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ORIGINAL ARTICLE – BREAST ONCOLOGY

Atypical Ductal Hyperplasia in Directional Vacuum-Assisted Biopsy of Breast Microcalcifications: Considerations for Surgical Excision

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ABSTRACT

Background. Our goal was to analyze clinicopathologic features of patients with atypical ductal hyperplasia (ADH) diagnosed on directional vacuum-assisted biopsy (DVAB) targeting microcalcifications to identify factors predicting the presence of carcinoma.

Materials and Methods. We retrospectively evaluated the clinical, mammographic, and histologic features of 140 patients with DVAB-diagnosed ADH who underwent either segmental excision (86.4%) or mammographic follow-up (≥2 years; 13.6%). Cases with mass lesions or ipsilateral cancer were excluded.

Results. In 16 cases, carcinoma was found on excision. All cases without excision showed no new abnormalities on mammographic follow-up. Only the amount of calcifications removed (≤95%) significantly correlated with the rate of upgrade of ADH to carcinoma ($P = .037$). Significant histologic predictors of upgrade to carcinoma included number of terminal duct-lobular units (TDLU; >2) involved ($P = .0306$), presence of significant cytologic atypia suspicious for intermediate or high-grade carcinoma ($P < .0001$), and necrosis ($P = .0006$). Among ADH cases without significant atypia and/or necrosis, the extent of ADH (≤2 vs. >2 TDLU involved) was not a significant predictor of carcinoma ($P = 1.0000$).

Conclusions. ADH associated with calcifications in the absence of a mass lesion can be categorized into different risk groups using a multidisciplinary approach with correlation of histologic and mammographic findings. ADH lesions with significant cytologic atypia and/or necrosis are most likely to be associated with carcinoma and should be excised. ADH without these features, regardless of extent of involvement, and with >95% removal of the targeted calcifications, is associated with a minimal risk (<3%) of carcinoma and may undergo mammographic follow-up only.

Up to 15% of image-guided core needle biopsies (CNB) of suspicious breast lesions yield a diagnosis of atypical ductal hyperplasia (ADH).[1–35] While the diagnosis of ADH on CNB often results in excision, the identification of patients who may be spared surgery is an area of active investigation. ADH is a proliferative, nonobligate precursor breast lesion and a marker of increased risk for breast carcinoma.[31] It is variably defined histologically as (1) a lesion with some, but not all, of the features of low-grade ductal carcinoma in situ (DCIS) or (2) a lesion with all the cytologic and architectural features of low-grade DCIS but involving no more than one duct or measuring less than 2 mm in diameter.[36–38] Because ADH may coexist with DCIS and its distinction from DCIS is partly quantitative, it is sometimes not possible to distinguish these two lesions in the limited samples provided by CNB.

The reported prevalence of carcinoma in surgically excised breast lesions after a CNB diagnosis of ADH has been variable. The reported rates of carcinoma range from

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11 to 88% for biopsies using a 14-gauge automated needle, compared with 0–38% for biopsies using a directional vacuum-assisted biopsy (DVAB) technique with larger probes (9 or 11 gauge).[1–10,12,13,15,16,18,20–30,32–35,39–55] The advantage of DVAB is that a greater amount of contiguous tissue can be extracted and sometimes with near-complete to complete removal of small lesions.[6,22,56–59] However, some studies indicate that the chance that a carcinoma may be missed by a DVAB is still too high to completely obviate the need for surgical excision.[2,3,5,7–9,13,14,18,22–25,29,30,32,35,45,46,48–52,60–65]

Many studies have examined the histologic characteristics of ADH on CNB to determine features that would predict carcinoma on excision. Some studies report that the rate of upgrade to carcinoma can approach 0% when the targeted calcifications were entirely removed and/or when ADH involved no more than 2 foci.[1,10,53,54,66–68] Others report that a micropapillary pattern of ADH and increased cytologic atypia are significantly associated with carcinoma.[28,46,68–70] Mammographic parameters such as size of the targeted calcification clusters, extent of residual calcifications after CNB, and volume of tissue extracted, have been found to be significant predictors of carcinoma.[2,22,30,54,67,71]

All of these studies suggest that several clinicopathologic features may be used to predict the presence of carcinoma and that perhaps not all patients with ADH diagnosed with CNB require surgical excision. It is difficult to obtain consensus on the management of ADH based on previous studies because of the heterogeneity of the study population, type of biopsy, and type of lesion targeted. The purpose of our study was to analyze multiple clinicopathologic features in a large cohort of patients with ADH who underwent either subsequent segmental mastectomy or clinical follow-up to identify factors associated with the presence of cancer. To our knowledge, our series is one of the largest to date, analyzing the significance of ADH found on DVABs targeting only microcalcifications.

METHODS

ADH was identified in 433 of the 4383 patients (9.9%) who underwent stereotactic DVAB of microcalcifications at The University of Texas MD Anderson Cancer Center (MDACC) from 1997 through 2009. Of 417 cases with slides available for review, 277 cases were excluded after review for the following reasons: (1) ADH was associated with a mass lesion or architectural distortion ($n = 43$), (2) the patient had a concurrent or remote history of ipsilateral breast cancer ($n = 111$), (3) ADH was not associated with microcalcifications and deemed incidental ($n = 22$), (4) the patient underwent total mastectomy ($n = 16$) (these cases were excluded because sampling of such cases included areas other than that sampled by the DVAB), (5) the patient had less than 2 years of follow-up ($n = 61$), and (6) the patient had no follow-up ($n = 24$). Of the 140 patients in the study, 121 patients (86.4%) underwent surgical excision and 19 patients (13.6%) underwent mammographic follow-up alone (minimum 24 months follow-up). Of these 19 patients, three underwent chemoprevention with either tamoxifen or raloxifene. This study was approved by the MDACC Institutional Review Board.

The processing of samples were carried out as previously described by Sneige et al.[53] Biopsy was performed using DVAB technique with a 14 g ($n = 3$), 11 g ($n = 75$), or 9 g ($n = 62$) needle. Mammographic characteristics of the calcifications were assessed by a breast imager (GJW) using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). The specimen radiographs were evaluated to confirm the presence of calcifications, and the postbiopsy radiographs were evaluated for residual calcifications after the DVAB procedure. For patients who did not undergo excision and were followed with mammography, absence of a change in lesion characteristics or absence of a new abnormality on follow-up was regarded as indicative of a benign lesion.

