-0.2	1	>530	>525		
Device 5 Setting 4	N/A	3.00			Max: 3.84 +/- 0.43	4.43			Single Pulse – 0.8 +/-0.2	0.9	>530	>525		
Device 5 Setting 5	N/A	3.00			Max: 4.27 +/- 0.43	5.05			Single Pulse – 0.8 +/-0.2	0.9	>530	>525		
Device 6 Setting 1	N/A	5.25			N/A	1.46			N/A	0.725	N/A	>450		
Device 6 Setting 2	N/A	5.25			N/A	1.53			N/A	0.75	N/A	>450		
Device 6 Setting 3	N/A	5.25			N/A	1.58			N/A	0.8	N/A	>450		
Device 6 Setting 4	N/A	5.25			N/A	1.62			N/A	0.85	N/A	>450		
Device 6 Setting 5	N/A	5.25			N/A	1.64			N/A	0.85	N/A	>450		
Device 7 Setting 1	N/A	No Adapter	Facial Adapter	Bikini Adapter	N/A	No Adapter	Facial Adapter	Bikini Adapter	N/A	34.5 base-to- base Too erratic for accurate measurement	N/A	No Adapter	Facial Adapter	Bikini Adapter
		2.85	2	1.9		8.93	8.30	8.70				>610	>530	>625
Device 7 Setting 2	N/A	2.85	2	1.9	N/A	9.05	8.26	8.69	N/A	Both 38 & 40 base to base Too erratic for accurate measurement	N/A	>610	>530	>625
Device 7 Setting 3	N/A	2.85	2	1.9	N/A	9.36	8.66	8.84	N/A	40mS base- to-base Too erratic for accurate measurement	N/A	>610	>530	>625
Device 7 Setting 4	N/A	2.85	2	1.9	N/A	9.74	9.01	9.21	N/A	41 base-to- base Too erratic for accurate measurement	N/A	>610	>530	>625
Device 7 Setting 5	N/A	2.85	2	1.9	N/A	9.95	9.20	9.41	N/A	43 base-to- base	N/A	>610	>530	>625

										Too erratic for accurate measurement			
Device 8 Setting 1	3	No Adapter	Facial Adapter	5	No Adapter	Facial Adapter	N/A	0.65	480-1200	>460			
		3.08	2		2.61	2.60							
Device 8 Setting 2	3	3.08	2	5	2.96	2.91	N/A	0.55	480-1200	>460			
Device 8 Setting 3	3	3.08	2	5	3.38	3.24	N/A	0.525	480-1200	>460			
Device 8 Setting 4	3	3.08	2	5	3.70	3.54	N/A	0.5	480-1200	>460			
Device 8 Setting 5	3	3.08	2	5	4.07	3.90	N/A	0.45	480-1200	>460			
Device 9 Setting 1	2.7	2.7		Max: 5	1.63		N/A	0.6	475-1200	>455			
Device 9 Setting 2	2.7	2.7		Max: 5	2.20		N/A	0.6	475-1200	>455			
Device 9 Setting 3	2.7	2.7		Max: 5	2.82		N/A	0.5	475-1200	>455			
Device 9 Setting 4	2.7	2.7		Max: 5	3.50		N/A	0.5	475-1200	>455			
Device 9 Setting 5	2.7	2.7		Max: 5	4.21		N/A	0.5	475-1200	>455			

Table 4 - Summary of all output measurements vs claimed outputs for all measured IPL devices.

5.1.1 Energy Density

Six of the nine devices from which energy density measurements were taken had five user selectable power settings. Devices 1, 2, and 3 had automated energy settings based on readings from a built-in skin tone sensor. The results are illustrated in Figure 5.3

Reference source not found.

The highest power and the 'sensitive level' power of device 1, the highest power of device 2 and the highest, lowest and a mid-range power setting of device 3, as the energy setting of these devices in normal use is decided by the skin contact sensor. While this meant that the complete range of output measurements of these devices were not collected, the gathered data is still sufficient to compare with the manufacturer's claims for energy density, as maximum energy output is given for the devices.

Manufacturers of six of the measured devices also provided claimed energy density values for their devices in the device user manuals. Only devices 4, 6, and 7 did not. Amongst those which did provide energy readings, only device 2 gave a reading which exceeded by >20% the claimed energy density for the device i.e. a claimed maximum output of 3 J/cm² but measured output of 4.14 J/cm², a difference of +27.53%. Devices 1, 8 and 9 (without adapter) had variations of between -10% and -20% from their claimed maximum outputs, while device 5 had readings of <7% difference for the highest 3 settings and were within the claimed range for the lowest two settings.

For the energy settings on all devices, the energy density (fluence) varied from the lowest at 1.64 J/cm² (device 6) to the highest at 9.95 J/cm² (device 7), as shown in Figure 5.3.

The variation between the highest and lowest fluence setting of each individual device ranged from 0.18 J/cm² for device 6 to 2.98 J/cm² for device 4. The small difference between settings on device 6 is partially related to its large spot size (5.25 cm²), however even when the spot size was not taken into account, the pulse energy difference between highest and lowest was just 0.95 J. As the settings given by the manufacturer are intended to be used as a guide for the suitability of use for different skin tones, it seems unlikely that a difference of 0.18 J/cm² would result in much difference in efficacy or potential side effects when using the device on darker skin tones. The fluence for the lowest power setting on device 9, which gave the subsequent lowest fluence readings, was 1.63 J/cm², only 0.01 J/cm² lower than the fluence of the highest setting of device 6.

The most inconsistent energy output came from device 7, with a variation between highest and lowest recorded values over 10 flashes at the same energy setting from the device of 1.15 J/cm² on setting 3 and 1.11 J/cm² on setting 4. The remaining devices were relatively consistent, with a variation between highest and lowest recorded values 0.04 J/cm² (device 6) and 0.38 J/cm² (device 4).

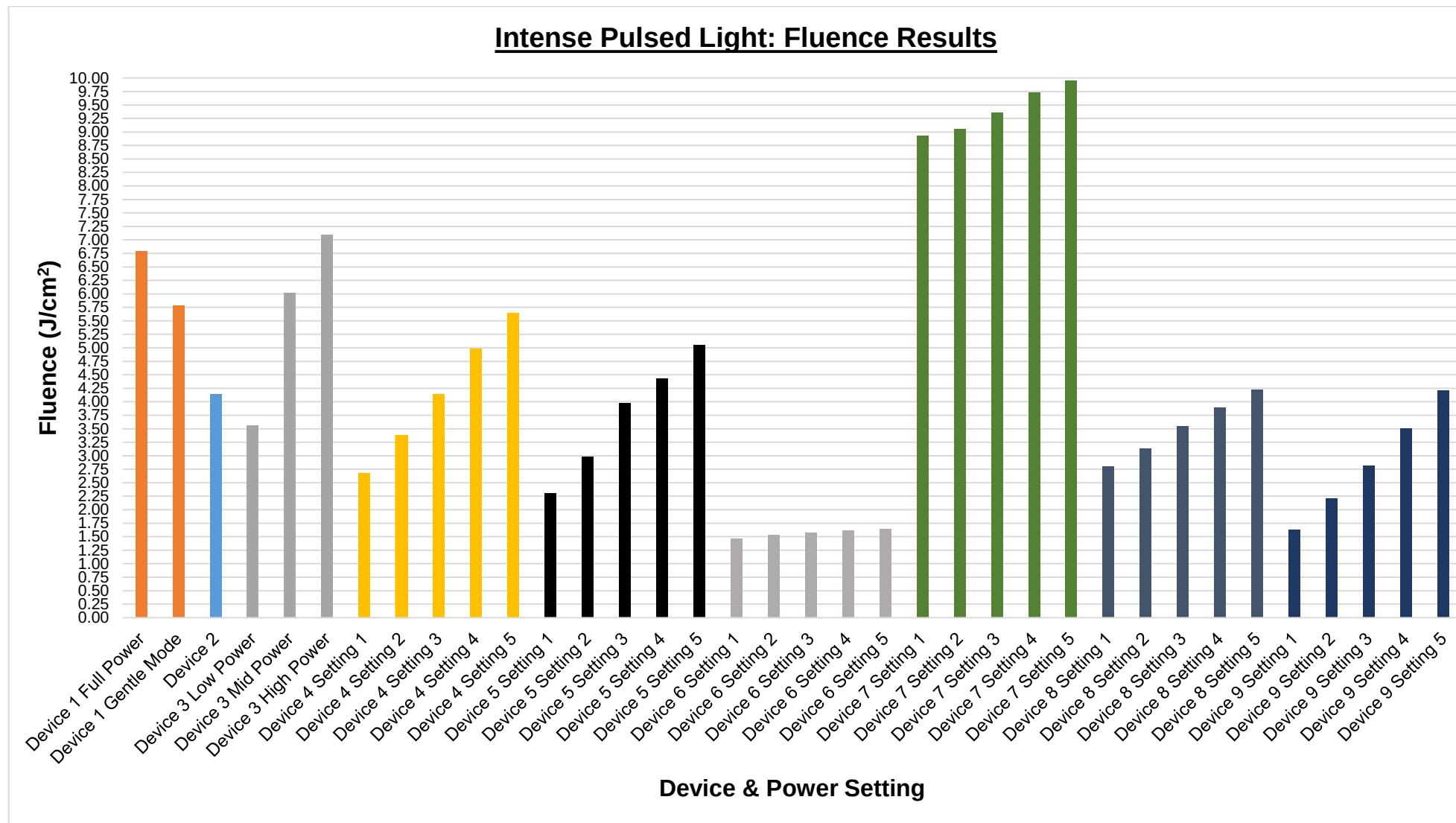


Figure 5.3 - Results of fluence readings for all measured IPL devices.

5.1.2 Pulse Duration Measurement

The pulse durations of nine devices were collected, with pulse durations for each available setting measured. Both the base-to-base and Full Width Half Maximum (FWHM) measurements were collected and all FWHM findings are given in Table 4 unless otherwise stated. The FWHM pulses across all devices ranged from 0.45 ms (device 8 setting 5) to 2.4 ms (device 1 Full Power). As with the energy density measurements, the pulse durations for some settings on devices 1, 2, and 3 were restricted by the automated energy settings based on skin tone measure by a built-in skin tone meter.

Of the nine devices evaluated, only four of the devices provided pulse duration information. Device 5 had a claimed pulse duration of 0.8 +/- 0.2 msec, with the pulse durations of all energy settings within range, except Level 1, with a 1.2 msec pulse duration, showing a deviation of +16.67%. Device 1 had a deviation of -7.69% at its highest setting and -15.38% on the Sensitive Mode; device 2 had a discrepancy of -10%; and the pulse durations measured for device 3 were substantially different from those claimed by the manufacturer with a -30.7%, -28.85%, and -38.46% difference at Full, Mid, and Low Power settings respectively.

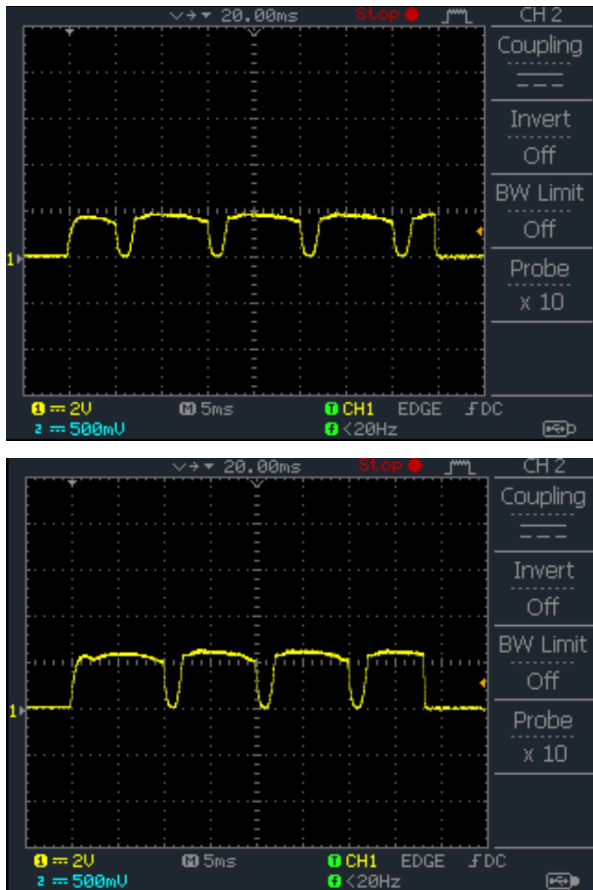


Figure 5.4 - Pulse durations for device 7 on the same setting are inconsistent.

The pulse durations for the device 7 were inconsistent between flashes on the same setting. As illustrated in Figure 3.4, the sub-pulses within a single pulse were different on two separate flashes of the device – the first showed four uneven square sub-pulses with a range of sub-pulse durations, while on the same setting, there were 5 uneven square pulses, where the final pulse appears to be half the size of the prior four sub-pulses. Varying pulse durations within a setting such as this might lead to under-treatment, as if the pulse duration is not close to or higher than the thermal relaxation time, the treatment may not be effective, while if the pulse is too long, it might lead to unwanted adverse effects.

5.1.3 Pulse Profiles

Most devices had free discharge style pulse shapes, with the exception of devices 6 and 7. Device 7 discharge pulse were having/approximating square-like profile but not perfectly shaped, which can be seen in Figure 5.4.

Device 6 had an unusual pulse shape, as shown in Figure 5.5, which appeared to begin as a free discharge shape, but cut off at the end of the pulse in the similar manner to that of a square pulse shape, meaning the pulse was not entirely sinusoidal.

