Reviewer's report

Title: Long term survival following the detection of circulating tumor cells in head and neck squamous cell carcinoma

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Reviewer: Jeffrey Chalmers

Reviewer's report:

General comments

The overall concepts of this interesting and relevant; however I have significant concerns about the sensitivity of the RT-PCR assays. While the authors of this study did attempt to measure the sensitive of their PCR detection technology, and correctly speculated that heterogeneity of gene expression in different cell line, this concept has already been quantitatively documents by Tong et al. 2007. In addition to citing this fact, and more importantly, the authors of this manuscript need to quantify the final concentrations of the contaminating PBL form the patient samples since this will effect the sensitivity of detection. While I respect that they demonstrated the sensitivity of their assay by spiking tumor cells from a cell line into blood, this is not the same as CTC from a patient, nor is the blood necessary the same in a cancer patient. Also, while I believe a positive results, I am not so sure of a “negative result”. If their final concnetration of contaminating PBL is significantly higher in the patients samples than in the spiking studies, a negative PCR result could be due to no CTC or, lack of sensitivity due to a dilution effect. Or, it could be that the CTC just does not express the mRNA for the particular target at a high enough level.

Specific Comments.

1. I found the results section tedious and hard to follow. It should be rewritten more concisely, and/or a better figure or table used to present all variations.
2. The use of the term “reconstruction experiments” is new to me. IT is typically called spiking studies. It is fine to use your own term, just compare it to the typical work “spiking”.
3. I am a little fuzzy on the actual protocol used on the patients. Was the blood sample first separated using magnetic beads targeting the cells, and then the immunobead RT-PCR technique performed? The results section seems to include optimization studies and actual patient studies mixed together so that it is not clear to the actual, final procedure used on the patients.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests.