Published in final edited form as:

Ann Surg Oncol. 2011 October ; 18(11): 3192–3197. doi:10.1245/s10434-011-1963-1.

Correlation of Ductal Lavage Cytology with Ductoscopy-Directed Duct Excision Histology in Women at High Risk for Developing Breast Cancer: A Prospective, Single-Institution Trial

Amy E. Cyr, MD¹, Julie A. Margenthaler, MD¹, Jill Conway, RN, BSN¹, Antonella L. Rastelli, MD², Rosa M. Davila, MD³, Feng Gao, PhD⁴, and Jill R. Dietz, MD⁵

Amy E. Cyr: cyra@wudosis.wustl.edu

¹Department of Surgery, Washington University School of Medicine, St. Louis, MO

²Department of Medicine, Washington University School of Medicine, St. Louis, MO

³Department of Pathology, Missouri Baptist Medical Center, St. Louis, MO

⁴Division of Biostatistics, Washington University School of Medicine, St. Louis, MO

⁵Women's Health Institute, Cleveland Clinic Foundation, Cleveland, OH

Abstract

Objectives—The study was designed to determine which histological lesions produce cellular atypia in lavage specimens and whether ductoscopy adds useful information for the evaluation of high-risk patients with atypical lavage cytology.

Methods—We prospectively recruited women 35 years at high risk for developing breast cancer. All underwent ductal lavage. Women found to have atypia underwent ductoscopy-directed duct excision (group 1). Women without atypia were observed (group 2). Data included patient demographics, risk assessment, cytologic and histologic findings, and outcomes. Descriptive statistics were utilized for data summary and were compared using Fisher's exact test.

Results—We enrolled 102 women; 93 (91%) were Caucasian. Their median age was 49 (range 34–73) years with a median follow-up of 80 (range 5–90) months. Overall, 27 (26%) had atypical lavage cytology (group 1), and 75 (74%) had benign cytology (group 2). Subsequent duct excision in group 1 revealed benign histology in 11 (44%), papillomas in 9 (36%), atypical hyperplasia (AH) in 4 (16%), and ductal carcinoma in situ (DCIS) in 1 (4%). At follow-up, three patients developed breast cancer, including one group 1 patient and two group 2 patients. There were no differences between groups 1 and 2 according to patient demographics, Gail scores, or risk for subsequent breast cancer ($P > 0.05$).

Conclusions—Although 20% of high-risk women with ductal lavage atypia have AH or malignancy on subsequent excision, the majority do not. Atypia identified by ductal lavage is not associated with a higher risk of developing subsequent breast cancer, even in this high-risk population.

Current screening for breast cancer involves physical and radiologic examination, unlike screening for gastrointestinal and gynecologic cancers, which involves direct visualization or cytologic evaluation of the epithelial tissue at risk. There are additional screening modalities, such as magnetic resonance imaging and ultrasound, which often are used as adjuncts to standard mammographic imaging for women at higher than average risk of developing breast cancer. In an attempt to identify these high-risk patients who may benefit from additional screening techniques, various models have been developed, none of which help to identify all high-risk patients. The Gail model, one of the most frequently used and validated risk-assessment models, has been modified and validated over time and its most

frequently used incarnation is known as the Breast Cancer Risk Assessment Tool (BCRAT).¹⁻⁴ The BCRAT calculates a woman's risk based on her age, menstrual and pregnancy history, the number of first-degree relatives with breast cancer, and previous breast biopsy history.⁵ It also has been modified to improve its validity in African-American women, although it has been less extensively studied for use in other ethnic populations. Its validity has not been demonstrated in women younger than age 35 years or women with a prior diagnosis of lobular carcinoma in situ (LCIS), and it does not take into account multiple non-first-degree affected family members. Finally, it only predicts for the risk of developing invasive breast cancer and does not include the risk of developing noninvasive disease.²

Nipple aspirate fluid (NAF) has been investigated as a way to identify markers of increased breast cancer risk. NAF is obtained by massaging the breast of an asymptomatic woman and collecting the resulting nipple fluid in a capillary tube. Cytology is then performed on the NAF. Early studies demonstrated that the presence of atypical cells on ductal lavage is associated with an increased breast cancer risk similar to that seen in women with atypical ductal hyperplasia (ADH) on histology.⁶⁻⁸ Unfortunately, limited specimen cellularity may limit the utility of this procedure. During a ductal lavage procedure, a duct producing NAF is cannulated and irrigated, and an exponentially larger number of epithelial cells can be collected for cytology. Studies of ductal lavage have demonstrated that high-risk patients are found to have atypia by this method up to 24% of the time.⁹