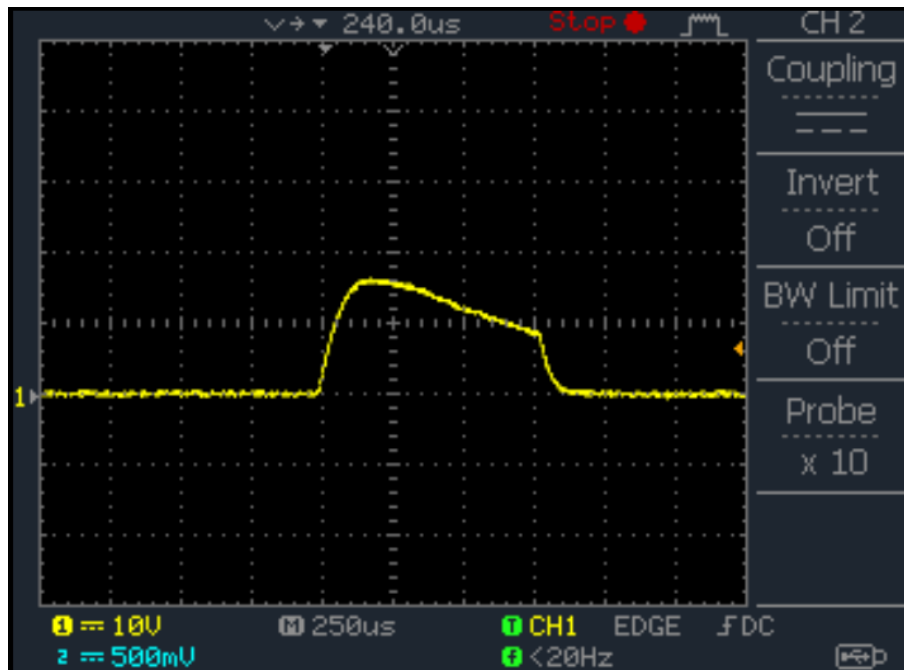


Figure 5.5 - The pulse shape of device 6 begins in the form of free discharge, however ends as though it is a square pulse.

Free discharge pulse shapes have been shown to be effective in heating a hair follicle sufficiently to cause damage, though may lead to variance in spectral distribution within each individual shot from the device. A typical train of square sub-pulses will heat the follicle to an optimal level, and sustain this heat throughout the sub-pulses in a more controlled manner than the heating achieved with free discharge energy pulses [131] though it is difficult to compare the measured pulse shape of the device 7 to a typical square pulse train since the sub-pulses are not perfect squares, vary in shape between sub-pulses, and the number and size of the sub-pulses vary from shot to shot from the device.

5.1.4 Spectral Measurement

The spectral output of an IPL device is an important factor in the efficacy and safety of the device as the chromophores targeted, including melanin in the hair follicle and its adnexa, will absorb certain wavelengths more strongly than others. The wavelength range of the device must be highly absorbed by the target chromophore, but not by the surrounding tissue in order to avoid unwanted adverse effects. For IPL hair removal, this is typically in the range between 500 nm and 1200 nm [132]. Wavelengths under 500 nm must be filtered out in order to avoid increased risk of injury to the eyes and skin [130].

Spectral output of nine IPL devices were measured, of which two devices had additional attachments which affected the spectral emission; devices 4 and 7, which both had a Facial Adapter and a Bikini Adapter. Device 8 also had a Facial Adapter which, however, had no effect on the spectral output of the device. The overall results are demonstrated in Figure 5.6.

Out of the nine devices measured, only five had manufacturer-provided data relating to the spectral output of the device, either giving the spectral range of the device or the lowest wavelength of the cut off filter. Device 5 claimed a cut off filter of 530 nm and was measured at 525 nm - a difference of less than a 1% between the claimed and measured values. Device 8 claimed a spectral range of 480 nm to 1200 nm, but the cut off filter was measured at 460 nm, showing a deviation of $< 5\%$ from the stated value - a similar finding to that of device 9, with a claimed range of 475 nm to 1200 nm and measured cut off filter of 455 nm. Device 4 had $< 10\%$ discrepancy between the stated cut off filters for the device with and without its attachments and those measured in this study.

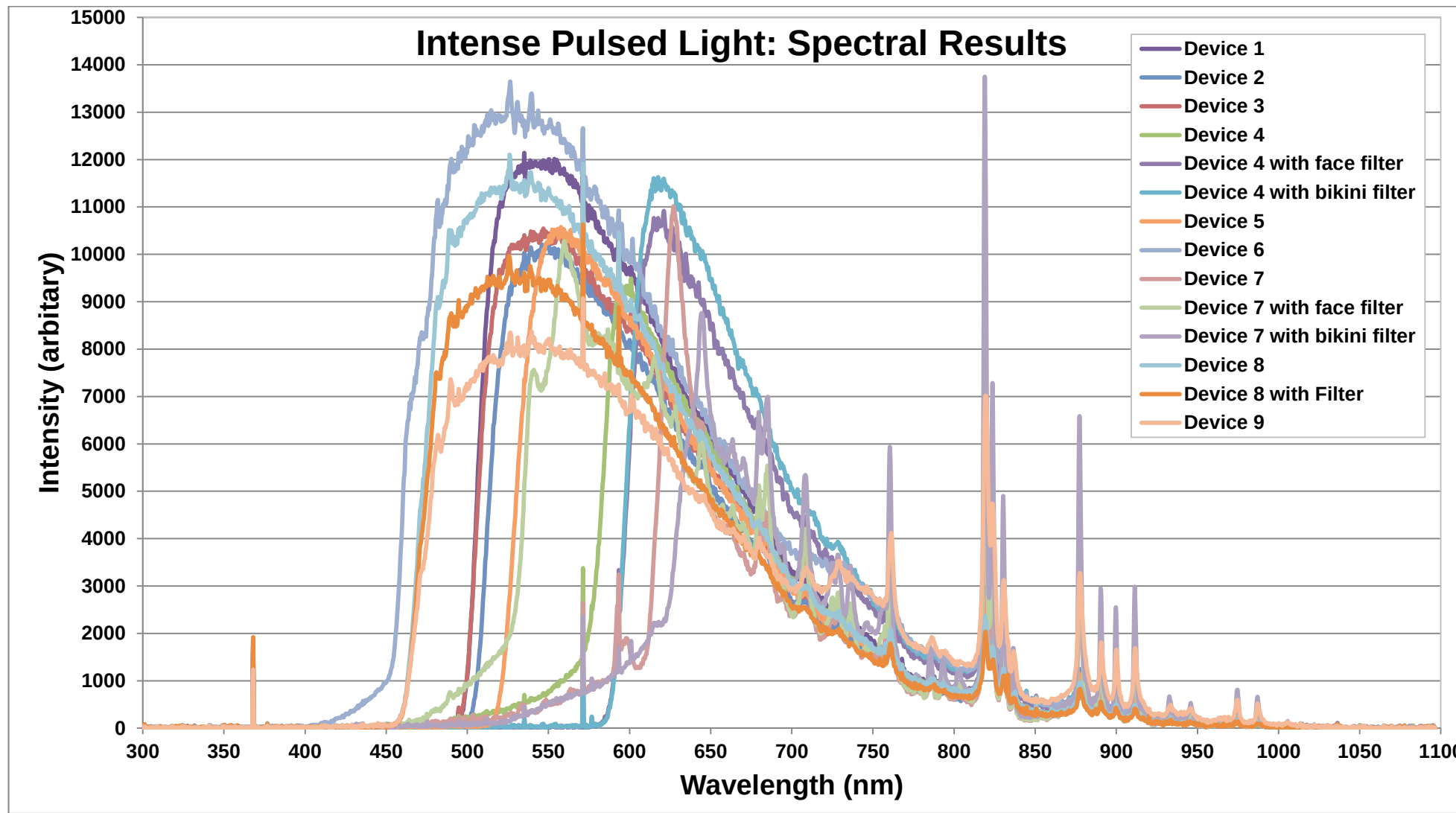
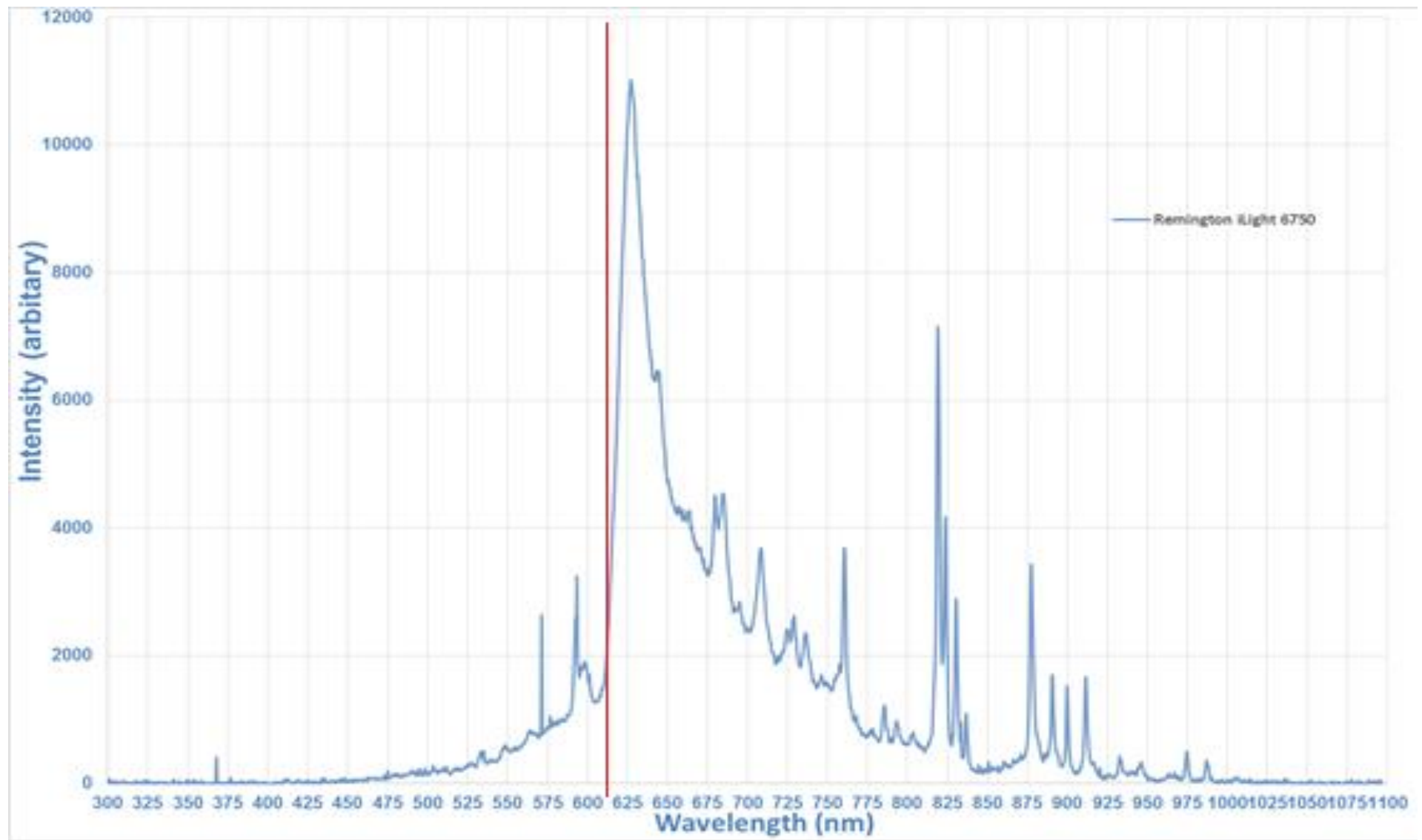
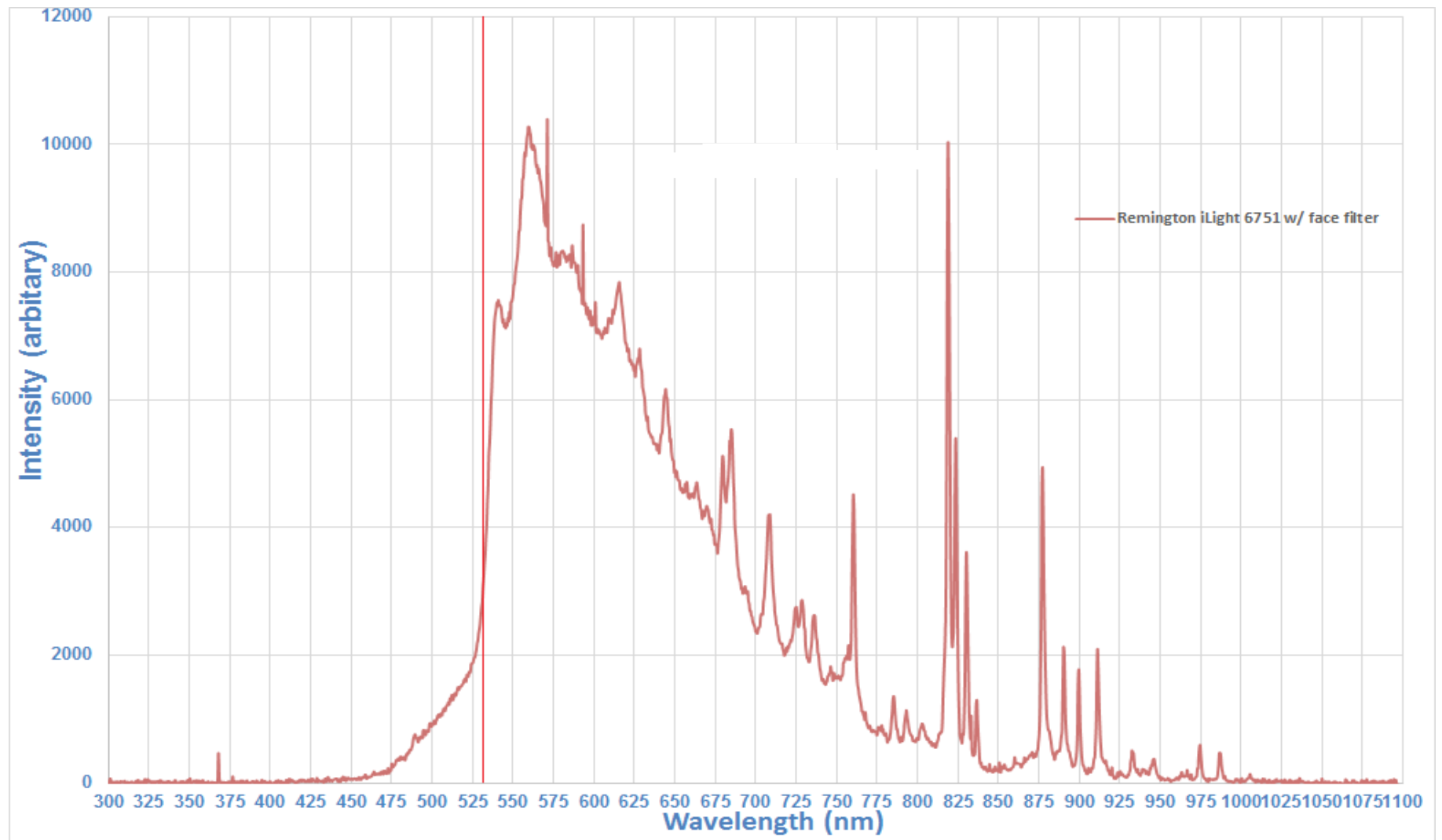


Figure 5.6 - Spectral outputs from all measured IPL devices.