The patients' electronic medical records were reviewed. The risk of carcinoma was calculated in a subset of patients ($n = 97$) using the Gail model risk assessment tool (http://www.cancer.gov/bcrisktool/). The model is not meaningful in patients with a history of breast carcinoma; therefore, such patients were excluded from the calculations.

All DVABs were retrospectively reviewed by three pathologists (CN, CTA, NS), two of whom are dedicated breast pathologists (CTA, NS). A consensus on the diagnosis of ADH was obtained using criteria as described by Page and Tavassoli.[36–38] The extent of ADH (number of terminal duct-lobular units [TDLU] or large ducts involved) was determined as described by Ely et al.[69] The histologic pattern of ADH (micropapillary vs. other), the presence of significant cytologic atypia suspicious for intermediate or higher-grade DCIS, and the presence of necrosis were also noted.

All statistical analyses were done using SAS software (version 9.1; SAS Institute Inc., Cary, NC). The association between two categorical variables was evaluated using Fisher exact test. The difference in the distribution of a continuous variable between two patient groups was tested using the Wilcoxon rank-sum test. All tests were two-sided, and P values less than .05 were considered statistically significant. When multiple comparisons were performed, the Bonferroni method was used.

RESULTS

Clinical and Mammographic Parameters

The study included 140 women, age 39–87 years (median age, 59.5 years) who presented with microcalcifications alone and had no associated mass, architectural distortion, or other lesion. There were 19 women who had clinical and mammographic monitoring only, with a median follow-up interval of 62.2 months (range, 29.6–132.9 months). None of the 19 cases without excision had new lesions or significant change in mammographic characteristics during follow-up (rate of upgrade to carcinoma of 0%). Of the 121 women who underwent surgery, 16 were found to have carcinoma on excision (rate of upgrade to carcinoma of 13.2%) (14 DCIS, 2 invasive carcinoma).

Clinical variables were evaluated and correlated with the rate of upgrade to carcinoma upon excision/mammographic follow-up (Table 1). In 28 cases there was either a remote or a concurrent history of contralateral breast cancer (7 DCIS, 21 invasive carcinoma). Gail model risk assessment calculations showed no statistical difference in the likelihood of finding cancer on excision or follow-up between patients with 5-year risks above or below 3.4% ($P = .114$) or between patients with lifetime risks above or below 18.1% ($P = .356$). Laterality of the lesion, family history of breast cancer, and history of contralateral carcinoma were also not significant predictors of carcinoma.

The size of the calcification groups detected on mammography ranged from 0.1 to 9.0 cm (median, 0.9 cm). Four cases were classified as BI-RADS 5, and 136 cases as BI-RADS 4. A median of eight cores (range, 4–22 cores) was obtained for each lesion. The percentage of calcifications removed was significantly different in cases that were upgraded to carcinoma (range, 20–100%; median, 85%) and cases that had no carcinoma (range, 10–100%; median, 90%) ($P = .0415$). There was also a significant difference in rates of upgrade to carcinoma between cases with >95% vs. ≤95% of calcifications removed ($P = .0371$). On the other hand, the number of cores obtained and the needle size were not associated with the rate of upgrade to carcinoma. A comparison of different calcification group sizes (≤0.5 cm, 0.6–2.0 cm, and >2.0 cm) showed no significant difference in rates of upgrade to carcinoma among these groups or the extent of ADH (data not shown). In cases with no residual calcifications, only one showed DCIS on excision. The core biopsy in this case showed extensive ADH (>5 foci) with focal necrosis.

Histologic Findings

Histologic variables were evaluated and correlated with the rate of upgrade to carcinoma (Table 1). These variables

TABLE 1 Correlation of clinicopathologic variables in relation to the rate of upgrade to carcinoma on excision ($n = 121$)/mammographic follow-up ($n = 19$)

Variable	No. of patients	No. of cases upgraded to carcinoma (% of cases)	Univariate *P* value (Fisher exact test)
Clinical and mammographic variables			
Patient age			
≤60 years	79	10 (12.7)	.7898
>60 years	61	6 (9.8)	
Laterality			
Left breast	83	9 (10.8)	.7934
Right breast	57	7 (12.3)	
First-degree relative with breast cancer			
Yes	29	6 (20.7)	.1004
No	81	7 (8.6)	
Race/ethnicity			
White	87	11 (12.6)	.4356
Black	11	0 (0)	
Hispanic	10	1 (10)	
Asian	4	1 (25)	
History of contralateral carcinoma			
Present	28	3 (10.7)	1.0000
Absent	112	13 (11.6)	
Gail 5-year risk			
≤3.4	50	3 (6)	.114
>3.4	47	8 (17)	
Gail lifetime risk			
≤18.1	49	4 (8.2)	.356
>18.1	48	7 (14.6)	
Size of calcification group			
≤0.5 cm	47	6 (12.8)	.6339
0.6–2.0 cm	64	5 (7.8)	
>2.0 cm	27	4 (14.8)	
No. of cores obtained			
≤8	76	9 (11.8)	1.0000
>8	64	7 (10.9)	
Amount of calcifications removed			
≤95%	94	14 (14.9)	.0371
>95%	42	1 (2.4)	
DVAB probe size			
14 gauge	3	0 (0)	
11 gauge	75	8 (10.7)	[a]
9 gauge	62	8 (12.9)	
Histologic variables			
No. of TDLUs involved			
≤2 TDLU	81	5 (6.2)	.0306
>2 TDLU	59	11 (18.6)	
Significant cytologic atypia			
Present	20	12 (60)	<.0001
Absent	120	4 (3.3)	

TABLE 1 continued

Variable	No. of patients	No. of cases upgraded to carcinoma (% of cases)	Univariate *P* value (Fisher exact test)
Focal necrosis			
Present	5	4 (80)	.0006
Absent	135	12 (8.9)	
Pattern of ADH			
Micropapillary	10	3 (30)	.0895
Other	130	13 (10)	

ADH atypical ductal hyperplasia, *DVAB* directional vacuum-assisted biopsy, *TDLU* terminal duct-lobular unit or large duct

[a] 11- vs. 9-gauge biopsies: $P = .7913$

included the number of TDLUs involved and the presence of significant cytologic atypia suspicious for intermediate or high-grade DCIS, necrosis, and micropapillary growth pattern. There was a statistically significant difference in the rate of upgrade to carcinoma between cases involving ≤2 TDLU vs. >2 TDLU ($P = .0306$). In addition, significant cytologic atypia and necrosis demonstrated a statistically significant association with carcinoma on excision/mammographic follow-up ($P < .0001$ and $P = .0006$, respectively). The presence of a micropapillary growth pattern was not significant ($P = .0895$).

