Determination of the pathological state of skin samples by optical polarimetry parameters

F. Fanjul-Vélez *[a], N. Ortega-Quijano[a], L. Buelta[b], J. L. Arce-Diego[a]
[1]Applied Optical Techniques Group, Electronics Technology, Systems and Automation Engineering Department, University of Cantabria, Av. de los Castros S/N, 39005 Santander, Cantabria, Spain

[2]Department of Medical and Surgery Sciences, University of Cantabria, Av. Herrera Oria S/N 39011 Santander, Cantabria, Spain

ABSTRACT

Polarimetry is widely known to involve a series of powerful optical techniques that characterize the polarization behaviour of a sample. In this work, we propose a method for applying polarimetric procedures to the characterization of biological tissues, in order to differentiate between healthy and pathologic tissues on a polarimetric basis. Usually, medical morphology diseases are diagnosed based on histological alterations of the tissue. The fact that these alterations will be reflected in polarization information highlights the suitability of polarimetric procedures for diagnostic purposes. The analysis is mainly focused on the depolarization properties of the media, as long as the internal structure strongly affects the polarization state of the light that interacts with the sample. Therefore, a method is developed in order to determine the correlation between pathological ultraestructural characteristics and the subsequent variations in the polarimetric parameters of the backscattered light. This study is applied to three samples of porcine skin corresponding to a healthy region, a mole, and a cancerous region. The results show that the method proposed is indeed an adequate technique in order to achieve an early, accurate and effective cancer detection.

Keywords: polarimetry, depolarization factor, porcine skin cancer.

1. INTRODUCTION

Skin cancer is known to be one of the most common types of cancer. There are three main types of skin cancer: basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma. Both BCC and SCC are unlikely to metastasize, so the lack of spreading to other parts of the body makes the chance of cure to be very high after the treatment. However, melanoma constitutes the most dangerous one: although it is not as common as BCC and SCC, it is likely to metastasize if it is not early diagnosed. This fact makes melanoma to be the major cause of skin cancer deaths.

The current techniques for melanoma detection are not sensitive enough, and subsequently it is hard to achieve an early detection. As a result, a lot of painful, costly and sometimes unnecessary biopsies have to be taken in order to make a correct diagnosis. Therefore, we find it necessary to develop more powerful cancer detection techniques that enable us to determine the presence or absence of cancer in a non-invasive way. Optical techniques have shown a big potential in this field [1, 2]. In particular, polarimetric techniques make it possible to characterize a sample taking into account some important properties that have a close relationship with the ultraestructural characteristics of the tissue. As long as these characteristics vary with the pathological state of the tissue, polarimetry can be used as a diagnostic technique.

In this work, we propose a comparative polarimetric method in order to study the differences between healthy skin, mole, and melanoma. In section 2, we will briefly present the theoretical corpus to be used in our work. In this way, subsection 2.1 is focused on Mueller matrix formalism, while subsection 2.2 summarizes the basics of Lu-Chipman polar decomposition. Section 3 shows the application of these techniques to skin, in particular to a healthy sample, a mole and a malignant cutaneous melanoma. After studying this pathology from a histopathological point of view, some optical parameters will be analysed. Finally, section 4 summarizes the most important conclusions of this work.

Corresponding author: *ffanjul@teisa.unican.es, tel:+34942201545; fax +34942201873; www.teisa.unican.es/toa,

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2. POLARIMETRIC CHARACTERIZATION OF BIOLOGICAL TISSUES

Biological tissues present a very high degree of heterogeneity. They are known to be a turbid medium in general, i.e., they strongly depolarize the optical radiation when irradiated with a light beam [1]. Due to this fact, the Mueller calculus is a very useful polarimetric technique in order to study polarization dependent interaction between light and tissues, as long as it can manage partial polarized light beams and devices that cause depolarization [3].

