Validation Study of Supervised and Unsupervised Calcification-Algorithms Used to Detection of Melanoma

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Abstract: Melanoma is a leading fatal illness responsible for 80% of deaths from skin cancer. It originates in the pigment-producing melanocytes in the basal layer of the epidermis. Melanocytes produce the melanin, (the dark pigment), which is responsible for the color of skin. As all cancers, melanoma is caused by damage to the DNA of the cells, which causes the cell to grow out of control, leading to a tumor, which is much more dangerous, if it cannot be found or detected early. Only biopsy can determine exact malformation diagnose, though it can rise metastasizing. When a melanoma is suspected, the usual standard procedure is to perform a biopsy and to subsequently analyze the suspicious tissue under the microscope. In this Paper, we provide a new approach using methods known as "Imaging Spectroscopy" or "Spectral Imaging" for early detection of melanoma. Spectral imaging can fill this gap of the classical imaging, which carries little spectral information while spectroscopy is severely limited in terms of measuring (potentially) inhomogeneous samples. Three different classifiers were applied, Maximum Likelihood ML and Spectral Angle Mapper SAM and K-Means. SAM rests on the spectral "angular distances" and the conventional classifier ML rests on the spectral distance concept. SAM and ML are two methods of the supported classification routines and K-Means is the known unsupported classification (clustering) algorithm.

Keywords: Melanoma, Spectral Imaging, Spectroscopy, Supported Classification, Unsupported Classification, Cancer Detection

1. Introduction

Melanoma is the most serious form of skin cancer. It originates in melanocytes, i.e. pigment cells within the skin, which turn malignant and develop into a tumor. Malignant melanoma can be diagnosed by clinical and histological means. The first step usually is a clinical examination, in-vivo and non-invasive. Here, the discrimination between melanoma and e.g. benign nevi is performed based on visual features like Asymmetry (A), Boundary (B), Color (C), and Depth (D), what is known as "ABCD-Diagnostic Rule" for melanoma detection[1],[2]. This examination is relatively cheap but frequently not sufficient for a reliable diagnosis. In many cases, the results are used as an indicator whether a patient should be referred to a biopsy of a suspect skin region. Here the application of Spectral imaging to detect the Melanoma has a number of advantages. First, the spectroscopic measurement allows to reliably contactless, non-invasive and in-vitro measure spectra for each pixel in the melanoma object, second it is purely harmless optical methods, additionally the spectral data contain information about the color, material and concentration of the tissue. Furthermore, when using the spectral imaging sys-tem, scanning e.g. a 2 x 5 cm² area of the skin takes about 30 s, with the detection-results being available practically instantaneously. This short detection time resolution allows monitoring the development of the melanoma over time, thus providing even more information. Practically, two major Spectral Imaging (SI) principles have emerged wavelength scanning SI, in remote sensing better known as “staring imaging”, and spatial scanning SI, also known as “push-broom scanning imaging” [4][5][6].

1.1. Wavelength Scanning SI

This method is essentially based on acquiring a number of single 2D-images of an identical sample, at different wavelengths. Hence, both spatial dimensions are acquired simultaneously, while the spectral information is acquired sequentially. Practically, the wavelength selection can be done either by a number of discrete filters, by tunable filters, namely acousto-optical tunable filters (AOTF) or liquid crystal tunable filters (LCTF) or by illumination of the sample...
at selected, discrete wavelengths. This method is highly useful in particular when only a few images at characteristic wavelengths have to be recorded. [7][8][9].

1.2. Push-Broom Imaging SI

More suitable for many high throughput applications would be spatial scanning SI. The frequently used term “push broom scanning” originates from remote sensing and implies the line-wise acquisition of the image data, making use of a constant, relative movement (linear feed) between sample (skin) and imager (Camera) as it shown in Figure 1. Instead of recording a two-dimensional image, a line across the sample, perpendicular to the direction of the relative movement, is projected into an imaging spectrograph. The radiation originating along this observation line is spectrally analyzed and the spectral information for each pixel along the investigate line projected along the second axis of the two-dimensional detector chip. The spectral encoding can be provided either by dispersive optics forming an imaging spectrograph or by linearly variable filters. Since the spatial information along the line is retained, the computerized images contain the spatial information along the first axis and the full spectral wavelength information along the second axis. The spectral and the first spatial dimension are simultaneously acquired, while the second spatial dimension is recorded sequentially due to the movement of the sample relative to the SI sensor. By combining the slices, the second spatial axis can be derived, resulting in a full image. [7][8][9].

