Reviewer’s report

Title: Cytologic Features of Nipple Aspirate Fluid Using an Automated Non-Invasive Collection Device: A Prospective Observational Study

Version: 1 Date: 28 April 2005

Reviewer: Hormoz Ehya

Reviewer’s report:

General

This paper describes an interesting new method for collection of NAF (nipple aspirate fluid). The manuscript is well written, and the methodology and results are clearly presented. I have a few suggestions, as described below.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. What was the length of time during which the study was conducted and how long was the follow up period?
2. Were all specimens examined by a single cytopathologist?
3. If multiple cytopathologists examined the specimens, were there any differences in percentage of cytologic diagnostic categories among different pathologists?
4. What was the protocol for follow up of patients with cytologic diagnosis of atypical hyperplasia?
5. Since all subjects were asymptomatic by design, how were the abnormal areas for biopsy identified in three cases (palpable mass? abnormal mammography?). What was the reason for a second biopsy in two of the subjects who initially had benign biopsies?
6. What is the follow up period for the two subjects with Category III cytology who did not have a biopsy?
7. The number of cells in each specimen has not been recorded. Then how do the authors claim that In the present study, 38% of the participants produced fluid with HALO NAF collection system, with higher cellularity than reported in the Dooley et al DL study (page 16, paragraph 2)?
8. Was there a learning curve for using the device? In our studies we had higher success in collecting fluid after some experience than in the early cases. Was this true in the current study?
9. Page 9, paragraph 1: For definition of Category II, please add that the cell arrangement was in cohesive cluster with >10-50 cells (as indicated in Table 1).
10. Reference number for Table I is incorrect.
11. Page 13 (Follow up results) and page 27 (Figure 6 A-D): The biopsy in one case with Category III cytology showed LCIS and duct hyperplasia. The atypical cells shown in Figure 6, in my opinion are unlikely to have come from LCIS. I suspect that they might have originated from areas of atypical duct hyperplasia or DCIS, not sampled by the biopsy. Do authors agree with this opinion? If so they should indicate this, as such patients should not be given false assurances that the abnormal area in their breast has been removed by surgery.
12. I believe it is necessary to include statistical analysis to demonstrate whether the differences in fluid producers v. non-producers (Table II) and diagnostic categories in different cohorts (Tables III, IV and V) are statistically significant.
13. In their conclusions, authors should make it more clear that NAF cytology in general, and the utility of HALO NAF instrument in particular should be considered experimental at this time and should not be recommended for clinical use until further studies with long-term clinical follow up have established the sensitivity and specificity of this method for detection of breast cancer and
precancerous conditions.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.