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Impact of digital dermoscopy analysis on the decision to follow up or to excise a pigmented skin lesion: a multicentre study

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Background: The quality of early malignant melanoma (MM) diagnosis is dependent on the experience of dermatologists, tools like dermoscopy and histopathology, and awareness and education of the studied population. Does a higher rate of excision of pigmented skin lesions (PSL) increase the rate of detected melanomas?

Material and Methods: The DB-MIPS objective tool, able to evaluate mathematical defined variables, has been used to verify the variability of measurements among PSL stored by five different centres located in Italy, Switzerland, and Germany.

Results: The objective analysis showed low differences in terms of moles' features among the different groups, arguing for robustness of the dermatological patient's PSL inspection. Differences in terms of false positives and predictive positive values have been detected. The tendency to follow up a lesion was proportional to the percentage of thin MM (<0.75 mm tumour thickness), while the interventism was proportional to the percentage of dysplastic moles. Similar percentage of thin melanoma has been observed in all the centres, indicating a standardization in early diagnosing among experienced dermatologists. The main difference among the centres was their mode of action, i.e. to follow up or remove suspicious PSL.

Conclusion: Interventism depends neither on the geographic site nor on the features of the observed moles. Higher removal rates do not correspond to higher MM detections: this means that an in-depth knowledge of melanoma patterns is required and follow-up of suspicious moles is highly suggested.

Key words: melanoma – nevus dermoscopy – digital dermoscopy analysis – follow-up

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CUTANEOUS MALIGNANT melanoma (MM) is a malignant tumour of melanocytes. A worldwide increase in MM incidence has been noted among the Caucasian population. In Italy, 1994–1998, the Cancer Registries calculated an incidence rate of 8.5 (males) and 1.9 (females) per 100,000 (1). In the central southern Italian Abruzzo region, an incidence rate of 14.1 per 100,000 inhabitants per year was seen in the years 2002 to 2005 (2). As shown by the Swiss Cancer Registries of Vaud and Neuchatel over the period 1978–2002, the age-standardized incidence of MM increased from 5.7/100,000 to 16.8/100,000 for men (+195%) and from 7.9/100,000 to 18.7/100,000 for women (+137%) (3). The incidence has tripled for both genders during the years from 1976 to 2003 as documented by the German Central Malignant Melanoma Registry and reached 10.3 (males) and 13.3 (females) per 100,000 per year (4).

Considering that advanced cutaneous melanoma is still incurable, an early diagnosis is of utmost importance to reduce the mortality rate. However, recognizing melanomas is not always easy. In the last two decades, dermoscopy become a non invasive tool for the diagnosis of pigmented skin lesions (PSL). This new non invasive technique also tends to reveal thicker MM and the supposed price to be paid is a higher number of false positives due to the difficulty of interpretation of malignant features and the high experience required (5–7).

A frequent discussion related to the accuracy in the diagnosis of MM refers in fact to the influence of the test sets. Many differences have been found in accuracy among multicentre studies using subjective assessments (8–10). It is supposed that the variation in accuracy is mainly caused by the different interpretation in using algorithms than in the nature of the PSL observed.

The results of the consensus internet meeting on MM diagnosis showed a very low concordance when using the seven-point checklist, the ABCD rule and other subjective 'algorithmic' methods (9–11). Different and more encouraging results have been obtained through the traditional dermoscopic inspection without using subjective algorithms (pattern analysis) (12–14).

To overcome the problem that occurred with the use of 'subjective algorithms', many computerized 'diagnosis oriented' systems have been developed in the last decade. The main advantage of computerized systems lies in not only the opportunity to store, retrieve and visually compare the lesions: some aided diagnosis tools also allow to objectively define and measure mathematically defined PSL features (15).

A computerized tool can instantly identify the border of the lesion and evaluate a defined number of variables expressing geometries, colours and colour islands inside the lesion identifying pigment distribution. It is possible to verify variables' reliability through multicentre studies (16).

In this multicentre study, the objective variables have been processed in order to evaluate their impact in the early diagnosis of analysed lesions during daily practice on large datasets. Moreover, we evaluated the impact of DDA on interventism defined as the number of removed lesions divided by the number of suspicious lesions observed.