Figure 1. Spectral imaging system- setup.

In contrast to the stop-motion requirement of wavelength scanning SI, spatial scanning SI has a motion requirement, i.e. a continuous relative movement between imager and sample is a necessary pre-requisite for the operation. In case this is not provided as part of the process to be monitored, opting for a staring image may well be a better choice, as no moving mechanical parts would have to be added [3].

However independent on the acquiring methods (Wavelength scanning or push broom method) the Spectral Data consist of 3D-Data Matrix (Spectral Data Cube) (x, y, λ), where x, y are the special information and the third dimension λ refers to the spectral information as it shown in figure 3.

2. Methodology

The acquiring system is capable of capturing an image with a spatial axis of 480 pixels and a spectral axis of 480 pixels. Therefore, the spectral range from 380 nm to 780 nm is divided to 270 locations (bands), with spectral resolution of (10 nm). The SI system is designed so that the object table is moved by a linear table to implement the necessary relative movement between camera and sample. The region of the image, which will be examined, is typically traversed in 400 lines. Theoretically, each pixel of the acquired images corresponds to a rectangular area of approximately 0.1 μm x 0.1 μm. The effectively achievable spatial resolution is physically limited by the diffraction limitation to the order of magnitude of the wavelength of the transmitted light, i.e. 380-780 nm.[3]. The system acquires the reflectivity of the light wave length, it is an indicator of the optical tissue properties in the wavelength range (in our study in VIS wavelength range). The reflectivity of each pixel in the measured object R(x,y) can be calculated using the following calibration equation:

$$R(x, y) = \frac{I(x, y) - I_{\text{black}}(x, y)}{I_{\text{white}}(x, y) - I_{\text{black}}(x, y)}$$  \hspace{1cm} (1)$$

where I(x,y) is the Intensity of measured pixel in the image, $I_{\text{black}}(x,y)$ and $I_{\text{white}}(x,y)$ are the intensities of black- and white current consequently. Black current is the intensity if zero
illumination (lens is covered) comes into the camera chip, while the white current is the intensity if the maximum illumination comes into the camera chip[5].

2.1. Skin, Melanoma and Moll Spectral Signatures

Reflectance spectra in the wavelength region from 380 nm to 700 nm were measured from 200 volunteers as training data and from 300 volunteers as test data[8]. The spectral signature of the Melanoma, healthy skin and moll areas in figure 4 (A) are shown in figure 4 (B).

Figure 4. 2x2 cm-image of melanoma object (left); spectral signature of melanoma, Moll and Healthy skin (right).

2.2. Detection Algorithms

Spectral classification methods were developed specifically for use on hyperspectral data, but they provide an alternative method for classifying multispectral data, often with improved results that can easily be compared to spectral properties of materials. In this Paper, the supervised as well as the unsupervised classification were used to cluster pixels in a dataset into classes corresponding to user defined training classes. It requires, using the supported classification, a training set, which must be defined for use as the basis for machine learning to build the discrimination function (recognition model). Two supervised methods are then applied in this study to determine if a specific pixel qualifies as a class member [5]. The first one is the Maximum Likelihood (ML) while the other is the Spectral Angle Mapper (SAM) [5].

The k-means as unsupervised classification routine is used to order automatically each pixel in the spectral image in one class of different classes based on the squared Mahalanobis distance of each pixel to the centers of each clusters.

\[
(x - \mu)^T \sum^{-1} (x - \mu) \tag{2}
\]

2.2.1. Maximum Likelihood (ML)

Maximum likelihood classification is a supervised classification method derived from the Bayes theorem, which assumes that the statistics for each class in each band are normally distributed and calculates the probability that a given pixel belongs to a specific class[8]. The probability that a pixel with feature vector \(\omega\) belongs to class i, is given by:

\[
P(\omega | i) = \frac{P(\omega | i)P(i)}{P(\omega)} \tag{3}
\]

where \(P(\omega | i)\) is the likelihood function, \(P(i)\) is the a priori information, i.e., the probability that class \(i\) occurs in the study area and \(P(\omega)\) is the probability that \(\omega\) is observed, which can be written as:

\[
P(\omega) = \sum_{i=1}^{M} P(\omega | i)P(i) \tag{4}
\]

