Non – Invasive Optical Detection of Squamous and Basal Cell Carcinomas

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Abstract: The early detection of skin cancer may highly increase the chances of its healing . In this research we designed and implemented the OIR reflectometry measuring system with a 650 nm diode laser source to aid physicians in diagnosing both squamous cell carcinomas (SCC) and basal cell carcinomas(BCC). The laser is delivered obliquely to the skin surface by an optical fiber fitted through a tube holder of CCD camera . The diffused reflected laser light from the skin is captured by the CCD camera and sent to a computer , which is supplied by a special prepared Matlab program to analyze these images in order to decide in a time whether the lesion is malignant or benign . For the fifty diagnosed cases in Iraq by this technique , the results were 85% accurate.

Keyword: skin cancer detection , diffusion theory , oblique incidence diffuse reflectance , reflectometry
consuming and painful. Laboratory results for the determination of histopathology of a suspected tumor may generally take several days. Since suspicious areas are identified by visual inspection alone, there are a significant number of false positives that undergo biopsy. Conversely, many malignant lesions can also be overlooked. There is an urgent need for objective criteria that would aid the clinician in evaluating whether biopsy is required[Seong G. Kong et al., 2006].

Nowadays there is a growing demand for accurate and fast models to predict the light distribution in biological tissues to deduce their optical properties from the measurable quantities [L. H. Wang and S. L. Jacques, 2000]. One of the measurable quantities is the diffuse reflectance. It is a function of the distance between the observation point and the incident point of a laser beam. The diffuse reflectance is defined as the photon probability of re-emission from inside a semi-infinite turbid medium per unit surface area (skin tissue). Measurements of the diffuse reflectance can be used to determine the optical properties of tissue non-invasively[L. H. Wang and S. L. Jacques, 2000].

Biological scatterers are primarily cell nuclei and mitochondria, with diameters ranging from 1 μm to 8 μm. As the laser light wavelength is smaller than these scatterers, then the light interaction can be predicted by Mie scattering theory, which is an exact analytical solution of Maxwell’s electromagnetic field equations, but when the scattering particles are much smaller than the wavelength, the light interaction can be predicted by Raleigh scattering theory, which is a limiting case of Mie theory. Scattering coefficient is defined as the probability of photon scattering per unit infinitesimal pathlength [Valery V. Tuchin, 2007].

In this paper we present a design and implementation of a non-invasive, painless and fast method to deduce the optical properties of skin cancerous suspicion lesions based on the application of the oblique incidence diffuse reflectance reflectometry (OIR) as originally conceived by Wang and Jacques [L. H. Wang and S. L. Jacques 1996, G. Marquez and L. H. Wang 1997]. The images of the diffused reflectance for both lesion and healthy adjacent skins of the same patient are captured by a CCD camera used for this purpose. These images are then analyzed and processed by a specially written Matlab program v.10 to perform a logical prediction (diagnosis) for the examined lesion for squamous and basal cancerous cells.

2- Theoretical Background

The significant changes that happen in malignant cells make it optically differentiable from benign cells due to the enlargement in their cell nuclei and mitochondria sizes, it is important to know that the nuclei and mitochondria are the major scatterers in the cells, therefore the enlargement of their size considered as the important indicator to the presence of cancer cells that cause increase in light scattering [Vinay Kumar 2005, Valery V. Tuchin 2007],

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When light enters a semi-infinite tissue, it will generally scatter many times before either being absorbed or escaping the tissue surface at a point other than its point of entry. The multiple scattered light that escape is called diffuse reflectance [Shao-Pow Lin et al 2005, Hua Jiang Wei et al 2009], as seen in Fig.(1).

![Fig.1: Light interaction in a scattering and absorbing media](image)

Because it is easier to model isotropic scattering than anisotropic scattering, the reduced or transport scattering coefficient $\mu_s'$ is introduced as the equivalent isotropic scattering coefficient of an anisotropically scattering medium $\mu_s' = \mu_s (1 - g)$, where $\mu_s$ is the scattering coefficient and $g$ is the average cosine of the scattering angle[Shao-Pow Lin et al2005, Markolf . H . Niemz 2007].

A sketch for the laser oblique incidence diffuse reflectance pattern from a semi-infinite turbid medium like the biological tissue is shown in Fig.(2).