Materials and Methods

This is a multicentre trial involving 3227 patients (aged between 12 and 80 years) with PSL in four centres, i.e. Dresden (Germany), Lucarno (Switzerland), Lugano (Switzerland), and Siena (Italy). All patients were evaluated clinically by dermatologists with >10 years of experience in a pigmented lesion clinic. In addition, data of the population of Capraia Island (Italy) have been obtained during a 2-day screening campaign. In total, 120 patients were investigated but only 91 (75%) of them were selected for the dermoscopic analysis as 25% had no PSL. The selection also included clearly benign PSL and small-size moles.

The images were stored and analysed using the DB-DM-MIPS© System (Biomips Engineering, S.R.L., Siena, Italy), which is a computerized tool providing digital dermoscopic images. A hand-held camera is connected to a personal computer and the true colour PSL images are automatically processed, evaluating 49 objective parameters. The variables are subdivided into three categories: geometries, colours, and islands of colours (Burroni Islands). Different optics can provide different magnifications: in this paper, we only discuss images with a magnification of $\times 16$ providing an image resolution of 45 pixels/mm corresponding to a field of view of 16.8 mm. The illumination is provided by halogen lamps. Each series of parameters is stored along with the coded image of the analysed lesion. Patient's data have been stored along with the 49 variables so that query reports have been allowed for advanced statistical comparisons. A module called DB-Dermo Search allowed objective queries on the huge databases. For each analysed mole, a proper variable has been set in order to specify the clinician's tendency to remove or follow up (the variable indicated three possible actions: remove, follow up, absolutely benign). Among 49 variables, 35 refer to geometries, colours and islands and 11 are a linear combination of the other. For this reason, we will report the statistics referring to 35 variables. For the three centres in Locarno, Lugano, and Dresden, each mole has also been signed for removal or follow-up purpose. The decision making was analysed for three centres involved in this study, while for the Siena centre, only the number of removed lesions has been set.

The diagnostic reliability is generally measured through two variables: sensitivity and specificity. The sensitivity identifies the percentage of correctly diagnosed melanoma. The specificity refers to the percentage of correctly classified benign non-melanoma lesions. An MM misdiagnosed with a mole is called a false negative while a mole identified as MM is called a false positive. Most efforts tend to reduce the number of false negatives, limiting, at the same time, the number of false positives.

The tendency to follow up (wait and see) is defined as the ratio of (number of suspicious lesions – removed lesions)/suspicious lesions. Interventism is defined as the number of removed

lesions divided by the number of suspicious lesions. Clinicians's false positive can be defined as the number of excisions–melanoma/total of stored lesions. The predictive positive value (PPV) indicates the probability of rightly predicting melanoma and it is defined as PPV = true positives/(true positives+false positives). We should point out the fact that the PPV is influenced by the incidence of MM. The difference in the PPV values do not indicate the quality of the diagnosis but, instead, indicate the kind of population studied when compared with the absolute number of lesions. Pre-selected populations should reveal higher values of PPV when having similar values in false positives.

Morphological analysis has been used to study the moles' features on the observed population just to take into consideration the aspect bias and influence.

Statistical analysis

Having four centres plus the Capraia Island screening to be analysed and a large amount of data considering that each mole leads to many variables, the best way to perform a comparison among the five classes consists in using multivariate analysis. We tried to understand datasets considering groups of variables instead of single variables. For this reason, we used the Mathlab statistics toolbox and the principal component Analysis. Each principal component is a linear combination of the original variables. In this way, it is possible to obtain a visual indication of the distribution in a plane of each single lesion stored by different centres. Multivariate comparative plots identify different values on a plane. Similar clusters of values lead to closer points on the space. The descriptive statistics were analysed through the *N*-way analysis of variance (ANOVA) for large datasets. The ANOVA was used to provide not only the mean values and their standard deviations but also to verify through the *P*-values (Fisher's *P* of significance) when the significant variables able to distinguish between moles and MM were the same among different centres. In addition, the mean values of the most significant variables of moles and MM among the different centres have been compared.

Patients' comparison

The patient groups table has been divided by age and gender (Table 1). The age has been indicated just because pigmented lesions belonging to older patients could have been more irregular or dark, thus altering the objective statistics. The Lugano, Locarno, and Siena centres presented a similar age distribution (Table 1), with female/male ratios of 1.78, 1.50, and 1.69, respectively. The Dresden centre revealed a higher percentage of patients older than 50 years and a slight prevalence of males (female/male ratio 0.94). An older population with no gender preference was found on the small island of Capraia.