It is still unclear what histologic lesions are associated with atypia on lavage cytology. Ductoscopy, which allows visualization of the atypical cell-producing epithelium, may offer additional information for evaluation of high-risk patients with atypical ductal lavage specimens. Pre-malignant changes can be identified by cytology or direct visualization before a lesion is identifiable by radiology studies or physical examination. The primary objective of this prospective study was to determine which histological lesions produce cellular atypia in NAF. Our secondary objective was to determine if ductoscopy provided additional useful information for evaluation of high-risk patients with lavage atypia. Finally, we sought to determine whether the presence of atypia on lavage cytology in a group of high-risk patients translated to a subsequent elevated breast cancer risk over time.

METHODS

After obtaining Institutional Review Board approval for this prospective clinical trial, patients were recruited from the Joanne Knight Breast Health Center at Siteman Cancer Center at Washington University. An American Society of Cytopathology Institutional Support Grant (PI Dietz, total direct costs \$20,000) was obtained to perform the study. The accrual goal was 100 patients during 10 months. Eligible patients were age 35 years or older and at high risk of developing breast cancer defined by a previous diagnosis of breast cancer, a personal history of lobular carcinoma in situ (LCIS) or atypical ductal hyperplasia (ADH) on breast biopsy, a carrier of a BRCA gene mutation, or a 5-year Gail score >1.7%. All women had a normal clinical breast examination, normal mammogram within the previous 6 months, no prior circumareolar incision on the breast being evaluated, no current use of tamoxifen or other chemotherapy, and no prior breast radiation. All women were counseled that duct excision would result in the potential inability to breastfeed in the future.

After consenting to participate, patients underwent ductal lavage. All ductal lavage was performed by dedicated breast physicians experienced in the technique. Emla cream was placed over one or both nipples for 45 min before the procedure for local anesthesia. The patient was instructed to massage her breast, "milking" toward the nipple, for 10 min. Keratin plugs were removed from the nipple using a gentle facial abrasive or ultrasound

jelly. NAF was then elicited via a suction aspirator device or with manual compression. Ducts yielding NAF were marked on a data sheet grid. These ducts were then cannulated with a microcatheter, which was taped into place. One percent lidocaine was instilled into the duct followed by 5–10 cc of sterile saline. The specimen was collected by massaging the breast and collecting the fluid in a syringe. Instillation of saline and collection of fluid was repeated several times. Specimens were then placed in RPMI media and sent to cytology. This procedure was repeated for each yielding duct, up to two ducts on each breast, using a fresh catheter for each new duct.

Cells in lavage fluid were pelleted and resuspended in RPMI media. Total cell counts were obtained. The equivalent of 10,000 cells were placed in CytoLyt and processed on the ThinPrep processor (Cytoc Corp, Boxborough, MA), according to the manufacturer's guidelines. One slide was prepared and Papanicolaou stained for cytologic analysis. All slides were read by one cytopathologist who was blinded to the origin of the specimens. Specimens were categorized as benign, indeterminate or mild atypia, marked atypia, and malignant as per the 1997 consensus criteria for breast fine-needle aspiration published by the National Cancer Institute.¹⁰ A statement regarding the number of cells present was added for hypocellular specimens (<10 epithelial clusters). Slides were reviewed to assess cellularity, papillary architecture, and nuclear atypia.

Patients with no NAF, acellular specimens, or specimens with benign ductal cells were encouraged to continue breast cancer screening and were asked to return in 1 year for a repeat ductal lavage. Patients with atypia on lavage were scheduled for an intraoperative ductoscopy with ductal washings and a direct duct excision of the duct producing the atypical cells.

Ductoscopy and duct excision were performed in the operating room using monitored anesthesia and injectable local anesthetic. Using the data grid sheet as a guide, NAF was elicited from the duct that yielded the atypical cells. The duct orifice was dilated and a ductoscope was inserted under direct visualization. Lidocaine was instilled into the ducts to clear debris, dilate the ducts, and provide further local anesthesia. Ductal washings were collected through the working port of the ductoscope and processed in the same manner as lavage specimens. The visual appearance of the ducts and any intraductal lesions was recorded. A directed duct excision was performed when a lesion was identified. If no lesion was identified, methylene blue dye was injected into the discharge-producing duct and a standard microdochectomy was performed. Histology was processed using routine formalin fixation and routine institutional processing. Postoperative management was based on the final pathology and patient/physician discretion. All patients were followed for subsequent cancer development.

