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Digital Image Analysis for Diagnosis of Skin Tumors

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Between 1987 and 2007, different groups developed digital image analysis systems for the diagnosis of benign and malignant skin tumors. As the result of significant differences in the technical devices, the number, the nature and benign/malignant ratio of included skin tumors, different variables and statistical methods any comparison of these different systems and their results is difficult. For the use and comparison of the diagnostic performance of different digital image analysis systems in the future, some principle basic conditions are required: All used systems should have a standardized recording system and calibration. First, melanocytic and nonmelanocytic lesions should be included for the development of the diagnostic algorithms. Critical analyses of the results should answer the question if in future only melanocytic lesions should be analyzed or all pigmented and nonpigmented lesions. This will also lead to the answer if only dermatologists or all specialities of medical doctors will use such a system. All artifacts (eg, hairs, air bubbles) should be removed. The number of variables should be chosen according to the number of included melanomas. A high number of benign skin lesions should be included. Of all lesions only 10% or better less should be invasive melanomas. Each system should be developed by a training-set and controlled by an independent test-set. Each system should be controlled by the user with the final decision and responsibility and tested by independent users without any conflict of financial interest.

KEYWORDS digital image analysis, skin tumors, melanoma, melanocytic nevi

During the past 2 decades dermoscopy (dermatoscopy, epiluminescence microscopy) has become an established noninvasive tool for improving the early detection of melanoma and nonmelanoma skin cancer while reducing unnecessary excisions of benign skin tumors.[1-3] Dermoscopy uses the recognition of submacroscopic morphologic structures as well as vascular patterns located in the different compartments of the skin (epidermis, dermoepidermal junction and upper dermis) to distinguish between benign and malignant skin tumors. Compared with the clinical diagnosis, there is an improvement of diagnostic sensitivity of 10-30% when using dermoscopy in skin tumors.[4] However, because of the complexity of patterns and their interpretation, the results of dermoscopic examinations have limitations, especially for beginners and users not trained specifically.[5,6] Therefore, the scientific endeavor exists to obtain an established and consistent classification between benign and malignant skin tumors by means of digital dermoscopy analysis.[7-38]

Between 1987 and 2007 different groups developed diagnostic systems of recorded images (slides or digital cameras; Table 1). Any comparison of the results reported in published studies is difficult. Only one study of which we're aware has been performed on a standardized calibration.[33] Different recording systems were used. In the reported studies, different data sets included melanocytic and, likewise, nonmelanocytic lesions. Different numbers of melanomas were included, which led to different ratios of benign and malignant melanocytic tumors. The melanomas under examination had varying median Breslow's tumor thickness. Different statistical methods with a different number of used variables were described. Often, the exact algorithms and formulas used for the diagnostic algorithm have not been disclosed in the literature. Also, the respective sets of images have been rarely analyzed by different approaches. In the reported studies the sensitivity ranged from 60.9% to 100% and the specificity from 60% to 100%.

Nevertheless, based on the results of the literature, the digital dermoscopy analysis of recorded images is and will be at least equal to the clinical and dermoscopic diagnostic sen-

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Table 1 Summary of the study groups that have developed digital dermoscopy analysis for digitized pictures

