Impact of Chromophores on Color Appearance in a Computational Skin Model

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ABSTRACT

Early diagnosis of skin cancer offers the patient more favorable treatment options. Color fidelity of skin images is a major concern for dermatologists as adoption of digital dermatoscopes is increasing rapidly. Accurate color depiction of the lesion and surrounding skin are vital in diagnostic evaluation of a lesion.

We previously introduced VCT-Derma, a pipeline for dermatological Virtual Clinical Trials (VCTs) including detailed and flexible models of human skin and lesions, which represent the patient in the entire dermatoscopy-based diagnostic process. However, those initial models of skin and lesions did not properly account for tissue colors.

Our new skin model accounts for tissue color appearance by incorporating chromophores (e.g., melanin, blood) into the tissue model, and simulating the optical properties of the various skin layers. The physical properties of the skin and lesion were selected from clinically plausible values. The model and simulated dermatoscope images were created in open modelling software, assuming a linear camera model. We have assumed ambient white lighting, with a 6mm distance to the camera.

Our model of color appearance was characterised by comparing the brightness of the lesion to its depth. The brightness of the lesion is compared through the variability of the mean gray values of a cropped region around the lesion. We compare two skin models, one without extensive chromophore content and one with. Our preliminary evaluation of increasing chromophore content shows promise based on the results presented here. Further refinement and validation of the model is ongoing.

Keywords: Skin lesion imaging, skin cancer, melanoma, lesion, computer simulation of skin anatomy, virtual clinical trials.

1. INTRODUCTION

Dermatoscopy is a non-invasive method of skin imaging. Dermatoscopes are the *de-facto* instrument of choice for dermatologists. Analog dermatoscopes have been used for many years and consist of a light source along with a magnifying lens to help the dermatologist visualize any irregularities with the lesion[1]. The dermatologist relies on visible light and what they see with their naked eyes through an analog dermatoscope to reach a diagnosis. Digital dermatoscopes are being adopted quickly and offer dematologists the ability to glean more from the lesion with the help of image processing

techniques to support the task of diagnosis[1]. Some digital dermatoscopes provide more than just visible light image in the form of multispectral information[2]. This can inform about the skin properties at varying depths based on the wavelength of the light used, additionally enhancing the diagnostic decision task.

Digital dematoscopes come in a variety of form factors such as large machines, to handheld devices, to smartphone add-ons[1,3]. Given the fact that most displays and camera devices apply some form of calibration and image processing to the image, it is very important to ensure that the digital image of the lesion that is viewed by the dermatologist is as close to the original lesion as possible. Lesion color is one the most likely characteristics to be unduly modified during such processing, which can potentially affect the final diagnosis[4].

It is critical to ensure that the characteristics of the lesion regarding color, border sharpness, and other that contribute in the clinical decision (such as Asymmetry, Border, Color, Dermatoscopic features)[5] all appear faithfully in the image to prevent misdiagnoses. Ensuring that digital dermatoscopes are of the required quality involves a number of iterations during the process of the device design as well as a number of clinical trials which admittedly are very expensive, and time consuming. Saving the cost and time of the real clinical trials is the reason why we have proposed the concept of Virtual Clinical Trials for Dermatology[6].

The VCT pipeline includes (i) software modules that simulate human skin with and without different types of skin lesions (in the form of the software skin phantom, i.e., the virtual patient), (ii) modules that simulate the effects of optical image acquisition resulting in simulated/virtual images of the skin (i.e., virtual dermatoscopic device), and (iii) modules to analyze the resulting images and infer the diagnostic decision (i.e., the virtual reader)[6].

In this manuscript we extend the skin phantom introduced in our earlier paper[6] by adding an improved chromophore representation. The extended skin phantom is characterised by the analysis of color appearance, assuming simulated melanoma.

2. METHODOLOGY

2.1 Influence of Color in Dermatoscopy

Dermatoscopy enables the visualisation of structures and colors beneath the surface of the skin, which are not routinely discernible to the naked eye[7]. To ensure an accurate diagnosis using dermatoscopy, clinicians and dermatologists need to understand the histopathological correlation. A lesion is generally characterised by several correlated features by which a dermatologist may reach a diagnosis. One of the more prominent being the color of the lesion. While invasive methods allow the dermatologist to see the entire breadth of the lesion in the horizontal plane, the structure and colors seen on dermatoscopy are generally limited in depth to the papillary dermis[7], which is the uppermost region of the dermis. Please refer to Figure 2 for an idea of the structure and layers of the skin.

