Reviewer's report

Title: Proteins and carbohydrates in nipple aspirate fluid predict the presence of atypia and cancer in women requiring diagnostic breast biopsy

Version: 2 Date: 14 September 2011

Reviewer: Robert T Chatterton

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Major points

1. High uPA and PAI-1 concentrations and age were independent predictors of disease in premenopausal women, and when TF was added the classification of disease was close to 100%. However, the contribution of age to these relationships is not presented. What percentage of the variation was attributed to age and how much to the biochemical factors?

2. Results of logistic regression analyses conducted with women with PND and NAF were equivalent to results obtained from analyses conducted with women only providing NAF. The data showing this should be presented so that the reader can judge for himself.

3. First paragraph on page 10: Statements are made about uPA being higher in premenopausal women with cancer and PAI-1 higher in postmenopausal women with cancer but the data for uPA in postmenopausal women with cancer and PAI-1 in premenopausal women are not presented. What were the results for uPA in postmenopausal women and PAI-1 in premenopausal women, and what was the significance of the difference?

4. The Figure presents data on AUC for only uPA in premenopausal women. What about the combined biomarkers? According to the conclusions of the paper, these should be better. Why are they not shown? Showing the various comparisons of uPA seems unnecessary. One of the figures would illustrate the point about uPA.

5. It seems that the nature of the suspicious breast lesions had little influence on the relationships with the control groups. This should be emphasized in the Discussion and in the Conclusion.

6. If the data were log-transformed as stated in the Methods section, the means presented should be geometric means. Is this the case? It is not indicated.

Minor concerns

1. page 2, line 14: “and” is misspelled
2. page 6, first sentence: commas are missing between the locations
3. page 7, “Preparation” Was the volume of discharge or NAF measured?
4. page 8, line 6: HRT and hormone replacement are listed as though they were
separate treatments.

5. page 9, line 15: change “conducted with only women” to “conducted with women only”

6. page 10, line 4: Do you mean “abnormal/benign” as in the table or “abnormal than benign?”

7. page 10: the last paragraph should be part of the Discussion not under Results.

8. page 15, reference #9: the date is missing

9. Table 2: the combined uPA + POAI-1 had a lesser AUC than uPA. This should be commented upon in the Discussion and a possible explanation should be given.

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.