

## Reviewer Report

**Title:** High precision registration between zebrafish brain atlases using symmetric diffeomorphic normalization

**Version:** Original Submission    **Date:** 4/19/2017

**Reviewer name:** Shengwei Zhang

### Reviewer Comments to Author:

The authors proposed an upgraded Zebrafish Brain Browser atlas, constructed by ANTs SyN registration algorithm, with information from the scans in both the previous atlas construction and the construction of Z-Brain atlas. The registration parameters were optimized separately for both live and fixed tissue scans. Multi-reference channel optimization provided better alignment between Z-Brain and ZBB with better performances in terms of precision and morphology. An additional visualization of the updated atlas was generated for enhanced user experience.

The use of a large number of scans and the application of a more powerful registration algorithm are the main advantages of the upgraded atlas. The results and figures presented promising enhancements compared with the previous version of atlas.

My specific comments/recommendations mainly concern the registration part:

- In "Methods - zebrafish lines", the sentence in page 4 line 103 "Aside from..." should be moved to registration section.
- The "Results - optimization of ANTs of live scans" section contained extensive descriptions that should be moved to "Methods - registrations", e.g. the explanation of choosing SyN for registration, the calibration of registration conditions, choice of SyN parameters. The "results" section should present the outcomes of the methods applied, rather than the methods used. The same also applies to "optimization of ANTs for fixed tissue" and "inter-atlas registration".
- In page 7 line 205, the MLD was calculated from values given by 3 blinded experts. Was there any inter-rater performance analyses?
- The whole processes of ANTs registration parameter optimizations, for live scan or fixed tissue or multi-channel combination, can be organized better by using flow charts for presentation. In the current format, it is not conspicuous for readers to follow such processes.
- In page 10 line 287, were those 167 tERK stained brains part of the 197 scans or new ones? Please clarify.

- In page 12 line 359-61, were the MLDs also obtained from 3 experts? Please clarify.
- In figure 2, J & K in the label should be j & k.
- In figure 3, Syn in e & f should be SyN. Same for the figure legends.
- In figure 4a, please separate M1 & M2 from other values because it is difficult to compare them.

### **Methods**

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Yes

### **Conclusions**

Are the conclusions adequately supported by the data shown? Yes

### **Reporting Standards**

Does the manuscript adhere to the journal's guidelines on [minimum standards of reporting?](#) YesChoose an item.

### **Statistics**

Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Yes, and I have assessed the statistics in my report.

### **Quality of Written English**

Please indicate the quality of language in the manuscript: Acceptable

### **Declaration of Competing Interests**

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