Classical analog dermatoscopes[1] were limited in this way as dermatologists would be essentially looking into a magnifying lens for detailed observation of skin lesions. The advent of digital dermatoscopes, which came with an integrated camera, allowed dermatologists to take dermatoscopic images of skin lesions thus allowing for the possibility of processed images that could help improve diagnosis of lesions.

One of the earliest methods to aid in diagnosis was the ABCDE algorithm[8]. It has been developed to question whether a melanocytic lesion under investigation was benign, suspicious or malignant. It is based on a score derived from the quantification of lesion's asymmetry (A), border (B), color (C), diameter / dermatoscopic structures (D), as well as, the evolution (E) of the lesion over time, as can be seen in Figure 1. below.

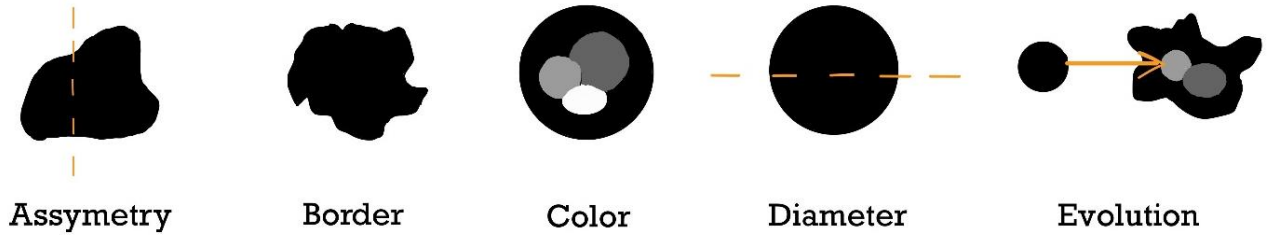


Figure 1 – ABCDE assessment of a lesion (modified from[9])

Of these five assessments, color is one of the most important determining factors for a lesion[4]. The number of colors discernible, as well as their spatial distribution are key to making correct clinical diagnoses. The observation of multiple colors in a lesion indicates that the lesion is more likely to be malignant than benign. Benign lesions (usually) reveal only one or two colors whereas malignant lesion (for example melanomas) frequently reveal three or more colors. The colors themselves help determine the seriousness of a lesion. With respect to melanoma, the presence of red, white, and/or blue/grey colors in a lesion are more likely to imply a malignancy as compared to just shades of brown. The distribution of the colored regions in a melanoma are often focal, asymmetrical, and irregular.

In the original ABCD-rule data[7], 56% of melanocytic nevi had two colors, 29% had three colors, and only 10% had more than three colors. In contrast, 85% of melanomas manifested three or more colors, and 40% of melanomas revealed five to six colors[7]. In determining the color score, the following six colors are considered important: white, red, light brown, dark brown, blue-grey, and black.

Most of these colors are only visible with the help of dermatoscopes as they are not very discernible with the naked eye. Dermatoscopes allow the dermatologist to identify specific colors and characteristics which are intrinsic to specific dermatoscpic features occurring at specific layers / depths of the skin.

Some colors, especially when associated with select dermatoscopic structures, also have important histopathologic correlates, such as white globules (associated with balloon-cell changes), homogeneous yellow to orange areas (associated with cell xanthomization) or black lacunae (associated with blood thrombosis)[10].

The importance of color assessment has led to a number of studies focusing on or employing color features as a constituent part of their skin analysis systems[4]. In the skin, the color is mainly dependent on the chromophores present in the selected region of interest. Chromophores are light-absorbing and scattering molecules, that are dependent on the wavelength of light incident upon them. They are responsible for complex elastic and inelastic scattering events.

Most of the colors present in the skin originate from an increase in a given chromophore on the skin, such as pigment (brown, black, gray, blue), lipids or keratin (yellow), collagen (white) or blood (red). The most important chromophore in pigmented lesions is melanin. The quantity and location of melanin, together with that of the blood vessels, vascular volume, keratinocytes, and collagen all contribute to the colors seen during dermoscopy[10].