TABLE 1. Our study population

	Capr1	Capr2	Lugano	Locarno	Dresden	Siena
Total number of patients	24	67	345	468	495	1919
Males	11	32	124	187	255	713
Females	13	35	221	281	240	1206
0<age<8 years	8%	16%	5%	4%	7%	2%
9<age<16 years	9%	4%	11%	8%	8%	11%
17<age<30 years	6%	13%	21%	30%	15%	28%
31<age<50 years	33%	34%	49%	41%	40%	46%
Older than 50	52%	51%	17%	17%	30%	15%

The patients are subdivided into percentage distribution by sex and age intervals.

Interventism vs. follow-up

One of the most recurring sentences concerning the early diagnosis of melanoma is related to the question of whether a follow-up is more powerful than interventism, i.e. the excision of slightly doubtful lesions, in the practical approach. The follow-up consists of the storage of a lesion and subsequent observation at prefixed time intervals. The two centres located in Locarno and Lugano present a high similarity of patients and observed moles (the maximum diameter, gradient, and darkness of the lesion are almost the same). A closer comparison between the two Swiss centres has been carried out because they have the same histologist and a comparison in terms of *situ* MM and dysplastic moles has been performed.

The histology of the Locarno centre reveals the same percentage of *situ* MM (20%) as the Lugano. The percentage of melanoma with a thickness <0.75 mm is in the same range (Locarno with 50% and Lugano with 40%). However, a significant difference exists in interventism and follow-up tendency among the two centres: in the Locarno centre, the interventism is 36.3% with respect to the 76% of the Lugano centre. The tendency to follow up of the Locarno centre (63%) is higher than that of the Lugano centre (24%). In the Dresden centre, the mean value of

interventism is 56.2% and that of follow-up is 43.8%. The percentage of MM with a thickness of <0.75 mm is similar to the Swiss centres. The different tendency among the centres in follow-up and interventism could influence the early diagnosis: the tendency to follow up could help to detect a higher percentage of MM with thickness <0.75 mm. Follow-up of slightly doubtful lesions could be useful in the daily routine.

The percentage of *situ* MM of the Siena centre is much higher than that in Swiss centres or Dresden, with 41%. However, the percentage of MM with a thickness <0.75 is not in the same range. This probably indicates a histological bias: the histological reproducibility related to the differential diagnosis between dysplastic moles and *situ*-melanoma is actually an open debate (17, 18).

Counting the total percentage of *situ*-MM and MM with a thickness <0.75, we note (Table 2) very similar values among the Lugano, Locarno, Dresden and Siena centres, corresponding to 60%, 70%, 66%, and 65%, respectively. The statistical analysis indicates a high standardization in the early diagnosis of melanoma among expert dermatologists in different situations. The population studied has obviously not altered early MM diagnosis in daily routine.

The lowest percentage of dysplastic moles of removed lesions was seen in the Dresden centre (14.7%), corresponding to the lowest percentage of false positives (6.6%). On the contrary, the Lugano centre reported 80.7% of dysplastic moles and showed the highest number of false positives (13.8%). For all the centres, a higher percentage of false positives seems to be correlated to a higher percentage of dysplastic moles. This tendency is also confirmed for the *situ* MM.

The number of MM less than 0.75 in thickness including also the *situ* MM is very similar among all four centres, where different dermatologists analysed patients from different countries, indicating how experienced dermatologists use the dermoscopic tool as a standardized process. Also, the influence of the diagnosis machine could have contributed to the standardization in the early diagnosis. In the Siena, Dresden, Lugano and Locarno centres, the different percentage in terms of false positives, which, however, remains low, does not alter the diagnostic ability of the clinicians, which is very similar.

The PPV is generally used to describe the population/specificity relationship. The PPV indicates the probability that a clinician's 'alarm' actually indicates a MM but this variable is strictly correlated with the incidence of melanoma and it should be considered carefully. However, in our study, the PPV is not found to be dependent on the tendency to follow up or remove (Table 2). The PPV values of the Siena centre, 17.5%, are very similar to the values reported in a nearby Florence centre, with PPV = 13.7% (12), in a study also measuring the sensitivity through a skin cancer registry comparison.

