Reviewer's report

**Title:** Prediction of melanoma metastasis by the Shields index based on lymphatic vessel density

**Version:** 1  **Date:** 10 November 2009

**Reviewer:** Antonio Piñero

**Reviewer's report:**

**Discretionary Revisions:**
- In the Introduction: the authors say that the follow-up is every three months for five years but they should define the follow-up after the fifth year (I suppose that it is every year).
- In Discussion: the authors should comment about the sensitivity of LYVE-1 and its specificity as lymphatic marker or as lymphovascular marker.

**Minor Essential Revisions:**
- The authors must change “then” for “than” in the sentence of Methods in the Abstract.
- The authors should write the first time for the abbreviation SLN in the Introduction (not only SLNB).
- They must specify the reference about the difference in lymphatic vessel density surrounding primary malignant melanoma (beginning of the second paragraph in page 4).
- They should substitute “lymphatic vessel density” by “LVD” in the text (twice at the end of page 4 and in page 8).
- The authors say that “specific components of the REMARK guidelines are identified in the text by numbers in square brackets”, so how can be the references from literature identified?.
- The sentence “..., and without ulceration or in situ tumour or were used”(page 6) should be rewritten.
- I am not able to find the references 14 and 18 in the text (they should be in pages 11 and 14, respectively).
- In the conclusions paragraph (page 16) they should use present tense (is) instead of past tense (was) when they say “...the use of the index described by Shields et al in 2004 was the most specific...” because they are describing their findings in this work.

**Major Compulsory Revisions:**
- A more clear definition of “metastatic outcome” must be done, as in Methods as in Results.
- How were the patients “randomly selected”?.
- Can you specify what does “clinically occult metastasis” mean? Does it refer to patients without metastasis? If they are “occult” how do you know about them?.
- If you talk about LVD and you count every lymphatic within 350 µm border around the tumour edge, how do you estimate the area to calculate the density (it is not the same the border of a 0.5 cm diameter lesion that the border of a 1 cm diameter lesion, … and density is the number of lymphatics per unit of area).
- I think that evaluation of digital images by a software analysis technique should be a more accurate method than a “visual counting”.
- The differences (no significant differences) between the metastatic and non-metastatic group that are described in page 9 should be showed as a Table.
- In Results, the authors say 45 patients developed metastases (page 11), but all of them were lymphatic metastases only or they include visceral metastases and, in this case, what type of metastases?.
- In this paper there is not any reference to normal dermis so how do the authors know that LVD is ion the same range that densities found in the normal dermis? (page 11). I suppose they refer to literature data. If it is they should specify any range or figure from literature (¿reference number11?).
- The number of sample cases in hot spot analysis must be specified in page 12. Did the authors compare 24 cases versus 102 cases or did they compare 24 cases versus 78 cases?.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.