Below is a short summary on some of the chromophores that are modelled in our skin model:

Melanin[11]: This is one of the principle components that determine the color of the skin. Melanin is produced by melanocytes which are located at the epidermal-dermal boundary of the skin (Figure 2). Depending on its location in the skin, the appearance of melanin varies. It appears black when located in the stratum corneum, brown when located at the dermo-epidermal junction, grey when located in the papillary dermis, and blue when located in the deeper dermis. Melanin, when present in multiple layers of the skin can also appear black.

Melanin mainly consists of two pigments: eumelanin and pheomelanin. The ratio of these pigments determines a person's skin type[12]. Eumelanin is a dark brown-black pigment while pheomelanin is a reddish-pink pigment. Persons with light complexioned skin mostly produce pheomelanin, while those with dark complexioned skin mostly produce eumelanin.

Abnormal growth of melanocytes is the cause of the most common type of skin cancer in the world - melanoma. Clinically observed lesions show an abnormal / cancerous growth of melanocytes in the skin, which starts at the epidermal-dermal boundary and penetrates deeper into the skin as the severity increases. Our skin model contains a lesion which is approximated to be a melanoma; and this is detailed in Section 3.

Haemoglobin[13]: After melanin, it is haemoglobin that next most influences the color of the skin. It is present in blood cells which are found distributed between two blood networks located in the upper and deep blood net dermis (refer Figure 2). The blood in these capillaries differ in color depending on whether they contain oxygenated (arterial) or deoxygenated (venous) blood, where the former is a brighter shade of red as compared to the latter. The veins sometimes appear bluish due to the scattering properties of the capillary walls if they are present at a greater depth. Blood vessels and vascular volume are responsible for the red and pink hues.

Carotene[14]: This is a yellow-pigment that is usually present in the fat cells of the dermis (refer Figure 2). As we have not modelled any fat cells (subcutaneous tissue), we have introduced a slight yellow-orange color into the dermal layers to compensate for this. It is also present in small quantities in the epidermis of the skin. Carotene is similar to the pigment bilirubin, which is yellow in color and the cause of the yellowing of the skin during jaundice.

Collagen: These are fibres that are present in the dermis of the skin and is responsible for the multi-scattering effect of the dermis. They do not contribute any specific color to the skin, but they are one of the causes of scattering in the skin. White coloration can be due to depigmentation, fibrosis, alterations in the collagen matrix, or keratin within cysts[7].

2.2 How the VCT-Derma skin model layers account for chromophores

The model of the skin was created using open software (Blender[15] v 2.79), a 3D modelling tool commonly used to create artefacts and structures to be employed in game engines. Blender makes use of luxcorerender[16], a physically based unbiased rendering engine, which can produce realistic images of photographic quality. It is based off the physically based rendering technique (pbrt)[17] algorithm which is an approach to render graphics in way that accurately simulates the flow of light, as would be observed in the real world[18].

The developed skin model is comprised of 6 layers, namely the stratum corneum, the epidermis, the papillary dermis, the upper blood net dermis, the dermis, and the deep blood net dermis. Two blood networks have been created in the upper and deep blood net dermis respectively which have been connected via interconnecting blood vessels spanning the width of the dermis[6], as can be seen in the Figure 2..

