Review 1: "A handheld point-of-care system for rapid detection of SARS-CoV-2 in under 20 minutes"

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As POC diagnostics for SARS-CoV-2 are of general interest, I will review from the view of a nonspecialist audience. LAMP technology is broadly pursued to diagnose. To properly assess novelty vs. the large landscape of LAMP preprints, I refer to the editor.

Comments:

Overall, a valid approach and high quality experiments were conducted. This is a high-interest approach and having a POC diagnostic device performing at similar benchmark sensitivity and accuracy as qPCR gold standard is highly desirable.

However, the paper does not allow a clear head-to-head comparison of both assays, which is information that needs to be included for this to be published. Authors go to great lengths to compare TTP, which is a minor point relative to the fact that a POC diagnostic assay needs to be accurate to be useful. They show that it's faster, and that it brings back results, but there was no clear comparison in terms of sensitivity (only the LAMP numbers are quoted, no PCR numbers for comparison).

The table comparing classification as positive opens several questions as a large number of qPCR positives does not seem to be detected by LAMP (n=12). For some reason, supplemental data is not available in the pdf and also could not be found online. It seems a lot of key information is in the supplemental data, which should not be the case.

Detailed comments:

- False positive/neg rate needs to be discussed for both assays (LAMP/qPCR) in light of Bayes' Theorem, coming up with realistic numbers of false negatives/pos assuming certain numbers of tests conducted - this will be more instructive for real world applications than just comparing sensitivity/specificity
- Fig 2B unclear - would be good to clearly state / color code which sequences can be detected by LAMP and if there are any known SARS Cov2 sequences that cannot be detected by the primers chosen
- Fig 3 A/B cannot be followed from figure legend, only in main text - rephrase figure legends to explain better
- Fig 3C/D points should be "jittered" along x axis to see where bulk of points are a box plot like in Fig 3C/D should be shown for actual positive/negative results for both qPCR/LAMP to see where they all fall. Table is insufficient to show that data

- Table 1 needs p-values / statistical analysis to determine if qPCR and LAMP experiments are different or not; visualization needed - sensitivity and specificity of qPCR assays should be listed as comparators for LAMP, including discussion in light of Bayes' theorem
- It would be good to include several qPCR assays here as comparison, not just the CDC one, to get a better idea where the LAMP falls in comparison to the several assays being run
- RnaseP assay is not introduced or described enough for a general audience
- Focus on TTP comparison is misleading as TTP is roughly similar between assays and it's not going to make a difference for patients if one assay takes 20min or 1 h
- The difference is that one of them is a POC assay; TTP is a minor point, focus should be on accuracy of detection
- Discuss timing of assays
- LAMP will likely be a pre-screen, POC, and then if positive assumption is patients will visit doctor's office to get qPCR; fact that there are false negatives with the LAMP (12) needs to be discussed in more detail.
- This paper gives a good overview about deriving predictive values from sensitivity/selectivity analysis:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6173138/>
- Ct is not introduced or explained for a general audience