TABLE 2. Classification of pigmented skin lesions

Centres	Lugano (%)	Locarno (%)	Dresden (%)	Siena (%)
MM/total lesions	0.6	0.8	2.8	2.4
In situ MM/all MM	20	20	12	41
Thin MM/all MM	40	50	54	24
(*In situ*+thin MM)/all MM	60	70	66	65
Dysplastic moles/total lesions	11.6	8.7	1.3	5.8
Dysplastic moles/removed	80.7	80.9	14.7	42.4
Tendency to follow up	24	63.7	42.3	ND
Interventism	76	36.3	57	ND
False positives	13.8	10.7	6.6	11.5
Predictive positive value	4.4	7.7	30.3	17.5

The interventism indicates in percentage the ratio between the number of removed lesions compared with those indicated as 'suspect'. The tendency to follow up is given by '100 – interventism'. The false positives describe the percentage of benign lesions indicated as malignant and removed. The predictive positive value of a centre indicates the probability that a lesion indicated as 'suspect' in that centre is a malignant one. Predictive positive values = true positives/(true positives+false positives). ND (not done) indicates that in the Siena centre, the field indicating 'suspect' was not implemented. The interventism is, however, proportional to the false positives. The values are expressed in percentage to be independent by the patient's number.
MM, malignant melanoma.

Multivariate plots

The multivariate distribution plots (Figs 1–5) provide a 'summer' of all the 35 variables: in this way, a simplified graph can be obtained. Each element indicates a lesion. Similar clusters of values lead to closer points on the space. Figure 1 shows the different distributions of the PSL belonging to different centres. The magenta circles corresponding to the Capraia Island's population lie on every side of the plane, indicating a bias of selection. The Siena and Dresden centres also spread wider on the plane. The Lugano and Locarno PSL are a subset of the Siena and Dresden PSL.

The similarities among Dresden and Siena and Lugano and Locarno coupled centres can be observed in Figs 2 and 3. Figure 4 shows the similar selection performed by different clinicians in the Capraia experience. The distribution resulting from the 35 variables of the lesions

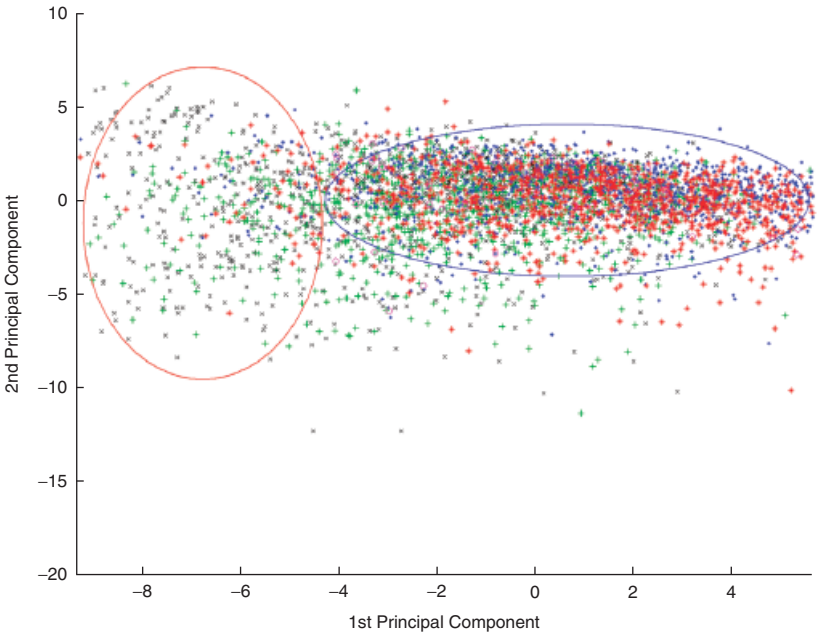

Fig. 1. The comparative plot in the multivariate plane shows the different distributions of benign lesions between the five centres. The multivariate distribution provides an 'abstract' of all the 35 variables: in this way, a simplified graph can be obtained. Each element indicates a lesion. Similar clusters of values lead to closer points on the space. The blue circle marks the region where the benign lesions show similar features among all the centres. The red circle indicates the area where the lesions stored in Dresden and Siena are prevalent. The Capraia Island population, identified by small magenta circles, lies on the entire plane, indicating the pseudo-random distribution. Green '+', Siena centre black; 'x', Dresden Hospital red;'', Locarno centre blue; '.', Lugano centre magenta; 'o' = Capraia Island.*