For all devices, we measured several small emission peaks below the measured cut-off filter wavelength, notably at approximately 370 nm in the UVA band. This phenomenon also occurred with devices 4 and 7 with the intensity of visible light appearing to rise slowly from 475 nm, as illustrated in Figure 5.6. These emission values outside the cut-off wavelength are to be expected when dichroic filters are employed with highly divergent light sources such as IPLs compared with lasers where the coherent laser beam is always perpendicular to the filter surface.



(a)



(b)

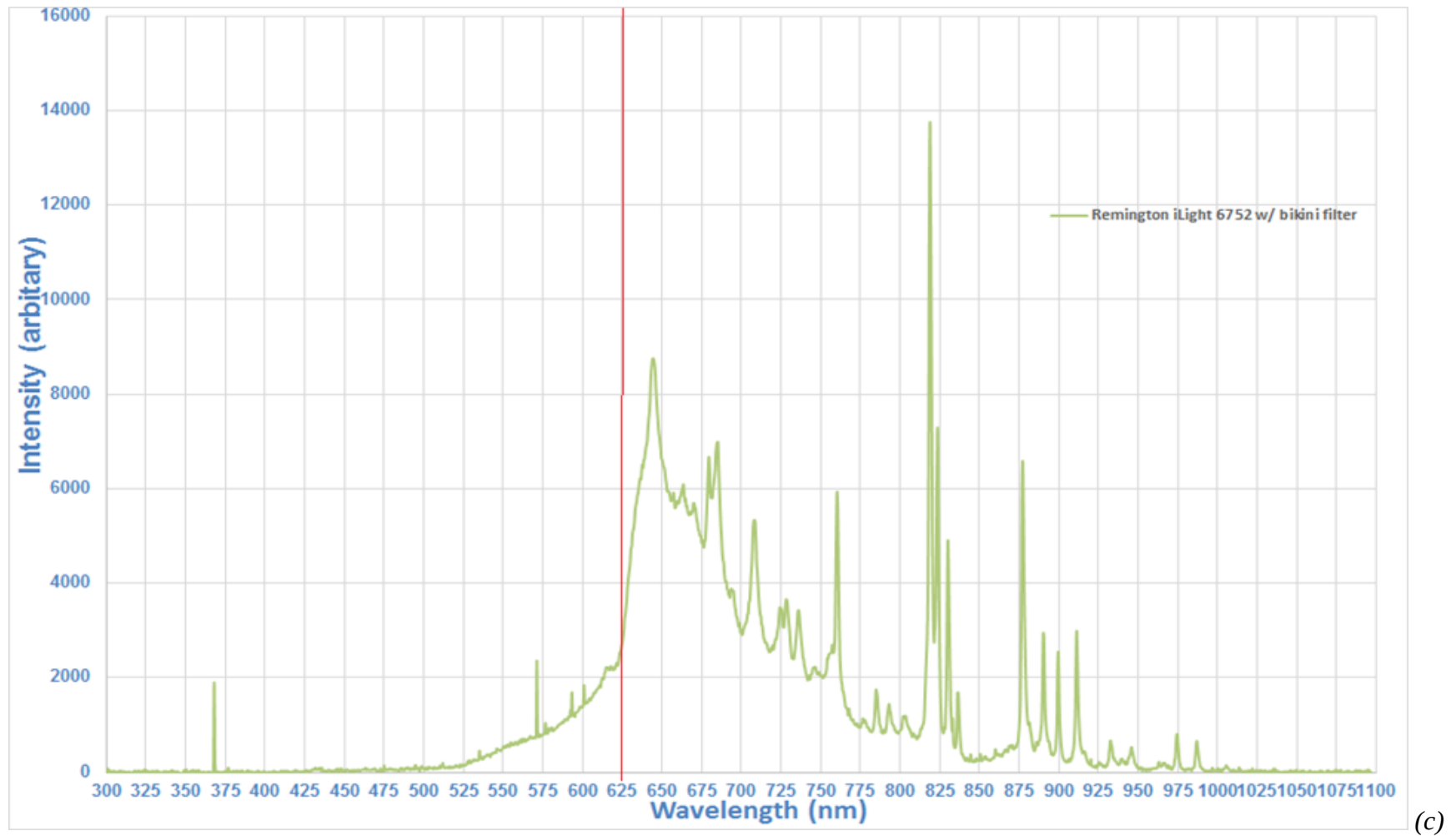


Figure 5.7 - Spectral results for Device 7 with no filter (a), with facial filter (b), and with bikini filter (c). Where the cut off filter begins is highlighted by the red line, at 530nm. Before this line, there should be no spectral readings, however as illustrated there is a single spike at approximately 370nm and it begins to rise before the cut-off point

5.2 Conclusion

It was not possible to override the safety features of devices 10 or 11. While this meant it was not possible to measure the output of the devices and assess their likely efficacy, it does show that it is very unlikely that the device could be misfired or misused by a consumer.

The spatial profiles of the IPL devices were not collected in this study, meaning whether the energy is distributed evenly across the treatment window or not was not established. This means that there may be areas within the treatment window which have more energy output than others, possibly resulting in uneven treatment of the hair follicles, which could lead to adverse side effects [133].

The time-resolved spectral data of the IPL devices were also not collected, meaning that how the wavelengths of light are distributed across the pulse duration cannot be determined. Therefore, we cannot tell whether or not the optimum wavelengths of light are being utilised at the highest intensity of the pulse and fully establish its efficacy for photons to reach the hair follicle [134].

It is difficult to make solid conclusions about how the measurements collected in this study affect the performance of the devices without a clinical trial or peer review study on these devices assessing how well the devices remove hair to compare to. While device 9 does have a peer reviewed clinical paper evaluating its efficacy, this is the only IPL tested in this study which does. There are also questions raised about the reliability of many of the peer-reviewed clinical studies published, due to the short periods of time over which the efficacy of the devices are assessed, the small number of participants, and some studies not being controlled or randomised.

It is recommended that manufacturers are more forthcoming about the output parameters of their devices in order to allow transparency to consumers about the product they are purchasing, and to help professionals in cosmetology give more specific advice to their patients. By accompanying this information with published studies about the performance of the device, this will lead to a more well-rounded knowledge about the best device for the different needs of patients and consumers.

Chapter 6 - Computational Modelling of Intense Pulsed Light Devices

Introduction

Using the data collected from the home use IPL devices in the previous chapter, the next step is to develop a calibrated computational model using the data from 9 devices. In this chapter, the Monte Carlo and Alternating Direction Implicit (ADI) methods will be used in conjunction with the experimental data to assess if the devices are able to effectively heat the hair follicle enough to cause damage. It will also be used to assess if the device when used correctly, and used incorrectly, would cause damage to the skin.

6.1 Parameters of the Computational Models

A calibrated version of the computational program TODDY will be used. TODDY is a custom 2 dimensional Monte-Carlo and ADI Modelling system, and its program can assess the thermal damage caused by the hair removal devices measured. The model was calibrated using the results of the experimental work, discussed in chapter 5. This chapter will demonstrate the parameters used, and the results of the computational runs.

6.1.1 Monte-Carlo

During the initial part of the program, the Monte-Carlo method assesses the movement, absorption and scattering of photons from a user input spectrum of light – in this scenario, taken from the experimental results given in the previous chapter - in a two dimensional representation of a hair follicle and the epidermis, dermis, and lower dermis, with the parameters of which is also input by the user. The figures assessed were the maximum temperature of the follicle and maximum temperature of the skin, as well as the damage caused to both the skin and the hair follicle.

For all devices, a Monte-Carlo run was completed based on Fitzpatrick Skin Type I (0.4% melanin in the epidermis) and dark hair (42% melanin in the hair), as shown in Figure 6.1. These skin parameters were chosen as research has shown that when IPL devices are used on pale skin and dark terminal hairs, the best results are yielded [6].

A separate, second run was also conducted for devices 6 and 7. The reason that these devices were separated from the other devices was due to their lack of skin tone sensor. This means that these devices could be used incorrectly, and therefore this model was designed to assess whether if the incorrect power setting on a darker skin tone was used, how much potential damage the devices could cause to human skin. As these were the only

devices which did not have skin tone sensors which directly interacted with the skin while the device was being used, no other devices were assessed using this second run. For the chosen devices, the second set of skin parameters were skin type IV (15.9% melanin in the epidermis) and black hair (99% melanin in the hair) as demonstrated in Figure 6.2. These parameters were chosen as some research has shown that in self-assessment reports of Fitzpatrick Skin Type IV is not as accurate as a dermatologist report of the same skin type [135].

RADIATIVE PROBLEM DEFINITION

MONTE CARLO PARAMETERS

Number of photons
100000000

limit i
500

limit j
5000

RADIATION SOURCE

Beam Width (um) MUST NOT BE GREATER THAN TISSUE WIDTH
20000

☐ Single Wavelength

Wavelength(nm)
409

☒ Broadband

Broadband filename
device7.txt

incident angle (deg)
0

incident anisotropy factor
0.9

Scaling factors

Epi Scatt SF
1

Dermis Scatt SF
1

Target Scattering Scaling Factor
1

START OR RESTART

☐ Restart

read from Monte Carlo results file
Dumpfile.txt

☒ New Run

Save to Monte carlo results file
Device7Damage.txt

TISSUE DATA

Layer Thickness (um)

Anisotropy factor

Tissue width(um) MUST BE GREATER THAN BEAM WIDTH
20000

Epidermis
70
0.789

Upper dermis
30
0.789

Lower dermis
800

Percentage Melanin in Epidermis
15.9

Percentage Melanin n Hair
99

PPIX FLUORESCENCE PARAMETERS

Quantum Efficiency
1

PPIX Concentration in target(mg/litre)
0

PPIX concentration in surrounding dermis (mg/litre)
0

Molecular weight (g)
562.658

PPIX concentration in epidermis (mg/litre)
4

Scaling Factor PPIX
10

AUTO FLUORESCENCE PARAMETERS

Quantum Efficiency
1

flavin concentration in target (mg/litre)
0

flavin concentration in surrounding tissue (mg/litre)
0

Molecular weight (g)
785.55

Scaling Factor Flavin
10

BLOOD CONCENTRATION

Blood conc in tissue
3000

Blood conc in target
0

Molecular weight(g)
1500

TUMOUR POSITION AND DIMENSIONS

Lower lateral edge of target (um)
9900

Lateral width (um)
200

tumour length(um)
500

anisotropy factor
0.8

OK

Cancel

Figure 6.2 - Fitzpatrick Skin Type IV and black hair.

The spectral data which is used within the model are the broadband spectrums collected for each individual device, as provided in the previous chapter. Some devices required multiple runs due to having different spectral results when using a filter designed for different types of the body – for example, device 4 required a separate run for the body filter, bikini filter and face filter.

All other settings in the parameters remained the same for each run, ensuring that all differences in results were directly due to the light spectrum of the device or the skin type and hair parameters used.

6.1.2 Alternating Direction Implicit (ADI) Method

During the second part of the TODDY program, using the data from the initial Monte Carlo run, the program runs an ADI method to assess the subsequent thermal effect of the absorbed photons. This part of the model was calibrated using the following work conducted in this and the previous chapter:

- The Monte Carlo models for each device.
- The energy outputs for each device which were collected, as described in the previous chapter, shown as the energy in Figure 6.3
- The pulse shape and durations for each device which were collected, as described in the previous chapter, input as a pulse temporal file, and the duration influencing the t_{max} , both shown in Figure 6.3.

Thermal data dialog

Thermal properties

	k (W/m/K)	rho (Kg/m3)	C (J/Kg/K)
Epidermis	0.21	1200	3600
Dermis	0.53	1200	3800
Target	0.24	1210	1500

Number of pulses

1

If pulse count > 3 then only Pulse 1 used

Pulse characteristics

pulse temporal file

device3pulse.csv

Toff (s)

1

Energy (J)

21.28

Thermal calculation parameters

NI	500	dt (s)	0.0002
NJ	5000	tmax (s)	0.054
dx (um)	4.00080016	plot every	2 time steps
dy (um)	4.00080016		

OK

Cancel

Execution type

Perform PDT damage calculation

Surface Heat transfer convect coeff (W/m2/K)

10

Ambient temperature C

20

Tissue temperature C

34

Calibration factor

30

Figure 6.3 - The input parameters for ADI Thermal Solver.