First author	Year	Variables (n)	Source	Statistical method	Lesions	Trainings-set	Melanoma	Sensitivity (%)	Specificity (%)
Cascinelli[7]	1987	no spe.	slides	no spe.	mel. + non-mel.	20	no spe.	no spe.	no spe.
Cascinelli[8]	1992	8	patients	no spe.	mel. + non-mel.	169	43	96	60
Schindewolf[9]	1993	23	slides	CART	mel.	353	215	94	88
Schindewolf[10]	1994	no spe.	patients	CART	mel.	309	80	89	88
Green[11]	1994	22	patients	discr.-anal.	mel. + non-mel.	164	18	89	89
Ecral[12]	1994	14	slides	neur.-netw.	mel. + non-mel.	326	136	80	86.3
Menzies[13]	1997	no spe.	slides	log. regr.	mel. + non-mel.	170	75	93	67
Husemann[14]	1997	no spe.	patients	neur.-netw.	no spe.	215	no spe.	>95	>95
Seidenari[16]	1998	22	patients	discr.-anal.	mel.	917	65	93	95
Binder[17]	1998	16	slides	neur.-netw.	mel.	120	39	90	74
Seidenari[18]	1999	26	patients	discr.-anal.	mel.	383	18	100	92
Handels[19]	1999	26	patients	neur.-netw.	mel.	44	19	97.7	100
Andreassi[20]	1999	13	patients	discr.-anal.	mel.	147	57	88	81
Blum[21]	1999	3[a] 6[b]	patients	factor an. + log. regr.[a,b]	mel. + non-mel.[a,b]	116[a] 51[b]	10[a] 27[b]	90[a] 70.4[b]	81.1[a] 70.4[b]
Stolz[22]	2000	no spe.	patients	log. regr.	mel.	466	125	86.4	92.7
Bauer[23]	2000	38	patients	neur.-netw.	mel. + non-mel.	315	42	92.9	97.8
Elbaum[24]	2001	13	patients	lin. class. + ROC	mel.	246	63	100	85
Rubegni[26]	2002	10	patients	neur.-netw.	mel.	147	57	93	92.8
Hoffmann[29]	2003	no spe.	patients	neur.-netw.	mel. + non-mel.	2.218	187	no spe.	no spe.
Burroni[30]	2004	10	patients	lin. class. + ROC	mel.	840	391	98	79
Blum[31]	2004	3[a] 6[b]	patients	factor an. + log. regr.[a,b]	mel.[a,b]	605[a] 232[b]	25[a] 59[b]	80[a] 82.7[b]	82.4[a] 84.1[b]
Menzies[33]	2005	103	patients[c]	[d] + ROC	mel. + non-mel.	2.430	382	91	68
Manousaki[35]	2006	3	patients	log. regr. + mult. mod. + ROC	mel.	132	23	60.9	95.4
Fikrle[37]	2007	2	patients	log. regr.	mel.	260	46	91.3	90.7
Wollina[38]	2007	35	patients	no spe.	mel. + non-mel.	3544	52	90-95	79.6-93.3

Abbreviations: no spe., no specification; CART, Classification And Regression Trees; discr.-anal., discrimination analysis; neur.-netw., neuronal network; factor an., factor analysis; log. regr., logistic regression; lin. class., linear classification; ROC, Receiver Operating Characteristics; mel., melanocytic skin lesions; non-mel., non-melanocytic skin lesions; mult. mod., multivariate model.

[a]=small, completely imaged lesions

[b]=large, partially imaged lesions

[c]=images were calibrated

[d]=discriminant variables with associated weighting factors and relationship features.

