Hong Kong J Radiol. 2022;25:284-92 | https://doi.org/10.12809/hkjr2217345

ORIGINAL ARTICLE

Underestimation of Ductal Carcinoma In Situ and Invasive Ductal Carcinoma in Specimens Obtained with Stereotactic-Guided Vacuum-Assisted Biopsy

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ABSTRACT

Objective: *We sought to determine the underestimation rates of ductal carcinoma in situ (DCIS) and of invasive ductal carcinoma (IDC), diagnosed as atypical ductal hyperplasia (ADH) and DCIS, respectively, occurring with stereotactic-guided vacuum-assisted breast biopsy (VABB) of suspicious microcalcifications.*

Methods: *We retrospectively reviewed cases of ADH and DCIS diagnosed by stereotactic-guided VABB between 2010 and 2019 in our institution. The biopsy results were correlated with the subsequent surgical histopathology results.*

Results: *A total of 44 ADH lesions and 83 DCIS lesions were sampled with stereotactic-guided VABB during the 10-year study period. All lesions were categorised as BI-RADS (Breast Imaging Reporting and Data System) 4. Most lesions had either 6 or 12 cores taken during the biopsy. The upgrade rate of VABB-diagnosed ADH was 18.2% (7 upgraded to DCIS and 1 to IDC out of 44 VABB diagnoses of ADH), while that of VABB-diagnosed DCIS was 9.6% (8 upgraded to IDC out of the 83 biopsy-diagnosed DCIS). Amorphous calcifications in ADH lesions were associated with a lower rate of malignancy upgrade (p = 0.019). No other predictors of upgrade for either ADH or DCIS were identified. When the pathology results of specimens without visible microcalcifications were reviewed separately, we found a very low rate of upgrade in the absence of histological microcalcifications or in the presence of a benign pathologic entity.*

Conclusion: *A significant proportion of stereotactic-guided VABB-diagnosed ADH and DCIS were underdiagnosed when compared to surgical histopathology. Surgical excisional biopsy is recommended for all VABB-diagnosed ADH and DCIS lesions for definitive pathology.*

Key Words: *Breast; Carcinoma, Intraductal, Noninfiltrating; Biopsy/IS; Pathology, Surgical; Neoplasms*

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Submitted: 21 Feb 2021; Accepted: 12 May 2021.

Contributors: ALCC, KHW, KYT and PYT designed the study. ALCC and YYM acquired the data. ALCC, KHW and PYT analysed the data. ALCC drafted the manuscript. All authors critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of Interest: All authors have disclosed no conflicts of interest.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability: All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval: This study was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (Ref: 2020.441). The patients were treated in accordance with the Declaration of Helsinki. Consent regarding data retrieval was waived by the Committee.

中文摘要

用立體定向引導真空輔助活檢獲得的標本中導管原位癌和浸潤性導管癌分級的低估

陳洛之、黃健開、譚家盈、文欣欣、鄧佩儀

目的：當對於可疑微鈣化立體定向發生引導真空輔助乳房活檢（VABB）診斷非典型導管增生（ADH）和導管原位癌（DCIS）時，了解DCIS和浸潤性導管癌（IDC）分級的低估率。

方法：回顧性總結我院2010至2019年立體定向引導VABB診斷的ADH和DCIS病例。活檢結果與隨後的手術組織病理學結果相驗證。

結果：在為期十年的研究期間，使用立體定向引導的VABB對44個ADH病變和83個DCIS病變進行了採樣。所有病變都歸類為BI-RADS 4。大多數病變取了6或12個活檢核。VABB診斷ADH的升級率為18.2%（44例VABB診斷的ADH中，7例升級為DCIS，1例升級為IDC），而VABB診斷DCIS的升級率為 9.6%（83例活檢診斷的DCIS中，8例升級為IDC）。ADH病變中的無定形鈣化提示較低的惡性腫瘤升級概率（p = 0.019），並沒有發現其他影響ADH或DCIS升級的預測因素。當單獨核對沒有可見微鈣化標本的病理學結果時，在沒有組織學微鈣化或存在良性病理實體的情況下升級率非常低。

