Reviewer’s report

Title: Prognostic value of metabolic response in breast cancer patients receiving neoadjuvant chemotherapy

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Reviewer: Geoffrey S Payne

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“Prognostic value of metabolic response in breast cancer patients receiving neo-adjuvant chemotherapy”

By MD Cao et al.

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Summary

This manuscript describes MRS of biopsy samples taken pre- and post-treatment using neo-adjuvant chemotherapy in a cohort of patients with locally advanced breast cancer. While the metabolic response does not appear to related to clinical response, they did correlate with 5-year survival. The important discriminating metabolites were identified as lactate, glycine, choline-containing metabolites, and glucose. This is a very useful finding, and should be of interest to many readers. The study was well conducted and in general the manuscript is well- written. I recommend publication subject to the points listed below.

Specific Points

Page Para Line Comment

2 3 8 Suggest replacing “could not be” by “were not”

6 1 3 Suggest inserting, “at end of treatment” or similar after “tumor size”

8 2 7 Is the “between subject variation” described by the “population distribution” of the average of repeat observations on the same subject?

9 1 Eq1 This needs more explanation. It appears that “control” is simply “-treatment”, which seems rather redundant.

10 1 12,13 The GPC levels did not always decrease, only on average.

11 2 1 Suggest rephrasing as “The patients were also divided into two groups…”

13 2 3-4 This seems a repeat of lines 1-2. If there is an additional thought then please clarify

14 2 3-4 Please check function of anthracyclines

14 3 1 “Patient” should be plural. More importantly this statement needs to be toned down, as it suggests clear discrimination between metabolite profiles, whereas there is some degree of overlap.

15 1 2 Replace “incident” with “incidence”
15 1 10 Replace “evading” with “evade”
15 2 1 (and elsewhere), replace “aerobe glycolysis” with “aerobic glycolysis”
15 2 Last “In coherence”?? Please rephrase and clarify.
19 1 4 Suggest inserting “at the end of treatment” after “stable disease”.
27 Tab2 Re-order title so multilevel PLS-DA is first (as this is order in table)
28 Tab3 For convenience, please specify number of survivors and non-survivors in table
30 Fig1 The loadings plots require more explanation as they are quite different to conventional loadings plots.
31 Fig2 The 3d plot is very hard to interpret (as is usually the case). I would be inclined to omit.

**Level of interest:** An article of importance in its field

**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'