Four groups were defined in terms of extent (≤2 or >2 TDLU) and presence or absence of significant cytologic atypia and/or necrosis (Table 2) (Figs. 1, 2). An upgrade to carcinoma occurred in 2 of 74 cases (2.7%) in which ADH involved ≤2 TDLU without significant cytologic atypia and/or necrosis. One case had ADH with a micropapillary pattern with 90% of calcifications removed by the DVAB procedure. The second case had only 30% of the calcifications removed by the DVAB procedure. In cases with ADH in >2 TDLU but without significant cytologic atypia and/or necrosis, 1 of 43 cases (2.3%) was upgraded to carcinoma. While this patient had 95% of her calcifications removed, excision demonstrated focal DCIS away from the biopsy site. Overall, in the absence of significant cytologic atypia and/or necrosis only 3 of 117 (2.6%) cases were upgraded to carcinoma. In contrast, in the presence of significant cytologic atypia and/or necrosis up to 13 of 22 (59.1%) were upgraded to carcinoma ($P < .0001$). In Table 2, when the extent of ADH was compared among cases without significant cytologic atypia and/or necrosis, there was no statistically significant difference in the rate of upgrade to carcinoma between cases involving ≤2 TDLU vs. >2 TDLU ($P = 1.0000$). These results suggest that the presence of significant cytologic atypia and/or necrosis, more than the extent of involvement by ADH, is more likely to be significantly predictive of carcinoma. Of note, there was no appreciable difference in the percent calcifications removed among the ADH groups: cases with ADH in ≤2 TDLU without significant cytologic atypia and/or necrosis (range, 10–100%; median, 90%), cases with ADH in >2 TDLU without significant cytologic atypia and/or necrosis (range, 20–100%; median, 90%), and cases with significant cytologic atypia and/or necrosis regardless of extent of ADH (range, 20–100%; median, 90%).

In the 19 cases that underwent clinical/mammographic follow-up, the percentage of calcifications removed by the DVAB procedure ranged from 10 to 100% (median, 90%). There were nine cases that had ADH in ≤2 TDLU without significant cytologic atypia and/or necrosis, two cases that had ADH in >2 TDLU without significant cytologic atypia and/or necrosis, and three cases that had significant cytologic atypia and/or necrosis. The reasons for not excising these cases were either caused by (1) removal of the majority of calcifications, (2) limited involvement by ADH, or (3) patient refusal for surgical excision.

DISCUSSION

In this study we have examined the characteristics of ADH detected in DVABs targeting calcifications alone with no associated mass lesions. Our findings suggest that cases of ADH can be stratified into different risk groups based on mammographic and histologic parameters. Our

TABLE 2 Comparison of histologic findings (number of TDLU involved by ADH and presence of significant cytologic atypia and/or necrosis) in relation to rate of upgrade to carcinoma

Extent of ADH on DVAB	Presence of significant cytologic atypia and/or necrosis	Corresponding surgical excision/mammographic follow-up		Univariate *P* value (Fisher exact test)
		No carcinoma ($n = 124$)	DCIS/invasive carcinoma ($n = 16$)	
≤2 TDLU	No	72 (97.3%)	2 (2.7%)	.0038
	Yes	4 (57.1%)	3 (42.9%)	
>2 TDLU	No	42 (97.7%)	1 (2.3%)	<.0001
	Yes	5 (33.3%)	10 (66.7%)	

ADH atypical ductal hyperplasia, *DCIS* ductal carcinoma in situ, *DVAB* directional vacuum-assisted biopsy, *TDLU* terminal duct-lobular unit or large duct

