Melanoma-nevus differentiation by multispectral imaging

Ilze Diebele*a, Ilona Kuzmina a, Janis Kapostins b, Alexander Derjabo b, Janis Spigulis a

aInst. of Atomic Phys. and Spectroscopy, Univ. of Latvia, Raina Blvd. 19, Riga, Latvia, LV-1586;
bLatvian Oncology Centre, Hipokrata str. 4, Riga, Latvia, LV-1006

ABSTRACT

A clinical trial on multi-spectral imaging of malignant and non-malignant skin pathologies comprising 22 melanomas and 59 pigmented nevi was performed in Latvian Oncology Center. Analysis of data obtained in the spectral range 450–950 nm using multispectral camera have led to a novel image processing algorithm capable to distinguish melanoma from pigmented nevi and different areas of activity of melanoma. The proposed methodology and potential clinical applications are discussed.

Keywords: melanoma- nevus differentiation, multi-spectral imaging

1. INTRODUCTION

Cutaneous melanoma currently represents 5% of newly diagnosed cancer in men and 6% in women. It is the leading fatal illness arising in the skin and is responsible for 80% of deaths from skin cancer. Melanoma arises from the malignant transformation of melanocytes at the dermal-epidermal junction or from the nevomelanocytes of dysplastic melanocytic nevi, or congenital nevomelanocytic nevus that become invasive and metastasize1. By now only biopsy can determine exact malformation diagnose. Though biopsy can rise metastasizing, therefore noninvasive diagnostics is preferable.

The penetration depth of optical radiation in the skin tissues depends on wavelength2. Diffuse reflectance from skin provides morphological information from different depths, and using multispectral imaging camera it is possible to get this information for various wavelengths. The optical properties of melanin and histological transition (dysplastic nevi → melanoma in situ → melanoma) have been investigated by contact diffuse reflectance3. Optical properties of benign and malignant pigmented lesions have also been estimated by oblique incidence diffuse reflectance spectrometry4, 5. Multispectral imaging provides spectral information over the whole lesion area and has promising potential for in vivo skin diagnostics, including melanoma diagnostics6-9. Previous investigations indicate that reflectance of the benign nevus at 940-950 nm is close to that of the surrounding skin, whereas pigmentation of the melanoma is still detectable6,8. Consequently, NIR-image analysis might help to distinguish melanomas from other skin malformations.

2. METHODS AND EQUIPMENT

2.1 Experimental set-up and processing algorithm

This clinical trial comprised 81 pigmented lesions was performed in Latvian Oncology Centre by multispectral imaging in the spectral range 450 – 950 nm with half-bandwidth 15 nm and 10 nm step. Overall 22 melanomas and 59 nevi were investigated in this study.

The set-up contained multispectral imaging camera Nuance EX with additional halogen lamps and polarizing film around the Nicon objective (Fig. 1). The Nuance Imaging Module contained the principal imaging components in a single compact enclosure: high-resolution, scientific-grade CCD imaging sensor, solid-state liquid crystal filter with a polarizer, wavelength tuning element, spectrally optimized lens and internal optics10. The Nuance program CRi was used to acquire image cubes and to average spectra of pigmented and normal skin areas.
Overall 51 images at different wavelengths were taken from each pigmented malformation. Before the measurement, the multispectral image of white etalon reproducing the illumination spectrum was taken. White paper with correction was taken as a reference. This solution has been found as most suitable to get initial light intensity on skin surface. Since white paper is not an ideal diffuse reflector, correction is necessary. *Avantes WS-2* reference tile was utilized to get difference between ideal reflector and white paper. This correction (Fig. 2) is further added to the captured image array.

![Fig. 1. Set-up: multispectral camera *Nuance EX*, halogen light source, polarizer, and computer.](image1)

![Fig. 2. Correction. Optical density difference between *Avantes WS-2* reference tile and white paper.](image2)

To avoid light reflection from the skin surface, which causes artifacts, cross-polarization filtering was used. Incident light was polarized with the polarizers at the light source and the light reflected from the skin surface, which didn’t change the polarization plane, was removed by second perpendicular polarizer located in the *Nuance EX* camera.

To remove artifacts from pulsed light, caused by altering current, halogen lamps were equipped with a DC source. With this approach the observed spectra obtained from skin had much smoother profile.

The patients were deposited on the couch to minimize motion artifacts in the process of pathology image capture at different wavelength. During the acquiring process the patients were asked to hold the breath about 30 seconds. All acquiring process took approximately 2 – 5 minutes, depending on the location of formation. In
cases when the motion artifacts were difficult to remove, a free image stabilization program ImageJ\textsuperscript{12} was used. An ImageJ plugin TurboReg\textsuperscript{13} was used for automatic alignment of source image to remove pathology motion artifacts.