結論：與手術組織病理學相比，相當比例的立體定向引導VABB診斷的ADH和DCIS診斷不足。建議對所有VABB診斷的ADH和DCIS病變進行手術切除活檢以明確病理診斷。

INTRODUCTION

Clustered microcalcifications on mammography may be associated with underlying breast malignancy. These microcalcification clusters may be sonographically visible, especially when there is an associated mass, which enables biopsy to be performed under sonographic guidance.[1] Sonographically occult microcalcification clusters can be biopsied using stereotactically guided vacuum-assisted breast biopsy (VABB). It is a minimally invasive and cost-effective tissue sampling method, which is safely performed in an outpatient setting as part of the workup for suspicious breast lesions.

Atypical ductal hyperplasia (ADH) is associated with a high risk for breast cancer, with cytopathological appearances that resemble but fail to meet a diagnosis of low-grade ductal carcinoma in situ (DCIS).[2] It can coexist with ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC). DCIS is the direct precursor of IDC.[3] The histopathological distinction between ADH and DCIS is hampered by significant inter-observer variation, probably related to differences in the interpretation of specific histological features and diagnostic field selection.[4,5]

It is known that lesions with an initial histopathologic diagnosis of ADH or DCIS using VABB may be upgraded from ADH to DCIS or IDC, or from DCIS to IDC after surgical excision and complete histological examination. A previous study has shown the underestimation rate of 11-gauge VABB lies between 10% and 27% for ADH and 5% and 18% for DCIS.[6] Surgical excision is advocated for these lesions for definitive histopathology.[7-9]

We sought to determine the underdiagnosis rate of DCIS and IDC with stereotactic-guided VABB performed on an Asian population in the radiology department of our institution comprising two regional hospitals in Hong Kong and to identify factors associated with underdiagnosis.

METHODS

Patients

This retrospective study included 127 lesions from 126 patients from two hospitals. Institutional approval was obtained for this retrospective study. The radiology information database for cases of stereotactic-guided VABB from January 2010 to December 2019 was reviewed. Patients were referred from the breast surgical team and underwent complete diagnostic workup with mammography and breast ultrasound. Patients who had suspicious microcalcifications detected on mammogram

with no corresponding abnormalities identified on ultrasonography were recommended for stereotactic-guided VABB.

Our study included patients with ADH or DCIS diagnosed by stereotactic-guided VABB of suspicious microcalcifications, who had undergone subsequent surgical excision. Cases with no corresponding surgical histopathology correlation at sites of VABB were excluded, instead undergoing follow-up for 2 to 9 years.

Biopsy Procedure and Postprocedural Assessment

Stereotactic-guided VABBs were carried out in the prone position on a biopsy table with either a 10- or 9-gauge biopsy needle (LORAD MultiCare Stereotactic Breast Biopsy System; Hologic, Marlborough [MA], US) equipped with a 10G EnCor biopsy needle (Bard; Murray Hill [NJ], US) from 2010 to 2016 in one centre, and with the Affirm Prone Biopsy Table (Hologic) and ATEC Breast Biopsy and Excision System (Hologic) with a 9G Eviva biopsy needle (Hologic) from 2016 to 2019 in another centre. All biopsies were performed by one of the breast radiologists with 10 to 20 years of experience in our institution. During the biopsy, at least six cores were obtained by a 360-degree rotational probe, allowing sampling from different angles without repeated removal and re-insertion of the needle into the breast. Specimen radiographs were obtained to ensure adequate inclusion of the microcalcifications initially identified on mammography. The specimens were separated according to the presence or absence of microcalcifications on the radiograph (Figure), and placed into two separate formalin bottles, labelled as 'with microcalcifications' and 'without microcalcifications' from the same biopsy site.