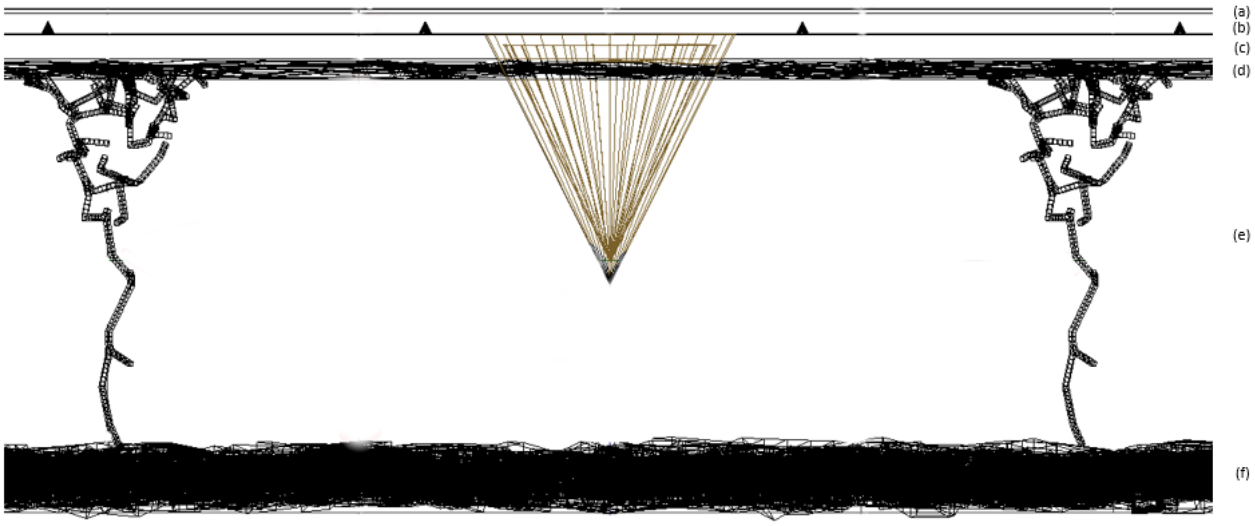


Figure 2 - Cross section of the skin model used in VCT-Derma[6] – (a) Stratum Corneum (b) Living Epidermis (c) Papillary Dermis (d) Upper Blood Net Dermis (e) Dermis (f) Deep Blood Net Dermis

Table 1 - List of chromophores employed in their corresponding layers in VCT-Derma Skin Model

Layer	Melanin		Blood		Carotene	Collagen
	Eumelanin	Pheomelanin	Oxyhaemoglobin	Deoxyhaemoglobin		
Stratum Corneum	Yes	Yes			Yes	
Living Epidermis	Yes	Yes			Yes	
Papillary Dermis					Yes	Yes
Upper Blood Net Dermis			Yes	Yes		
Dermis					Yes	Yes
Deep Blood Net Dermis			Yes	Yes		
Lesion	Yes					

Table 1. lists the chromophores that we addressed in our skin model, as well as which layer accounts for which chromophore. Each layer is assumed to have uniform properties throughout; the individual layers are dependent on the optical (absorption and scattering) properties of the corresponding chromophores. These properties include an approximation of the color (RGB) for the pigment (in line with those mentioned earlier in section 2.1), the index of refraction, and the absorption depth to an extent. Table 2. gives an idea of some of these values obtained from literature[19]. The phantom is illuminated with an ambient source of white light to simulate better the natural viewing conditions.

Table 2 - Optical Properties of Caucasian Skin at 600nm[19]

Skin Layer	Thickness (μm)	Scattering Coefficient (mm^{-1})	Absorption Coefficient (mm^{-1})	Absorption Depth (mm)	Anisotropy factor	Index of Refraction
Stratum Corneum	20	100	0.02	0.001	0.9	1.53
Living Epidermis	80	40	0.015	0.001	0.85	1.34
Papillary Dermis	150	30	0.07	0.001	0.8	1.4
Upper Blood Net Dermis	80	35	0.1	0.001	0.9	1.39
Dermis	1500	20	0.07	0.1	0.76	1.4
Deep Blood Net Dermis	170	35	0.1	0.001	0.95	1.39
Lesion	1000			0.1		1.7

The camera model employed is the generic camera model available in the Blender luxcorerender. It is located 6mm from the surface of the skin phantom, as this is the distance between the glass and sensor of the dermatoscope[2] to be modelled in the VCT-Derma pipeline[6].