All data were transferred to a single spreadsheet (Excel; Microsoft, Redmond, WA). Data were compared using Fisher's exact test. All statistical analyses were performed using a statistical package SAS (SAS Institutes, Cary, NC). $P < 0.05$ was taken to indicate significance.

RESULTS

A total of 102 high-risk patients were enrolled in the trial. The median age was 49 (range 34–73) years. Ninety-three (91%) were Caucasian. The median Gail score was 2.5 (range 0.6–8.4). Median follow-up was 80 (range 5–90) months. Other demographic characteristics and risk factors are detailed in Table 1. Twenty-seven women had atypia on ductal lavage and were included in group 1, whereas 75 did not have atypia and were included in group 2. The median age of group 1 was 46.5 (range 35–69) years, and the median age of group 2

was 50 (range 34–73) years. Twenty-five patients of group 1 were Caucasian (93%) and 68 patients of group 2 were Caucasian (91%). The median Gail score for group 1 was 2.45 (range 0.06–7.7), and the median Gail score for group 2 was 2.5 (range 0.07–8.4). There were no significant differences between the two groups in terms of demographics or risk factors (Table 1).

Of the 27 women in group 1 found to have atypia on ductal lavage, 25 underwent attempted ductoscopy and duct excision. Ductoscopy revealed intraductal mass lesions in 11 women in group 1. Six of these correlated with papillomas on final pathology: five without atypia and one with atypia. One intraductal mass seen on ductoscopy was associated with a radial scar on excision pathology. Four of the women with intraductal mass lesions seen on endoscopy were found to have only benign histology at excision. Intraductal webs were identified endoscopically in three patients. Two were diagnosed with papillomas at excision and one was diagnosed with AH. Two women in group 1 had normal ductoscopies; at excision, one was found to have benign histology and one was found to have an intraductal papilloma without atypia. Ductoscopy was limited by ductal diameter in nine patients. In these patients, injected methylene blue dye guided microdochectomy. Excision pathology revealed a papilloma in one of these women, benign histology in five, AH in two, and DCIS in one woman. The patient found to have DCIS at duct excision also was found to have a previously undiagnosed T1a contralateral breast cancer at the time of bilateral mastectomies and tested positive for a BRCA2 mutation. She did not undergo ductal lavage of the contralateral breast for the study. One patient in group 1 with benign ductal histology on excision was subsequently diagnosed with breast cancer. This patient's mother, who also had breast cancer, tested negative for a BRCA mutation. None of the other women in group 1 subsequently developed cancer (Fig. 1). Two patients (7%) in group 1 underwent prophylactic mastectomy subsequent to their participation in the trial, and no malignancy was found on final pathology for either patient. Neither woman underwent BRCA testing.

Two patients (3%) in group 2 underwent prophylactic mastectomy subsequent to their participation in the trial, and no malignancy was found on final pathology for either patient. One woman was evaluated for Cowden Syndrome based on her family history but was negative. The second woman was a BRCA2 mutation carrier. Two patients (3%) in group 2 ultimately developed breast cancer during follow-up. One of these patients had been treated for a prior contralateral breast cancer and also had a striking family history with multiple maternal relatives who also had breast cancer, although she tested negative for a BRCA mutation. The other woman had a known BRCA-2 mutation.

DISCUSSION

Cytologic evaluation of NAF has been evaluated as a potential technique for identifying women at high risk of breast cancer and may help to identify atypical lesions before they become detectable by physical examination or radiographic screening. Poor cellular yield, however, has limited the utility of this technique. The addition of ductal lavage produces greater cellular yield,⁹ and the addition of ductoscopy allows direct visualization of the epithelium at risk.