![Fig.2: Single wavelength oblique incidence diffuse reflectance pattern](image)
The spatial distribution of diffuse reflectance of an oblique incident laser beam from a semi-infinite turbid medium like the biological tissue has been modeled according to Wang and Jacques by two isotropic point sources; one positive source located below the tissue surface and one negative image source above the tissue surface, as shown in Fig.(4). The positive source is buried at distance \(d_s\) from the point of laser incidence on the skin, this distance is considered practically to be three times greater than the diffusion coefficient “D” as in the mean free path Eq. (1) [G. Marquez and L. H. Wang 1997, Markolf. H. Niemz 2007, Yaqin Chen et al 2011]:

\[
1 \times e^{D}d_{s} = 3D - \frac{1}{0.35\mu_{a} + \mu_{s}}
\]

(1)

The modified dipole source diffusion theory model gives diffuse reflectance at the skin boundary \(R(x)\), by using Eq.(2) which can be scaled to fit a relative reflectance profile that is in absolute units.

\[
R(x) = \frac{1}{4\pi} \exp\left(-K_{eff}p_{2}\right)
\]

(2)


Where;

\(\alpha_i\) : is the angle between the incident laser beam and the normal line on the tissue surface.
\( \alpha_t \): is the angle of light transmission into the tissue, could be calculated according to Snell’s law which is used to measure the new optical path where the isotropic positive point is locate, as seen in Fig(4).

\( r \): is the distance between the normal line between the positive and negative point and the observation point.

\( x \): is the distance between the point of observation and the point of light incidence (origin point).

\( \rho_1, \rho_2 \): are the distances from the two point sources to the point of interest.

\( z_b \): is the distance between the virtual boundary and the surface of the tissue.

\( A \): is the parameter related to the internal reflection which can be calculated using either Fresnel reflection coefficients or using empirical variable \( r_i \) and relative reflection coefficient \( n_{rel} \) of the tissue ambient (air) interface as following:

\[
A_{rel} = \frac{n_{tissue}}{n_{ambient}} 
\]  

\( r_i = -1.448n_{tissue}^2 + 0.710n_{tissue} + 0.663 + 0.0035n_{rel} \)  

\[
A = \frac{1 + r_i}{1 - r_i} 
\] 

\( A \): is unity for a matched boundary [Shao-Pow Lin et al 2005].

\( \Delta z \): is the depth of the positive point source from the surface of skin.

\[
\Delta z = \frac{\cos(\alpha_t)}{\mu_a + \mu_g} = \Delta x \tan^{-1}(\alpha) 
\] 

\( \Delta x \): is the distance shift between the point of laser incidence and the center of the most symmetrical circle, as seen in Figs(2),(3) and(4).

\[
\Delta x = \frac{\sin\alpha_t}{0.3(\mu_a + \mu_g)} 
\] 

Ones the distance shift \( (\Delta x) \) was found, the diffusion coefficient \( D \) could be calculated from Eq.(8):
\[ D = \frac{\Delta x}{3 \sin(\alpha_t)} \]  

(8)

\[ \mu_{\text{eff}} \] is the effective attenuation coefficient:

\[ \mu_{\text{eff}} = \sqrt{\frac{\mu_a}{\mu_s}} \]  

(9)

The \( \mu_{\text{eff}} \) value could be found by using a last-square fitting to Eq.(2).

Now it is possible to find the skin optical properties \( \mu_s' \) and \( \mu_a \) from Eqs.( 10 and 11) as following:

\[ \mu_a = \frac{\mu_{\text{eff}} \cdot \Delta x}{3 \sin(\alpha_t)} \]  

(10)

and

\[ \mu_s' = \frac{\sin(\alpha_t)}{\Delta x} - 0.35 \cdot \mu_a \]  

(11)

3- Experimental Work

A) Material

Fifty patients were examined for a suspicion of skin cancerous lesions by using the setup that is shown in Fig.(5), which was implemented for this purpose. These practical experiments carried on at the dermatology advisory clinical section in the Governmental Marjan Teaching Hospital in Babylon state, Iraq. Physicians sent the patients with suspicion skin lesions for a biopsy routine test after finishing this OIR reflectometry measurements and analysis.

B) Experimental Setup

The oblique incidence diffused reflectance reflectometry (OIR) system that is designed in this work to measure the skin optical properties is sketched in Fig.(5). It includes the following components:

1- 650 nm laser diode source.
2- Multimode fiber optic of 0.22 NA and 200µm in diameter, fitted by a guiding needle at 45° angle with the central normal imaginary line of CCD camera.

3- Charge coupled device (CCD) camera.

4- Computer with special written analytical Matlab program v.10.