Data Collection

Data on patients' demographics, including age of patients when the biopsy was performed, were collected (Tables 1 and 2). The suspicious microcalcifications on the preprocedural mammogram were categorised with reference to the fifth edition of the Breast Imaging Reporting and Data System (BI-RADS) developed by the American College of Radiology. Location and size of the lesions (measured as the single greatest dimension) were documented. The dates of the preprocedural mammogram, biopsy and surgery, and the time interval between the preprocedural mammogram and biopsy, and between the biopsy and surgery, were recorded. The needle size and number of cores taken during biopsy were obtained. The post-biopsy mammogram was evaluated to assess for the presence of residual calcifications. The final histopathological results of the VABB samples and subsequent surgical specimens, and the number of ADH foci in the VABB specimens were recorded. We reviewed the final histopathology of specimens with and without microcalcifications obtained during the VABB.

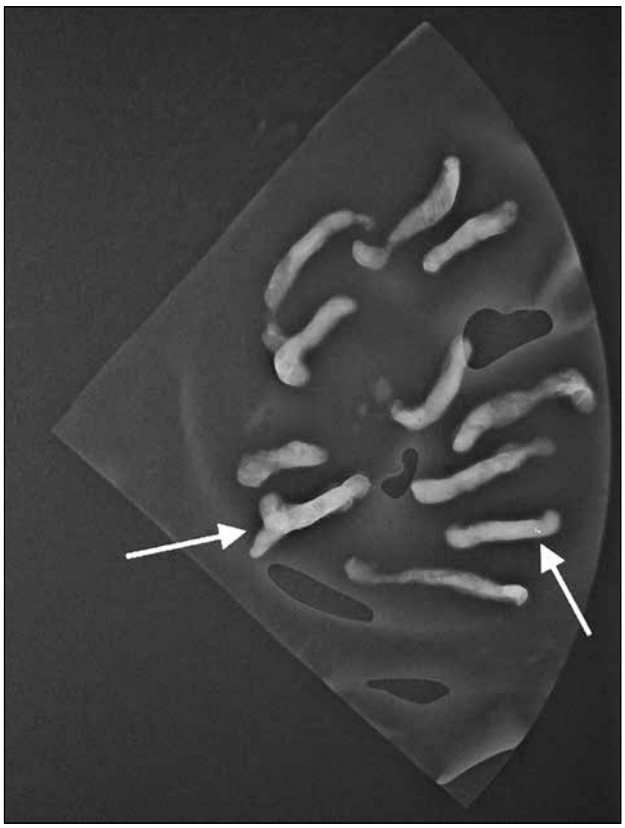

Figure. Radiograph of specimens obtained at stereotactic-guided vacuum-assisted breast biopsy showing microcalcifications (arrows). Specimens with visible microcalcifications and rest of the specimens without calcifications were placed into two separate formalin bottles.

Data Analysis

Underestimated DCIS or IDC diagnoses refer to lesions with an initial VABB diagnosis of ADH that was upgraded to DCIS or IDC, or DCIS that was upgraded to IDC, in the surgical specimen histopathology. DCIS cases with pathological evidence of microinvasion were considered invasive.

Data were analysed with SPSS (Windows version 23.0; IBM Corp, Armonk [NY], US). To identify factors that affected underestimated DCIS and IDC diagnoses, the association between categorical variables was evaluated

Table 1. Clinical, mammographic, and histological data compared with the upgrade to malignancy (n = 8) in the atypical ductal hyperplasia group (n = 44).*

Variable	No. of patients	Upgraded to malignancy	p Value
Patient age (mean = 51 y; range, 38-69)			
<50	15	3	1.000
≥50	29	5	
Laterality			
Left	22	4	1.000
Right	22	4	
Needle size			
9-gauge	24	5	1.000
10-gauge	20	3	
No. of cores taken			
6	8	2	0.581
12	31	6	
Others (range, 10-24)	5	0	
Morphology of calcifications			
Amorphous	23	1	0.019
Fine pleomorphic	21	7	
Size of microcalcifications (mean = 7.2 mm; range, 2-29)			
≤5 mm	23	3	0.324
6 mm-1 cm	9	3	
>1 cm	6	1	
Unknown	6	2	
No. of calcifications removed			
All or almost complete removal	23	3	0.432
Incomplete removal	17	4	
Unknown	4	1	
No. of atypical ductal hyperplasia foci			
<2	13	1	0.402
≥3	31	7	
Time interval between biopsy and surgery (mean = 161 d; range, 39-529)			
<90 d	16	3	1.000
≥90 d	28	5	