2.1 Mueller matrix formalism

The Mueller calculus is a well-known 4x4 matricial method that characterizes a light beam by means of a 4-element column vector S={I, Q, U, V} (the Stokes vector) and a certain device by means of a 4x4 matrix composed of real elements (the Mueller matrix). In this way, if a light beam interacts with a device which is characterized by its Mueller matrix M, the output beam can be calculated by S'=MS [4]. Given a certain Stokes vector, it is possible to obtain the degree of polarization by the following equation:

$$dop^{tot} = \frac{\sqrt{Q^2 + U^2 + V^2}}{|I|}, \tag{1}$$

which is used to calculate the total degree of polarization of the light beam. The degree of linear polarization is

$$dop^{lin} = \frac{\sqrt{Q^2 + U^2}}{|I|}, \tag{2}$$

while the degree of circular polarization is given by

$$dop^{circ} = \frac{\sqrt{V^2}}{|I|}. \tag{3}$$

In order to study the variation of polarization properties caused by a certain sample, a set of crosstalk polarization parameters is defined. In this way, the horizontal-to-vertical crosstalk (HVC) is determined for an horizontally polarized incident beam, being defined as the ratio:

$$HVC = \frac{par - perp}{par + perp} \tag{4}$$

where *par* corresponds to the intensity of the horizontal polarization output component when irradiating the tissue with horizontally polarized light, and *perp* is the intensity associated to the vertical component. The vertical-to-horizontal, left-to-right and right-to-left crosstalk parameters can be defined in an analogous way. All these parameters are in the range of [–1, 1]. On one hand, if they take the value of 1, it means that the corresponding polarization state is maintained. On the other hand, a value of –1 corresponds to a situation in which a concrete incident polarization state would result in the opposite polarization state.

2.2 Lu-Chipman polar decomposition

It is possible to extract precise information about the depolarization, retardance and diattenuation of a Mueller matrix by means of the so-called polar decomposition proposed by Lu and Chipman [5]. This method decomposes this matrix in a product of three components, $M = M_\Delta \cdot M_R \cdot M_D$.

The calculation process of these decomposition components will be briefly described now. First of all, the diattenuation component is calculated. From the first row of the Mueller matrix, the diattenuation vector $\vec{D}$ is obtained, and from its unitary vector and module, the submatrix m_D is constructed. The diattenuation matrix appears then as:

$$M_D = m_{00} \begin{bmatrix} 1 & \vec{\mathrm{D}}^t \\ \vec{\mathrm{D}} & \mathrm{m_D} \end{bmatrix}. \tag{5}$$

The calculus of the depolarization component M_Δ requires that of the submatrix m_Δ, that is carried out by the following expression:

$$m_\Delta = \varepsilon\left[m'(m')^t + \left(\sqrt{\lambda_1\lambda_2} + \sqrt{\lambda_2\lambda_3} + \sqrt{\lambda_1\lambda_3}\right) I \right]^{-1} \cdot \left[\left(\sqrt{\lambda_1} + \sqrt{\lambda_2} + \sqrt{\lambda_3}\right) m'(m')^t + \sqrt{\lambda_1\lambda_2\lambda_3}\, I \right]. \quad (6)$$

With this equation, the final expression results:

$$M_\Delta = \begin{bmatrix} 1 & \vec{0}^t \\ \vec{P}_\Delta & \mathrm{m}_\Delta \end{bmatrix}. \quad (7)$$

The retardance matrix M_R can be calculated from the previous ones, and from this matrix several parameters like the total retardance R, the linear retardance δ, the optical rotation ψ and the fast axis orientation respect to the horizontal axis θ can be obtained [5].

An ideal and pure depolarizer, with null retardance and diattenuation, can be expressed by the following Mueller matrix:

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & \mathrm{a} & 0 & 0 \\ 0 & 0 & \mathrm{b} & 0 \\ 0 & 0 & 0 & c \end{bmatrix}, \qquad |\mathrm{a}|,\ |\mathrm{b}|,\ |\mathrm{c}| \le 1. \quad (8)$$

A natural consequence is that the component M_Δ from the Lu-Chipman decomposition will resemble this matrix, but it will not be completely identical, due to the fact that in spite of the heterogeneous structure of biological tissues, in general samples measured do not behave like totally depolarizing media.