Optical density was calculated by the \textit{CRi Nuance} program as

$$\text{OD}(\lambda) = - \log \left( \frac{I(\lambda)}{I_0(\lambda)} \right)$$

(1),

where $I(\lambda)$ – intensity of the skin-reflected light and $I_0(\lambda)$ – intensity of the light reflected from the white etalon (at the same distance).

For differentiation between melanoma and nevus, the following algorithm of parametric imaging was proposed:

$$p = \text{OD}_{650} + \text{OD}_{950} - \text{OD}_{540}$$

(2),

where $p$ is the differentiation parameter, $\text{OD}_{540}$ is the optical density at 540 nm, $\text{OD}_{650}$ is the optical density at 650 nm and $\text{OD}_{950}$ is the optical density at 950 nm. Wavelength 540 nm corresponds to maximum absorption of blood\textsuperscript{14-15}, while at 650 nm the greatest difference between melanoma and healthy skin was observed and 950 nm is the longest available wavelength corresponding to the deepest penetration under the skin surface\textsuperscript{2}.

3. RESULTS AND DISCUSSION

Fig. 3 presents the spectra of optical density for healthy skin (blue curves) and melanomas (red curves).

![Fig. 3. Optical density spectra for melanomas (red curves) and healthy skin (blue curves).](image)

To illustrate results of proposed algorithm, Fig. 4 compares ordinary color RGB and parametric images of melanomas, and Fig. 5 compares RGB and parametric images of nevi. In the second case of Fig. 4, near melanoma the nevus is also seen.
In all cases after processing melanoma had areas with notably higher $p$ values than the skin around malformation, but nevus vanished or had lower $p$ values than healthy skin. These areas, where parameter $p$ had higher values than normal skin, coincided with the suspicious regions of melanoma confirmed by oncologists. Consequently, the criterion $p > p_n$, where $p_n$ is related to the surrounding healthy skin, may be regarded as indication to melanoma. The mean parameter $p$ values for melanomas and nevi were determined as average values over the whole area of pathology, but no convincing correlations have been obtained so far.

During diagnostic test, sensitivity, specificity, positive predictive value and negative predictive value were calculated (Tab.1.). After analysis of the 22 available melanoma multi-spectral image sets, 19 showed clear response accordingly to the above-mentioned criterion (true positives or TP), and the 3 remaining cases also generally corresponded to that, but with some deviations (false negatives or FN). After analysis of 59 nevi, 54 pathologies showed a lower parameter values than the surrounding skin, which coincides with the established criteria (true negatives or TN), and 5 cases did not meet the criterion (false positive or FP). Sensitivity of this test is 86%, specificity = 92%, positive predictive value = 79% and negative predictive value = 95%.

Fig. 4. RGB images and parametric $p$-images of two melanomas.

Fig. 5. RGB images and parametric $p$-images of two pigmented nevi.
Table 1. Diagnostic test using newly developed image processing algorithm (2).

<table>
<thead>
<tr>
<th>Patients with melanoma (as confirmed by oncologist)</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic test using algorithm (2)</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>True Positive (TP) = 19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>False Positive (FP) = 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive predictive value (PPV) = TP / (TP + FP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>= 19 / (19 + 5) = 79%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>False Negative (FN) = 3</td>
<td>True Negative (TN) = 54</td>
</tr>
<tr>
<td>Negative predictive value (NPV) = TN / (FN + TN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>= 54 / (3 + 54) = 95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity = TP / (TP + FN) = 19 / (19 + 3) =</td>
<td></td>
<td>Specificity</td>
</tr>
<tr>
<td>86%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity = TN / (FP + TN) = 54 / (5 + 54) =</td>
<td></td>
<td>92%</td>
</tr>
<tr>
<td>92%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. CONCLUSIONS

The newly developed image processing methodology may be helpful for in–vivo melanoma differentiation from nevus by distant optical biopsy. The first results show that sensitivity of this approach is 86 % and specificity is 92 %. Further development of software being able to replace the visual assessment (Fig.4, Fig.5) by automatized selection is necessary. Additional studies by use of this methodology would promote better understanding of the photophysiological processes that take place in human skin and its lesions.

ACKNOWLEDGMENTS

The financial support of European Social Fund (grant #2009/0211/1DP/1.1.1.2.0/09/APIA/VIAA/077) is highly appreciated.

REFERENCES