* Difference in morphology of calcifications was significant ($p < 0.05$).

using Fisher's exact test or the Chi-squared test. A p value <0.05 was considered significant. For specimens without microcalcifications, the positive predictive value and negative predictive value (NPV) of the presence of histological microcalcifications or pathology (ADH/DCIS) with respect to upgrade to DCIS/IDC in the surgical specimen were calculated. Missing or unknown data were excluded from statistical analysis.

RESULTS

During the 10-year study period, a total of 171 patients were diagnosed with ADH (n = 78) and DCIS (n = 93) by stereotactic-guided VABB, of which 35 patients in the ADH group and 10 patients in the DCIS group with no corresponding surgical histopathology correlation at sites of VABB were excluded. The study finally included 43 patients (mean age = 51 years; range, 38-69) with 44 lesions in the ADH group, and 83 patients (mean age = 53 years; range, 37-78) with 83 lesions in the DCIS group. One patient in the ADH group had bilateral lesions and underwent two separate biopsies.

Atypical Ductal Hyperplasia Group

Clinical, mammographic, and histological data were evaluated and correlated with the underestimation rate (Table 1).

The mean age of the patients was 51 years, with equal distribution of the lesions in the right and left breasts. The size of microcalcification clusters detected on the preprocedural mammogram ranged from 2 to 29 mm (mean = 7.2). Out of the 44 lesions, 24 were removed via 9-gauge needles, while 20 of them were removed via 10-gauge needles. Most lesions had either 6 or 12 cores taken. Some lesions had more specimens taken depending on individuals' clinical circumstances

Table 2. Clinical, mammographic, and histological data correlating with false-negative IDC (n = 8) and false-negative higher-grade DCIS (n = 6) in the DCIS group (n = 83).

Variable	No. of patients	False-negative IDC	p Value	False-negative higher-grade DCIS	p Value
Patient age (mean = 53 y; range, 37-78)					
<50	27	1	0.264	4	0.177
≥50	56	7		2	
Laterality					
Left	41	5	0.483	1	0.200
Right	42	3		5	
Needle size					
9-gauge	37	5	0.457	1	0.679
10-gauge	46	3		5	
No. of cores taken					
6	19	2	0.311	1	1.000
12	48	3		4	
Others (range, 10-34)	16	3		1	
Morphology of calcifications					
Amorphous	32	2	0.505	3	1.000
Fine pleomorphic	43	5		3	
Linear branching	6	1		0	
Unknown	2	0		0	
Size of microcalcifications (mean = 9.7 mm; range, 3-35)					
≤5 mm	23	2	0.699	2	0.916
6 mm-1 cm	33	3		2	
>1 cm	25	3		2	
Unknown	2	0		0	
Proportion of calcifications removed					
All or almost complete removal	36	3	0.415	2	0.285
Incomplete removal	23	4		1	
Unknown	24	1		3	
Grade of DCIS					
Low	10	0	0.051	3	0.346
Intermediate	26	1		3	
High	42	7		-	
Unknown	5	0		0	
Time interval between biopsy and surgery (mean = 83 d; range, 21-776)					
<90 d	66	7	1.000	5	1.000
≥90 d	17	1		1	

Abbreviations: DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma.

