COMPUTER AIDED DIAGNOSIS OF CONFOCAL LASER SCANNING MICROSCOPY IMAGES OF MELANOCYTIC SKIN TUMOURS

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Abstract

The aim of this study is to check the application of machine learning algorithms for the computer aided diagnosis of confocal laser scanning microscopy (CLSM) views of skin lesions. The images were dissected in equal square elements where the features, based on spectral properties of the wavelet transform, were calculated out. The images were discriminated according their features by several machine learning algorithms, based on tree classifiers, function classifiers and lazy classifiers. The results were evaluated and show that tree classifiers allow the best discrimination between CLSM views of benign common nevi and malignant melanoma.

1. Introduction

Confocal laser scanning microscopy (CLSM) is a novel imaging device enabling the non-invasive examination of skin cancer in real-time [1-3]. CLSM is well suitable for preventive medical check-ups and early recognition of skin tumours. In contrast to the conventional examination, where suspicious skin tumours have to be excised, embedded in paraffin and stained, the method is much more agreeable for the patient and faster. However, training and experience is necessary for successful and accurate diagnosis in this new and powerful imaging technique. To diminish the need for training and to improve diagnostic accuracy, computer aided diagnostic systems are required. Automated diagnostic systems need no input by the clinician but rather report a likely diagnosis based on computer algorithms. In a previous study we developed and evaluated a system (TCA: Tissue Counter Analysis) for automated image analysis of CLSM images [4]. In this previous study several texture features, based on spatial and frequency domains, were evaluated for applicability and the best features were selected. The system was tested in a clinical environment and the results compared with the prediction success of an independent human observer. In this study we check and compare several machine learning algorithms for their applicability in the tissue counter system.

Pre-selected CLSM images from the centre of tumours are used in this study. The study set emphasis 50 images of benign common nevi and 50 images of malignant melanoma. In contrast to blood cells, which are well separated and therefore enable segmentation without problems, the histological tissue show structures arranged in a variety of patterns. To avoid the segmentation of the skin

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tissue, which is the main difficulty in automatic image analysis, the images are divided into square elements of equal size. The features, based on spectral properties of the Daubechie 4 wavelet transform, are calculated for each square element of the respective image. These features have been shown to be well suitable for the automatic analysis of CLSM images because they enable an exploration of architectural structures at different scales. The tissue of benign common nevi often show pronounced structures such as tumour cell nests and arrangements of nevi cells around basal structures. Contrary to this, the tissue of malign melanoma often shows melanoma cells and connective tissue without architectural structures. The experience shows that such architectural structures play an important role for the diagnosis of CLSM images. After the feature extraction the square elements are classified by different machine learning algorithms. In this study we evaluate several algorithms of tree classifiers, function classifiers and lazy classifiers. The algorithms are checked for their applicability for the automatic discrimination of benign common nevi tissue and malign melanoma tissue.

2. Material

2. 1. Convocal laser scanning microscope

Confocal laser scanning microscopy is performed with a near-infrared reflectance convocal microscope (Vivascope 1000, Lucid Inc., Rochester, NY, USA). The microscope uses a diode laser at 830 nm wavelength and a power of <35mW at lissue level. A x30 water-immersion objective lens with a numerical aperture of 0.9 is used with water (refractive index 1.33) as an immersion medium. The spatial resolution is 0.5-1.0 µm in the lateral and 3-5 µm in the axial dimension. Usually an examination depth of 350 µm can be reached. The laser beam is focused by an objective lens to an illuminated spot at a specific layer of the skin tissue. The vertical position (depth of the layer) is controlled by a pinhole in front of the laser source. The images are gained from the reflected light where the contrast in the images results from variations in the refractive index of microstructures within the skin. The reflected light from each point of the plane, which goes the same way back through the objective, is separated from the incident laser beam (by a beam splitter) and deflected to the detector. A CLSM examination takes 3-5 minutes per lesion. Up to 16 layers per lesion can be scanned.

2. 2. Convocal laser scanning microscopy images

All images were monochrome images with a resolution of 640x480 pixels and 8 bits per pixel. They are stored in BMP file format. The images contain a field-of-view of 0.5x0.5 mm on the skin tissue providing insights into cellular structures. They show horizontal sections of the lesions. Overall, 50 images of benign common nevi and 50 images of malignant melanoma are used as study set. The images are taken from the centre of the tumours representing the dermo-epidermal junction.