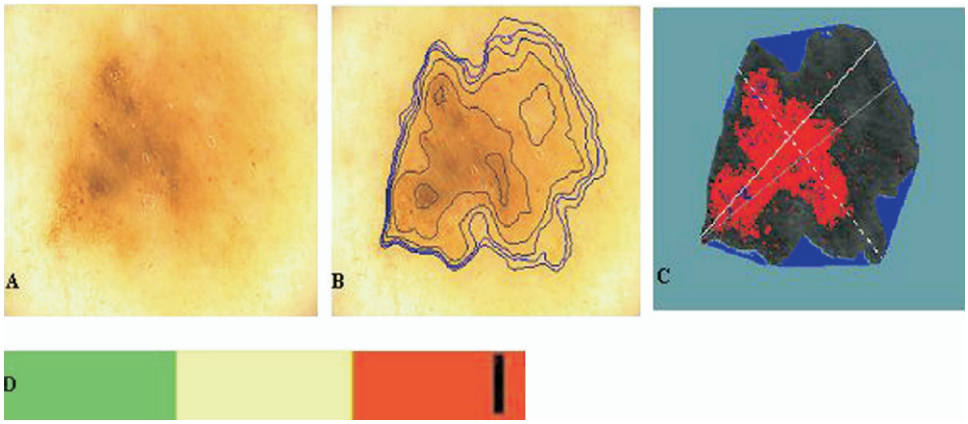

Figure 1 (A) Initial melanoma in situ with a distinct asymmetric hyperpigmentation. (B) Finding of the border and areas of different pigmentation. (C) Definition of the diameter, surface and different colors of the tumor. (D) Classification according the training- and testset into the area of suspicious lesions.[21,31] (Color version of figure is available online.)

sitivity and specificity obtained by a trained expert of dermoscopy (Fig. 1).[26] An advantage of a digital dermoscopy diagnostic system would be that the instrument and analyzing works independent of time. The digital system will not be influenced by different levels of attention as in human beings. Additionally, it might be a useful tool, particularly for centers without expertise in dermoscopy. On the other hand, it is not likely that the digital system will completely substitute the expert in dermoscopy. Well-trained users will recognize certain, significant details in melanocytic lesions which lead to the diagnosis of a disease with malignant potential.[1-3] These details, just visible in one small area of the entire lesion, couldn't have the impact to change the lesion from benign to malignant for the computer algorithm yet (Fig. 2).

Computer diagnostic algorithms could also be used in the follow-up of patients with atypical moles (Fig. 3).[34] The comparison of images recorded at different times is helpful in these patients. In addition, the results of computer diagnostic algorithms of the lesion could be useful for decisions in clinical management of patients with atypical mole syndrome.[27,34]

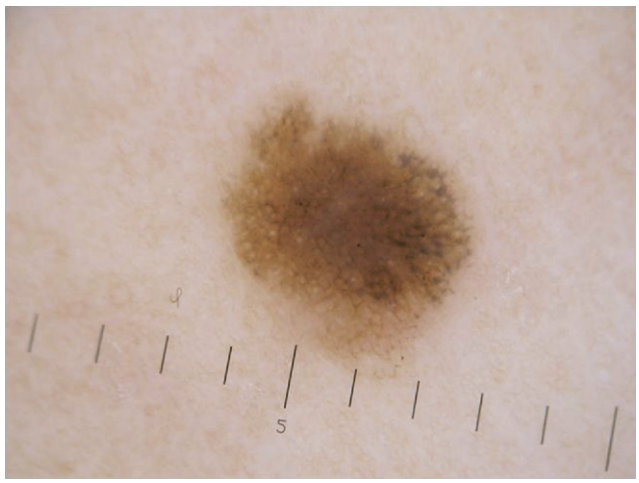

Figure 2 Severe dysplastic nevus proven by histopathology. In dermoscopy, distinct atypical network and starting radial streaming can be seen on the right side of the tumor. (Color version of figure is available online.)

For using and comparison the results of digital image analysis in future, some principle conditions are proposed[39]:

- All used systems should have a standardized recording system of the lesions of the patients. This includes the use and correct interpretation of immersion contact or polarized light dermoscopy with or without contact.[40,41]
- All used systems should have a standardized calibration of the camera that should be applied regularly.
- First, melanocytic and nonmelanocytic lesions should be included for the development of the diagnostic algorithms. Critical analyses of the results should answer the question if in future only melanocytic lesions should be analyzed or all pigmented and nonpigmented lesions. This will also lead to the answer if only dermatologists or all specialties of medical doctors will use such a system.
- All artifacts (eg, hairs, air bubbles) should be removed.
- The number of variables should be chosen according to the included melanomas (ratio between 1:10 and 1:100).
- A high number of benign melanocytic and nonmelanocytic lesions should be included.
- To represent the routine setting of a mole clinic, only 10% or better less of all lesions should be invasive melanomas.[31]
- Each system should be developed by a training-set and controlled by an independent test-set with the same ratios of benign and malignant tumors.
- Each system should be controlled by the user with the final decision and responsibility and tested by independent users without any conflict of financial interest.