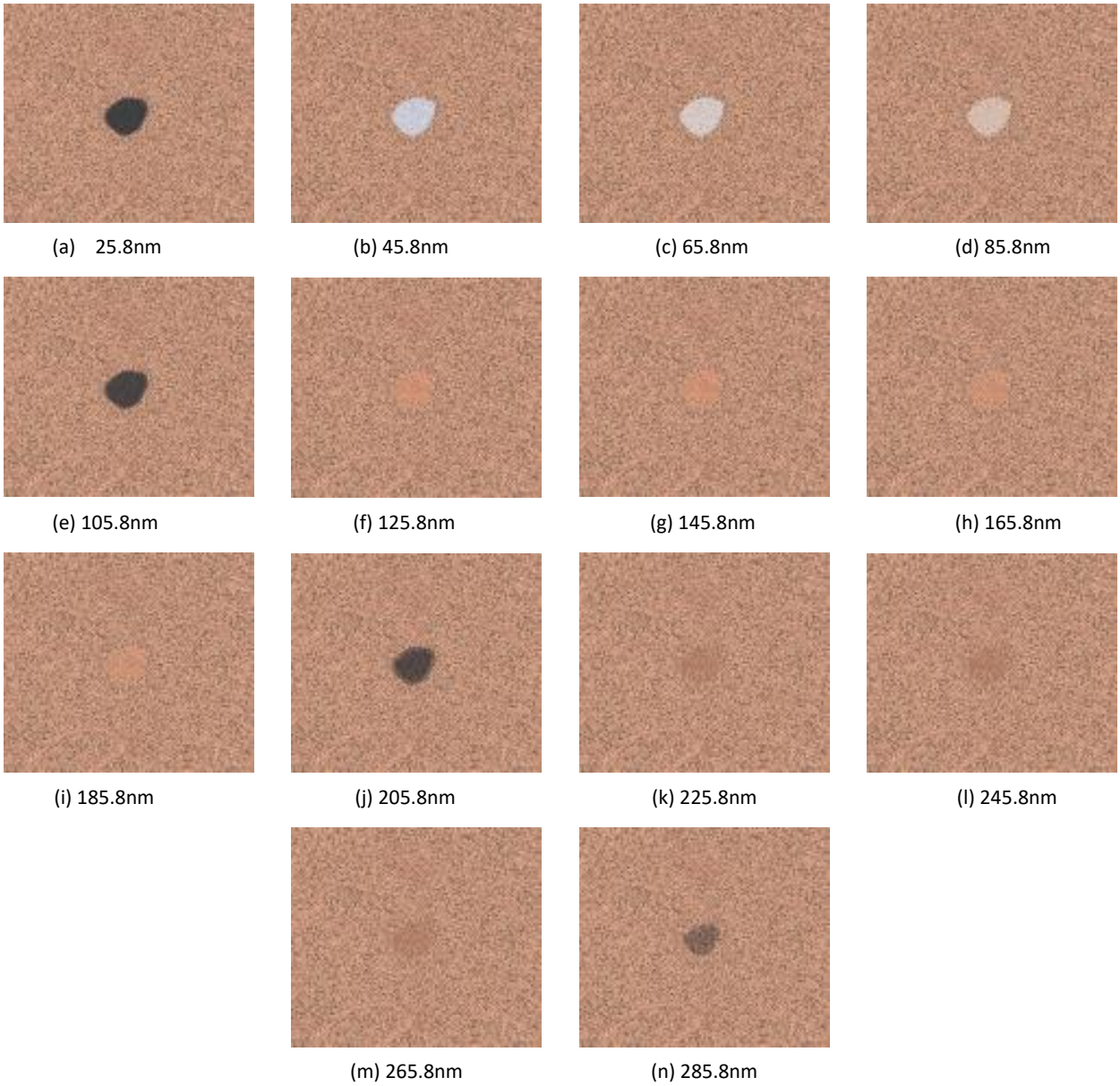
As mentioned in section 2.1, in the case of melanoma, lesion color varies with the position of melanin in the skin, from dark brown-black for melanoma residing in the stratum corneum, brown in the epidermis/papillary dermis, bluish white in the dermis, and finally black as it penetrates deeper into the dermis. Therefore, in our skin model we insert lesions at various depths and generate simulated images for each of those.

This experiment is conducted with two skin models, Model 1 (lacking extensive chromophores)[6], and Model 2 (accounting for all chromophores mentioned in Table 1). The mean grey values of the images are calculated and plotted against the depth of lesion in the model (in mm) to quantify lesion variation with depth, as well as to observe any / all variation based on increased chromophore concentration. The results for the same can be seen in the Results and Discussion section below.

3. RESULTS AND DISCUSSION

A lesion of 1mm thickness is lowered within our skin model in steps of 0.02mm/20nm from the stratum corneum to the papillary dermis-upper blood net dermis border (Figure 2). Figure 3. shows simulated images of the lesion as we increase the depth from the stratum corneum to the papillary dermis - upper blood net dermis border of Model 1; Figure 4. shows the corresponding lesion images for the Model 2. The clarity of simulated lesion appearance on the skin surface is progressively reduced as their depth increases; in line with observation of clinical images[7].

Further research is ongoing on how we could adequately simulate the so-called Tyndall effect[20] when light propagates further into the dermis. The Tyndall effect is where short-wavelength visible light (blue) is dispersed and reflected more than long-wavelength light (red). This results in the blue color of otherwise black melanin, based on the depth of the pigment deep in the dermis. This can be viewed in the image (E) of the Figure 5.