147

For device 7, two separate thermal runs were completed as the pulse shape and durations were found to be erratic in the previous chapter. Therefore, two pulses were created in order to assess if this affected how the device heated the skin or hair follicle – the two pulse shapes are demonstrated in Figure 6.4.

As with the Monte Carlo parameters, all other input options were kept the same in order to ensure that any results were as a result of the differences of the devices, such as the energy output of pulse durations.

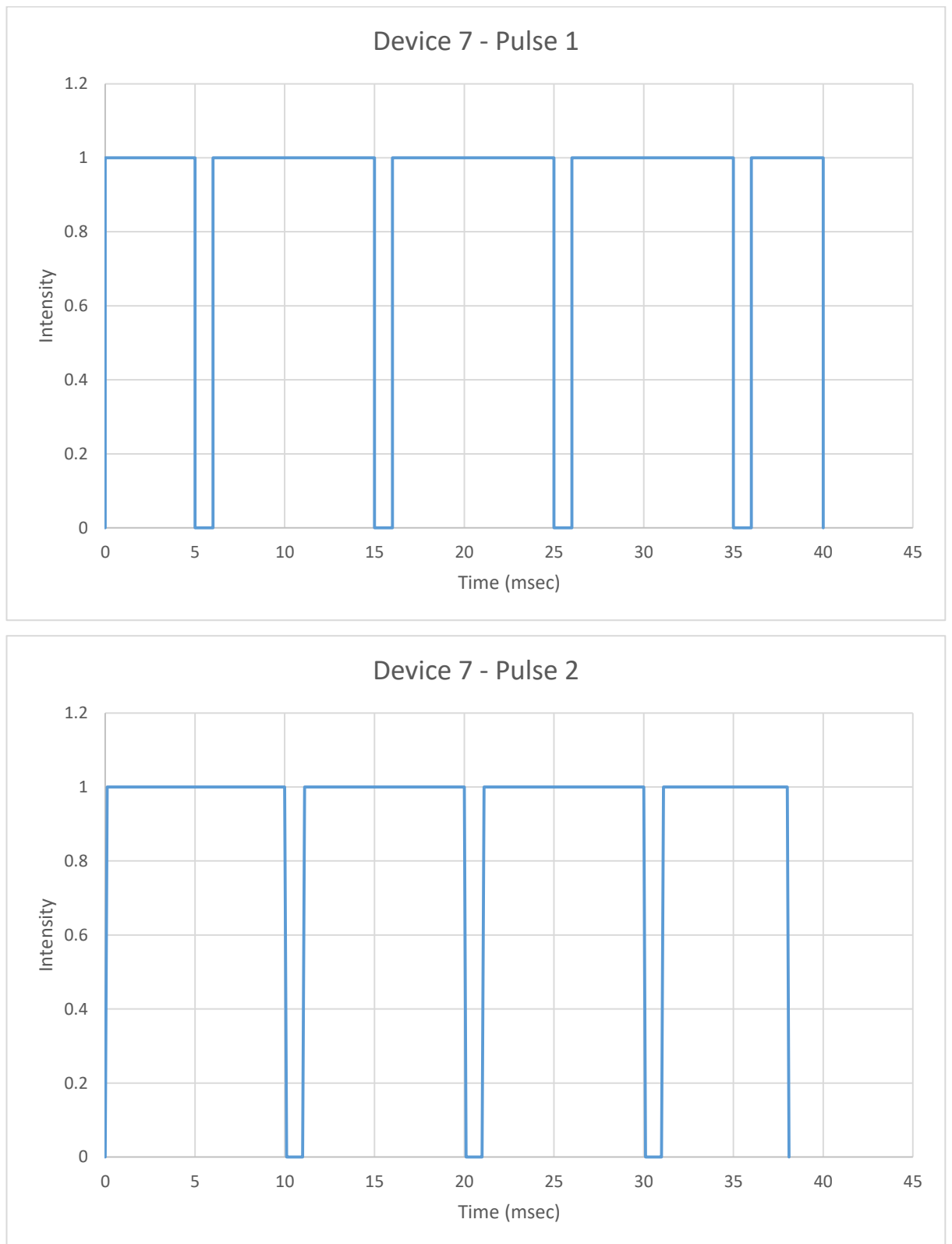


Figure 6.4 - Pulse shapes and durations for Device 7.

6.2 Computational Analysis Results & Discussion

During the computational modelling stage of the research, a total of 24 calculations were completed. These calculations covered each device and their accompanying filters being used on Fitzpatrick Skin type I with a dark hair colour. In addition, devices 6 & 7 were run with Fitzpatrick skin type VI, as these devices did not have a skin tone sensor attached to the head of the device, meaning that they could be used with a high power on a darker skin tone. The skin tone sensors on the other devices prevents this type of misuse. Therefore, this second run was conducted to illustrate the potential damage which could be caused if the device was used incorrectly, as the device does not prevent this type of misuse. The results of the computational modelling are given below, followed by a discussion of results given.

6.2.1 Thermal Results

Out of all 24 calculations which were conducted, 18 indicated that the devices could sufficiently heat hair follicles to the temperature threshold for damage, being 44°C [82], and each device individually was indicated to meet this threshold on at least one run, as shown in Figure 6.5. For the devices which were shown did meet this threshold, the temperatures which the hair follicles reached ranged from 45.5°C (device 7, with damage parameters and using pulse duration 2) to 72.1°C (device 4 with the bikini filter). When taking into account the devices which result indicated did not heat the hair follicles to a sufficient temperature to reach damage threshold for the hair follicle, as shown in Figure 6.6, the lowest temperature was from device 6 with damage parameters, heating the follicle to 40.4°C.

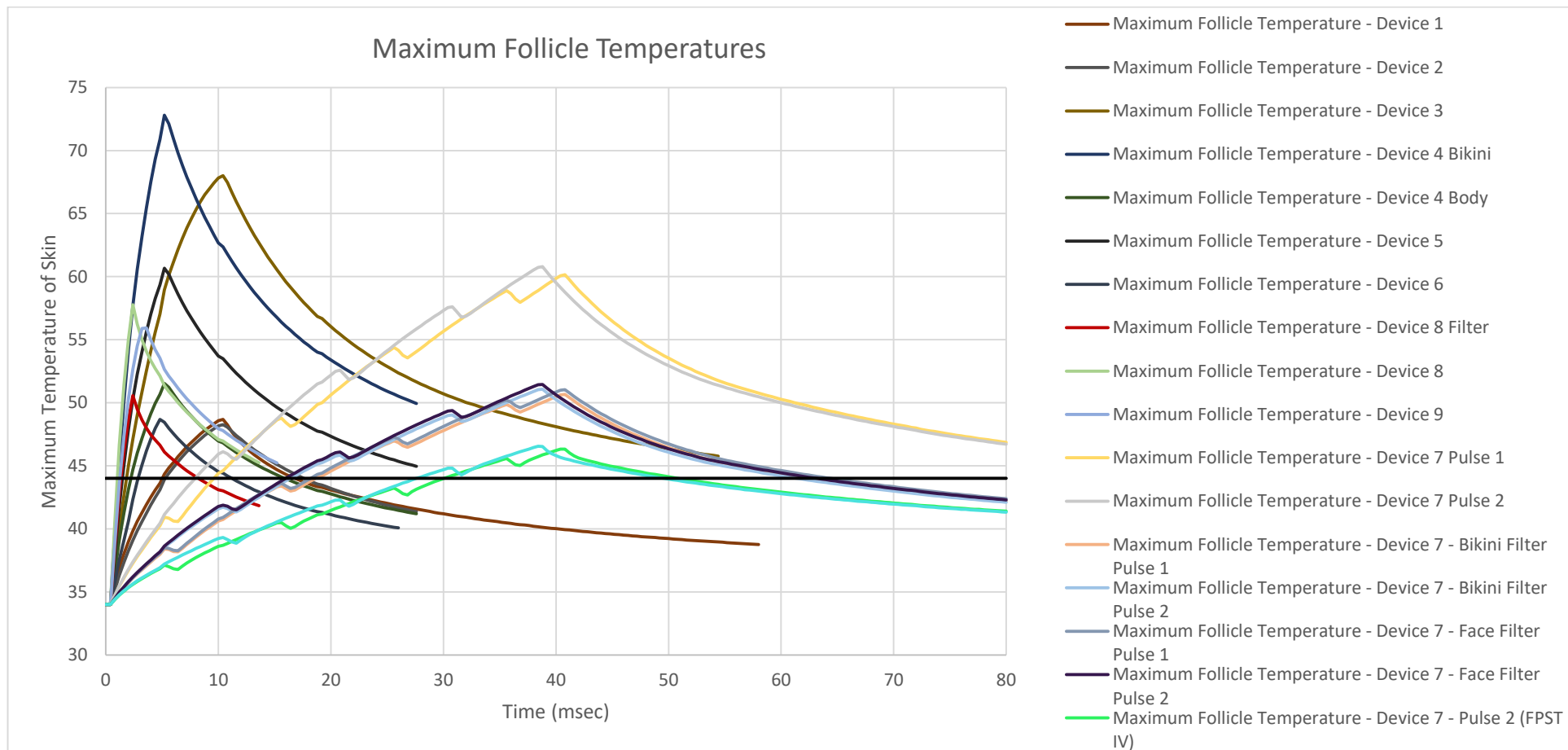


Figure 6.5 – The devices which could heat hair follicle to the point of where irreversible damage begins.

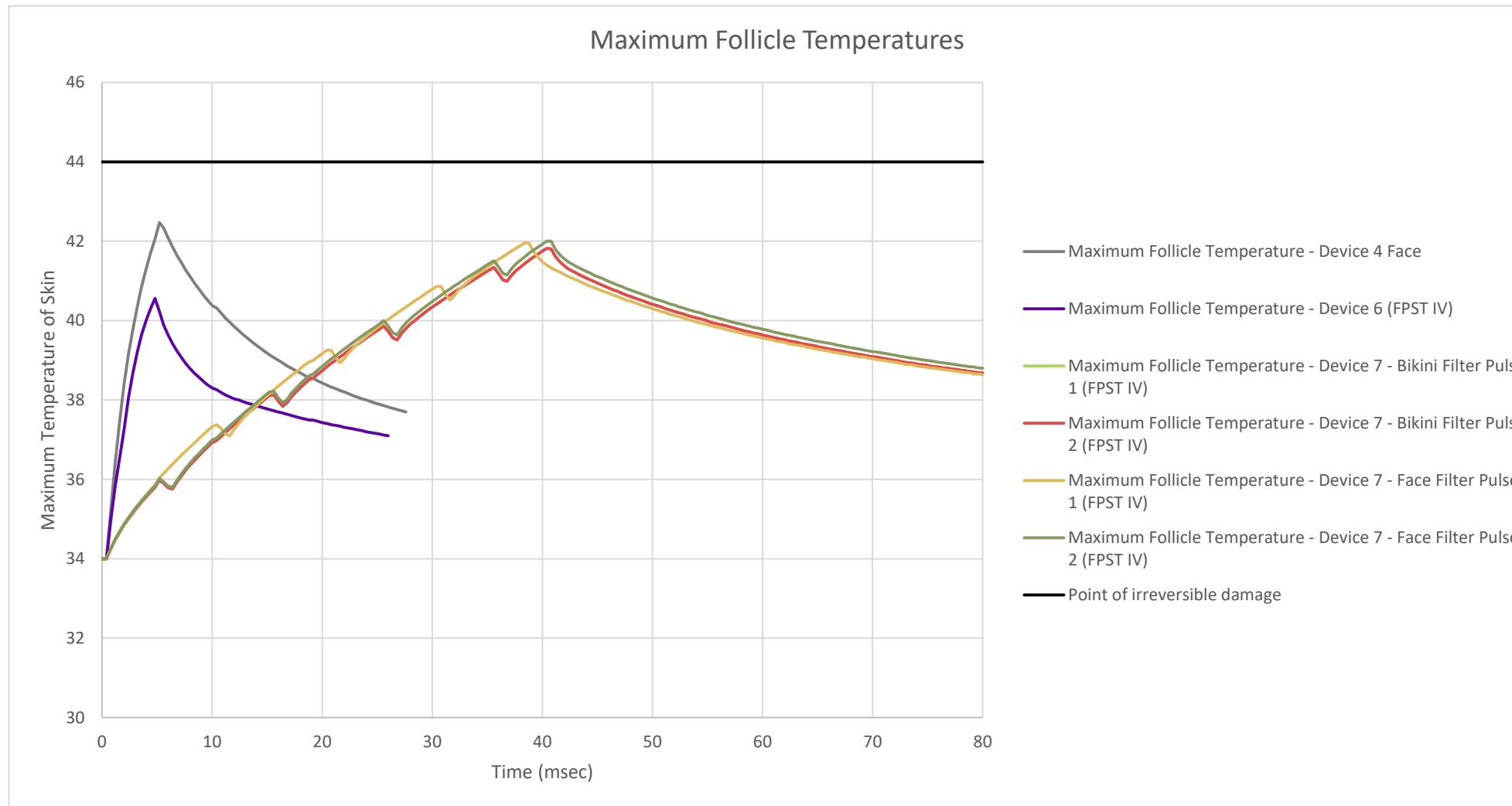


Figure 6.6 - The devices which were not able to heat hair follicle to the point of where irreversible damage begins.