The final and unsolved question until now is: Who will use this technology?

If automated diagnostic systems will be used by general practitioners or in pharmacies and shopping centers, these systems should be work with very high sensitivity and reasonably good specificity. Therefore, malignant tumors would

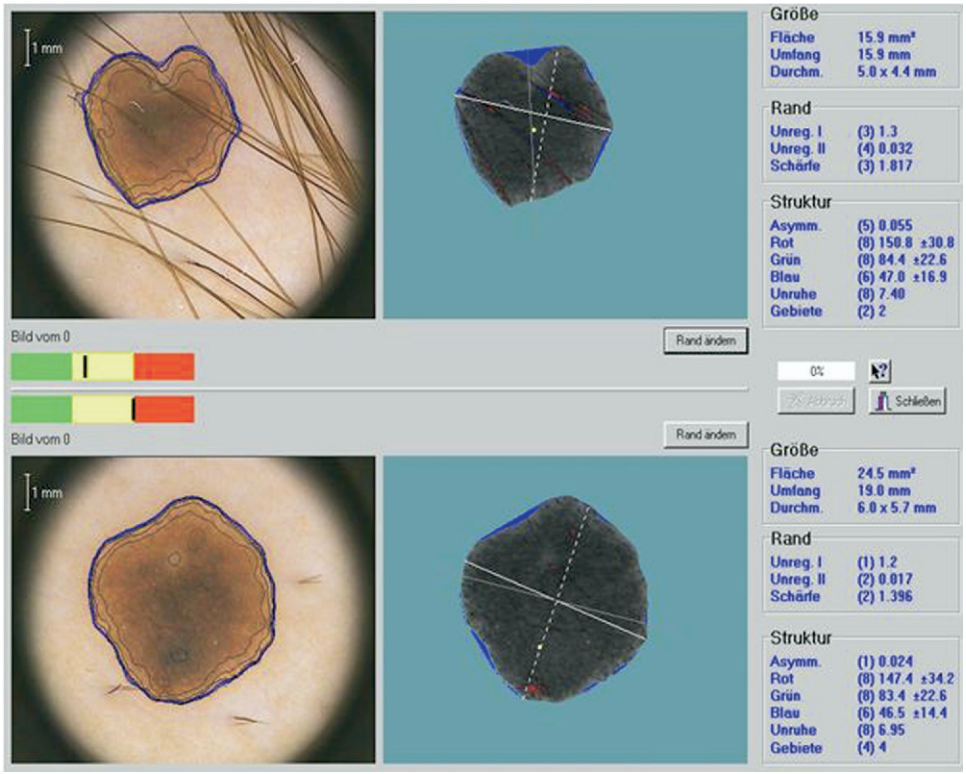

Figure 3 Computer-assisted analyzing of nevus in the follow-up over a period of 6 months: upper lesion is smaller (area 15.9 mm^2) and lower lesion is bigger (area 24.5 mm^2) with a symmetric growth. A distinct change from the yellow to the yellow-red area is seen in the classification of both lesions.[21,31] (Color version of figure is available online.)

be detected in early stage and unnecessary excision of benign lesions would be avoided. If the target is the "nonexpert" user, studies should be designed to test the accuracy of automated systems on a broad range of benign and malignant, melanocytic and nonmelanocytic pigmented and nonpigmented skin lesions. Atypical lesions such as Spitz nevi, atypical nevi, or seborrheic keratoses could still be missed by the analyzing system but would be more easily diagnosed by a good dermatologist using his/her clinical experience and additional criteria (eg, ugly duckling sign, clinical history) that can not be evaluated by an automated system.

If the target is the "expert" user, studies should be designed with the aim to help clinicians in distinguishing atypical benign lesions from malignant tumors of the skin. An increase in specificity might be the goal for an automated system directed to expert users together with a sensitivity at least equal to that achieved by the expert.

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