One of the key assumptions in the statistical model is that BRCA1/2-mutated and sporadic tumors require a similar number of driver mutations for initiation. However, this may not be valid, as germline BRCA1/2 mutations could act as oncogenic drivers, theoretically reducing the number of additional somatic driver mutations required for tumorigenesis. Additionally, the authors should clarify whether loss-of-heterozygosity (LOH) or other second-hit events in BRCA1/2 genes were considered in the analysis, as germline mutations alone do not necessarily lead to complete functional loss of BRCA1/2, and secondary inactivating events may serve as independent rate-limiting drivers.

Yves:

The statistical model needs to account the gBRCA1/2 LOH/second-hit event in the “two-hit” hypothesis:

* Determine this new feature
* Include it to *calculate\_mutation\_rate\_ratio*

Currently, the mutation rates are determined for: CNA, DEL, INDEL.Include LOH as part of CNA event counts: changes in *format*\_*mutation*\_*counts* code.

We thank the reviewer for requesting these details. We agree that providing specific information on the matching process is important for reproducibility. First, we have updated the Methods section for clarification, “… …Non-carrier breast and ovarian cancer samples were matched to BRCA1 or BRCA2 carrier samples separately, ensuring equal sample sizes within each cancer type and carrier status. We performed this matching using a weighted random sampling procedure, implemented via custom scripts in R. For breast cancer, non-carrier tumors were matched based on the distribution of PAM50 subtypes (Luminal A, Luminal B, HER2-enriched, Basal-like, Normal-like) and pathologic stages (I-IV) to match the sample size of BRCA1 or BRCA2 carriers. For ovarian cancer, matching was performed based on clinical stage distribution. … …” and [YVES] will add a new supplementary table to provide these details.

The current code does not perform the sampling based on the distribution of subtypes in BRCA1 or BRCA2 carriers, same for OV cancer: easy to fix.