While 44°C is the threshold for causing damage to the skin [82], a prolonged period at this temperature is required to cause any significant damage to skin [83]. Moritz & Henriques [85] suggest that when cells are heated above 51°C, this is when destruction can occur within shorter periods. The results of the bio-physical computational model indicate that many of these devices did not cause damage to the surrounding skin, and most of those which did caused more damage to the hair follicle.

Device 7 was the only device which was shown to be able to heat the skin tissue above 44°C, as demonstrated in **Error! Reference source not found.** This was not the case for all of the calculations with device 7 – only when no filter was used did the device heat skin to such temperatures. The highest the skin was heated to was 47.8°C when the device was used with Fitzpatrick skin type IV.

The pulse shapes of the devices were reflected in the way in which they heated the device – all devices except device 7 had free discharge pulse shapes, and the thermal results of these devices showed the initial increased peak of heat as the device flashes, then the heat decrease over the rest of the of pulse time. Device 7 had a square pulse train, therefore the temperature would rise with the first pulse, and then drop a little, then rise again with the second pulse and so on. After the final pulse, the heat decreases at a slightly slower rate than is seen with free discharge devices. The comparison between the two types of heating is shown in Figure 6.8.

The pulse shape only appears to affect the way the follicle is heated when using the optimum skin and hair parameters – the heating of the skin follows same pattern no matter the pulse shape, which is starting out low and slowly rising after the pulse, as demonstrated by Figure 6.9.

However, when using Fitzpatrick skin type IV and dark hair, the heating of the skin reflected the same pattern of heating as the hair follicle, seeing the high initial peak for a free discharge device, and a steady rise, and small drop in heat then rising again with the next pulse, as shown in Figure 6.10.

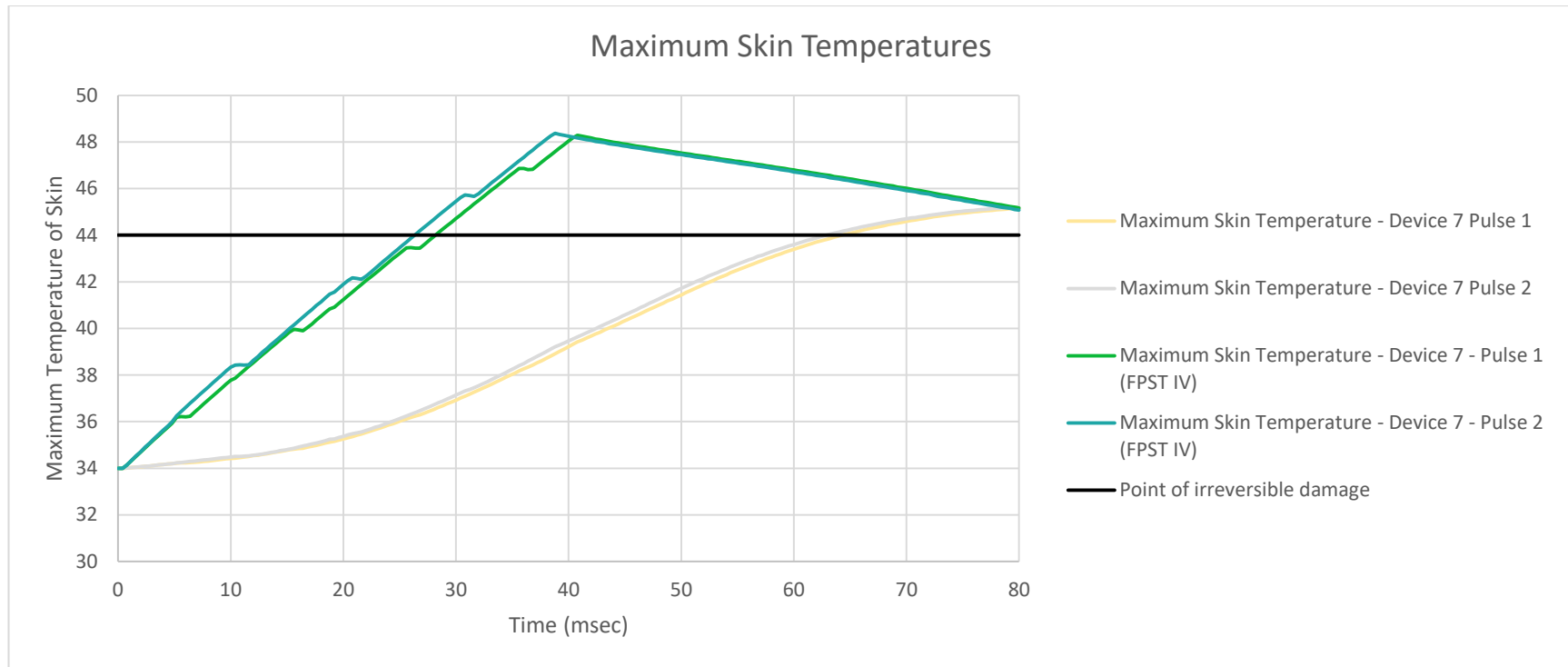


Figure 6.7 - Device 7 which heated skin to the point of potential damage.

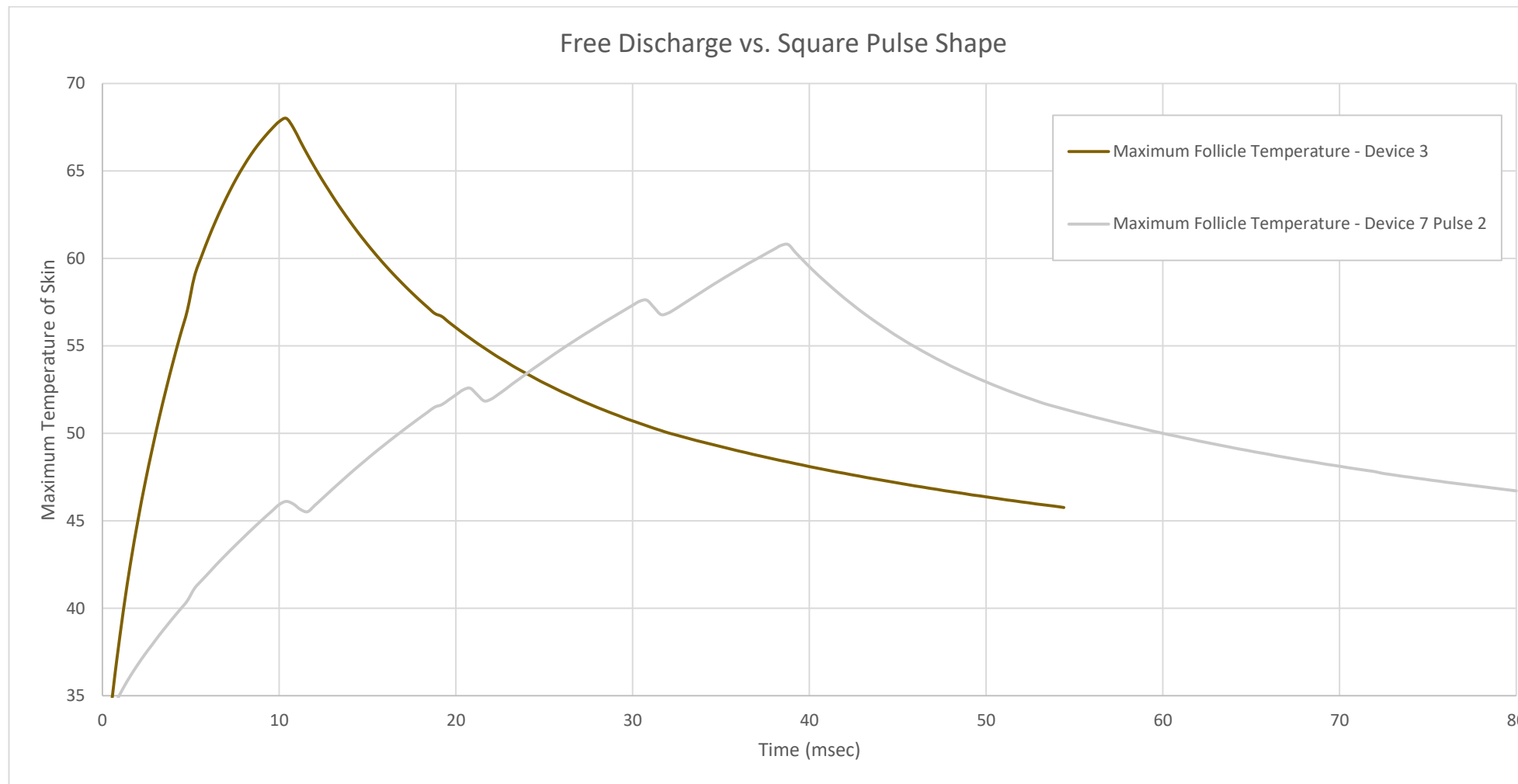


Figure 6.8 - Device 3 has a free discharge pulse shaped, illustrated by the high peak of heat, then drop in temperature. Device 7 has a square pulse train, highlighted by the steady rise, and small drop in heat repeated by the number of pulses.

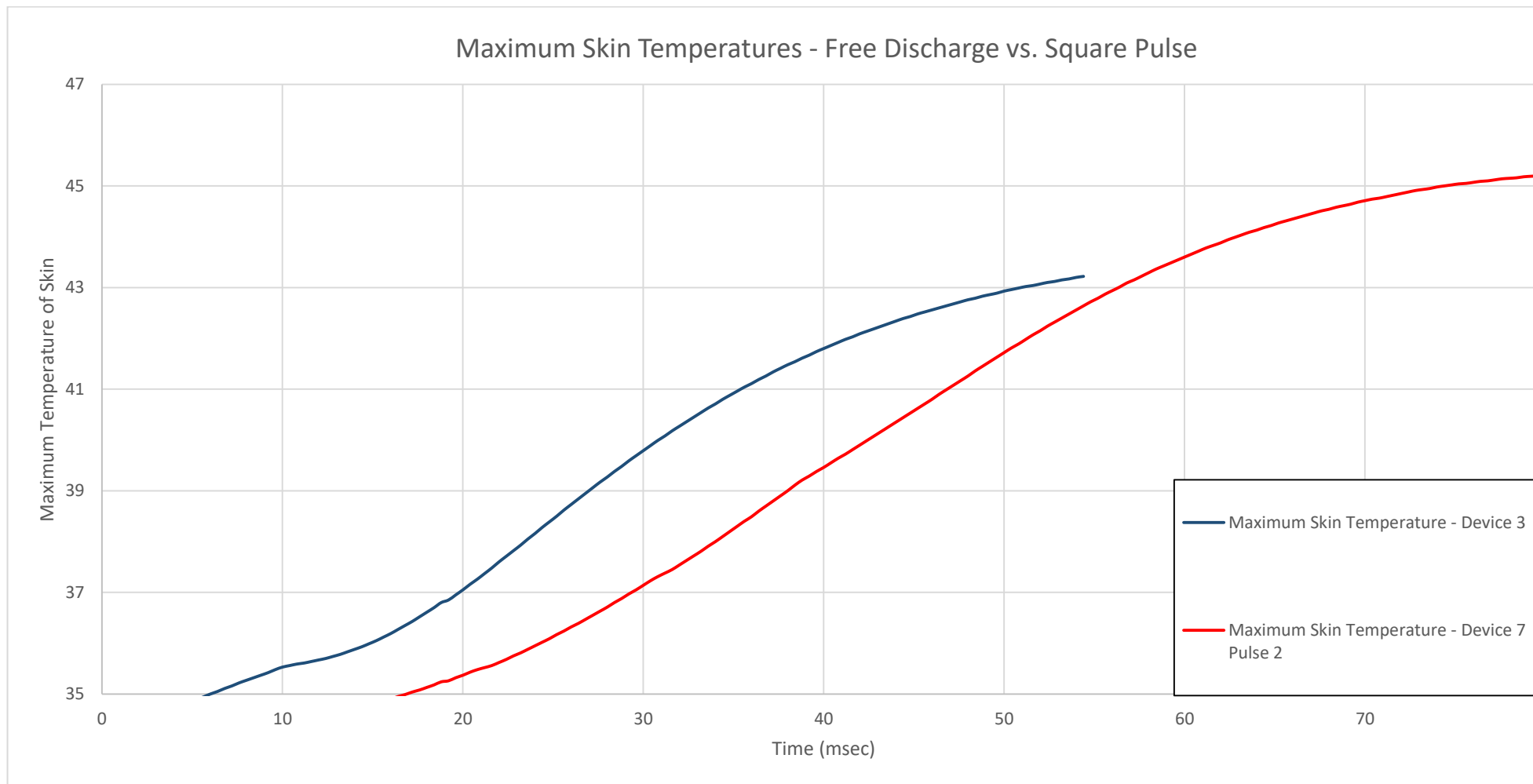


Figure 6.9 - Device 3 has a free discharge pulse shape while device 7 has a square pulse shape, however the heating of the skin follows the same pattern

