Reviewer’s report

Title: Immunohistochemical detection improves the prognostic value of lymphatic and blood vessel invasion in primary ductal breast cancer

Version: 5
Date: 23 May 2014

Reviewer: Niamh Conlon

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Discretionary Revisions

1. The first paragraph of the Background is based on out-of-date statistics. I believe lung carcinoma is now the leading cause of cancer death in women and almost 50,000 women are diagnosed in the UK each year (refer to SEER data (US) or Cancer research UK data 2011 (available online)).

2. Methods: I can’t see any data in the methods that documents the Stage of these patients. Are they all Stage I and II, or are there any Stage III patients? This would be useful to know. If you include stage in your multivariate analysis, is LBVI as statistically significant?

3. Discussion: There is no review of the results of the survival analysis in the discussion section. I think a discussion of the significance of LBVI H&E vs LVI D2-40 and BVI FVIII would be appropriate, e.g. why LBVI H&E was not found to be statistically significant on multivariate analysis in this cohort, but the LBVI IHC was significant. This is an important point, as it backs up the authors’ recommendation that the introduction of routine IHC for assessment of LBVI may be indicated.

4. Discussion: I think that the Discussion is very much improved since the last draft but it still needs some stylistic editing. The first sentences of paragraphs two and three should be re-drafted as they lack coherence. Likewise the syntax in paragraph twelve needs to be reworked. Overall, I think the whole discussion could be more succinct.

Minor Essential Revisions

1. In the Abstract, abbreviations such as LBVIIH&E etc need to be written as subscripts, like in the rest of the paper.

2. Background paragraph 2 sentence 3 – re-write.

3. Results, paragraph 7 sentence 2 – I think you mean “younger age” rather than older age?

4. Discussion paragraph 13, sentence 1 – insert the words “detection of” between the words “of” and “LBVI”.

5. Figure 1 – I think that the figure legend is wrong or images E, F, G and H may
be in the wrong order, as image F is referred to in the legend as a positive Factor
VIII stain, when it is actually negative, and G is called a negative stain when it
appears to be positive.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.