Reviewer’s report

Title: BCL-2 expression aids in the immunohistochemical prediction of the Oncotype DX breast cancer recurrence score

Version: 1 Date: 25 Oct 2018

Reviewer: David Geffen

Reviewer’s report:

This paper is a very well written report of the use of techniques of straining for BCL2 and a mathematical transformation in addition to image analysis staining for ER PR and HER2 to predict Oncotype DX results. The ability to predict Oncotype results from locally obtained clinical-pathologic information would be of great benefits where the expense of Oncotype is too great a burden to enable doing the test.

I am not a statistician so I suggest statistical review of the transformation techniques.

I am not a pathologist so I cannot comment on the techniques of IHC and image analysis other than to say that as a breast oncologist the techniques and results in this study seem very reasonable.

I suggest adding to the paper a note that with a total of 158 patients spread over 7 years the numbers in each category are relatively small and this study should be regarded as hypothesis generating to be verified in a larger group patients. From the data presented it would seem that RS can be predicted in 60% or so of cases, potentially saving resources significantly.

I would replace reference 49 or add to the references another study by Gage et al recently published - Combined pathologic-genomic algorithm for early stage breast cancer improves cost-effective use of the 21 gene recurrence score assay. Annals of Oncology 29:1280, 2018. They report on the use of their algorithm in 1268 patients with 5 year clinical followup using just ER and PR staining, and were able to show that they could predict as well as the RS for low and high risk patients and could avoid doing the RS in about 44% of patients.

A minor point - in the text response to the previous reviewer you mentioned the incorrect journal where the TAILOR-X trial was reported. It was as you reference correctly reported in the New England Journal of Medicine.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

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