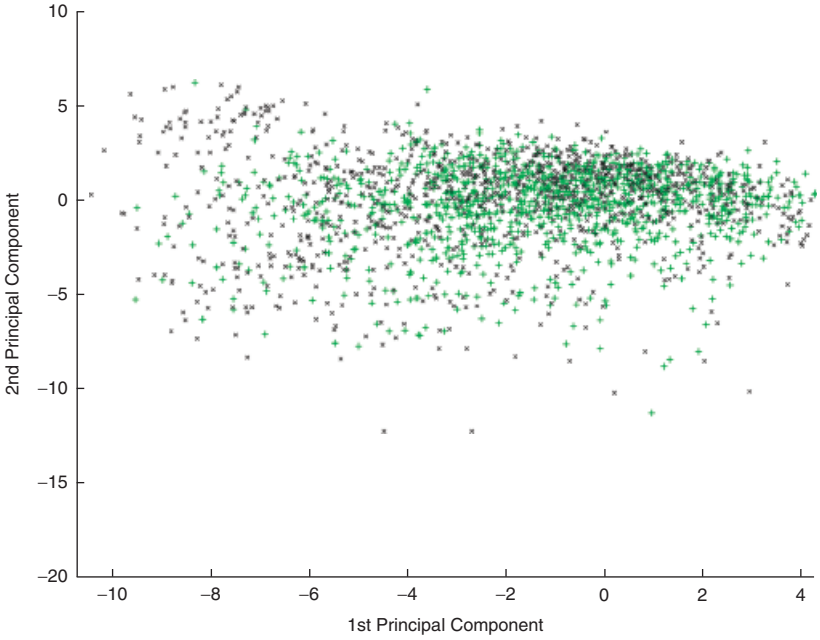

Fig. 2. The comparative plot in the multivariate plane shows the homogeneity of distribution of benign lesions between the Siena and Dresden centres. The different distribution compared with the Swiss centres (Fig. 3) indicates a different bias. Green '+', Legatumori Siena centre black; 'x', Dresden Hospital.

demonstrates that there is no evident separation between the two groups. This indicates that different dermatologists decided to store only moles presenting standardized aspects. The similar distributions of the distant Dresden and Siena populations illustrate standardized aspects. In other words, it is possible that the selection of PSL features is not clinician dependent but population dependent. Expert dermatologists tend to store the same kind of PSL in homogeneous

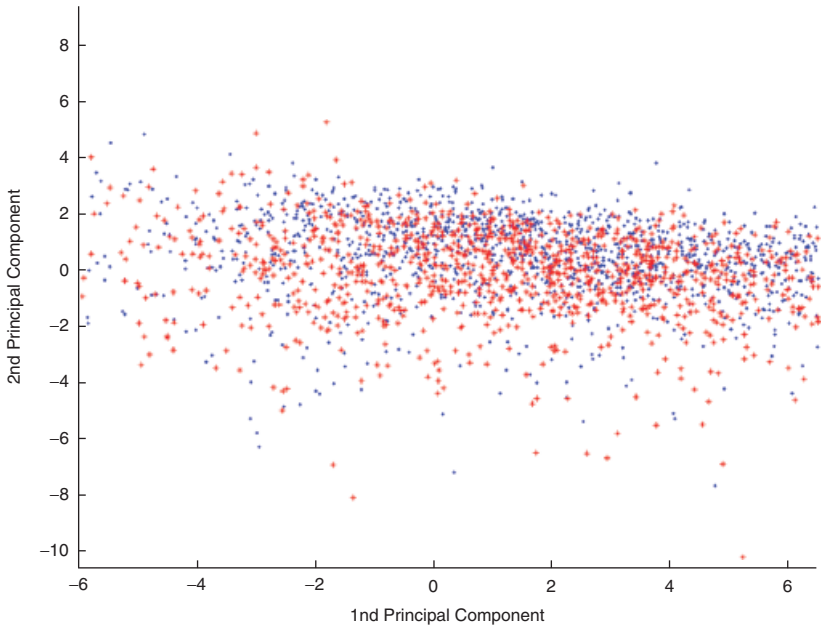

Fig. 3. The comparative plot in the multivariate plane shows the homogeneity of distribution of benign lesions between the Lugano and Locarno centres. The different distribution with respect to the Siena and Dresden centres (plot A and plot B) indicates a different bias. Red '', Locarno centre blue;'.', Lugano centre.*

