

# Nipple Aspirate Fluid as an Additional Tool for Comprehensive Risk Assessment

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## Background

Atypia in nipple aspirate fluid has been shown to be a marker of increased risk in large longitudinal studies since the 1950's.<sup>1,2,3,4</sup> But manual collection of nipple aspirate fluid had been impractical in all but the research setting. A new device for collecting nipple aspirate fluid in the primary care setting is being employed in the Southern California catchment area of our dedicated breast practice. Local primary care physicians are targeting women aged 25-55. The objective is to find women who may require detailed breast cancer risk assessment and follow up.



*HALO® Breast Pap Test  
(NeoMatrix)*

Studies have shown that California has some of the highest breast cancer rates in the United States; these rates also have substantial regional variations within the state. Women in our region of California have a 10% higher risk of developing breast cancer than other regions of California,<sup>6</sup> second only to the San Francisco Bay Area.

During 2008, 17 new patients were referred to our practice with atypia found with this new device (HALO Breast Pap Test).

## Objective

We sought to understand if and how information provided by HALO atypia findings influenced our care path during the first year HALO atypia patients presented in our practice.

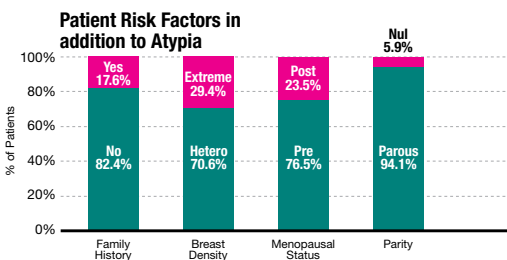
TISSUE(S)	LEFT BREAST NIPPLE DISCHARGE, CYTOLOGY
GROSS DESCRIPTION:	Received is a left breast nipple discharge sample submitted in a liquid-based cytology vial from which one ThinPrep slide is prepared. ja/HL:vmw
MICROSCOPIC DESCRIPTION:	Left breast nipple discharge cytology sample above shows a few small to intermediate-sized tight, some papillary groups of predominantly mild to moderately atypical ductal cells with occasional overlapping nuclei. Several individual and small aggregates of foamy cells noted. Scattered degenerated apocrine metaplastic cells and occasional inflammatory cells. Background has degenerated blood-mixed proteinaceous material.
FINAL DIAGNOSIS:	A FEW PAPILLARY GROUPS OF PREDOMINANTLY MILD TO MODERATELY ATYPICAL DUCTAL CELLS PRESENT. (Please see comment)
COMMENT:	Cytological findings of presence of papillary groups are usually associated with intraductal papilloma or complex papillary lesion (intraductal papilloma with associated ductal hyperplasia or cystic change). Current slide is compared with the most recent sample (GB-08-8787 from 3/25/08) which has similar findings, but current sample has more papillary groups of ductal cells. Since MRI and mammographic findings are not indicative of malignancy, suggest close clinical follow-up with repeat evaluations as felt to be clinically indicated.

## Methods

A complete medical history is taken. HALO atypia is considered along with other risk factors such as family history, genetic profile, and breast density in our comprehensive risk assessment. Either diagnostic mammography or ultrasound is performed on the patient as a first step.

## Results

- Patient age range was 38-53 with a mean age of 45.5
- All but 2 of the patients had previous normal mammograms or mammograms with a stable finding, but only 4 of the 15 or 23.5% had had a screening mammogram or other imaging exam within the last 12 months
- A majority of the patients had benign or probably benign findings on their initial imaging exams making subsequent imaging more complicated.
- All 17 patients had dense to extremely dense breasts, conferring additional risk to those women over age 45. 11/17 or 64.7% of the referred women were 45 or older.<sup>5</sup>
- 5/17 patients or 29.4% had moderate to strong family history of breast and/or ovarian cancer, but only one of the patients had family history that might suggest the need for BRCA1-2 testing. Only one of the patients with family history had a suspicious finding on imaging that resulted in a biopsy.
- 2 out of 17 patients or 12% had Polycystic Ovary Syndrome.
- The majority of patients were parous (86%)



- Core and/or excisional biopsies were done on 6 patients out of 17 patients with suspicious imaging findings (35.3%)
  - 2 had a finding of papilloma;
  - 2 had a finding of fibroadenoma;
  - 1 had ADH and 1 had ALH along with a papilloma.
- One atypia was associated with lactational changes in a women aged 38. Follow up recommendation is mammography at age 40.
- Patients with findings of papilloma, ADH, ALH and HALO atypia will be followed in a regular program of high risk follow up. This includes mammography and MRI once a year, staggered at 6 month intervals. Patients with HALO atypia plus dense breasts will also be followed in this fashion.

Result after Evaluation	Follow up
Normal lactational changes	Follow up mammography at age 40
Normal imaging results but very dense breasts, over age 45	Annual Mammography/MRI on a staggered 6 month basis.
Normal imaging results plus one or more additional risk factors	Clinical follow up. Imaging on a case by case basis depending on overall risk profile.
Papilloma	Surgical removal. Imaging on a case by case basis depending on patient's overall risk profile.
Papilloma and/or ADH, ALH	Surgical removal. Annual Mammography/MRI on a staggered 6 month basis. Case by case referral to medical oncology for chemoprevention.

## Conclusions

- Patients who otherwise would not have had risk assessment have been seen by our practice and are now being followed with specialized breast care
- Patients with atypia are more closely examined and triaged for imaging studies
- Patients eligible for screening mammography who had neglected having the exam, had mammography or other imaging studies based on a finding of atypia
- Biopsies on patients with atypia and positive imaging studies confirmed findings that confer additional risk and these women will be very closely followed by our practice.
- HALO is helping our community primary care physicians better identify patients who require further evaluation for breast cancer risk

## Questions to Consider as we Move Forward

- Does a positive HALO test result improve screening imaging compliance in women who are age appropriate for mammography?
- Halo tests will be administered by our community's primary care physicians on average every 12 months. At what point can or should patients with positive HALO results return to normal breast screening and follow up?
- What is the appropriate time interval for repeat HALO on patients who have positive HALO results but normal imaging and no other significant risk factors?

An interesting case highlights how HALO might be used in the care path

A 52-year old postmenopausal women with no family history of breast or ovarian cancer and previously normal mammograms, got referred to our practice because of an atypical HALO result. We performed a diagnostic mammogram and ultrasound. The mammogram was unchanged from previous mammograms. The ultrasound was normal. She had a follow up HALO three months later; the HALO showed atypia again with an increase in the atypical cells in the NAF sample. An ultrasound was performed and a small lesion found. This lesion was biopsied with a finding of sclerosing adenosis and ADH. This patient will be followed by our practice and referred to medical oncology for possible chemoprevention.

## References

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