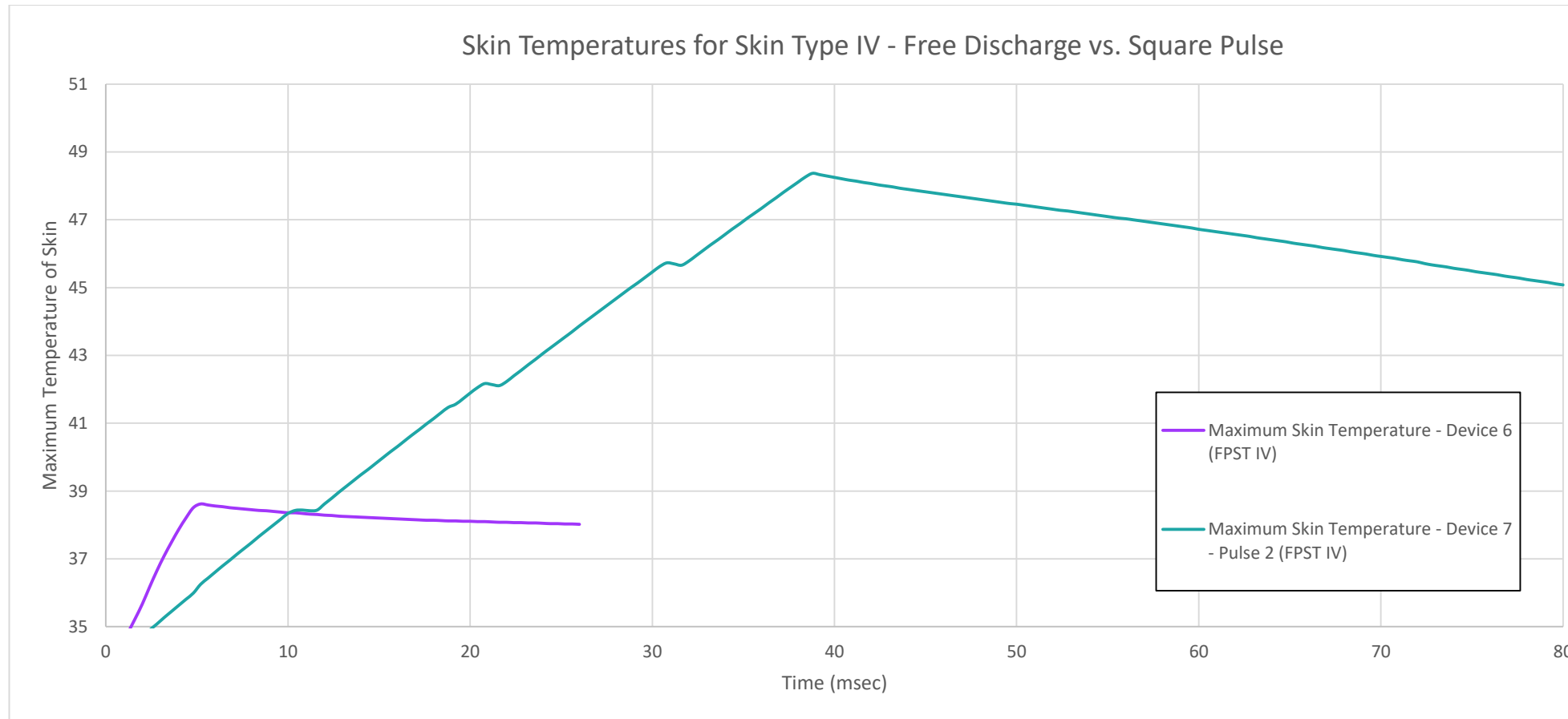


Figure 6.10 - The maximum power settings for both devices 6 & 7 were used on Fitzpatrick Skin Type IV – the way that the skin is heated reflects the pattern of the heating of the hair follicle and the pulse shape, being partially free discharge for Device 6 and square pulse for Device 7.

6.2.2 Damage Results

While the thermal results give us an indication of how the devices interact with the skin in the form of the maximum temperatures reached within the skin and the targeted hair follicle, the calibrated TODDY model is also able to demonstrate how much damage could be caused to the skin and hair follicle.

Figure 6.11 shows the damage values which were reached for each run in both the skin and hair follicle for Fitzpatrick Skin Type I. The results indicate that nearly all the devices heat the hair follicle more than they heat the surrounding skin tissue. There was only one exception, with the results from one device suggesting it could not significantly cause damage to the hair follicle or the skin.

Figure 6.12 illustrates the damage values for both the hair follicle and skin which were reached for each run when using Fitzpatrick Skin Type IV. Only the interaction of 2 devices with these skin parameters were used, as both devices did not have a skin tone sensor on the head of the device. In the results of each of these calculations, it was indicated that when using the devices incorrectly, more damage is caused to skin than to the hair follicle.

A further two calculations, both for device 7, indicated that the devices caused very minimal damage to the hair follicle. Nine calculations, consisting of seven separate devices, suggested that the devices were not able to heat the hair follicles enough meet a damage value of 1, which is the equivalent of 66% damage to the targeted cells. Only nine calculations showed that some devices were able to heat hair follicles enough to exceed the damage value of 1 for the hair follicle, from devices 3 and 7.

In terms of damage caused to the skin, sixteen calculations showed that devices were able to heat the hair follicle without causing any skin damage at all. Eight calculations did show that the devices caused some damage to the surrounding skin tissue, all of which derived from device 7. Only two of the calculations which showed that the device did cause damage exceeded the damage value of 1, which was from the use of device 7 without a filter on Fitzpatrick skin type IV.

While these results cannot be taken as concrete results, due to this being a theoretical model of how these types of devices interact with skin, as the model has been calibrated to the devices being used from the data collected in chapter 5, it can be concluded that the

differences between damages caused by the devices to the hair follicle and to the skin tissue will be similar. Therefore, where some devices may appear not to cause significant damage to the hair follicle, this may not be the case in practice. We can conclude, however, that the difference between the devices ability to heat the hair follicle and to heat the skin tissue will likely remain the same.

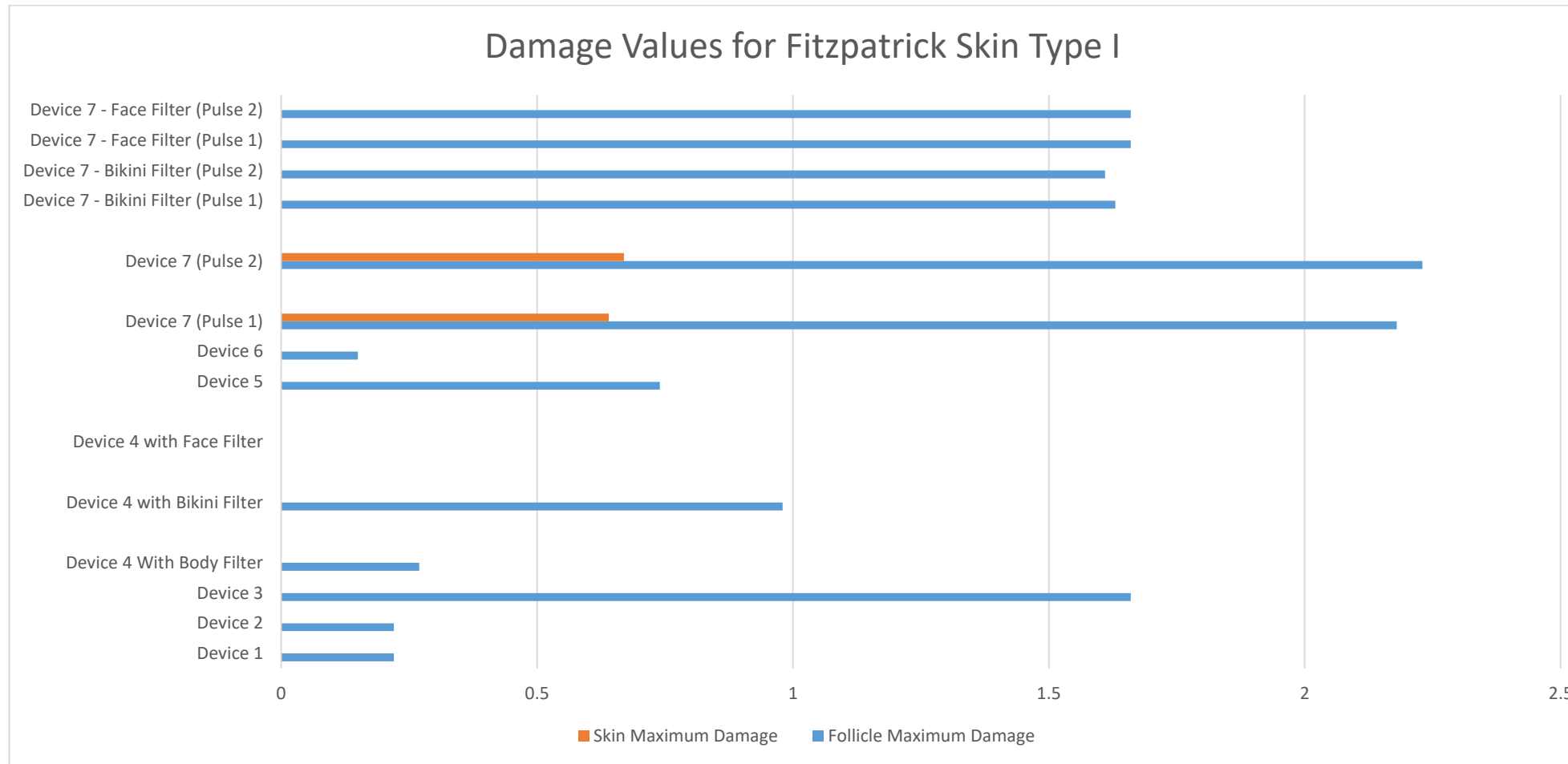


Figure 6.11 - This table illustrates the damage indicated for skin and hair when using the TODDY computational model calibrated for Fitzpatrick Skin Type I and dark hair.

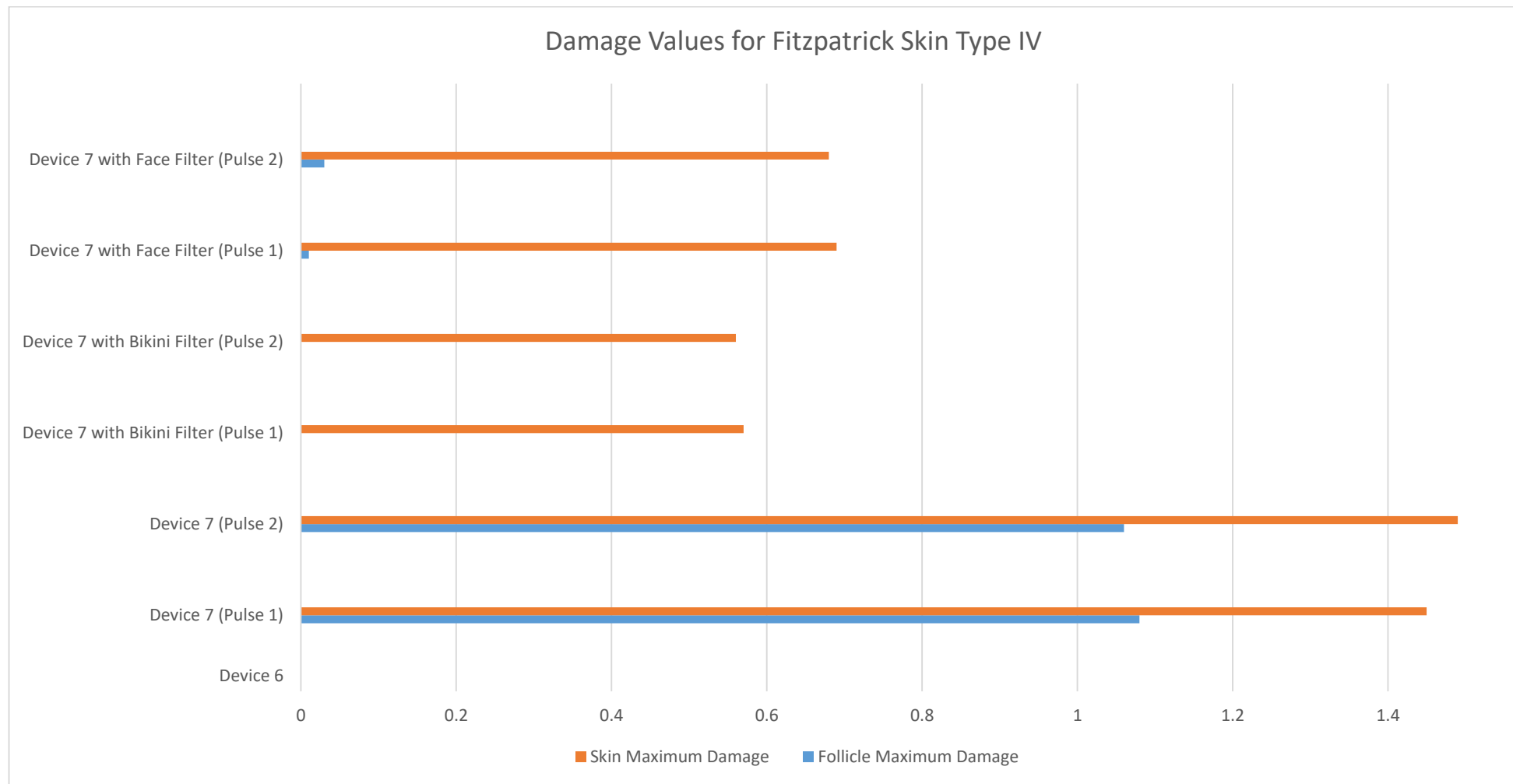


Figure 6.12 - This table illustrates the damage indicated for skin and hair when using the TODDY computational model calibrated for Fitzpatrick Skin Type IV and dark hair.

6.2.3 Discussion

The computation assessments which have been conducted have been done on a selection of IPL devices available on the market for consumers to use at home. Therefore, the results found are designed to be an indication of how these devices across the market perform in their abilities to damage hair follicles without causing damage to the surrounding tissues.

When using the parameters which research describes to give optimum results from home use IPL devices – pale skin and dark hair – no calculations indicated that the devices caused damage to the skin with the exception of device 7, which will be examined in further detail further in this section. In addition, all devices caused the follicle to heat to temperatures of 44°C or above. However, in many cases, the temperatures reached did not reflect in the damage caused, which many results showing less than 66% damage to the targeted follicle.

