Author's response to reviews

Title: Computer-aided dermoscopy for diagnosis of melanoma

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Author's response to reviews: see over
Dear Editor
BMC Dermatology

Thank you for considering our manuscript for review. I am really grateful to the referees for their thorough review. They helped us to revise our manuscript and write a better one.

We revised the manuscript according to the referees' comments. However, if you think that there is still anything in the manuscript that should be changed, please kindly contact us. We are ready for further revision with your help.

Please find our response to the referees' comments and description of the changes made to the manuscript at the end of this message. Some minor changes have been addressed after response to referees. We hope that you and the referees will be satisfied with the revised version.

Response to reviewer 1, Dr Giuseppe Argenziano
Major Compulsory Revisions
Comment:
The main criticism concerns the discussion that is too short and should be improved by the authors, especially in the context of possible limitations of this technique that, in my view, could be too less effective in terms of cost/benefit ratio in a population where the prevalence of melanoma is very low.
Response:
We completed the discussion with referring to the previous studies and comparing them with our study. (Page 6: we added line 6-8 and 10-21; Page 7: we added line 1-2)
We mentioned in the conclusions that the cost benefit ratio of using this system needs to be assessed in developing countries with a low incidence of melanoma.
(Conclusions: we added line 5-6)

Minor Essential Revisions
Comment:
In the abstract, the authors should add the number of melanomas included in this study as diagnosed histopathologically.
Response:
We mentioned the number of melanomas in the abstract of the revised version of the manuscript. (Abstract, Results: we added line 1)

Response to reviewer 2, Dr Ketty Peris
Major Compulsory Revisions
Comment 1:
The low overall number of melanomas and lesions with an equivocal clinical and/or dermoscopic diagnosis (so-called simulators of melanoma) might explain their high values of sensitivity and specificity.
Response:
We agree that this study with a low number of melanoma (a small sample size) may not have a high accuracy and narrow confidence intervals. However, if you mean that it may introduce a bias, we could say that prevalence of a disease in the population could affect Positive Predictive Value of a test. However, prevalence of the disease in the population and the sample size have no effect on the calculated sensitivity or specificity that are calculated by following formulae:

\[ \text{Sensitivity} = \frac{TP}{TP+FN} \]
\[ \text{Specificity} = \frac{TN}{TN+FP} \]

Therefore, we believe that low number of melanoma in this study do not introduce any bias.

Comment 2:
The authors should specify in the text the clinical and dermoscopic diagnoses of the pigmented skin lesions included in their study and not to illustrate them only in Table 1.
Response:
I apologize because I think we could not understand what the reviewer wants to say. There was not any "dermoscopic diagnosis" in our study, because we did not examine the lesions with dermoscope to make a diagnosis. We only analyze them and recorded a score for each lesion in order to draw a ROC curve that is the best indicator of sensitivity and specificity of this system.
We mentioned in the revised version that we had 6 melanoma in our study. (Page 5: we added line 1-2)
We also have a more thorough description of our method regarding clinical diagnoses in the revised version. (Page 4: line 4-6)
We had 122 lesions with 14 different pathological diagnoses. Each lesion had one "the most likely clinical diagnosis" and some "clinical diagnostic considerations". Describing all of the clinical diagnostic considerations and dermoscopic score of all lesions (or at least groups of lesions with a pathological diagnosis as in table 1) in the text needs about 300-2000 words in a long manuscript.

Comment 2.1:
How was the interobserver agreement between the two physicians (an attending dermatologist and a 3rd year resident) regarding the clinical diagnoses of melanoma or suspected melanoma?
Response:
For each patient, there was only one list including clinical diagnostic considerations of both clinicians after their consultation. The first diagnostic consideration in the list was the most likely clinical diagnosis made by them after consultation. They did not record their diagnoses in separate lists. Therefore, we could not compare the two observers with each other.

Comment 3:
The authors report an output value of the software ranging from 0 to 10. They should better specify how they established the cut-off point of 7.88 and 7.34 and what is their meaning.
Response:
The cut-off points of 7.88 and 7.34 are not important points and have no use or meaning when calculating or reporting specificity and sensitivity of the test or working with this system. We calculated the specificity and sensitivity of clinical
examination. Then, we drew the ROC curve for dermoscopy score. After that, we chose the points on the curve that had specificity and sensitivity near that of clinical examination. These points were found to be 7.88 and 7.34. Therefore, these points have been selected only for comparison with clinical examination in this study and do not have any other value or meaning. We mentioned this point in the revised version of the manuscript. (Page 5: we added line 8-11)

Comment 4:
Were the lesions included in their study randomly or consecutively selected?
Response:
Thank you for your point. We mentioned in the revised version of the manuscript that the sampling was consecutive. (Methods: line 1)

Comment 5: The authors should further clarify what is the difference between a suspected melanoma and a most likely clinical diagnosis of melanoma. Does it mean that in the second case, the final clinical and/or dermoscopic diagnosis was melanoma?
Response:
We explained more exactly in the revised version of the manuscript about clinical considerations. We defined "the most likely diagnosis" and "clinical diagnostic considerations". We omitted the term "suspected diagnoses" and "suspected melanoma". When clinical findings of a lesion were compatible with more than one diagnosis, the clinicians recorded all of these diagnoses as "clinical diagnostic considerations" in a list. The first diagnosis in this list was the diagnosis that they believed that was most compatible with clinical findings of the lesion and called "the most likely clinical diagnosis". (Page 2: line 15; Page 4: line 4-6; Page 4: line 19; Page 5: line 5; Legend of Table 2)
We recorded the "clinical considerations" before dermoscopy of the lesion, therefore, dermoscopic score and histologic findings were not used for making clinical diagnoses.

Comment 6:
Discussion would benefit from more exhaustive data on dermoscopy and automated-aided diagnosis and advantage of their system as compared to those reported in the literature or commercially available.
Response:
We completed the discussion with referring to the previous studies and comparing them with our study. (Page 6: we added line 6-8 and 10-21; Page 7: we added line 1-2)

Minor Essential Revisions
Comment:
Malignant melanoma should be simply reconsidered as melanoma.
Response:
We changed malignant melanoma to melanoma. (Title of manuscript; Page 2: line 5, 12, 14 and 17; Page 3: line 1, 4, 5, 6; Page 4: line 19; Page 5: line 2, 4, 8, 13; Page 6: line 7, 13 and 21; Page 7: line 3, 8, 10, 12; Title of Figure 1)
Minor changes in the revised version of the manuscript:
Page 7, line8: We changed the term "However" to "Nevertheless".

Thank you for considering this manuscript for review.
Faithfully yours,

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