(a) 25.8nm (b) 45.8nm (c) 65.8nm (d) 85.8nm

(e) 105.8nm (f) 125.8nm (g) 145.8nm (h) 165.8nm

(i) 185.8nm (j) 205.8nm (k) 225.8nm (l) 245.8nm

(m) 265.8nm (n) 285.8nm

Figure 3 – Model 1 - Increasing lesion depth by 20nm from (a) the Stratum Corneum, to (b) - (d) Epidermis, (e) - (i) Papillary Dermis, (j) - (m) Upper Blood Net Dermis, and (n) Dermis

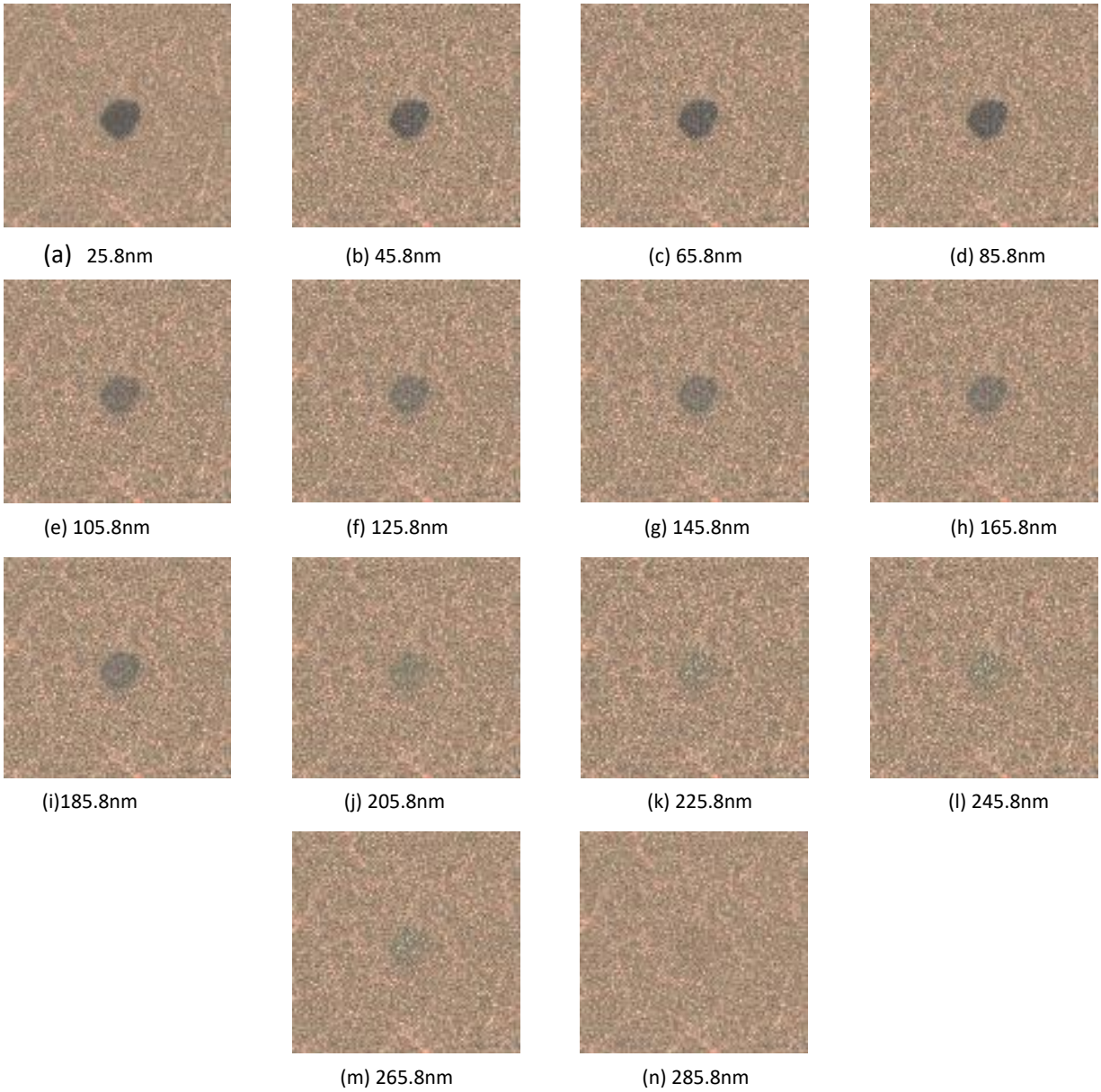


Figure 4 - Model 2 - Increasing lesion depth by 20nm from (a) the Stratum Corneum, to (b) - (d) Epidermis, (e) - (i) Papillary Dermis, (j) - (m) Upper Blood Net Dermis, and (n) Dermis