While the efficacy of the devices cannot be concluded from this data, the validation and calibration can define the difference between the devices' ability to heat skin tissue in comparison to its ability to heat hair follicles. Therefore, these results would suggest that these devices can damage the hair follicle more significantly than the surrounding skin tissue.

When assessing how home-use devices without appropriate safety parameters to prevent its misuse interacts with Fitzpatrick skin type IV and dark hair, the results showed that it would not successfully cause damage to the hair follicle, as would be expected. However when using device 6 in this manner, it also would not cause damage to the skin. When using device 7, some damage was caused to the skin, no matter which filter was used. Additionally, the damage to skin exceeded the damage to the follicle in each run, and when no filter was used, the amount of destruction caused to cells exceeded 66%.

These results highlight the importance of using safety mechanisms such as skin tone sensor, as without this skin tone sensor being used in conjunction with the IPL flashes, it can not only reduce the devices ability to heat hair follicles, it is also possible that such a device could cause damage to the surrounding skin tissues.

The way the skin is heated by devices 6 and 7 when used on Fitzpatrick Skin Type IV also gives some insight into why one device caused significant damage while the other did not. As the pattern of heating reflected the pulse shape, due to the large amount of photons

absorbed in the skin as well as the follicle, the partial free discharge shape meant that the skin was heated to its peak temperature when the pulse is applied, then the skin temperature drops afterwards. The square pulse train means that the skin is heated higher with each pulse in the train, and the heat is applied over a longer period of time. This agrees with research which shows that it takes prolonged heating to cause damage to the skin [83], therefore free discharge pulse shapes may not cause as much damage to the skin when the device is used on darker skin tones compared to square pulse trains. These results suggest that the pulse type used is not only important to consider when assessing a device's ability to heat the hair follicle, but it is a factor in the ability of a device to cause unwanted damage to the skin.

Both the thermal and damage results highlight that the filters for different parts of the body make a significant difference in the efficacy of the devices. As each filter is designed for a specific body area, it is likely they are intended to either decrease power for more sensitive parts of the skin, such as the face, or increase power for other parts of the skin, such as the bikini line. This was highlighted with device 4. When the face filter is attached to device 4, no damage is caused to the hair follicle, while when the bikini filter is attached, nearly 66% of the targeted cells in the targeted hair follicle are damaged.

Device 7 had a variety of calculations completed. As the pulses for each flash of the device changed, two different pulse shapes and durations were used. In addition, as it lacked an appropriate skin tone sensor, both the optimum skin parameters and a high power setting with inappropriate skin parameters were used. All calculations were then replicated without a filter, and with the bikini and face filters attached. The thermal results of device 7 only are highlighted in Figure 6.13 & Figure 6.14.

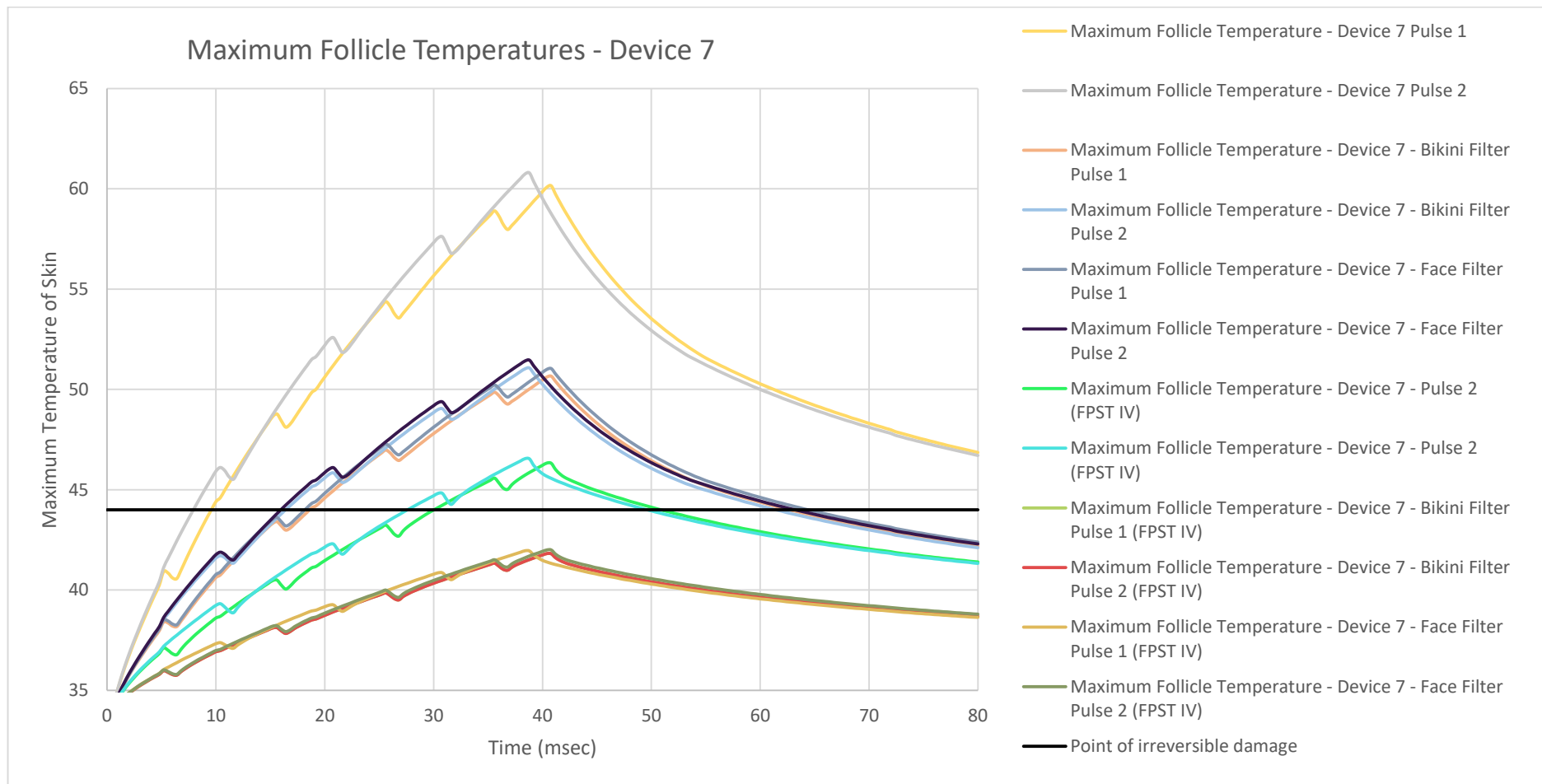


Figure 6.13 - The maximum temperatures reached in the follicle by Device 7.

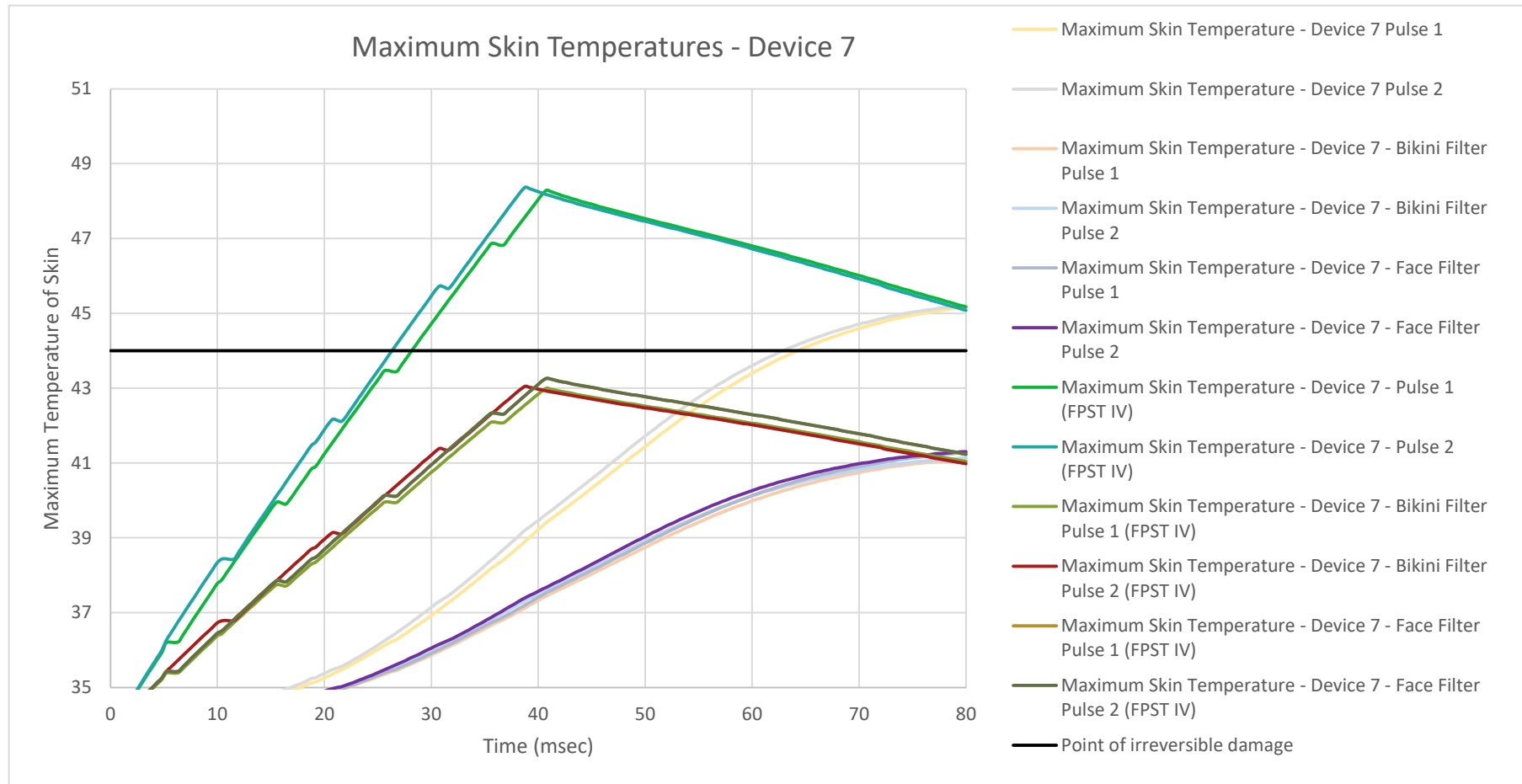


Figure 6.14 - The maximum temperatures reached in the skin by Device 7.

When the device was used as intended, the computational calculations suggest that only when a filter is not used could some damage be caused to the skin, though with filters it may not cause any skin damage. These results indicate that the intention of these filters do as they describe, and may be something which could be implemented to all devices to improve their efficacy and prevent potential unwanted skin damage during use.

When device 7 is used with Fitzpatrick skin type IV, it causes more damage to the skin than it does to the hair follicle. The high amounts of damage caused is likely due to the pulse shape, as the energy outputs are not out of the norm compared to the other devices, nor is the broadband of light used.

The different pulse shapes produced by the device between flashes did not appear to cause significant changes in the thermal or damage results from the device. While these results alone may indicate that some inconsistencies in pulse shape may not cause significant differences in a devices ability to heat hair follicles without causing damage to the surrounding skin tissues, the previous findings regarding how pulse shape does appear to make a difference to how the skin is heated must be taken into account. It is important that the pulse shapes of IPL devices are consistent in their output.

6.3 Conclusion

The results of the developed computational modelling highlighted that the devices available to consumers are safe to use when the correct parameters are used. These results indicated that all devices with sufficient safety parameters attached to the device do not cause significant, if any, damage to the skin surrounding the target tissue in comparison to the damage caused to the hair follicle.

The results indicated that in some cases a device's ability to heat a hair follicle sufficiently may be affected by the filters attached to a device. While these findings suggest that these filters provide some protection from the device causing unwanted damage to the skin tissue, a balance needs to be found between ensuring that no significant damage is caused to the skin, while still effectively heating the hair follicle.

Results also indicated that should a device be used on an inappropriate skin tone with a high power level, significant damage can be caused to the users' skin. This finding highlights that ensuring the appropriate safety mechanisms are fitted to the devices available on the consumer market, as this type of misuse is preventable when a device has skin tone sensors attached to the head of the device.

All the results found in this chapter cannot be directly applied to physically using an IPL device on the skin. The computational model used has limitations with regards to the results produced – the model is only two dimensional, which is not an accurate representation of human skin. In addition, the computational model runs on ideal parameters, such as the device being exactly perpendicular to the skin, and the temperature of the skin being exactly the same throughout, and the hair follicle being at a perfectly straight angle. While some safety mechanisms can encourage the user to ensure the device is perpendicular to the skin, it can be difficult to get the device at the perfect angle for optimum results for some areas it is designed to be used for, such as the underarms, especially as the devices are intended to be applied by the user, rather than applied by a professional.

The computational model used, however, has been validated and calibrated in line with the skin tones and hair colours used, and therefore the results are accurate with regard to damage calculations given when comparing a devices' ability to heat the hair follicle in comparison to its ability to cause thermal damage to the surrounding tissue.

Due to this, while these results do give an accurate indication of the efficacy and safety of the devices available on the market, conclusions cannot be drawn on computational results alone, and clinical studies to compare the results to would support these findings regarding how such devices interact with the skin and hair.

Chapter 7 - Discussion and Conclusions

7.1 Discussion

Home-use devices such as IPL devices allow people to bring light-based technology into their home and use such technology without professional guidance for a lower prices than regularly visiting a salon for a similar treatment conducted by a professional, and these types of devices are very popular.

The wide range of devices' available lack peer-reviewed research into their efficacy, and this can make it difficult for both the consumer to decide which product is best for them. This also means it can be hard for them to be given informed guidance from medical professionals regarding these products.

As these devices are designed to be used without professional guidance, their power is reduced and a variety of safety mechanisms are implemented on the device itself in order to reduce the likelihood of a user injuring themselves.