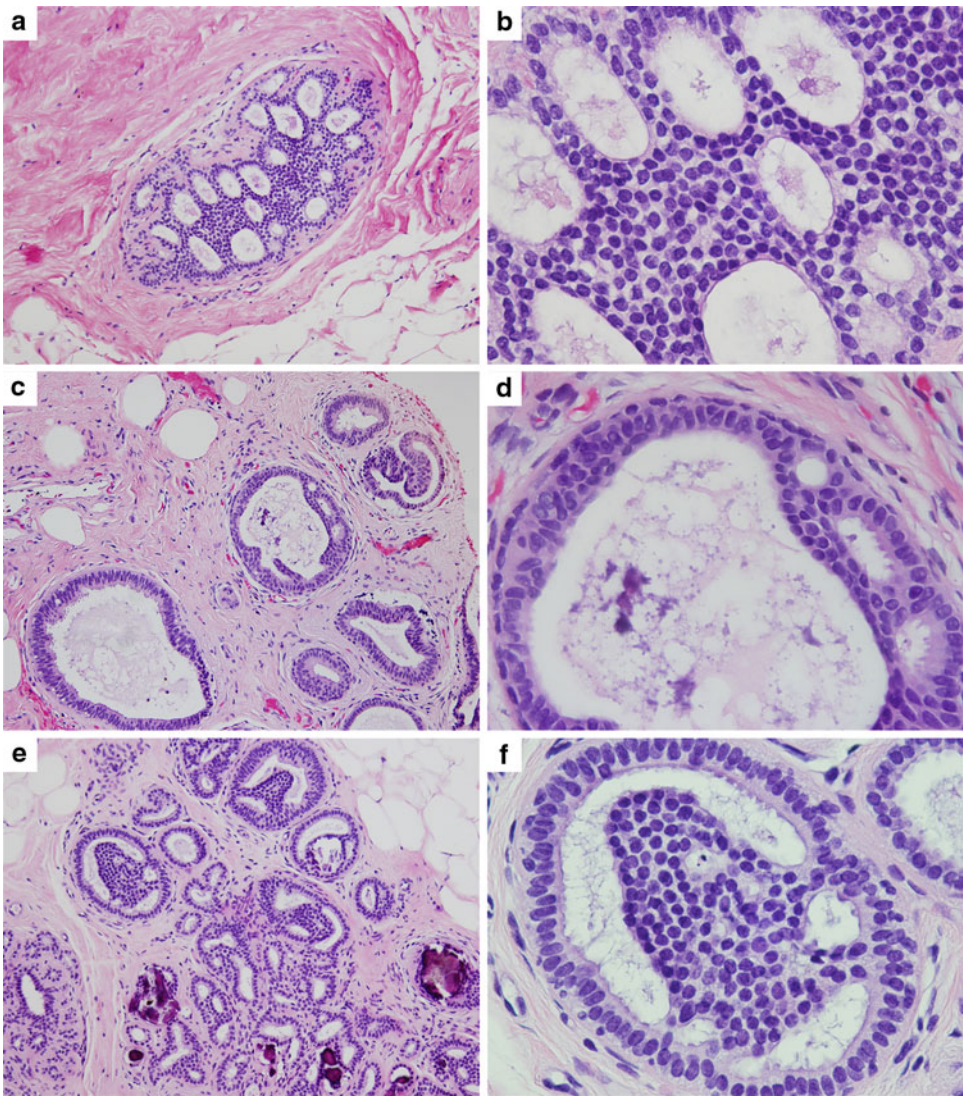

FIG. 1 Examples of ADH associated with minimal risk of upgrade to carcinoma on excision. These cases contained ADH involving ≤2 TDLU/large ducts and/or exhibited minimal cytologic atypia. On the left panels are low magnification (100×) and on the right panels are their respective higher magnifications (400×). Whole slide imaging is available through the website www.pathscholar.com by logging in with the following username (PathSlides) and password (pathslides)

results demonstrated a significantly lower rate of upgrade to carcinoma in DVAB with ADH involving ≤2 TDLUs (6.2%) and in DVAB with ≥ 95% removal of targeted calcifications (2.4%). However, cases with features suspicious for DCIS (significant cytologic atypia and/or necrosis) had a significantly greater chance of being upgraded to carcinoma (59.1%). We conclude that all ADH lesions with significant cytologic atypia and/or necrosis should be excised to exclude DCIS. Lesions without these features are amenable to imaging follow-up provided that the targeted calcifications were nearly completely removed. Thus, by reporting the extent of involvement (number of TDLUs) and the presence or absence of suspicious findings (significant cytologic atypia or necrosis), we can subcategorize cases of ADH into different risk groups.

Previous studies demonstrated a wide variation in the reported rates of upgrade of ADH on CNB to carcinoma on excision. This is probably secondary to differences in study design. Prior to 1997, the automated gun was used almost exclusively with the 14-gauge probe. The transition to the DVAB technique with larger 11- or 9-gauge needles occurred gradually over the next few years. The lower rates of upgrade to carcinoma in the later studies may reflect this change in the biopsy procedure. Many previous studies have included both patients with calcifications and those with mass lesions. In our institution, mass lesions usually warrant excision, regardless of the extent or features of ADH identified on CNB. For these reasons, in this study we focused exclusively on patients with suspicious microcalcifications only.

In our study, the overall frequency of upgrade to carcinoma for excised cases was 13.2%. This rate is among the lowest reported for DVAB compared with previous studies where it has ranged from 0 to 38% (Table 3). Our analysis showed a statistically significant difference in

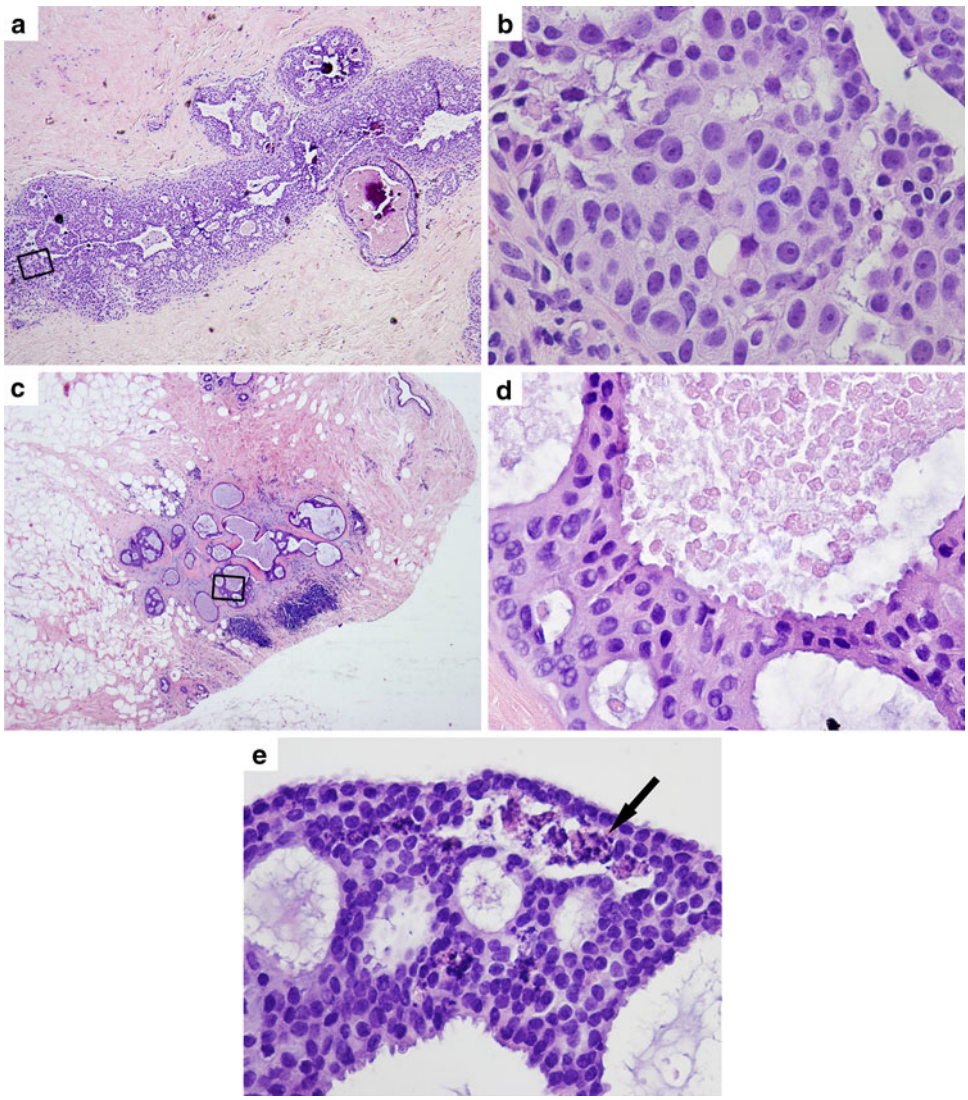

FIG. 2 Examples of ADH associated with high risk of upgrade to carcinoma on excision. **a**, **b**, significant cytologic atypia suspicious for intermediate to high-grade carcinoma (40× and 400×, respectively; square panel in **a** represents area magnified in **b**). **c**, **d**, significant cytologic atypia suspicious for intermediate-grade carcinoma (40× and 400×, respectively: square panel in **c** represents area magnified in **d**). **e** focal necrosis (*arrow*) (400×)