Due to this similarity, it is convenient to introduce a parameter, called depolarization power, which comes directly from a, b and c parameters. Like the entropy, it measures the depolarization introduced by the component M_Δ in a simpler way:

$$\Delta = 1 - \frac{|a| + |b| + |c|}{3}, \quad 0 \le \Delta \le 1. \quad (9)$$

3. APPLICATION TO CUTANEOUS MALIGNANT MELANOMA

3.1 Cutaneous malignant melanoma

Melanoma is a malignant tumor that originates in the melanocytes [6]. Melanocytes are the cells that produce melanin, a basic pigment that is found all over the skin, in the eyes and in the hair. They are located in the *stratum basale*, the deeper layer of the epidermis. Melanoma causes melanocytes to grow in an uncontrolled way, so the tumorous tissue spreads over the skin. According to this growth, four types of melanoma can be defined: 1) Superficial spreading melanoma (SSM). This is the most common type of cutaneous melanoma in Caucasians. This cancer spreads on the surface of the skin before penetrating into deeper tissues. 2) Nodular melanoma (NM). This type of melanoma grows vertically, and it rapidly invades the deeper tissues, being the most aggressive form of melanoma. 3) Acral lentiginous melanoma. This type of melanoma, also called subungual melanoma, is found most commonly in dark-skinned people and in Asians. It usually appears on the palms, soles and nail beds, without evidence of relationship with sunlight exposure. 4) Lentigo maligna melanoma. This is the slowest-spreading form of melanoma, showing a non-invasive growth. It is normally found in elderly people on sun-damaged skin.

The general evolution of melanoma shows both lateral spread and penetration towards deeper tissue layers [6], as it is shown in Figure 1. The tumor growth shows a lot of diversity, depending on the type of melanoma and each particular conditions. However, it is possible to define some general criteria in order to establish a practical, reproducible and applicable staging system that enables us to standardly summarize the spreading degree of cancerous tissue [7]. The

determination of the tumor stage is extremely important, as long as the effectiveness of the treatment relies on the accurate evaluation of cancer spread, which is crucial to determine a patient's prognosis.

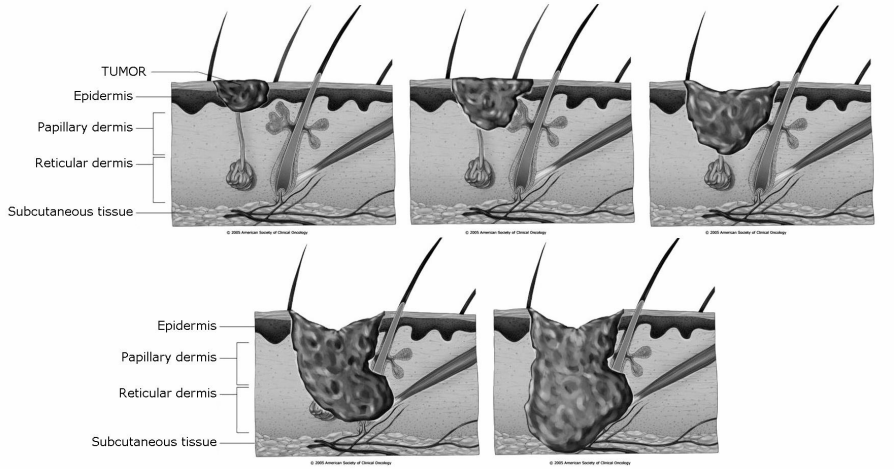

Fig. 1. General melanoma's growth [American Society of Clinical Oncology].

The first staging systems were only based on two main methods of classifying the thickness of a melanoma: the Breslow thickness, that fixes some critical depths of penetration and subsequently defines three types of melanoma, and the Clark's classification that comprises five tumor levels in terms of the skin layers it has reached. The most complete and widely used staging system is the so-called TNM classification that takes into account three relevant parameters: the tumor thickness and ulceration (T), the involvement of lymph nodes (T), and metastasis (M) [7].