(i.e., when microcalcifications were note detected on the first specimen radiograph). All lesions in the ADH group were categorised as BI-RADS 4B. Some of the radiographs (including the postprocedural mammogram) were not retrievable from the system and therefore some data are missing for some patients, yet at least 52.3% (n = 23) of lesions designated as ADH by VABB were completely or almost completely removed during the procedure according to available mammography. Approximately 30% (n = 13) of these lesions contained less than two ADH foci, while the rest (70%; n = 31) had more than two foci of ADH in the specimen. All of these lesions underwent subsequent surgical excision with a mean of 161 days between VABB and surgery.

Of the 44 lesions diagnosed with ADH by VABB, the final histopathologic diagnosis was also ADH in 36. In eight lesions (18.2%), seven DCIS and one IDC were diagnosed in the subsequent surgical specimen. Apart from one case in the underestimated DCIS/IDC group presenting with unilateral amorphous microcalcifications, the other seven had presented with fine pleomorphic microcalcifications (p = 0.019). All other variables including age, laterality of the lesion, size of needle, number of cores taken, size of microcalcifications, complete versus incomplete removal of the calcifications, number of ADH foci on VABB, and the time interval between biopsy and surgery showed no significant association with the underestimated diagnosis.

As mentioned earlier, we separated the specimens (of the same biopsy site) according to presence or absence of visible calcifications. In the pathology results of those without visible calcifications, NPV was high for malignancy in the absence of microcalcifications (0.88) or when benign pathology (0.84) was found in the specimens (Table 3).

Ductal Carcinoma In Situ Group

Clinical, mammographic, and histological data were evaluated and correlated in the DCIS underdiagnosis subgroup (Table 2).

The mean age of the patients was 53 years. The size of microcalcification clusters detected on the preprocedural mammogram ranged from 3 to 35 mm (mean = 9.7). Out of the 83 lesions, 37 lesions were retrieved via 9-gauge needles and 46 lesions via 10-gauge needles.

Table 3. Analysis of the atypical ductal hyperplasia group specimens without visible calcifications (n = 44), with correlation to surgical pathological upgrade to ductal carcinoma in situ or invasive ductal carcinoma.

Adverse event	Histological microcalcifications		VABB diagnosis	
	Present	Absent	ADH	Benign diagnosis
False-negative for malignancy	5	3	4	4
Accurate diagnosis	14	22	15	21
PPV of false-negative	0.26		0.21	
NPV of false-negative	0.88		0.84	

Abbreviations: ADH = atypical ductal hyperplasia; NPV = negative predictive value; PPV = positive predictive value; VABB = vacuum-assisted breast biopsy.

Table 4. Analysis of the ductal carcinoma in situ group specimens without visible calcifications (n = 83), with correlation to surgical pathological upgrade to invasive ductal carcinoma.

Adverse event	Histological microcalcifications		VABB diagnosis	
	Present	Absent	DCIS	Benign diagnosis
False-negative for malignancy	3	5	7	1
True-positive VABB	42	33	58	17
PPV of false-negative	0.07		0.11	
NPV of false-negative	0.87		0.94	

Abbreviations: DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; NPV = negative predictive value; PPV = positive predictive value; VABB = vacuum-assisted breast biopsy.

Most lesions had either 6 or 12 cores taken. Some lesions had more specimens taken depending on individuals' clinical circumstances. Most of the lesions (n = 75) were BI-RADS 4B lesions while a small proportion (n = 6) were BI-RADS 4C lesions. At least 43.3% (n = 36) of lesions were completely or almost completely removed during the VABB. The DCIS lesions were further categorised into low- (n = 10), intermediate- (n = 26) or high-grade (n = 42) lesions according to the Van Nuys DCIS Classification. All of these lesions underwent subsequent surgical excision with a mean of 83 days between VABB and surgery.

