Reviewer's report

Title: Automatic registration of multi-modal microscopy images for integrative analysis of prostate tissue sections

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Reviewer: Osamu Ukimura

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Authors reported their initial experience to assess feasibility of applying modern image analysis methods to automatic alignment of microscopic images from differently stained adjacent paraffin sections from prostatic tissue specimens. This is one of new approaches to more objective and less intra-inter variability in pathological analysis of prostate biopsy tissue. However, there are some concerns requiring revisions.

1) Authors tried to conclude the proposed method is fast; however, no data was shown to be faster. Need to clarify.

2) The performance of algorithm is not yet proven regarding correlation of clinical prognosis. Otherwise, the 2nd sentence of conclusion seems too strong.

3) It is not clear whether authors' determination of Gleason score also based on algorithm? or manual? If not automatical determination of Gleason score, there should be a significant bias. Gleason score should be determined by blind nature. Need to clarify.

4) In discussion, there is lack of "limitation of study section". Because of the nature of feasibility study, this technique must be validated with further studies, including actual time to conduct, cost, inter-/intra-variability with increased number of cases, and multi-institutional study.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
'I declare that I have no competing interests'