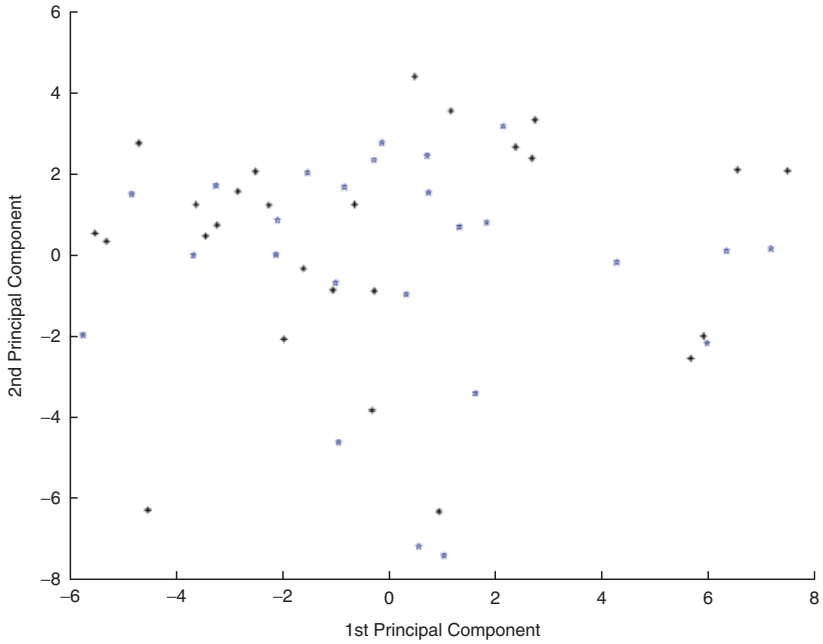

Fig. 4. Distribution of the Capraia Islands' benign lesions. The signs '+' and '' identify the two different ambulatories where expert dermatologists were working. The distribution resulting from the 35 variables of the lesions demonstrate that there is no evident separation between the two groups. This indicates that different dermatologists decided to store only moles showing standardized aspects.*

populations. The comparative plot in Fig. 5 shows the different distributions of MM between the five centres. Similar clusters of values lead to closer points on the space. The distribution of MM features among different centres does not reveal the same homogeneity as that observed in the diagrams related to benign lesions. Some of the Lugano and Siena MM can be separated by two lines from the others, indicating some peculiar aspects like the small diameter of the Lugano MM and the low gradient and lower darkness of MM from Siena.

Benign lesion's features

The study analysing the features of the stored lesions in Capraia indicates that there are no

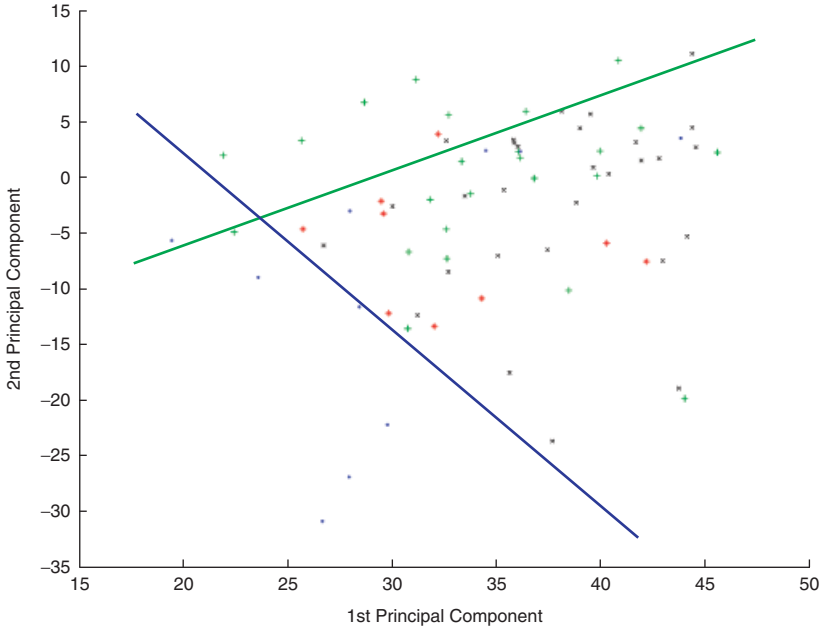

Fig. 5. The comparative plot in the multivariate plane shows the different distribution of malignant melanoma (MM) between the five centres. Similar clusters of values lead to closer points on the space. The distribution of MM features among different centres does not reveal the same homogeneity as that observed in the diagrams related to benign lesions. Some of the Lugano and Siena MM can be separated by two lines from the others, indicating some peculiar aspects like the small diameter of the Lugano MM and the low gradient and lower darkness of MM from Siena. Green '+', Legatumori Siena centre black; 'x', Dresden Hospital red;'', Locarno centre blue; '.', Lugano centre magenta; 'o', Capraia Island.*