Tables 3 and 4 depict the mean grey values of the images in Figures 3. and 4., as well as the standard deviation repsectively. It is observed that the standard deviation is lower in the Model 2 as compare to Model 1, showing the influence of the increased chromophore detail, in maintaining a more uniform mean grey value with variation in lesion depth. Due to the simplicity of the original model as well as the variation with lesion depth (Figure 5), the brightness of the lesion with depth was measured by converting the RGB pixels to gray scale. This was performed as an initial test to analyse lesion variation with depth. With the model being updated with improved chromophores, the similar mean gray value test was conducted in order to be able to compare the two models.

Table 3 - Mean grey values of four different positions of model 1 along with the standard deviation measured

Layer	SC	E			PD					UBND				D	Std.Dev
Depth (in nm)	25.8	45.8	65.8	85.8	105.8	125.8	145.8	165.8	185.8	205.8	225.8	245.8	265.8	285.8	
Model 1 - Mean (Grey)	148.54	151.42	151.32	151.06	148.39	150.31	150.31	150.32	150.28	148.71	150.03	149.96	149.92	149.59	0.92

SC - Stratum Cornuem; E - Epidermis; PD - Papillary Dermis; UBND - Upper Blood Net Dermis; D - Dermis; Std.Dev - Standard Deviation

Table 4 - Mean grey values of four different positions of model 2 along with the standard deviation measured

Layer	SC	E			PD					UBND				D	Std.Dev
Depth (in nm)	25.8	45.8	65.8	85.8	105.8	125.8	145.8	165.8	185.8	205.8	225.8	245.8	265.8	285.8	
Model 2 - Mean (Grey)	147.12	146.79	146.93	146.89	147.17	147.29	147.33	147.22	147.44	147.65	147.33	147.46	147.72	147.88	0.31

SC - Stratum Cornuem; E - Epidermis; PD - Papillary Dermis; UBND - Upper Blood Net Dermis; D - Dermis; Std.Dev - Standard Deviation

We have also compared the simulated and clinical lesion appearance, Figure 5. We have used clinical images of lesions located in the Stratum Corneum and Papillary Dermis, Figure 5(d), obtained from literature[7]. We have compared these two images by extracting some pixels from within the lesion to act as our region of interest. We then perform a comparison using the deltaE2000[21] metric which is a metric for understanding how the human eye perceives color differences. On a typical scale the delta values range between 0 and 100; 0 being identical while 100 being complete opposites. A deltaE <=1 is not perceptible by the human eye. Between 1 and 2 is perceptible through close observation. Between 2 and 10 is perceptible at a glance. Between 11 and 49, the colors are more similar than opposite[22].

When we compared the images, we obtained a deltaE of ~16 which is far from ideal. The best estimate as mentioned earlier would be to have deltaE <3. This is being investigated further. It must be noted that the lesions from the clinical images contain dermatoscopic structures, which the current model lacks. These features impart certain colors and properties as well, which may well be the cause for the large deltaE2000 value.

Simulated lesion images resemble the appearance of clinical skin lesions. They capture the effect of fading out with the increased depth. There are differences in the color content (seen in Figure 5), also reflected in the deltaE2000 calculation.