![Fig. (5): Schematic sketch of OIR setup.](image)

The design of CCD camera holder is shown in Fig.(6). The virtual center line (axis) of CCD camera was fitted particularly to be on the center of the horizontal plane, exactly at intersecting point with the needle tip.

![Fig.(6): Geometrical design of CCD camera holder.](image)

The CCD camera holder was painted by black color to reduce the effect of the outside light. The clinic lamb lights was turned off also during the examination. All the apparatus were placed on a small portable hospital cart as shown in Fig.(7) to move it easily in the patient examination room.
c) Work Procedure

The optical examination for skin cancer diagnosis was carried on by the sequence shown in Fig(8):

- Import the captured lesion and healthy images to the computer
- Morphological process to extract most symmetrical circle then analysis the extracted circle to find the center
- Calculate the reflectance at points along the diameter of image, then last square curve fitting procedure to data point w.r.t. image diameter (x-axis [mm]) Eq.(10)
- Calculate the \( \Delta x \) shifting, then calculate \( D \) by using Eq.(8)
- At point \( x \), calculating the value of \( \rho_1 \) and \( \rho_2 \) by Pythagoras law of triangles, then determine the fitted \( R(x) \) at the same point \( x \)
- Calculate the value of \( \mu_{\text{eff}} \) by Eq.(2), with error less than 0.0001, then calculate the value of \( \mu_a \) by Eq(10) and \( \mu_s' \) by Eq(11)
- Logical prediction for the optical properties
- Print the lesion prediction status

Fig.(7): The implemented OIR laser system for skin cancerous examination.
Fig(8): Work procedure block diagram.

Figures(9) shows a sample of the diffused reflected image of case no. 08 in table(1), it was a low grade malignancy cancer. It’s relative diffused reflectance curve resulted by the Matlab program computations is shown in Fig.(10).

Fig.(9): Diffused reflected image, showing the place of \( \Delta x \) shift, from needle tip (laser incidence point) to the center point of outer symmetrical circle of case no. 08 in table(1).

Fig.(10): Sample of relative diffuse reflectance curve for a lesion of case no. 08 in table(1).

For the same patient case no. 08 in table(1), Figs(11)and(12) show the diffused reflected image of the healthy adjacent skin area and it’s relative diffused reflectance curve resulted by the Matlab program computations respectively.
**4- Results**

The results are tabulated as shown for twelve samples out of the fifty examined cases presented in table(1). Our experimental non-invasive logical final decision, beside the invasive biopsy analysis result are shown in the table as well as the optical parameters of the lesion and the healthy skins for each patient.

**Table (1): Selected results**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patient gender and age</th>
<th>Lesion site</th>
<th>Skin lesion optical parameter $\mu_s$ [cm$^{-1}$]</th>
<th>Healthy adjacent optical parameter $\mu_s$ [cm$^{-1}$]</th>
<th>Logical prediction</th>
<th>Histological diagnosis (by biopsy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female, 30</td>
<td>Cheek</td>
<td>6.1033</td>
<td>0.4132</td>
<td>Low grade Malignancy</td>
<td>SCC</td>
</tr>
<tr>
<td>2</td>
<td>Female, 45</td>
<td>Breast</td>
<td>4.9191</td>
<td>0.2588</td>
<td>Low grade Malignancy</td>
<td>SCC</td>
</tr>
<tr>
<td>3</td>
<td>Male, 60</td>
<td>Cheek</td>
<td>20.1398</td>
<td>0.4108</td>
<td>Malignant</td>
<td>SCC</td>
</tr>
<tr>
<td>4</td>
<td>Male, 65</td>
<td>Cheek</td>
<td>40.4127</td>
<td>0.2058</td>
<td>Malignant</td>
<td>BCC</td>
</tr>
<tr>
<td>5</td>
<td>Male, 53</td>
<td>Cheek</td>
<td>15.5480</td>
<td>0.4267</td>
<td>Malignant</td>
<td>BCC</td>
</tr>
<tr>
<td>6</td>
<td>Male, 72</td>
<td>Cheek</td>
<td>15.9872</td>
<td>0.5949</td>
<td>Malignant</td>
<td>BCC</td>
</tr>
<tr>
<td>7</td>
<td>Male, 42</td>
<td>Cheek</td>
<td>2.0559</td>
<td>0.0603</td>
<td>Benign</td>
<td>Benign</td>
</tr>
<tr>
<td>8</td>
<td>Male, 46</td>
<td>Cheek</td>
<td>5.787</td>
<td>0.3832</td>
<td>Low grade Malignancy</td>
<td>SCC</td>
</tr>
<tr>
<td>9</td>
<td>Male, 35</td>
<td>Cheek</td>
<td>5.4704</td>
<td>0.3384</td>
<td>Low grade Malignancy</td>
<td>SCC</td>
</tr>
<tr>
<td>10</td>
<td>Male, 40</td>
<td>Leg</td>
<td>4.6936</td>
<td>0.2308</td>
<td>Benign</td>
<td>Benign</td>
</tr>
<tr>
<td>11</td>
<td>Male, 32</td>
<td>Shoulder</td>
<td>10.0599</td>
<td>0.8058</td>
<td>Malignant</td>
<td>SCC</td>
</tr>
</tbody>
</table>