TABLE 3. Differences in nevi clinical objective characteristics among the four centres

Nevi	Lugano	Locarno	Dresden	Siena	Capraia	Variable description
Diameter (mm)	4.88	5	6.22	6.7	5.6	Maximum diameter
Gradient	10.12%	12.61%	8.17%	7.8%	7.8%	Mean sharpness of lesion's border
Red average	19.95%	13.57%	18.20%	17.3%	17%	Mean red value of lesion's area
Red tenth	9.33%	9.8%	14.76%	13.6%	14%	Decile of red's histogram in the lesion's area
Peripheral dark	16%	19%	18%	16%	16%	Gradient of dark regions from centre to periphery
Unbalance	12%	12%	14%	11%	13%	Imbalance of pigment respect to the centre of gravity
Red multicomponent	23%	26%	32%	38%	27%	Multicomponent imbalance (red band)
Blue moment	13%	11%	6.7%	7%	10%	Imbalance of grey–blue areas

These 'significant' variables were derived from a multivariate selection of a total of 49 between nevi and melanomas.
MM, malignant melanoma.

differences among the lesions selected by the two different ambulatories (Fisher's P of significance in the N-way ANOVA analysis). In fact, in the two plots in the multivariate diagram (Fig. 4), there is no division line between the two classes (signed with * or +) but they are uniformly distributed and mixed, indicating that the trained dermatologists of each ambulatory decided to store moles with 'standardized' features. The eventual influence in features between a 'screening selection' and a daily ambulatory routine can be excluded considering the very minimal differences (Table 3) between the features of the PSL stored in the Capraia Island and the features stored in the daily routine ambulatory in the Siena centre. In this comparison, where an eventual influence by phototype can be excluded having the patients a common origin, we can deduce that dermatologists selection of PSL has been standardized.

The benign lesions stored in the Siena and Dresden centres (Table 3) reveal larger dimensions with a mean maximum diameter of 6.7 and 6.2 mm, respectively. The red tenth variable, proportional to the luminance of a lesion, reveals that the moles analysed in Dresden are lighter than those analysed in the two Swiss centres. The gradient variables, proportional to the borders' sharpness, indicate that the Dresden moles are less sharp than those of the two Swiss centres. The other variables appear similar among the centres.

Smaller lesions should lead to low false positives. The darker colours of PSL in the Swiss centres could indicate the difference in false positives. However, the lesions among the two Swiss centres are very similar both in colours and dimensions. Also, smaller and more regular-looking moles have been analysed in the other ambulatories with respect to the Dresden centre. Hence, it appears that the false positives could be more influenced by the clinician's interventism than by the features of the observed population.

Melanoma features

At 50%, the percentage of MM with a diameter <6 mm in the Lugano centre is much higher than that in Locarno, with 11%. The Siena and Dresden centres reveal a lower percentage of MM with a diameter <6 mm, i.e. 8.3% and 3.5%, respectively. The Lugano centre focused on smaller lesions. The mean gradient (23.6%), the red average (9.5%), and red tenth (5.5%) indicate sharper and darker MM compared with the other centres. The Lugano centre tends to identify small dark brown MM while the Locarno centre focuses more on the irregular distribution of pigments. The Locarno centre has a surgery room while the Lugano centre is mainly a secondary specialized prevention centre. The Dresden centre is equipped with dermato-surgery facilities, while the Legatumori in Siena is a primary care centre. On the other hand, the Siena centre collected slightly larger MM than Dresden, with a mean diameter of 10.7 vs. and 10.6 mm, and the percentage of MM with a diameter <6 mm is higher in Siena, with 8.3% vs. 3.5% in Dresden.

Overall, the largest MM (in diameter) were observed in the Siena and Dresden centres. Other features such as RAve and RTenth are very similar in these two centres (Table 4). It is important to focus on the standardization of measurements that can be reached when using objective calibrated instruments with respect to variable subjective assessments.

The tendency to observe larger moles and MM in Dresden and the smallest moles and MM in Lugano could also be influenced by the different bias in the observed population. Surprisingly, this does not alter the final percentage of early MM in our study. Further and more detailed studies are required in order to confirm this tendency.

