Reviewer’s report

**Title:** A comparison of landmark methods and time-dependent ROC methods to evaluate the time-varying performance of prognostic markers for survival outcomes

**Version:** 0  **Date:** 11 Dec 2018

**Reviewer:** Jianfei Zhang

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The manuscript mainly introduced how to estimate time-varying hazard ratio in the Cox model by means of changing the length of follow-up duration and making coefficients vary with time, and how to evaluate accuracy in terms of time-dependent AUC by comparing incident or cumulative cases with dynamic controls.

1. If I understand you correctly, the lines 152 - 155 mean that the regression coefficients are interpreted as the (average) HR which becomes the exponential of coefficients, as shown in line 214. Which one of \( \beta \) and \( \exp(\beta M) \) is the hazard ratio in line 104?

2. You say 'Hazard ratios are also sensitive to the scale on which the marker is measured' in line 518, that is, the model parameter coefficients are sensitive to the scale of variables? Is this an issue if you normalize every continuous variable, e.g., in the range of \([0,1]\)?

3. In page 16, the first paragraph involves the ties issue. Did you dichotomize the eight continuous markers in the process of AUC estimation?

4. In line 345, the precise representation could be like "the predictions for a comparable pair of subjects", as two controls (censored cases) are not comparable. The C-index is actually a generalization of AUC(t), is it possible to append the results in terms of C-index for each AUC curve in Figure 4(right)?

5. For ROC(p) and specificity=1-p in pages 9 and 10, what probability does p, in particular, refer to? Eq.1 has used such notation as the dimension of data. Similarly, k is reduplicate for a certain subject and a landmark time point (t^L_k) on page 9.

6. The ROC / AUC is sensitive to class/group imbalance. The landmark analysis would lead to short follow-up periods (e.g., 1-year study) and yield more Controls and fewer Cases. Did such an imbalance between cases and controls arise and affect the AUC performances?
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