rates of upgrade to carcinoma between cases of ADH that involved ≤2 TDLUs vs. >2 TDLUs ($P = .0306$). This is similar to the findings by Sneige et al., Ely et al., and Wagoner et al.[53,68,69] However, when we recategorized our cases of ADH based on extent of ADH (No. of TDLUs) and presence of suspicious features, we found that, in the absence of significant cytologic atypia and/or necrosis, the extent of ADH was not a significant predictor of carcinoma.

Furthermore, our studies showed that ADH cases with significant cytologic atypia and/or necrosis had a 59.1% risk of upgrade to carcinoma and were more likely to yield carcinoma upon excision than cases of ADH without these features. These findings are consistent with studies reported by Doren et al. and Bonnett et al.[46,67] Thus, the presence of ADH with significant cytologic atypia or necrosis on DVAB should prompt surgical excision, even if calcifications are nearly completely removed.

In contrast to other studies, we did not find that a micropapillary pattern significantly increases the risk of malignancy, even though 3 of 10 cases with this feature were shown to have DCIS on excision.[68,69] We found no clinical parameters that were helpful in predicting carcinoma. Previous reports have emphasized the significance of mammographic parameters including lesion size, percentage of residual calcifications, and number of cores obtained during DVAB (Table 3). Intuitively, one would expect higher rates of underestimation when sampling is less adequate, which would be more likely in the case of larger target lesions, more residual calcifications, or fewer cores obtained. However, when we compared the rates of upgrade to carcinoma by probe sizes (11 g vs. 9 g), the results were not statistically significant. In fact, the only mammographic parameter that was a significant predictor of carcinoma was the percentage of residual calcifications. Of note, Forgeard et al. found that the combination of

TABLE 3 ADH at stereotactic biopsy of calcifications with and without mass lesions: representative findings in the literature and predictors of upgrade to carcinoma

First author	DVAB needle gauge	Mean No. of cores (range)	Biopsy target	Number of cases with carcinoma/total cases (%)	Summary of predictors of upgrade to carcinoma
Burbank[6]	14	27	C, M	0/8 (0)	None upgraded.
Liberman[22]	11	14	C, M	1/10 (10)	Incomplete removal of calcifications
Brem[3]	11	13.4 (8–24)	C, M	4/16 (25)	No correlation between number of cores and upgrade
Philpotts[30]	11	13 (6–19)	C, M	14/86 for C (16.3) 1/64 for M (1.6)	Incomplete removal of calcifications
Ely[69]	(11 or 14, technique not stated)	11.6 (3–29)	C, M	17/47 (36.2)	(1) ≥4 foci of ADH (2) Pure micropapillary pattern
Maganini[49]	11	N/A	C, M	4/32 (13)	No parameters are predictive
Bonnett[67]	11 (except 26 with 14 g by US guidance)	20 (8–41) for 11 g 5 (2–10) for 14 g	C, M	12/121 (35)	(1) Mammographically extensive calcifications (2) Atypia is multifocal or associated with borderline cytologic features.
Pandelidis[29]	11	9 (3–20)	C, M	4/37 (13.5)	Calcifications measure >1.5 cm.
Winchester[35]	11	>6	NP	11/65 (17)	No parameters are predictive.
Bedei[2]	11	12 (6–36)	C, distortion, opacities	2/17 (11.8)	(1) Lesion size is >2 cm. (2) Sampling is inadequate.
Lourenco[24]	11 or 9	>6	C, M	11 g: 13/46 (28.3) 9 g: 8/27 (29.6)	No difference in upgrade rate between 11 g and 9 g core biopsy
Sohn[32]	11	9	C, M	14/78 (17)	Larger needle size reduces but does not eliminate upgrade to carcinoma.
Doren[46]	11	N/A (estimated 8–12)	C, M	17/51 (33)	Increased grade of cytologic atypia
Eby[9]	11 or 9	20.1 (6–20)	9 g: C, M; 11 g: C	26/123 (21.1)	No parameters are predictive.
Wagoner[68]	11 (except 7 with 14 g by US guidance)	10 (2–26)	C, M, distortion	16/41 (39) if >2 foci 6/82 (7) if ≤2 foci 0% if no residual lesion	(1) Incomplete removal of lesion (2) Micropapillary pattern (3) Extent of ADH (4) Degree of residual calcifications
Adrales[1]	11	6	C	9/62 (15)	(1) Marked ADH (2) Incomplete removal of calcifications (3) Previous contralateral breast cancer (4) Family history of breast cancer
Sneige[53]	11 (except 3 with 14 g)	10.8 (6–22)	C	3/42 (7)	(1) Incomplete removal of calcifications (2) ADH >2 lobules
Forgeard[10]	11	16	C	29/116 (25)	(1) Lesion size >20 mm (2) ADH in >2 lobules in smaller lesions (3) Incomplete removal of calcifications
Teng-Swan Ho[33]	11	N/A	C	14/61 (23)	No parameters are predictive.
Current study	11 or 9 (except 3 with 14 g)	8.9 (4–22)	C	16/121 (13.2)	(1) ADH has increased cytologic atypia or necrosis (2) Residual calcifications comprise ≥ 5%

ADH atypical ductal hyperplasia, *DVAB* directional vacuum-assisted biopsy, *C* calcifications, *M* mass, *N/A* not available, *g* gauge, *US* ultrasound, *NP* nonpalpable

extent of ADH and size of the calcification groups were predictive of underestimation of carcinoma.[10] However, in our study when we evaluated our cases using their classification, there was no statistically significant difference (data not shown).