**Fig.(11):** Diffused reflected image of lesion of case 08 in table(1).

**Fig.(12):** Sample of relative diffuse reflectance curve for healthy skin of case 08 in table(1).
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patient gender and age</th>
<th>Lesion site</th>
<th>Skin lesion optical parameter</th>
<th>Healthy adjacent optical parameter</th>
<th>Logical prediction</th>
<th>Histological diagnosis (by biopsy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Male</td>
<td>53</td>
<td>Cheek</td>
<td>$\mu_s' [\text{cm}^{-1}]$</td>
<td>$\mu_a [\text{cm}^{-1}]$</td>
<td>$\mu_s' [\text{cm}^{-1}]$</td>
</tr>
</tbody>
</table>

5- Discussion

This OIR measuring setup required at least 8 bit of dynamic range of CCD camera to measure the diffuse reflectance within a few centimeters radius of diffused reflectance image, without bring the CCD camera in saturation state.

The accuracy of $\Delta x$ shift value measurement was proportional to the resolution of the CCD camera in the setup. In our study, the size of pixel was 0.05 mm/pixel and the CCD camera dynamic range was 16 bit.

The sharpness and $\Delta x$ measurement accuracy of the diffused reflected images, as were shown in Fig.(9 and 11), increased after painting the camera holder tube by black color.

The red 650 nm diode laser was selected for these measurements due to its low absorption in the high scattering epidermal tissue, which increase the accuracy of the measured optical properties. The 620 – 670 nm visible light range is better for these applications than the UV and IR. To be sure practically, a green laser of 532 nm wavelength has been used to check out this phenomena, the result was no diffused reflected image seen.

The diagnostic logical decisions in table(1) was based on the $\mu_s'$ threshold value selection beside the increment in the $\mu_a$ value. Any increase in the reduced scattering coefficient value of lesion more than 1.8 cm$^{-1}$ over the reduced scattering coefficient value of normal healthy adjacent skin and combined with a small increment in the absorption coefficient of lesion over the absorption coefficient of normal healthy adjacent skin was referred to be a low grade malignancy lesion case. Also any increase in the $\mu_s'$ value of lesion more than 4 cm$^{-1}$ over the $\mu_s'$ value of normal healthy adjacent skin and combined with increment in the absorption coefficient of lesion over the absorption coefficient of normal healthy adjacent skin referred to be a malignant lesion case. Else, if the difference between the $\mu_s'$ value of the lesion and the $\mu_s'$ value of the normal adjacent healthy skin is less than 1.8 cm$^{-1}$, then this case considered as benign lesion case.

The threshold value was chosen according to case no.(09) in table(1), which is of a 35 year male with lesion in the cheek. The biopsy result was low grade malignant and the difference between the reduced scattering coefficient of lesion and adjacent healthy skin was 1.8511 cm$^{-1}$. Therefore, the low grade malignancy threshold considered to be ranged from 1.8 cm$^{-1}$ to 4 cm$^{-1}$.
6- Conclusion

Only the relative profile of the diffuse reflectance was used for the extraction of optical properties, which made the device insensitive to variations of some system parameters such as source power.

The accuracy of diagnostic decision depends on the image analysis and fitting accuracy to obtain optical properties of lesion and adjacent healthy skins. These results in turns depend on many factors such as the light source wavelength, resolution of CCD camera, and the procedure of estimating the center of the circles and determining the Δx shift, as well as the chosen μs⁺ threshold value.

The diagnosis accuracy achieved in this experimental study was 85%.

References
Hua Jiang Wei, Da Xing, Bo Hua He, Huai Min Gu, Guo Yong Wu and Xue Mei Chen, (2009). “Using an oblique incident laser beam to measure the optical properties of stomach mucosa/submucosa tissue”. BioMed Central Ltd, BMC Gastroenterology, UK.