2. 3. Image analysis software

The procedure for image analysis (feature extraction and calculation, relocation of the square elements in the images) was developed using the “Interactive Data Language” software tool (IDL 6.0, Research Systems, Boulder, CO, USA). The software runs on a PC under Windows.

2. 4. Machine learning software

For the discrimination of the square elements, according to the features of the different tissues, machine learning algorithms of the WEKA toolkit are used. WEKA (Waikoto Environment for Knowledge Analysis) was developed at the University of Waikato in New Zealand [5]. The system is written in Java and distributed under the terms of GNU General Public License). The tree classification is done by the CART (Classification and Regression Trees) analysis software from Salford Systems, San Diego, USA. Both software systems are running on a PC with Microsoft Windows operating system.

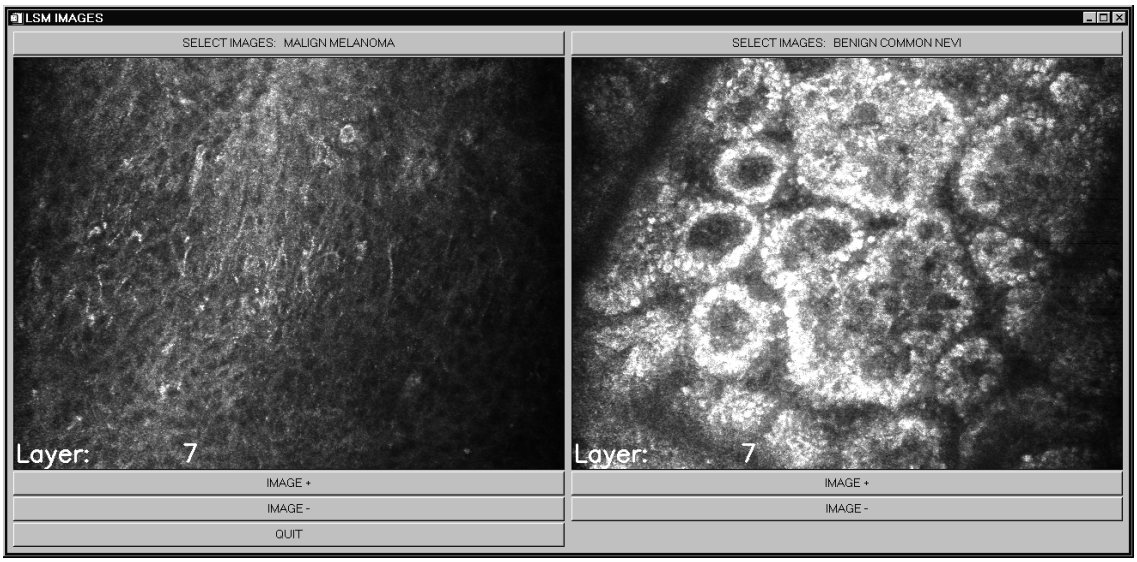

Figure 1: Confocal images of malignant melanoma (left) and benign common nevi lesions (right), showing typical cellular and architectural details.

3. Methods

CLSM views of skin tissue show structures arranged in a variety of patterns. To avoid the automatic segmentation of structures, such as: cells, vessels and other inclusions, which can not be done in a general approach, the images are dissected in square elements of equal sizes. For this study square elements of 256x256 pixels are used.

3. 1. Image analysis system

Tissue counter analysis (TCA) consists of three parts: the feature calculation and extraction; the classification and the relocation. In feature calculation, the different features are calculated inside each square element. In the classification procedure, machine learning algorithms splits the square elements, according to their features, into different classes representing the different kinds of tissue (benign common nevi and malign melanoma). In the relocation procedure, the classified square elements are superimposed on the corresponding image enabling the visualization and evaluation of the classification results.

3. 2. Texture features

Melanocytic cytomorphology and architecture and keratinocyte cell borders are taken into account for diagnostic decisions by the human observer. Because architectural structures play an important role for the rating of CLSM images, features based on the spectral properties of the Daubechie 4 wavelet transform are selected for the description of benign common nevi and malign melanoma tissues. Wavelets enable an exploration of tissue structures at different scales. In total, 39 different features are calculated from the wavelet transform representing large scale and low scale information in the different frequency bands.