Discussion

It is very important to reduce the burden of MM early diagnosis. Easy access of patients to dermatologists, information campaigns, and education of general practitioners are complementary approaches to improving early detection (19). Dermoscopy aids the clinician in improving his accuracy of melanoma and dysplastic melanocytic lesions' diagnosis, thus also reducing unnecessary benign excisions (20–22). By this means, unnecessary excisions of PSL can be reduced (23). In addition to analogue dermoscopy, digital dermoscopy offers easy comparability of findings among various centres (24–27).

Digital images for computer processing require an extremely high quality of image acquisition. For the clinical routine, high-speed image acquisition and processing and simplicity of handling are also necessary. There are different technical instruments on the market that allow digital dermoscopy analysis. The use of various equipment may be a

TABLE 4. Differences in the clinical characteristic, typology of centre, type of dermoscopy, and clinical objective characteristics among the four centres

Melanomas	Lugano	Locarno	Dresden	Siena	Description
Percentage of MM having a diameter <6 mm	50%	11%	3.5%	8.3%	% of lesions having a diameter <6 mm
Typology	Primary care	Primary care	Hospital	Primary care	Primary or secondary care prevention center
Optical dermoscopy	Yes	No? (only digital)	Yes?	Yes	Both digital and optical dermoscopy
Diameter (mm)	7.0	9.6	10.6	10.7	Maximum diameter
Gradient	23.6	19.3	17.6	13.8	Mean sharpness of lesion's border
Red average	9.5	13	17.4	16.25	Mean red value of lesion's area
Red tenth	5.5	7.2	11.1	11.3	Decile of red's histogram in the lesion's area
Peripheral dark	29%	48%	46%	33%	Gradient of dark regions from the centre to the periphery
Unbalance	20%	23%	24%	19%	Imbalance of dark pigment with respect to the centre of gravity
Red multicomponent	43%	66%	86%	72%	Multicomponent imbalance (red band)
Blue moment	31%	26%	19.3%	17%	Imbalance of grey–blue areas

These 'significant' variables were derived from a multivariate selection of a total of 49 between nevi and melanomas.
MM, malignant melanoma.

disadvantage when multicentre trials are performed (14, 28, 29).

In the present multicentre approach, the DM-MIPS© System was used for objective evaluation of PSL including MM. The sensitivity and specificity of DM-MIPS© System in previous studies were 94.3–99.1% and 72.5–93.8% depending on the decision probability used (11, 18, 23). Geometrics of lesions showed a reproducibility of 85%, with a colour reproducibility of 90%. These findings support not only the high accuracy of diagnosis but the reliability of the method (23, 30, 31).

The present investigation was performed under routine conditions. The low percentage of false positives reported by this study clearly indicates dermoscopy to be a valid tool for the daily observation and diagnosis of pigmented lesions. The variables analysed have been expressed in terms of percentages of the entire MM population.

In practice, excision of PSL is influenced by three major factors, i.e. the patient, the peculiarities of the individual PSL, and the experience of the physician. Some excisions might be driven primarily by the patient's wish spurred by fear or for aesthetic reasons. Patient education is important to reduce the risks of under- and overtreatment of PSL.

The individual PSL can be assessed with the naked eye, but imaging tools have been shown to improve accuracy and facilitate the diagnosis of early malignant lesions as discussed above. Technical equipment is no substitute for experience, but can support the objective assessment of PSL.

We analysed the interventism and follow-up according to their impact on the percentage of early MM. We found that higher levels of interventism among centres did not necessarily correspond to a higher percentage of thicker MM seen in this centre. In the Siena centre, for instance, the number of *situ*-melanoma was twice as high as in the other centres, while the number of melanoma with a thickness <0.75 mm as the same. This indicates the controversies and open questions related to the definition of *situ*-melanoma (32).

Another issue of interventism is the surgical removal of dysplastic naevi. Although studies have shown that most atypical nevi will never progress to melanoma, excision is commonly practiced (33). Although there is no doubt that a high number of dysplastic naevi represent an MM risk factor, this is not the case for the individual mole.

Our study is a photograph of what we see in four dermatological Centres. Moreover, it demonstrates the ability of highly experienced dermatologists to uniformly select and diagnose early MM using a well-standardized digital imaging tool. To reduce unnecessary excisions in a safe way, further investigations are necessary. The creation of a large database with objective measurements of PSL seems to be an essential step for decision making.

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