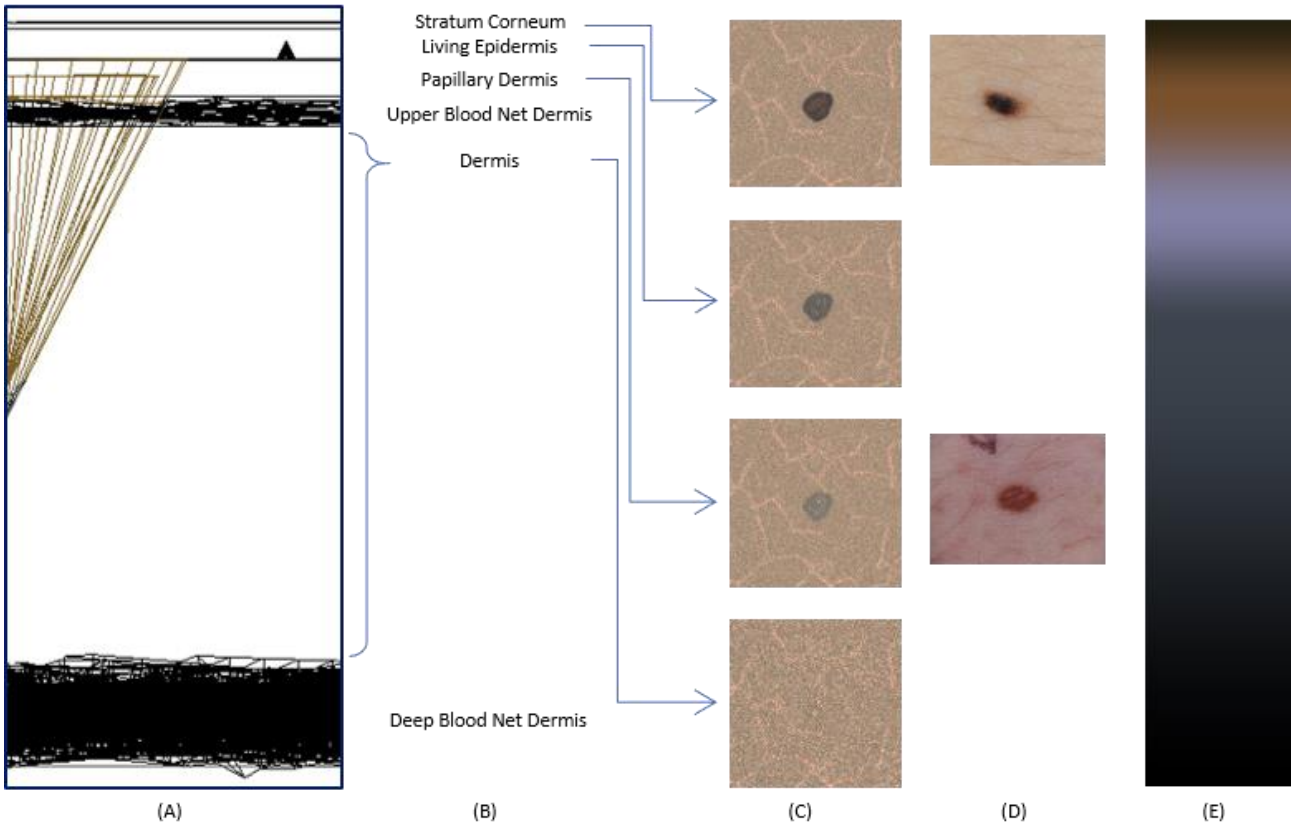


Figure 5 - (A): Cross-section of the model; (B): List of simulated tissue layers; (C): The corresponding synthetic images; (D): Sample images [7] of clinical lesions for visual comparison; and (E): The clinical lesion color variation with depth (modified from literature[7])

The current skin model has limited pixel intensity variations as compared to clinical skin images. This is due to the lack of irregular tissue boundaries, appropriate distribution of the blood networks, etc. Future work will include modifications to the model to add other dermatoscopic features[23], such as streaks, dots, grey/blue structures etc., as well as including a realistic simulation of tissue boundaries, further improving the realism of dermatological VCTs. The current image acquisition simulation assumes a generic camera model; it will be expanded to include properties of a real dermatoscope (e.g., the housing, optical stack etc.), with material characteristics of device components modelled in Blender. This is of importance as optical properties of the components (primarily the optical stack) may account for reflections. Further studies into the skin chromophore content, such as the progression of melanoma with time (evolution of a lesion), chromophores associated with dermatoscopic features etc., and lesion color fidelity are also ongoing.

4. CONCLUSION

We have presented an improved simulation of the skin for dermatological virtual clinical trials. Our previous model[6] has been extended to incorporate chromophores, which determine the color appearance of the skin lesions. Our results and preliminary visual assessment of the newly created synthetic dermatological images indicate clinically plausible appearance for the simulated lesions. The observed changes in simulated lesion clarity with lesion depth within the skin model suggests clinically expected relationship. Further work on extending the model of the skin with irregular grooves, and better representation of the chromophores is ongoing.

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