In our practice, ADH cases are usually presented at multidisciplinary conferences where the combination of histologic, mammographic, and clinical findings are reviewed for patient management. When ADH is limited to 2 TDLUs and there is little to no residual calcification, the recommendation at our institution is for clinical and mammographic follow-up, provided that there are no other suspicious clinical findings.[53] Based on the findings of the present study with a larger patient population, recommendations will be made to incorporate significant atypia or necrosis as one of our parameters.

In summary, our study demonstrates that by noting the extent of ADH and the presence or absence of features suspicious for DCIS (significant cytologic atypia and/or necrosis) on DVAB, ADH can be stratified into different risk groups. We propose that for ADH detected in DVABs that target calcifications alone without other associated mammographic lesions, all ADH lesions with significant cytologic atypia and/or necrosis should be excised regardless of the extent of involvement by ADH, as they are more likely to be associated with carcinoma. ADH lesions limited to 2 TDLUs, with >95% removal of targeted calcifications and no significant cytologic atypia and/or necrosis are associated with a minimal risk for carcinoma and may undergo mammographic follow-up every 6 months for 2 years and then annually. It should be emphasized that in our study the minimal risk group is a highly selected group of patients with ADH diagnosed on DVAB targeting calcifications (no associated mass lesion, near complete removal of calcifications, no atypia or necrosis). Multivariate analysis could not be performed because of the low incidence of carcinoma in this select group of patients. It will certainly be helpful in future studies to evaluate a much larger cohort of patients with long-term follow-up to see if this management strategy is truly a safe and appropriate option for these patients.

While translation of these recommendations into general community practice can be challenging, application of some of the principles of multidisciplinary care with correlation of clinicopathologic and mammographic features can only improve management of these patients. The importance of a multidisciplinary approach has been emphasized previously, and the findings from this study further support this approach.[19]

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REFERENCES

1. Adrales G, Turk P, Wallace T, Bird R, Norton HJ, Greene F. Is surgical excision necessary for atypical ductal hyperplasia of the breast diagnosed by Mammotome? *Am J Surg.* 2000;180:313–5.
2. Bedei L, Falcini F, Sanna PA, Casadei Giunchi D, Innocenti MP, Vignutelli P, et al. Atypical ductal hyperplasia of the breast: the controversial management of a borderline lesion: experience of 47 cases diagnosed at vacuum-assisted biopsy. *Breast.* 2006;15:196–202.
3. Brem RF, Behrndt VS, Sanow L, Gatewood OM. Atypical ductal hyperplasia: histologic underestimation of carcinoma in tissue harvested from impalpable breast lesions using 11-gauge stereotactically guided directional vacuum-assisted biopsy. *AJR Am J Roentgenol.* 1999;172:1405–7.
4. Brown TA, Wall JW, Christensen ED, Smith DV, Holt CA, Carter PL, et al. Atypical hyperplasia in the era of stereotactic core needle biopsy. *J Surg Oncol.* 1998;67:168–73.
5. Burak WE, Jr., Owens KE, Tighe MB, Kemp L, Dinges SA, Hitchcock CL, et al. Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. *Arch Surg.* 2000;135:700–3.
6. Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. *Radiology.* 1997;202:843–7.
7. Cangiarella J, Waisman J, Symmans WF, Gross J, Cohen JM, Wu H, et al. Mammotome core biopsy for mammary microcalcification: analysis of 160 biopsies from 142 women with surgical and radiologic followup. *Cancer.* 2001;91:173–7.
8. Darling ML, Smith DN, Lester SC, Kaelin C, Selland DL, Denison CM, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. *AJR Am J Roentgenol.* 2000;175:1341–6.
9. Eby PR, Ochsner JE, DeMartini WB, Allison KH, Peacock S, Lehman CD. Is surgical excision necessary for focal atypical ductal hyperplasia found at stereotactic vacuum-assisted breast biopsy? *Ann Surg Oncol.* 2008;15:3232–8.
10. Forgeard C, Benchaib M, Guerin N, Thiesse P, Mignotte H, Faure C, et al. Is surgical biopsy mandatory in case of atypical ductal hyperplasia on 11-gauge core needle biopsy? A retrospective study of 300 patients. *Am J Surg.* 2008;196:339–45.
11. Fuhrman GM, Cederbom GJ, Bolton JS, King TA, Duncan JL, Champaign JL, et al. Image-guided core-needle breast biopsy is an accurate technique to evaluate patients with nonpalpable imaging abnormalities. *Ann Surg.* 1998;227:932–9.
12. Gadzala DE, Cederbom GJ, Bolton JS, McKinnon WM, Farr GH Jr, Champaign J, et al. Appropriate management of atypical ductal hyperplasia diagnosed by stereotactic core needle breast biopsy. *Ann Surg Oncol.* 1997;4:283–6.
13. Jackman RJ, Birdwell RL, Ikeda DM. Atypical ductal hyperplasia: can some lesions be defined as probably benign after stereotactic 11-gauge vacuum-assisted biopsy, eliminating the recommendation for surgical excision? *Radiology.* 2002;224:548–54.
14. Jackman RJ, Burbank F, Parker SH, Evans WP 3rd, Lechner MC, Richardson TR, et al. Atypical ductal hyperplasia diagnosed at stereotactic breast biopsy: improved reliability with 14-gauge, directional, vacuum-assisted biopsy. *Radiology.* 1997;204:485–8.
15. Jackman RJ, Nowels KW, Rodriguez-Soto J, Marzoni FA Jr, Finkelstein SI, Shepard MJ. Stereotactic, automated, large-core