Of the 83 lesions with the post-biopsy diagnosis of DCIS, 75 lesions had the same pathology and eight lesions had IDC revealed on the subsequent surgical specimens; hence the underdiagnosis rate of invasive carcinoma was 9.6%. No variables, including patient age, laterality of the lesion, size of needle, number of cores taken, size/morphology of microcalcifications, complete or incomplete removal of the calcifications, or the time interval between biopsy and surgery were significantly associated with IDC. Among the 75 DCIS lesions without evidence of invasion on biopsy specimens, six of them (7.2%, 6/83) were upgraded to higher DCIS grades in the subsequent surgical specimen. This included three lesions with an initial diagnosis of low-grade DCIS (2 of them upgraded to intermediate-grade and 1 to high-grade), and three lesions with intermediate-grade DCIS (upgraded to high-grade). There were again no variables significantly associated with upgrade to a higher grade of DCIS.

Similarly, we reviewed the pathology results of specimens without visible microcalcifications. There were high NPVs for pathological upgrade when no histological microcalcifications (0.87) or benign pathology (0.94) were found in the specimens (Table 4).

DISCUSSION

This study included a highly selected group of patients with ADH or DCIS diagnosed by VABB, with microcalcifications depicted by mammogram and not by ultrasound. Stereotactic-guided VABB is a minimally invasive and reliable technology for sampling of mammographic microcalcifications.[10] Underestimation of carcinoma and/or invasion associated with VABB-proven ADH and DCIS are unavoidable. In our cohort, 18.2% of patients diagnosed with ADH by VABB had malignancy found in the subsequent surgical specimen and 9.6% of patients underdiagnosed with DCIS had

Table 5. Underdiagnosis of atypical ductal hyperplasia and ductal carcinoma in situ at stereotactic vacuum-assisted breast biopsy.

Source	Needle gauge	No. (%)
Atypical ductal hyperplasia underdiagnosis		
Liberman et al, 1998[11]	11	1/10 (10.0%)
Philpotts et al, 1999[12]	11	4/15 (26.7%)
Eby et al, 2008[13]	9 or 11	26/123 (21.1%)
Forgeard et al, 2008[14]	11	29/116 (25.0%)
Ho et al, 2008[15]	11	14/61 (23.0%)
Nguyen et al, 2011[10]	9 or 11 (except 3 patients with 14-gauge)	16/121 (13.2%)
Current study	9 or 10	8/44 (18.2%)
Ductal carcinoma in situ underdiagnosis		
Liberman et al, 1998[11]	11	1/21 (4.8%)
Jackman et al, 2001[16]	11	107/953 (11.2%)
Pfarl et al, 2002[17]	11	11/91 (12.1%)
Liberman et al, 2002[18]	11	17/120 (14.2%)
Kettritz et al, 2004[19]	11	49/422 (11.6%)
Current study	9 or 10	8/83 (9.6%)

IDC. These underdiagnosis rates were similar and comparable to other studies (Table 5).[10-19]

All the specimens in this study were sampled by either 9-gauge or 10-gauge needles, and inclusion of an adequate number of microcalcifications was confirmed on specimen radiography. Lourenco et al[6] showed no significant difference between 11-gauge and 9-gauge biopsy needles in the underdiagnosis of ADH and DCIS. The use of 9- or 10-gauge biopsy needles in our study had no significant impact on the underdiagnosis rate ($p = 1.000$ and 0.679 for the ADH and DCIS groups, respectively). Most specimens had either 6 or 12 cores of tissues retrieved, equivalent to 180° and 360° of probe rotation if a specimen was taken at each clock position, respectively (the degree of probe rotation may vary with the location of the microcalcifications and operator preference). A few had >12 cores taken, mainly due to difficult localisation of the lesion or lesions with scarce microcalcifications. According to Lomoschitz et al,[20] the highest diagnostic yield was achieved with 12 specimens per lesion, although underdiagnosis still occurred with retrieval of 20 specimens per lesion. Our study demonstrated no significant correlation of the underdiagnosis rate with the number of specimens taken.