An in-depth description of how light interacts with skin, and how certain types of home-use devices has been given in this thesis. Further detail is given with regards to Intense Pulsed Light devices for hair removal, and the theory behind how the devices operate is also given.

A literature review was conducted on the already published work on home-use devices, which highlighted the lack of peer-reviewed research conducted on home use devices, with the majority of research available focusing on IPL devices. Of the studies discussed, there were a number of problems highlighted, including small sample sizes, short-term follow ups despite claims of long term hair removal, and a large range of results from similar or the same devices. It was concluded that this was due to poorly controlled parameters in the studies which had been conducted.

The literature review also highlighted that many devices do make claims of long term, and sometimes permanent, hair removal and that the devices do not pose safety concerns for users. Some studies have raised questions regarding these claims, as there is potential for thermal and electrical injuries to users [5], [114].

This thesis intended to highlight the gaps in knowledge regarding the use, effectiveness and safety of such devices. To do so, a range of devices available on the market were investigated, investigating the outputs of the devices, and how they compared with the

claimed outputs described by the manufacturers of the devices. This selection of devices was chosen as a representation of the devices available on the market. Using these results, the potential for damage to both the hair follicle, to reduce hair growth, and skin was assessed using a calibrated version of program TODDY. This program uses Monte Carlo and ADI methods to indicate the interaction of the light emitted from the device with the skin and hair, providing an indication of damage caused and the temperatures to which the skin and hair follicle was heated to through the interaction of these devices with the skin.

The experimental results showed that many devices fell within the claimed outputs of their manufacturers, when they were provided. The findings for energy output for device 2 had more than a 20% difference compared to the claimed output from its manufacturer. The pulse duration for device 3 had a difference of between 28.85% and 38.46% compared to the claimed pulse durations for the settings on this device. Device 7 had erratic pulse shapes which changed with each flash of the device. In the following chapter, the effect of the changing pulse shapes for device 7 were investigated. The spectral results showed that many devices had emissions of light in the wavelengths before the cut off filter on the devices, though it was concluded that this was likely due to the dichroic filters used on these devices.

These examples highlighted that many devices on the market are not upfront about the technical specifications of their devices, and in some cases, the devices outputs can vary from the manufacturers' claims. It is concluded that it is important for the manufacturers to be upfront to consumers about their devices outputs, and to ensure that they are as accurate as possible.

With regard to safety findings, all devices had safety mechanisms implemented. All devices had separate power settings, designed for different skin types and skin sensitivity – some devices, such as device 2, automatically assessed the power needed using the skin tone sensor on the device. Others, such as device 4, allowed the user to decide which power setting they wished to use. All devices except device 6 required the device to be in full contact with the skin before it could be used. Skin tone sensors were present on all devices except device 6, and device 7 had the skin tone sensor separate from the head of the device – for this reason, the use of these of the highest power of these devices on Fitzpatrick Skin type IV was investigated in the computational results chapter. Devices 4, 7 and 10 had filters designed for certain body areas – the effect of these filters were assessed in the computational results.

The safety findings of our sample of devices suggest that while many devices are adequately equipped with the safety mechanisms required to ensure that the devices are used correctly, it is not an industry requirement that devices have mechanisms in place which prevent misuse, such as sensors to ensure that the device is in contact with the skin before use.

Using the data collected from the devices, Monte Carlo and ADI models were conducted to assess the ability of the devices to heat and damage the hair and skin. Results showed that all devices were able to effectively heat the hair follicle to 44°C, the heat at which irreversible damage begins. Despite this, damage results showed that many devices were not able to heat the follicle sufficiently to cause a significant amount of damage. However, the temperatures found themselves cannot be taken as concrete, and the results instead suggest that most devices do cause significantly more damage to the hair follicle than the surrounding tissue, as intended.

The computational modelling highlighted that the filters provided with some devices had a significant effect on the damage caused to the hair follicle by the device, however this is not something that all devices were fitted with. As they did have such an impact on the damage, or lack thereof, on hair follicles in comparison to the surrounding skin tissue, this is something manufacturers should consider as part of the safety mechanisms which can be included on a device.

When assessing potential damage to skin when devices without skin tone sensors were used incorrectly, interesting results were noted – device 6, with a partial free discharge pulse shape caused no damage to the skin or hair follicle, while device 7 caused significant damage to the skin in comparison to the hair follicle – in all cases, more damage was caused to the skin than the hair follicle. The reason behind these findings was discussed to be related to either the power of the device, as one device had not been able to significantly damage the hair follicle either, or the pulse shape of the devices. One device had a pulse train, repeatedly raising the temperature of the skin, while the other had a single, free discharge style pulse, only raising the temperature of skin and follicle once.

This chapter concluded stating that further investigation would be required to support the findings of the computational methods, as it is not an accurate reflection of a person physically using the device on the skin.

7.2 Conclusions

7.2.1 Meeting the aims and objectives

This thesis had two purposes, two aims, and two main objectives. How each of these has been met will now be addressed.

The first purpose of the thesis was to “give an impartial assessment on the safety and efficacy of various branded home-use IPL devices currently available on the market”. This purpose was met in chapters 4, 5 and 6 – chapter 4 began by giving an overview of the research which had already been published with regards to home use devices. Chapter 5 then assessed the safety mechanisms on the devices, and collected the outputs of each devices being investigated. Finally, the collected data was used alongside computational models in chapter 6 to assess the ability of the devices ability to heat a hair follicle, and whether it subsequently causes damage to the skin. The findings indicated that the devices available on the market are adequately safe to use, though some improvements could be made. In addition, most devices were able to heat the hair follicle significantly more than the surrounding skin tissue.

The second purpose was to “create a bio-physical computer model which can measure the heating effects of the chosen home-use Intense Pulsed Light (IPL) devices”. This purpose was met in chapters 3 and 6. Chapter 3 described a variety of computation models which described heat transfer within biological tissues, and two of these models – the Monte Carlo method and the ADI method – were utilised in chapter 6 to assess the ability for the chosen devices to heat the hair follicles and the skin. These models were calibrated using data from chapter 5 in order to assess the sample of devices used. This aim was met by the development of the computational model to analyse and explain the outputs of typical home-use IPL devices available on the market.

The second aim of the thesis was to “To assess if the devices being investigated can successfully destroy the hair follicle without causing damage to the users’ skin.” This aim was met in chapter 6, which showed that most devices were able to heat hair follicles without causing significant damage to the surrounding skin tissue.

7.2.2 Implications of the Thesis Findings

In chapter 4, a literature review was conducted. The literature review highlighted the lack of peer-reviewed research available regarding home use light based devices. It also

demonstrated that many of the studies available to the scientific community lacked appropriate parameters and controls, with difference results for the same device shown in separate studies. The studies also had small sample sizes, typically only used one device, and only showed results over a short period of time, despite the study intending to indicate long term results.

In chapters 5 & 6, outputs of the devices were collected, and then assessed using a computational modelling program. The results of the computational modelling suggested that many of the devices assesses can heat hair follicles without causing significant damage to the surrounding skin tissue. These chapters also highlighted a potential in the safety mechanisms of some available devices, which could lead to them to be used inappropriately, which could lead to adverse effects. This was only possible due to these devices lacking a skin tone sensor on the head of the device, a mechanism which was included on all other devices investigated. Device 7 in fact did have a skin tone sensor, however due to the fact it only requires a fingerprint to assess skin tone, this means it cannot accurately assess the skin tone of the location that the device is being used on. This finding highlights the importance of ensuring these devices are fitted with complete and appropriate safety mechanisms available to manufacturers.

These chapters also highlighted that the outputs of these devices sometimes do not conform to the outputs suggested by their manufacturers, and are sometimes not uniform. One device showed its energy output was the most varied compared with the other devices tested, and the measured pulses differed between flashes. The computational results showed that the heating abilities of this device were enough to potentially cause damage to the skin as well as the hair follicle, and could cause more damage if the device was used against safety recommendations.

7.2.3 Contributions to Knowledge

This thesis had two intended knowledge contributions. The first was to calibrate a bio-physical computation model which could be used with home-use IPL devices to assess their thermal effects on human skin and hair follicles with specific skin parameters. This was achieved, as detailed in chapter 6 – a Monte Carlo model was calibrated to the devices using the findings from chapter 5 to assess the movement of photons in 2 skin models. The first model simulated Fitzpatrick Skin Type I with black hair, while the second model simulated Fitzpatrick Skin Type 2 with brown hair. The second part of the model, which used the ADI Method, was calibrated to assess how these devices could theoretically heat

human skin, and assess if they could potentially successfully damage hair follicles to a temperature which would induce reduction of re-growth. This was also able to successfully assess the comparative potential these devices had for damage to human skin.

The second was to create a comprehensive list of the dielectric properties of human skin, between frequencies of 200kHz and 6MHz. The list was successfully created, and was provided in chapter 3. This information was compiled through the limited literature available, as much previous work had been investigating the conductivity and permittivity of skin at higher frequencies. All of the data compiled was specifically based on human tissue only, as some available literature used animal skin to provide their results as an indication of general skin properties.

7.2.4 Recommendations

Following the findings of chapters 5 & 6, it is recommended that manufacturers review and appropriately assess the outputs of its devices. Experimental results showed that while many devices were well within the accepted 20% boundary of its claimed outputs, some devices were out of this range for its energy and pulse durations. Some manufacturers did not state the expected output of the device, though findings would suggest that some devices had outputs which were unlikely to be intended by the manufacturer, with erratic pulse shapes and durations, and a large range of energy outputs between flashes. Some devices may also have the capability to cause skin damage to the user when using this device.

It is also noted that many of the devices provide low enough powers to ensure that they cannot pose a danger of heating the skin to the point of damage during use, however these finding suggest they may not be able to sufficiently heat hair follicles to the point of damage in comparison to their ability to not cause damage to the surrounding tissue, which is the claim being made by manufacturer of these devices. Following these findings, it is also recommended that all manufacturers being forthcoming with the outputs of the devices, in order for independent investigations of the devices to be conducted and assessed.

To ensure the safe use of these devices, it is recommended that all devices are equipped with the appropriate safety mechanisms as standard, including skin tone sensors on the head of the device to ensure that the skin that the device is being directly used on is being detected, and additionally sensors which ensure devices are in full contact with the skin

when being used. By implementing a skin tone sensor to this type of device, it would mean that the device could not be used when it is out of contact with the skin. The findings of chapter 6 highlight that should these devices be misused, there is potential for skin damage to the user.

Another area which could increase the safe use of IPL devices would be the implementation of filters designed for certain body areas, to adjust the power of the device according to skin sensitivity. Chapter 6 highlights that these filters can have a significant effect on the damage a device can cause to hair follicles, however a balance would need to be found between reducing adverse effects and ensuring that a device can still significantly heat the target tissues.

7.2.5 Limitations of the Thesis

This thesis only assesses these devices in a laboratory setting with regard to the output of the devices, and in a theoretical setting with regards to their interaction with skin. Due to this, definitive conclusions cannot be drawn regarding whether these devices do meet their claims of safety and efficacy – for a more complete indication of the devices efficacy, and potential for damage to the skin, a well-controlled clinical study would need to be conducted alongside the computational model.

The chosen computational model was a two dimensional model of the broadband of light interacting with skin, which is not a true representation of how skin and light interact in practical settings, as skin is not a two dimensional construct. The way which photons can move is limited in the TODDY model, and cannot give a precise representation of how an IPL device would interact with and heat skin or hair follicles.

The safety findings of this thesis were focused only on the outputs of the devices, and their physical safety mechanisms. To give a full overview of the safety of home use light based devices, all available devices would need to be inspected with these parameters. Other areas of safety would also need to be assessed, such as ocular safety for devices which do not need to be in complete contact with the skin to be used, and whether these devices meet safety standards and regulations.

This study only assesses two potential areas of efficacy and safety when interacting with skin, being the highest power settings of these devices with Fitzpatrick skin type I and dark hair, and Fitzpatrick skin type IV and black hair. To give a full assessment of the safety

and efficacy of these devices, a full range of skin tones and hair colours with different power settings would need to be investigated. This thesis only gives a partial indication of the safety and efficacy of these devices.

7.2.6 Further Research

Following the limitations discussed in this chapter, further work which could be carried out to give a more in depth and accurate answer to the research questions posed in this thesis will be discussed here.

Controlled clinical trials, which are independently assessed and are conducted over a 12 month period with a statistically significant number of participants of different skin tones and hair colours, with multiple cohorts and different target hair locations on the body would give a more rounded indication of the efficacy and safety of these devices. With clear results from the physical interaction of these devices with skin, it will give a good comparison tool to create context for the technical and computational findings of this thesis.

Clinical trials are limited, however, as by using the devices in a manner which is not recommended by manufacturers, a risk is posed to a participant in the form of adverse effects on to their skin, and therefore would be against ethical guidelines. By using a three dimensional computational modelling system alongside clinical trials, the use of the higher energy settings on the devices on darker skin tones could give a more accurate indication of how intense pulse light devices interact with all skin tones. It is important to assess the damage which these devices could potentially cause in order to ensure the safety mechanisms on devices are appropriate.

Additionally, looking at all devices available on the market with a range of energy settings, hair colours and Fitzpatrick skin types would give provide a more versatile indication of all the results that these devices can produce, rather than just when the optimum parameters are used for some devices, or the devices is used against some safety recommendations.

This thesis is limited to assessing devices which use intense pulse light technology to treat hair removal at home. The market of home use devices is much wider, with devices using different types of technology to treat cosmetic conditions such as wrinkles, acne, and alopecia, all of which have even less research conducted than research based on IPL devices. Further work should look into investigating the safety of these devices, and their ability to do as they claim, theoretically and practically.

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