Despite these advantages with lavage and ductoscopy, these techniques have limitations. The success rate of obtaining adequate lavage cytology is variable in the literature. Visvanathan et al. reported data on 69 high-risk women enrolled in a ductal lavage study. Only 65% of premenopausal women and 41% of postmenopausal women produced NAF, and only 72% of those women underwent successful ductal lavage.¹¹ Even when lavage is completed, failure to obtain adequate cellular material for cytology is common. Wood et al. published data for 23 women who were diagnosed with breast cancer.¹² These women

underwent bilateral nipple aspiration and ductal lavage of the ducts producing NAF. NAF was identified in 72% of breasts that subsequently underwent ductal lavage. Only 55% of lavage specimens were adequate. Loud et al. reported adequate cellularity in only 41% of women in BRCA mutation families.¹³ Our study focused on correlation of atypia on lavage, ductoscopy findings, and histology, and therefore, only women who successfully underwent ductal lavage were included in our cohort.

Various studies comment on the lack of reproducibility in lavage specimens. When ducts are found on lavage to have atypia, repeat lavage often fails to demonstrate atypia a second time.^{11,14,15} The concordance between NAF cytology and breast pathology also may be unreliable. Only 16.6% of samples from malignant breasts contained an abnormality in the study by Wood et al.¹² Khan et al. found ductal lavage to have a sensitivity of only 13–42% in breasts with known cancers.¹⁶ In our study, only 20% of women with atypia in NAF were found to have atypical or malignant histology at duct excision, and only one of the remaining women were diagnosed with malignancy during the follow-up period. Most of the women with atypia on lavage were ultimately diagnosed with benign ductal histology, although benign papillomas were seen more commonly than in the general population. Our findings corroborate data published by Carruthers et al. In their study, ductal lavage was performed on 116 high-risk patients.¹⁷ Twenty-five patients were found to have atypical or papillary-like cells on cytology. Fifteen of those patients underwent further workup consisting of ductoscopy, MRI, or biopsy, and all had benign findings. Two patients of the 116 enrolled subsequently developed cancer; neither had atypia on lavage. No patient with atypia on lavage subsequently developed cancer. Longer follow-up may better correlate lavage atypia with future cancer risk.

Although ductoscopy allows visualization of the at-risk duct epithelium, visual abnormalities are not always associated with cytologic or histologic abnormalities, and vice versa. Danforth et al.¹⁸ compared ductoscopic findings with lavage cytology in 25 patients. Eighty-three percent of their patients with atypical cytology had intraductal lesions seen on endoscopy. It is not always clear, however, that the visual findings are the source of the atypical cells. In one of our patients, a luminal mass visualized during ductoscopy proved to be a papilloma with atypia, and in another patient diagnosed with AH, a web was identified at ductoscopy. Two patients found on excision to have atypia and one patient found on excision to have DCIS had no identifiable intraluminal lesions. Ductoscopy was limited in these three patients, however, due to small duct diameter. Our results are similar to those published by Louie et al.¹⁹ Of 188 patients who underwent ductoscopy and duct excision, 14 were diagnosed with malignancy, but only 8 of those had duct wall abnormalities or masses. Liu et al. reported significantly better sensitivity of ductoscopy for identifying malignancy (94.2%) but specificity was limited; of 437 patients with ductoscopic findings, only 12.3% were diagnosed with atypia or malignancy at excision.²⁰

Lack of consistent reimbursement and poor patient acceptance of the procedure has been cited as a barrier to increased use of ductal lavage and ductoscopy. All of the women in our study underwent both procedures simultaneously in the operating room. When ductoscopy is omitted, however, as it is in many studies in the literature, the lavage is usually performed without sedation. Loud et al. surveyed 165 high-risk women and found that the anticipated and experienced discomfort was significantly higher for ductal lavage compared with mammogram, MRI, or nipple aspiration.²¹ Finally, there are practical considerations limiting the use of ductoscopy and ductal lavage. Ductoscopy and ductal lavage are expensive, time-consuming, and require additional training.^{22,23}

CONCLUSIONS

Benign nonproliferative ductal changes and benign papillomas were the most commonly seen histologies associated with atypia on ductal lavage. Ductoscopy allows visualization of obvious pathology, including papillomas, and literature supports its usefulness in decreasing the need for preoperative localization studies, the extent of duct excisions, and increasing the proliferative yield in patients with pathologic nipple discharge.^{24–26} However, in asymptomatic, high-risk patients, there is poor concordance with histology and addition of ductoscopy adds little to the evaluation. Finally, ductal lavage and ductoscopy identified histologic atypia or malignancy in only 5 of 102 (5%) high-risk women in our study, even though cytologic atypia was identified in 26%. Although the numbers are small, there is no apparent difference in the risk of future breast cancer development between those with atypia on ductal lavage and those without at 6 years of follow-up. Therefore, cytologic evaluation of ductal lavage and ductoscopy specimens appears to be of limited utility for stratifying or monitoring women at high risk of developing breast cancer. However, previous data suggest that bio-molecular studies performed on specimens obtained during ductal lavage and/or ductoscopy-directed excision may provide better risk-stratifying information with potential to improve the positive predictive value of ductoscopy.^{27,28} Future studies should focus on these molecular analyses.