3. 3. Classification

Different machine learning algorithms, based on of tree classifiers, function classifiers, lazy classifiers and metalearning algorithms are used in this study. Tree classifiers are based on divide-and-conquer strategies for the construction of decision trees. By the *CART* (Classification and Regression Trees) analysis the square elements are automatically separated into homogeneous terminal nodes corresponding to the different tissues. The splitting rules, which are generated automatically by the *CART* algorithm, are used as diagnostic rules. Function classifiers include algorithms that can be written down as mathematical equations. Several function classifiers are used: *Logistic*; *Simple logistic*; *SMO* and *Multilayer perceptron*. *Logistic* build a linear logistic regression model. *Simple logistic* uses a linear logistic regression model with build in attribute selection. *SMO* uses a sequential minimal optimization algorithm for support vector classification. *Multilayer perception* is a neural network with backpropagation. Lazy classifiers store the training instances and do no real work until classification time. *IBk* and *IB1* are used. *IB1* classifier is a basic nearest-neighbour instance based learner. *IBk* is a k-nearest-neighbour classifier. Metalearning algorithms take classifiers and turn them into more powerfull learners. As representatives of metalearning algorithms, the *Multi Class Classifier* and the *Threshold Selector* are used. *Multi Class Classifier* uses a two-class classifier for multiclass datasets. *Threshold Selector* optimizes the F-measure for a probabilistic classifier.

4. Results

The percentage of square elements correctly classified as benign common nevi and the percentage of square elements correctly classified as malignant melanoma for al the 100 cases are shown in *Table 1*. The best result is obtained with the *CART* algorithm showing 96.0% of correct classified elements of benign common nevi and 97.0% of correct classified elements of malignant melanoma. The correctly classified instances are 96.50% and the incorrectly classified instances are 3.50%.

Table 1: Classification results for the square elements of common benign nevi and malignant melanoma by use of different machine learning algorithms

Machine learning algorithm		Nevi [%]	Melanoma [%]
Function classifiers	Logistic	80.0	83.5
	Simple Logistic	73.5	73.0
	SMO	70.5	71.5
	Multilayer perception	80.0	80.5
Tree classifier	CART	96.0	97.0
Lazy classifier	IB1	79.0	81.5
	IBk	79.0	81.5
Metalearning	Multi Class Classifier	80.0	83.5
	Threshold Selector	74.5	87.0

The correctly classified instances for the other classifiers are: 81.75% for *Logistic*, 73.25% for *Simple Logistic*, 71.00% for *SMO*, 80.25% for *Multilayer Perceptor*, 80.25% for *IB1*, 80.25% for *IBk*, 81.75% for *Multi Class Classifier*, 80.75% for *Threshold Selector*. Then the incorrectly classified instances are: 18.25% for *Logistic*, 26.75% for *Simple Logistic*, 29.00% for *SMO*, 19.75% for *Multilayer Perceptor*, 19.75% for *IB1*, 19.75% for *IBk*, 18.25% for *Multi Class Classifier*, 19.25% for *Threshold Selector*.

5. Discussion

Delayed recognition of skin malignancies puts the patient at risk of destructive growth and dead from disease once the tumour has progressed to competence for metastasis. Therefore preventive and periodical skin checkups are of special importance. Technological advancements in imaging systems have led to the development of convocal laser scanning microscopy. This technique enables the examination of skin lesions in vivo and significantly higher prediction success than reported for dermoscopic examination can be achieved for the diagnosis of melanoma. However due to the fact that the CLSM method is relatively new, there is still a lack of experiences with the diagnostic features and an intensive training is necessary for the clinician. Computer aided diagnosis providing automated decisions can be used as an expert second opinion or help and assist the non-experienced physician in the diagnostic procedure.

To evaluate the performance of our automated image analysis system, it was tested in a real life environment and the prediction results were compared with the prediction success of an independent human observer. A total of 857 CLSM images including 408 benign common nevi and 499 melanoma images were evaluated. The CART algorithm was used for classification. 97.55% of the malign melanoma images and 96.32% of the benign common nevi were correctly classified (overall performance 96.94%). In contrast, sensitivity and specifity of 85.52% and 80.15% could be reached by the human observer (overall performance 82.84%).

6. Conclusion

In conclusion, image analysis together with machine learning algorithms provide a powerful tool for automated diagnosis of CLSM images of skin lesions. This study demonstrates the applicability of the system for the discrimination of CLSM views of malignant melanoma and benign common nevi. As possible clinical application the system can be used as a screening tool to improve preventive medical checkups and the early recognition of skin tumours.

7. References

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