There is lack of universal consensus on predictors associated with underdiagnosis of pathology across various studies.[10] Our study demonstrates that the presence of amorphous calcifications is associated with a lower rate of malignancy underdiagnosis in ADH lesions ($p = 0.019$). Oligane et al[21] showed similar findings in stereotactic biopsy of clustered amorphous calcifications, which were rarely associated with aggressive malignancy, yet biopsy of the amorphous calcifications remained necessary, with a malignancy rate of 7%. Amorphous calcifications, however, were not a significant predictor in the DCIS underdiagnosis subgroup ($p = 0.505$) or in other similar studies.[15,22,23]

A few studies[11,24,25] have demonstrated no underdiagnoses among cases of ADH in which the entire lesion seen on mammography was removed at VABB. In our series, 23 ADH lesions with microcalcifications were completely removed during the biopsy, with three (13%) of them upgraded to DCIS on the subsequent surgical specimen. Similarly for DCIS, three out of 36 (8.3%) lesions with microcalcifications completely removed during biopsy were underdiagnosed. Our study also demonstrated that lesion size was not a significant predictor of underdiagnosis for either the ADH ($p = 0.324$) or DCIS subgroups ($p = 0.699$) [Tables 1 and 2].

The mean time intervals between VABB and surgery were 161 and 83 days for the ADH and DCIS groups, respectively. While it is logical to deduce underdiagnosis of pathology could be the result of disease progression during the lag time between biopsy and surgery, our results demonstrated no significant differences in the underdiagnosis rates related to this factor. Indeed, out of nine lesions with a final diagnosis of IDC in the DCIS group, seven of them had had surgery done within 3 months of the biopsy.

Histologically, there was no significant difference in the

underdiagnosis rate in lesions with fewer than three ADH foci (p = 0.402) compared to lesions with greater than three ADH foci. Among 13 lesions with fewer than three foci in our study, one lesion containing a focus of ADH had malignancy (intermediate-grade DCIS) detected in the surgical specimen. This finding is in contrast to that reported by Sneige et al[26]: within a cohort of 42 cases, none of the 16 patients with one or two foci of ADH was found to have DCIS or invasive cancer at surgery.

For the DCIS/IDC underdiagnosis subgroup, none of the patients with low-grade DCIS was found to have invasive cancer at surgery (n = 10), yet this was not statistically significant as a predictor (p = 0.051), and was probably related to the relatively small number of patients with low-grade DCIS compared to the number of patients with intermediate- (n = 26) and high-grade DCIS (n = 42). According to Meurs et al,[27] in a study of 2892 DCIS biopsies, the underdiagnosis rate was the lowest (15%) for low-grade DCIS compared to intermediate- (20%) and high-grade subgroups (23%) in their model, which was comparable to our findings.

We specifically analysed the pathological results for specimens without visible microcalcifications. We found high NPVs for underdiagnosis (0.84-0.94) in both ADH and DCIS groups without visible microcalcifications on mammography when no histological microcalcifications or benign pathology were found in the specimens. These results suggest that underdiagnosis is less likely under these circumstances. Nonetheless, the presence of histological microcalcifications or positive pathology (ADH/DCIS according to the group) in the specimens without visible calcifications were not useful predictors of underdiagnosis (positive predictive value = 0.07-0.26). Recent studies[22,23] have also demonstrated that analysis of specimens without microcalcifications may be beneficial in determining the likelihood of underdiagnosis. Further studies with larger cohorts to verify this hypothesis are necessary.

We identified a few weaknesses in this retrospective study. Our relatively small sample size and the retrospective nature of the study based on data, mammography, and specimen radiograph review might have influenced the statistical analysis. Some of the data and radiographs could not be retrieved, resulting in a smaller sample size for several parameters. Inter-observer variability of histopathological analysis cannot be excluded.

CONCLUSION

Our study showed that the DCIS/IDC underdiagnosis rates of ADH and DCIS diagnosed with vacuum-assisted biopsies with 9- or 10-gauge needles were 18.2% and 9.6%, respectively. Our study demonstrated that the presence of amorphous calcifications was associated with a lower rate of malignancy upgrade in ADH lesions. No other predictors of underdiagnosis for both ADH and DCIS were identified. Surgical excisional biopsy is recommended for all biopsy-proven ADH and DCIS lesions for definitive pathology.

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