References

1. Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, Mulvihill JJ. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst.* 1989; 81:1879–86. [PubMed: 2593165]
2. <http://www.cancer.gov/bcrisktool/about-tool.aspx>.
3. Constantino JP, Gail MH, Pee D, Anderson A, Redmon CK, Benichou J, Wieand HS. Validation studies for models projecting the risk of invasive and total breast cancer incidence. *J Natl Cancer Inst.* 1999; 91:1541–8. [PubMed: 10491430]
4. Gail MH, Constantino JP, Pee D, et al. Projecting individualized absolute invasive breast cancer risk in African American women. *J Natl Cancer Inst.* 2007; 99:1782–92. [PubMed: 18042936]
5. <http://www.cancer.gov/bcrisktool/>.
6. Wrensch MR, Petrakis NL, King EB, et al. Breast cancer incidence in women with abnormal cytology in nipple aspirates of breast fluid. *Am J Epidemiol.* 1992; 135:130–41. [PubMed: 1536131]
7. Petrakis NL, Ernster VL, King EB, Sacks ST. Epithelial dysplasia in nipple aspirates of breast fluid: association with family history and other breast cancer risk factors. *J Natl Cancer Inst.* 1982; 68:9–13. [PubMed: 6948129]
8. Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med.* 1985; 312:146–51. [PubMed: 3965932]
9. Dooley WC, Ljung BM, Veronesi U, et al. Ductal lavage for the detection of cellular atypia in women at high risk for breast cancer. *J Natl Cancer Inst.* 2001; 93:1624–32. [PubMed: 11698566]
10. The uniform approach to breast fine needle aspiration biopsy. *Am J Surg; NIH Consensus Development Conference*; 1997. p. 371–85.
11. Visvanathan K, Santor D, Ali SZ. The reliability of nipple aspirate and ductal lavage in women at increased risk for breast cancer: a potential tool for breast cancer risk assessment and biomarker evaluation. *Cancer Epidemiol Biomarkers Prev.* 2007; 16:950–5. [PubMed: 17507621]
12. Wood ME, Stanley MA, Crocker AM, Kingsley FS, Leiman G. Ductal lavage of cancerous and unaffected breasts: procedure success rate and cancer detection. *Acta Cytol.* 2009; 53:140–5.
13. Loud JT, Theibaut AC, Abati AD, et al. Ductal lavage in women from BRCA 1/2 families: is there a future for ductal lavage in women at increased genetic risk of breast cancer? *Cancer Epidemiol Biomarkers Prev.* 2009; 18:1243–51. [PubMed: 19336560]