needle biopsy of nonpalpable breast lesions: false-negative and histologic underestimation rates after long-term follow-up. *Radiology.* 1999;210:799–805.
16. Jackman RJ, Nowels KW, Shepard MJ, Finkelstein SI, Marzoni FA Jr. Stereotaxic large-core needle biopsy of 450 nonpalpable breast lesions with surgical correlation in lesions with cancer or atypical hyperplasia. *Radiology.* 1994;193:91–5.
17. Jang M, Cho N, Moon WK, Park JS, Seong MH, Park IA. Underestimation of atypical ductal hyperplasia at sonographically guided core biopsy of the breast. *AJR Am J Roentgenol.* 2008; 191:1347–51.
18. Lai JT, Burrowes P, MacGregor JH. Diagnostic accuracy of a stereotaxically guided vacuum-assisted large-core breast biopsy program in Canada. *Can Assoc Radiol J.* 2001;52:223–7.
19. Lee AH, Denley HE, Pinder SE, Ellis IO, Elston CW, Vujovic P, et al. Excision biopsy findings of patients with breast needle core biopsies reported as suspicious of malignancy (B4) or lesion of uncertain malignant potential (B3). *Histopathology.* 2003;42: 331–6.
20. Liberman L, Cohen MA, Dershaw DD, Abramson AF, Hann LE, Rosen PP. Atypical ductal hyperplasia diagnosed at stereotaxic core biopsy of breast lesions: an indication for surgical biopsy. *AJR Am J Roentgenol.* 1995;164:1111–3.
21. Liberman L, Dershaw DD, Glassman JR, Abramson AF, Morris EA, LaTrenta LR, et al. Analysis of cancers not diagnosed at stereotactic core breast biopsy. *Radiology.* 1997;203:151–7.
22. Liberman L, Smolkin JH, Dershaw DD, Morris EA, Abramson AF, Rosen PP. Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy. *Radiology.* 1998;208: 251–60.
23. Lin PH, Clyde JC, Bates DM, Garcia JM, Matsumoto GH, Girvin GW. Accuracy of stereotactic core-needle breast biopsy in atypical ductal hyperplasia. *Am J Surg.* 1998;175:380–2.
24. Lourenco AP, Mainiero MB, Lazarus E, Giri D, Schepps B. Stereotactic breast biopsy: comparison of histologic underestimation rates with 11- and 9-gauge vacuum-assisted breast biopsy. *AJR Am J Roentgenol.* 2007;189:W275–9.
25. Meyer JE, Smith DN, Lester SC, Kaelin C, DiPiro PJ, Denison CM, et al. Large-core needle biopsy of nonpalpable breast lesions. *JAMA.* 1999;281:1638–41.
26. Moore MM, Hargett CW, 3rd, Hanks JB, Fajardo LL, Harvey JA, Frierson HF Jr, et al. Association of breast cancer with the finding of atypical ductal hyperplasia at core breast biopsy. *Ann Surg.* 1997;225:726–31; discussion 731–3.
27. Nguyen M, McCombs MM, Ghandehari S, Kim A, Wang H, Barsky SH, et al. An update on core needle biopsy for radiologically detected breast lesions. *Cancer.* 1996;78:2340–5.
28. O'Hea B, Tornos C. Mild ductal atypia after large-core needle biopsy of the breast: is surgical excision always necessary? *Surgery.* 2000;128:738–43.
29. Pandelidis S, Heiland D, Jones D, Stough K, Trapeni J, Suliman Y. Accuracy of 11-gauge vacuum-assisted core biopsy of mammographic breast lesions. *Ann Surg Oncol.* 2003;10:43–7.
30. Philpotts LE, Lee CH, Horvath LJ, Lange RC, Carter D, Tocino I. Underestimation of breast cancer with II-gauge vacuum suction biopsy. *AJR Am J Roentgenol.* 2000;175:1047–50.
31. Rosen PP. Rosen's Breast Pathology. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009.
32. Sohn V, Arthurs Z, Herbert G, Keylock J, Perry J, Eckert M, et al. Atypical ductal hyperplasia: improved accuracy with the 11-gauge vacuum-assisted versus the 14-gauge core biopsy needle. *Ann Surg Oncol.* 2007;14:2497–501.
33. Teng-Swan Ho J, Tan PH, Hee SW, Su-Lin Wong J. Underestimation of malignancy of atypical ductal hyperplasia diagnosed on 11-gauge stereotactically guided Mammotome breast biopsy: an Asian breast screen experience. *Breast.* 2008;17:401–6.
34. Tocino I GB, Carter D. Surgical biopsy findings in patients with atypical hyperplasia diagnosed by stereotaxic core needle biopsy. *Ann Surg Oncol.* 1996;3:483–8.
35. Winchester DJ, Bernstein JR, Jeske JM, Nicholson MH, Hahn EA, Goldschmidt RA, et al. Upstaging of atypical ductal hyperplasia after vacuum-assisted 11-gauge stereotactic core needle biopsy. *Arch Surg.* 2003;138:619–22; discussion 622–3.
36. Page DL, Dupont WD, Rogers LW, Rados MS. Atypical hyperplastic lesions of the female breast. A long-term follow-up study. *Cancer.* 1985;55:2698–708.
37. Page DL, Rogers LW. Combined histologic and cytologic criteria for the diagnosis of mammary atypical ductal hyperplasia. *Hum Pathol.* 1992;23:1095–7.
38. Tavassoli FA. *Pathology of the Breast.* Stamford, CT: Appleton & Lange, 1999.
39. Acheson MB, Patton RG, Howisey RL, Lane RF, Morgan A. Histologic correlation of image-guided core biopsy with excisional biopsy of nonpalpable breast lesions. *Arch Surg.* 1997;132:815–8; discussion 819–21.
40. Dahlstrom JE, Jain S, Sutton T, Sutton S. Diagnostic accuracy of stereotactic core biopsy in a mammographic breast cancer screening programme. *Histopathology.* 1996;28:421–7.
41. Dahlstrom JE, Sutton S, Jain S. Histological precision of stereotactic core biopsy in diagnosis of malignant and premalignant breast lesions. *Histopathology.* 1996;28:537–41.
42. Dershaw DD, Morris EA, Liberman L, Abramson AF. Nondiagnostic stereotaxic core breast biopsy: results of rebiopsy. *Radiology.* 1996;198:323–5.
43. Harvey JM, Sterrett GF, Frost FA. Atypical ductal hyperplasia and atypia of uncertain significance in core biopsies from mammographically detected lesions: correlation with excision diagnosis. *Pathology.* 2002;34:410–6.
44. Ioffe OB, Berg WA, Silverberg SG, Kumar D. Mammographic-histopathologic correlation of large-core needle biopsies of the breast. *Mod Pathol.* 1998;11:721–7.
45. Philpotts LE, Shaheen NA, Carter D, Lange RC, Lee CH. Comparison of rebiopsy rates after stereotactic core needle biopsy of the breast with 11-gauge vacuum suction probe versus 14-gauge needle and automatic gun. *AJR Am J Roentgenol.* 1999; 172:683–7.
46. Doren E, Hulvat M, Norton J, Rajan P, Sarker S, Aranha G, Yao K. Predicting cancer on excision of atypical ductal hyperplasia. *Am J Surg.* 2008;195:358–61; discussion 361–2.
47. Faour I, Al-Salam S, El-Terifi H, El Taji H. The use of a vacuum-assisted biopsy device (Mammotome) in the early detection of breast cancer in the United Arab Emirates. *Ann N Y Acad Sci.* 2008;1138:108–13.
48. Liberman L, Kaplan JB, Morris EA, Abramson AF, Menell JH, Dershaw DD. To excise or to sample the mammographic target: what is the goal of stereotactic 11-gauge vacuum-assisted breast biopsy? *AJR Am J Roentgenol.* 2002;179:679–83.
49. Maganini RO, Klem DA, Huston BJ, Bruner ES, Jacobs HK. Upgrade rate of core biopsy-determined atypical ductal hyperplasia by open excisional biopsy. *Am J Surg.* 2001;182:355–8.
50. Margolin FR, Kaufman L, Jacobs RP, Denny SR, Schrumpf JD. Stereotactic core breast biopsy of malignant calcifications: diagnostic yield of cores with and cores without calcifications on specimen radiographs. *Radiology.* 2004;233:251–4.
51. Plantade R, Hammou JC, Fighiera M, Aubanel D, Scotto A, Gueret S. Underestimation of breast carcinoma with 11-gauge stereotactically guided directional vacuum-assisted biopsy. *J Radiol.* 2004;85:391–401.
52. Rao A, Parker S, Ratzer E, Stephens J, Fenoglio M. Atypical ductal hyperplasia of the breast diagnosed by 11-gauge directional vacuum-assisted biopsy. *Am J Surg.* 2002;184:534–7; discussion 537.