Where \(M\) is the number of classes. ML often assumes that the distribution of the data within a given class \(i\) obeys a multivariate Gaussian distribution. It is then convenient to define the log likelihood (or discriminant function)

\[
g(\omega) = \ln P(\omega) = -\frac{1}{2}(\omega - \mu)_{i}^{T} C_{i}^{-1}(\omega - \mu)_{i} - \frac{N}{2} \ln(2\pi) - \frac{1}{2} \ln |C| \tag{5}
\]

Pixel \(x\) is assigned to class \(i\) by the rule:

\[
X \in i \text{ if } g_{i}(\omega) > g_{j}(\omega) \text{ for all } j \neq i \tag{6}
\]

Each pixel is assigned to the class with the highest value of \(g\). Each pixel is assigned to the class with the highest likelihood or labelled as unclassified if the probability values are all below a threshold set by the user [6].

2.2.2. Spectral Angle Mapper (SAM)

Spectral Angle Mapper algorithm computes the "spectral angle" between the pixel spectrum and the training's pixel spectrum, i.e. (SAM), is a common distance metric, which compares an unknown pixel spectrum to the reference spectra \(d_{i}\), \(i = 1,..,K\), for each of \(K\) references and assigns \(t\) to the material having the smallest distance: This technique is comparatively insensitive to illumination and albedo effects. Smaller angles represent closer matches to the reference training's spectra. The result indicates the radian of the spectral angle computed using the following equation[6].

\[
\alpha = \cos \left( \frac{\sum_{i=1}^{m} T_{i} d_{i}}{\sqrt{\sum_{i=1}^{m} T_{i}^{2}} \sum_{i=1}^{m} d_{i}^{2}} \right) \tag{7}
\]

Where \(m\) = the number of bands; \(T_{i} = (t_{xi},t_{yi})\) is the i-pixel spectrum ; \(d_{i}\) = reference spectrum in training’s data and \(\alpha\) = radian of the spectral angle, (see figure 4).

The spectral angle classifiers we applied here rests on the spectral "angular distances," while the conventional classifier maximum likelihood rests on the spectral distance concept.[5]

If \(\alpha_{i} = \min(\alpha_{j,k})\), then \(x \in x_{j,k}\)

where: \(x_{i}\) the spectral angel of the pixel \(x\) in test set; \(x_{j,k}\) spectral angel of the pixel \(x\) the class \(k\) in training set.

We can measure the similarity between two spectra \(x\) and \(y\) by using the Euclidean distance measure

\[
| x - y | = \sqrt{\sum_{k=1}^{m} (x_{k} - y_{k})^{2}} \tag{9}
\]
2.2.3. Training Set for the Supervised Classification

Using the spectral data of clinical diagnosed melanoma objects of 200 volunteers, we built a training set to learn the classification machine (classification routine) the scatterplot of training data is shown in the following figure:

Figure 6. Spectrums of the Training data.

2.2.4. K-Means Unsupervised Algorithm

K-Means unsupervised classification calculates initial class means evenly distributed in the data space, then iteratively clusters the pixels into the nearest class using a minimum-distance technique. Each iteration recalculates class means and reclassifies pixels with respect to the new means. All pixels are classified to the nearest class unless a standard deviation or distance threshold is specified, in which case some pixels may be unclassified if they do not meet the selected criteria. This process continues until the number of pixels in each class changes by less than the selected pixel change threshold or the maximum number of iterations is reached. It is clear that the probability in the equation (4) is large when the squared Mahalanobis in equation (2) is small. Suppose that we merely compute the squared Euclidean distance $|x_k-\mu_i|^2$, find the center of the cluster (the mean $\mu_m$) nearest to $x_k$ and approximate the probability as

$$
\hat{P}(W_i|X, \theta) = \begin{cases} 
1 & \text{if } i = m \\
0 & \text{Otherwise}
\end{cases}
$$

(10)

It is to minimize the function of the square distance in each iteration and compare it with its previous value up to reach the smallest different between the actual and previous values of the distance as it illustrated in the following figure.

Figure 7. The mean value of the centroids in each iteration.

From a statistical point of view, it may be inappropriate to use K-Means clustering since K-Means cannot use all the higher order information that PCA or ICA provides. There are several approaches that avoid using K-means. However, for large images this algorithm fails to converge. A 2-stage K-means clustering strategy is developed that works particularly well with skin data:

1. Drop spectral data that contain only noise or correspond to artifacts.
3. Those clusters that correspond to healthy skin are taken together into one cluster. This cluster is labelled as skin.
4. Perform a second run of K-Means clustering on the remaining clusters (inflamed skin, lesion, etc.). This time use 3 clusters. Label the clusters that correspond to the mole and melanoma center as mole and melanoma. The remaining clusters are considered to be ‘regions of normal skin or unclassified regions’.
In Table 3 the confusion matrix of the classification of each class using the unsupervised K-means algorithm, based on the truth-values used in the training set (diagnosed by dermatologist).
Table 1. Confusion matrix of k-means unsupervised classification.