Malignant melanoma is clinically detected by means of the "ABCDEF" method, which takes into account several characteristics to identify the pathology [8]: Asymmetry, Border irregularity, Color variation, Diameter, Evolutionary change and Funny-looking lesion. This method provides the physicians with a series of valuable features in order to make the diagnostic. However, it is not a sensitive enough technique, and subsequently it does not enable an effective early detection. As a result, a lot of painful, costly and sometimes unnecessary biopsies have to be taken in order to make a correct diagnosis. Applying the polarization techniques described in the previous section can provide the practitioners with an accurate, fast, non-invasive and in situ diagnostic technique.

3.2 Polarimetric characterization

The samples measured in this work correspond to Sinclair swine models. They are a particular breed of black minipigs, and they display congenital cutaneous melanoma that suffers a tumor regression process by means of depigmentation [9]. They show lesions that are very similar to human nevi and to cutaneous malignant melanoma. In particular, their invasive cutaneous melanomas are analogous to the superficial spreading melanomas (SSM) observed in humans [9]. This resemblance, as well as the fact that the pig skin and human skin have very similar optical properties, makes the Sinclair swine a proper model in order to study this pathology.

The Mueller matrices have been measured in backscattering configuration for a wavelength of 633.8 nm with such a detection angle that the specular reflection is avoided [10]. The resulting matrices are included in Table 1.

Table 1. Mueller matrices of healthy skin, mole, and tumor of Sinclair swine samples.

Healthy skin	**Mole**	**Tumor**
$\begin{pmatrix} 1 & 0 & 0 & 0 \\ -0.05 & 0.3 & -0.07 & 0 \\ 0.02 & -0.05 & -0.3 & 0.015 \\ -0.015 & 0.03 & 0 & -0.23 \end{pmatrix}$	$\begin{pmatrix} 1 & 0 & 0.01 & -0.005 \\ -0.02 & 0.57 & -0.13 & 0 \\ 0.3 & -0.1 & -0.5 & -0.001 \\ -0.03 & 0.07 & 0.01 & -0.44 \end{pmatrix}$	$\begin{pmatrix} 1 & -0.09 & 0.008 & -0.07 \\ -0.1 & 0.64 & -0.16 & 0 \\ 0.3 & -0.12 & -0.605 & -0.001 \\ -0.035 & 0.09 & 0 & -0.55 \end{pmatrix}$

From these matrices, the Lu-Chipman polar decomposition is applied, and then the depolarization power of each sample has been calculated. The results are shown in table 2. It can be observed that normal skin depolarizes light in a

strong way. Benign mole depolarizes less, and the melanoma sample produces the lower depolarization. These results will be discussed later.

Table 1. Depolarization power of the samples measured.

	Depolarization
Normal skin	0.719
Benign mole	0.487
Cancerous lesion	0.389

As well as the depolarization power, we have calculated a series of degrees of polarization. The notation used here is dop_{input}^{type}, where *input* determines the polarization state of the irradiated light beam considered, and *type* determines whether we are calculating the total dop, the degree of linear polarization, or the degree of circular polarization. The results for linear polarization states are included in Table 2, while Table 3 shows the parameters for the circular ones.

Table 2. Degrees of linear polarization.

	dop_H^{lin}	dop_H^{tot}	dop_V^{lin}	dop_V^{tot}	$dop_{mean\_lin}^{lin}$	$dop_{mean\_lin}^{tot}$
Normal skin	0.2518	0.2522	0.3569	0.3598	**0.3083**	**0.3093**
Benign mole	0.5852	0.5866	0.7128	0.7198	**0.5930**	**0.5956**
Cancerous lesion	0.6255	0.6284	0.7806	0.7890	**0.6758**	**0.6792**

Table 3. Degrees of circular polarization.