14. Patil DB, Lankes HA, Nayar R, et al. Reproducibility of ductal lavage cytology and cellularity over a six-month interval in high risk women. *Breast Cancer Res Treat.* 2008; 112:327–33. [PubMed: 18097749]
15. Johnson-Maddux A, Ashfaq R, Cler L, et al. Reproducibility of cytologic atypia in repeat nipple duct lavage. *Cancer.* 2005; 103:1129–36. [PubMed: 15685620]
16. Kurian AW, Mills MA, Jafee M, et al. Ductal lavage of fluid-yielding and non-fluid yielding ducts in BRCA1 and BRCA2 mutation carriers and other women at high inherited breast cancer risk. *Cancer Epidemiol Biomarkers Prev.* 2005; 14:1082–9. [PubMed: 15894656]
17. Carruthers DC, Chapleskie LA, Flynn MB, Frazier TG. The use of ductal lavage as a screening tool in women at high risk for developing breast carcinoma. *Am J Surg.* 2007; 194:463–6. [PubMed: 17826056]
18. Danforth DN, Abati A, Filie A, et al. Combined breast ductal lavage and endoscopy for the evaluation of the high-risk breast: a feasibility study. *J Surg Oncol.* 2006; 94:555–64. [PubMed: 17048242]
19. Louie LD, Crowe JP, Dawson AE, Lee KB, Baynes DL, Dowdy T, Kim JA. Identification of breast cancer in patients with pathologic nipple discharge: does ductoscopy predict malignancy? *Am J Surg.* 2006; 192:530–3. [PubMed: 16978968]
20. Liu GY, Lu JS, Shen KW, et al. Fiberoptic ductoscopy combined with cytology testing in the patients of spontaneous nipple discharge. *Breast Cancer Res Treat.* 2008; 108:271–7. [PubMed: 17473979]
21. Loud JT, Beckjord EB, Nichols K, Peters J, Giusti R, Greene MH. Tolerability of breast ductal lavage in women from families at high genetic risk of breast cancer [abstract]. *BMC Womens Health.* 2009; 14:20. [PubMed: 19602282]
22. Fabian CJ, Kimler BF, Mayo MS, Kahn SA. Breast-tissue sampling for risk assessment and prevention. *Endocr Relat Cancer.* 2005; 12:185–213. [PubMed: 15947097]
23. Fabian CJ, Kimler BJ, Mayo MS. Ductal lavage for early detection—what doesn't come out in the wash. *J Natl Cancer Inst.* 2004; 96:1488–9. [PubMed: 15494592]
24. Dietz JR, Crowe JP, Grundfest S, et al. Directed duct excision by using mammary ductoscopy in patients with pathologic nipple discharge. *Surgery.* 2002; 132:582–8. [PubMed: 12407341]
25. Vaughan A, Crowe JP, Brainard J, et al. Mammary ductoscopy and ductal washings for the evaluation of patients with pathologic nipple discharge. *Breast J.* 2009; 15:254–60. [PubMed: 19645780]
26. Kapenhas-Valdes E, Feldman SM, Cohen JM, Boolbol SK. Mammary ductoscopy for evaluation of nipple discharge. *Ann Surg Oncol.* 2008; 10:2720–7. [PubMed: 18685898]
27. Yamamoto D, Tanaka K. A review of mammary ductoscopy in breast cancer. *Breast J.* 2004; 10:295–7. [PubMed: 15239786]
28. Fackler MJ, Rivers A, Teo WW, et al. Hypermethylated genes as biomarkers of cancer in women with pathologic nipple discharge. *Clin Cancer Res.* 2009; 15:3802–11. [PubMed: 19470737]

FIG. 1.
Outcomes for 102 women at high risk for developing breast cancer who underwent ductal lavage

TABLE 1

Demographics, risk factors, and follow-up for 102 women at high risk for developing breast cancer who underwent ductal lavage

	Total N = 102 N (%)	Group 1, Atypia on ductal lavage N = 27 N (%)	Group 2, No atypia on ductal lavage N = 75 N (%)	P
Demographics				
Median age, yr (range)	49 (34–73)	46.5 (35–69)	50 (34–73)	0.18
Caucasian	93 (91)	25 (93)	68 (91)	>0.99
African-American	8 (8)	2 (7)	6 (8)	
Asian	1 (1)	0	1 (1)	
Postmenopausal	64 (63)	14 (52)	50 (67)	0.25
Risk factors				
Used HRT	43 (42)	11 (41)	32 (43)	>0.99
Median age of first live birth (range)	24 (16–40)	24 (17–38)	26 (16–40)	0.42
Median age of menarche (range)	13 (9–16)	12.5 (10–16)	13 (9–16)	0.69
Mother with breast cancer	49 (48)	11 (41)	38 (51)	0.5
Sister with breast cancer	38 (37)	14 (52)	24 (32)	0.1
Daughter with breast cancer	1 (1)	0	1 (1)	>0.99
No. of other relatives with breast cancer	78 (76)	21 (78)	57 (76)	>0.99
Median Gail score (range)	2.5 (0.6–8.4)	2.45 (0.6–7.7)	2.5 (0.7–8.4)	0.86
Previous atypia	13 (13)	5 (19)	8 (11)	0.32
Previous lobular carcinoma in situ	5 (5)	1 (4)	4 (5)	>0.99
Previous malignancy	10 (10)	1 (4)	9 (12)	0.28
Follow-up				
Subsequent malignancy	4 (4)	2 (7)	2 (3)	0.29
Subsequent prophylactic mastectomy	4 (4)	2 (7)	2 (3)	0.29
Median follow-up (mo)	80	79	80	