<table>
<thead>
<tr>
<th>Classes</th>
<th>Class1</th>
<th>Class2</th>
<th>Class3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unclassified</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Class1</td>
<td>16117</td>
<td>2227</td>
<td>7</td>
<td>18351</td>
</tr>
<tr>
<td>Class2</td>
<td>0</td>
<td>1288438</td>
<td>14738</td>
<td>170176</td>
</tr>
<tr>
<td>Class3</td>
<td>0</td>
<td>50131</td>
<td>48303</td>
<td>98434</td>
</tr>
<tr>
<td>Total</td>
<td>16117</td>
<td>180796</td>
<td>90048</td>
<td>286961</td>
</tr>
</tbody>
</table>

Confusion Matrix (Memory1) 512x512x1
Overall Accuracy (192858/286961) 67.2070%

Table 2. Confusion matrix of LM supervised classification.

<table>
<thead>
<tr>
<th>Classes</th>
<th>Class1</th>
<th>Class2</th>
<th>Class3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unclassified</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Class1</td>
<td>16114</td>
<td>14798</td>
<td>0</td>
<td>18192</td>
</tr>
<tr>
<td>Class2</td>
<td>3</td>
<td>114645</td>
<td>30645</td>
<td>143141</td>
</tr>
<tr>
<td>Class3</td>
<td>66003</td>
<td>59403</td>
<td>0</td>
<td>125406</td>
</tr>
<tr>
<td>Total</td>
<td>16117</td>
<td>180796</td>
<td>90048</td>
<td>286961</td>
</tr>
</tbody>
</table>

Confusion Matrix (Memory1) 512x512x1
Overall Accuracy (192858/286961) 67.2070%

Table 3. Confusion matrix of SAM supervised classification.

<table>
<thead>
<tr>
<th>Classes</th>
<th>Class1</th>
<th>Class2</th>
<th>Class3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unclassified</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Class1</td>
<td>99.98</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Class2</td>
<td>0.02</td>
<td>63.51</td>
<td>34.03</td>
<td>50.68</td>
</tr>
<tr>
<td>Class3</td>
<td>0</td>
<td>36.51</td>
<td>63.49</td>
<td>43.37</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

In table 1 and table 2 the confusion matrix of the classification of each class using the supervised LM and SAM algorithms, based on the truth-values used in the training set (diagnosed by dermatologist). In table 3 the confusion matrix of k-means algorithm for pixel classification.

Table 4. Classifier true positive results using ML, SAM and K-means.

<table>
<thead>
<tr>
<th>Class</th>
<th>ML</th>
<th>SAM</th>
<th>Kmeans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>88.28%</td>
<td>81.83</td>
<td>79</td>
</tr>
<tr>
<td>Moll</td>
<td>92.28%</td>
<td>86.98</td>
<td>84</td>
</tr>
<tr>
<td>Healthy skin</td>
<td>93.17%</td>
<td>87.92</td>
<td>85</td>
</tr>
</tbody>
</table>

The sensitivity, specificity, positive predictive value and negative predictive value of each class is calculated using the true positive, true negative, false positive and false negative arguments.
4. Conclusion

In this report, we have proposed a new scheme that allows to classify melanoma as pigmentation lesions of skin using multi-spectral images applying three different classification algorithms: ML, SAM as supervised classifiers and K-means as unsupervised classifier. The obtained results on 300 melanoma objects in clinical study tend to show that the spectral imaging method as new technology is robust and usable in Vivo and non-invasive diagnostic method.

The fact that the supervised classification algorithms interacts at the last step of the classification can be seen as a benefit tool compared with the unsupported classification algorithms. Because it allows to both make a miss or over classification control and make the classification to be based only on machine learning techniques, which are often controllable and evaluable.

In a possible application, where the physician is assisted by a system which pre-screens patients, we have to take care about high sensitivity which is typically accompanied with a loss in specificity. Preliminary experiments showed that a true positive of 88% using ML or 81% using SAM is possible at the cost of less than 15% false-positives using MI and SAM. K-Means provided only 7% true positive.

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References