	dop_R^{circ}	dop_R^{tot}	dop_L^{circ}	dop_L^{tot}	$dop_{mean\_circ}^{circ}$	$dop_{mean\_circ}^{tot}$
Normal skin	0.2450	0.2525	0.2150	0.2208	**0.2300**	**0.2366**
Benign mole	0.4724	0.5602	0.4080	0.5065	**0.4402**	**0.5333**
Cancerous lesion	0.6290	0.7146	0.4813	0.5653	**0.5552**	**0.6399**

In order to obtain more information about the polarization behavior of the samples, we have also calculated the polarization crosstalk parameters included in Table 4. They do not present any type of strong crosstalk asymmetry between polarization states.

Table 4. Polarization crosstalk parameters of the samples.

	HVC	**VHC**	**RLC**	**LRC**
Normal skin	0.2500	0.3500	-0.2450	-0.2150
Benign mole	0.5500	0.5900	-0.4724	-0.4080
Cancerous lesion	0.5934	0.6789	-0.6290	-0.4813

The depolarization power observed for each sample shows a clear difference between them. Depolarization in biological tissues is mainly related to scattering, and therefore it varies with the number of scattering events undergone by the photons, as well as with the density of scatterers, their dimensions and their composition [1]. We hypothesize that the main factor that affects the depolarization power is related to the absorption coefficient, and in particular to the melanin content, as long as it is the most relevant histopathological characteristic of the tumorous lesion considered in this work. Skin absorption is dominated by melanin that shows a strong absorption in the visible range. It is the dominant chromophore in skin. Therefore, the absorption coefficient of skin directly depends on the melanin presence. Melanin is contained in the melanosomes. Nevus are characterized by a higher melanosome content than healthy skin. In the case of melanoma, malignant melanocytes continue to produce melanin in their cancerous state. Therefore, as the tumor grows, melanosomes proliferate in the epidermis layer and, depending on the melanoma stage, can also appear in the dermis [11]. This causes that, in the particular melanoma type considered in this work, the tumorous tissue shows a very high melanin content. This has a double effect: both the penetration depth and the amount of backscattered light are drastically reduced. We propose that, as long as light penetrates less into the tissue, it undergoes less scattering events, suffering less depolarization. As well as this, it is known that cancerous tissues typically show increased blood perfusion compared to normal tissues. In particular, malignant melanoma usually has a peripheral blood net around it in order to

obtain enough nutrients to maintain its growth [11]. Hemoglobin is the dominant absorber in the short-wavelength end of the therapeutic window, which is in the range of the wavelength used in this work. As a result, this additional hemoglobin content may also contribute to the overall absorption increase of melanoma.

The results included in Tables 2 and 3 show that linearly polarized light is maintained over a slightly longer distance than circularly polarized light. According to this, such depolarization behaviour corresponds to a Rayleigh scattering regime, although it is near the Rayleigh-Mie transition regime. However, the dominant scatterers are thought to be Mie-sized. This is the case of mitochondria, for example. The results obtained here, that show an agreement with other previous works, suggest two possibilities [12]. The first one is that scattering may be dominated by smaller subcellular organelles that are Rayleigh-sized. The second one is that, when the scatterer concentration is very high, correlated scattering effects can appear, and subsequently the polarization behaviour is modified. This is a complex issue that remains unclear and has to be investigated in a very profound way.

4. CONCLUSION

A comparative polarimetric method to determine the pathological state of a sample has been proposed. In particular, the depolarization power has been proved to show a significant difference between healthy skin, mole, and cancer. We have hypothesized that it is due to the melanin content of the skin samples considered, based on its optical properties effects as well as the fact that it is the most relevant histopathological feature observable in mole and melanoma samples in comparison with healthy skin. However, there are more factors that should be studied in future works in order to achieve a better knowledge about this pathology and its detection possibilities by means of optical techniques. As well as this, the depolarization influence over linear and circular polarization states has been analyzed. The results are in agreement with other important works, which highlight the need for further studies that completely clarify the ultraestructural scattering behaviour in biological tissues.

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