53. Sneige N, Lim SC, Whitman GJ, Krishnamurthy S, Sahin AA, Smith TL, et al. Atypical ductal hyperplasia diagnosis by directional vacuum-assisted stereotactic biopsy of breast microcalcifications. Considerations for surgical excision. *Am J Clin Pathol.* 2003;119:248–53.
54. Travade A, Isnard A, Bouchet F, Bagard C. Non-palpable breast lesions and core needle biopsy with Mammotome 11G: is surgery required in patients with atypical ductal hyperplasia? *J Radiol.* 2006;87:307–10.
55. Zografos GC, Zagouri F, Sergentanis TN, Nonni A, Koulocheri D, Fotou M, et al. Minimizing underestimation rate of microcalcifications excised via vacuum-assisted breast biopsy: a blind study. *Breast Cancer Res Treat.* 2008;109:397–402.
56. Jackman RJ, Marzoni FA, Jr., Nowels KW. Percutaneous removal of benign mammographic lesions: comparison of automated large-core and directional vacuum-assisted stereotactic biopsy techniques. *AJR Am J Roentgenol.* 1998;171:1325–30.
57. Liberman L, Dershaw DD, Morris EA, Abramson AF, Thornton CM, Rosen PP. Clip placement after stereotactic vacuum-assisted breast biopsy. *Radiology.* 1997;205:417–22.
58. Parker SH, Klaus AJ, McWey PJ, Schilling KJ, Cupples TE, Duchesne N, et al. Sonographically guided directional vacuum-assisted breast biopsy using a handheld device. *AJR Am J Roentgenol.* 2001;177: 405–8.
59. Perez-Fuentes JA, Longobardi IR, Acosta VF, Marin CE, Liberman L. Sonographically guided directional vacuum-assisted breast biopsy: preliminary experience in Venezuela. *AJR Am J Roentgenol.* 2001;177:1459–63.
60. Houssami N, Ciatto S, Bilous M, Vezzosi V, Bianchi S. Borderline breast core needle histology: predictive values for malignancy in lesions of uncertain malignant potential (B3). *Br J Cancer.* 2007;96:1253–7.
61. Houssami N, Ciatto S, Ellis I, Ambrogetti D. Underestimation of malignancy of breast core-needle biopsy: concepts and precise overall and category-specific estimates. *Cancer.* 2007;109: 487–95.
62. Liberman L, Holland AE, Marjan D, Murray MP, Bartella L, Morris EA, et al. Underestimation of atypical ductal hyperplasia at MRI-guided 9-gauge vacuum-assisted breast biopsy. *AJR Am J Roentgenol.* 2007;188:684–90.
63. Orel SG, Rosen M, Mies C, Schnall MD. MR imaging-guided 9-gauge vacuum-assisted core-needle breast biopsy: initial experience. *Radiology.* 2006;238:54–61.
64. Stolier AJ. Stereotactic breast biopsy: a surgical series. *J Am Coll Surg.* 1997;185:224–8.
65. Wiratkapun C, Wibulpholprasert B, Lertsithichai P, Pulpinyo K, Wongwaisayawan S. Breast cancer underestimation rate of atypical ductal hyperplasia diagnosed by core-needle biopsy under imaging guidance. *J Med Assoc Thai.* 2005;88:460–6.
66. Tourasse C, Sebag P, Denier J, J, Rouyer N, Donné C. Value of stereotactic breast core biopsy in patients with atypical ductal hyperplasia. *J Radiol.* 2008;89:40–6.
67. Bonnett M, Wallis T, Rossmann M, Pernick NL, Bouwman D, Carolin KA, et al. Histopathologic analysis of atypical lesions in image-guided core breast biopsies. *Mod Pathol.* 2003;16:154–60.
68. Wagoner MJ, Laronga C, Acs G. Extent and histologic pattern of atypical ductal hyperplasia present on core needle biopsy specimens of the breast can predict ductal carcinoma in situ in subsequent excision. *Am J Clin Pathol.* 2009;131:112–21.
69. Ely KA, Carter BA, Jensen RA, Simpson JF, Page DL. Core biopsy of the breast with atypical ductal hyperplasia: a probabilistic approach to reporting. *Am J Surg Pathol.* 2001;25:1017–21.
70. Yeh IT, Dimitrov D, Otto P, Miller AR, Kahlenberg MS, Cruz A. Pathologic review of atypical hyperplasia identified by image-guided breast needle core biopsy. Correlation with excision specimen. *Arch Pathol Lab Med.* 2003;127:49–54.
71. Renshaw AA, Cartagena N, Schenkman RH, Derhagopian RP, Gould EW. Atypical ductal hyperplasia in breast core needle biopsies. Correlation of size of the lesion, complete removal of the lesion, and the incidence of carcinoma in follow-up biopsies. *Am J Clin Pathol.* 2001;116:92–6.