Reviewer’s report

Title: Hereditary and non-Hereditary Branches of Family eligible for BRCA test: Cancers in other sites.

Version: 0 Date: 08 Apr 2017

Reviewer: Cecilie Heramb

Reviewer’s report:

Thank you for the invitation to review this paper.

Generally, a very interesting model for describing cancer types related to BRCA1/2.

Grammar/written English: Unfortunately, there are in general too many unclear paragraphs, this may be due to grammar issues mainly.

There is an arbitrary use of capitol letters in the middle of sentences, which is not common in written English. The paper should be reread by someone fluent in English before submitting again.

Some examples:

p 4 l "The frequency of Other Cancers of H- Branch resulted significantly higher," should be rewritten. I.e "were significantly higher" , "there were a significantly higher frequency of...
"etc

p.4 l. 53 "HBOC generally accounts for germ line mutations in BRCA1/2", it is the other way around, mutations accounts for cancer.

p.5 l. 1 and 2 : the word "stressing" is confusing. line 9 and 10 is confusing as as well : Are you commenting on "modifiers" - this issue is only presented here, and not discussed any further. Maybe you either should leave it out or, if you keep it, elaborate upon it in discussion section.

Some other mistakes regarding verbs / prepositions are unfortunately too abundant as well :

p.4 l 60 alterations HAVE,

p5 l. 16 "those" information - unusual use of "those"

p. 6 l.27 the frequency OF different cancers

etc.
Abbreviations: There are some inconsistencies in the use of abbreviations H-Brach, NH-Branch, N-H vs nH and n-H. Please be consistent.

You include H& N cancers in your abstract/results/conclusion, but never define this abbreviation. I believe you mean head and neck cancers, but in results larynx cancer is the only cancer listed, and no "head"/cerebral cancer?

Methodology:

My main concern: Are all hereditary branch subjects proven mutation carriers, and vice versa, all non-hereditary branch subjects non-carriers?

You have designed an interesting model for comparing distributions of cancer, but I think it needs to be clarified whether you are comparing mutation carriers (H-branch?) vs non-mutation carriers (NH-branch?) or not. Did you screen all included subjects with sequencing or only H-branch? And could you please comment on why you did not check for copy number variants with MLPA?

A BRCAPRO limit of 20% is rather high in my opinion, and I wonder what the N-Branch score is?

Results: Striking results indeed, for lung, liver, larynx cancer. Very interesting.

But it is also striking that prostate and pancreas are n.s. (not significantly different?) between H-branch/NH-branch in your study (table 2.)

This is opposing previous knowledge on non-breast/ovarian cancer in BRCA1/2 carriers, and is worthwhile commenting on in the discussion section. How do you explain this?

Discussion: Please include how you think your lung cancer findings could be confirmed in a different study model.

Best wishes, Cecilie Heramb

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An article whose findings are important to those with closely related research interests

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