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Upgrade rates of high-risk breast lesions diagnosed on core needle biopsy: a single-institution experience and literature review

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Optimal management of high-risk breast lesions detected by mammogram yielding atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar without atypia on core needle biopsy is controversial. This is a single-institution retrospective review of 5750 core needle biopsy cases seen over 14.5 years, including 249 (4.3%), 72 (1.3%), 50 (0.9%), 37 (0.6%), and 54 (0.9%) cases of atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar without atypia, respectively. Patient age, radiologic characteristics, needle gauge, and excision diagnoses were recorded. Of 462 high-risk cases analyzed, 333 (72%) underwent excision. Upgrade rate to ductal carcinoma *in situ*, pleomorphic carcinoma *in situ*, or invasive mammary carcinoma was 18% for atypical ductal hyperplasia, 11% for flat epithelial atypia, 9% for atypical lobular hyperplasia, 28% for lobular carcinoma *in situ*, and 16% for radial scar. Carcinoma diagnosed on excision was more likely to be *in situ* than invasive, and if invasive, more likely to be low grade than high grade. Overall, cases that were benign (*vs* high risk or carcinoma) on excision were less likely to have residual calcifications after biopsy (17% *vs* 27%, $P = 0.013$), and more likely to have a smaller mass size (< 1 cm) (82% *vs* 50%, $P = 0.001$). On subgroup analysis, atypical ductal hyperplasia cases that were benign (*vs* high risk or carcinoma) on excision were more likely to have smaller mass size (< 1 cm) ($P = 0.025$). Lobular neoplasia diagnosed incidentally (*vs* targeted) on core needle biopsy was less likely to upgrade on excision (5% *vs* 39%, $P = 0.002$). A comprehensive literature review was performed, identifying 116 studies reporting high-risk lesion upgrade rates, and our upgrade rates were similar to those of more recent larger studies. Careful radiological–pathological correlation is needed to identify high-risk lesion subgroups that may not need excision.
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To excise or not to excise is the question posed when certain non-malignant but high-risk breast lesions are diagnosed on core needle biopsy after imaging detection. The appropriate post-core needle biopsy management of these lesions causes debate, with a variety of practices including surgical excision, close-clinical follow-up with short-term repeated imaging and possible consideration for risk-reducing medication. Currently, high-risk lesions are diagnosed in fewer than 9% of core needle biopsy cases, but volumes will likely increase as advances in breast imaging techniques increase lesion detection.[1–4]

Core needle biopsy diagnoses such as atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar are some the non-malignant lesions that are considered high risk for carcinoma. Patients with radial scar and atypical ductal hyperplasia were found to have a two-fold and up to five-fold increased risk of breast cancer over the general population, respectively.[5–7] Increased risk of ipsilateral breast cancer was seen in patients with atypical lobular hyperplasia and lobular carcinoma *in situ*.[8] And histologic and genetic similarities have been described between flat epithelial atypia and carcinoma.[9–11]

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Notably, these high-risk lesions are not only markers of future carcinoma, but also indicators of concurrent carcinoma missed due to biopsy sampling. Upgrade rates to ductal carcinoma *in situ* or invasive carcinoma from core needle biopsy to excision in the literature range from 0 to 62% for atypical ductal hyperplasia, 0 to 21% for flat epithelial atypia, 0 to 67% for atypical lobular hyperplasia, 0 to 60% for lobular carcinoma *in situ*, and 0 to 16% for radial scar.[12–21] Given these data, it is not surprising that the management of high-risk breast lesions seen on core needle biopsy is controversial. More defined upgrade rate data are needed and may prevent over- and undertreatment.

The present study evaluates excision results for patients with non-malignant high-risk lesions, including atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar without atypia diagnosed on core needle biopsy at our institution. Additionally, we investigate the predictive role of clinicopathological features including patient age, Breast Imaging Reporting and Data System (BI-RADS) score, calcification span, mass size, and needle gauge on management and excision diagnosis. This is one of the largest studies elaborating on variables that predict benign diagnosis on excision, in addition to establishing baseline upgrade rates. We subsequently present the most comprehensive literature review to date, and conclude with a summary of our statistically significant findings with recommendations, providing a reference for the management of high-risk breast lesions diagnosed on core needle biopsy.

Materials and methods

After obtaining IRB approval, our pathology database was searched using the terms atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar on breast core needle biopsy cases from 1 January 2003 to 30 June 2014. Both imaging-targeted lesions and incidental pathologic findings were included. Radiologists at our institution used smaller 11- to 14-gauge needles from 2003 through 2005, and then larger 9-gauge needles were introduced and used almost consistently after 2007. Over the duration of the study, four subspecialized breast pathologists classified cases. Original slides were not re-reviewed for the purposes of this study. However, per institutional quality assurance policy, every breast core needle biopsy case was reviewed by a second pathologist within 1 week of original sign out. In addition, diagnoses were confirmed by a second pathologist during tumor board for excisional biopsy cases upgraded to ductal carcinoma *in situ* and/or invasive carcinoma.

For analysis, cases were assigned to appropriate high-risk entity categories (Figure 1). We excluded atypical ductal hyperplasia bordering on ductal carcinoma *in situ*, pleomorphic lobular carcinoma *in situ*, other variants of lobular carcinoma *in situ* such as florid/distended lobular carcinoma *in situ* with central necrosis, and radial scar associated with any type of epithelial atypia. Core needle biopsy cases with juxtaposed known synchronous ipsilateral breast carcinoma were also excluded. For flat epithelial atypia, cases from 2003 diagnosed using historical names such as 'columnar cell change with atypia', 'columnar cell hyperplasia with atypia', or 'columnar alteration with prominent apical snouts and secretions' were included. Only pure flat epithelial atypia cases were included in the flat epithelial atypia category for this study. If flat epithelial atypia was seen with lobular neoplasia, we tabulated the case under either atypical lobular hyperplasia or lobular carcinoma *in situ*. If flat epithelial atypia was seen with atypical ductal hyperplasia, then we tabulated the case under atypical ductal hyperplasia. Cases with focal and incidental lobular neoplasia seen with atypical ductal hyperplasia were included in the atypical ductal hyperplasia analysis. Other mixed atypical lesions were excluded.

From the electronic medical record, clinical and radiologic data for core needle biopsy cases were recorded, including patient age, Breast Imaging Reporting and Data System (BI-RADS) score, imaging findings (ie mass or calcification), calcification span, mass size, whether or not residual calcifications were noted after core needle biopsy, and needle gauge. Only cases with radiographic findings were included in this study. During the 14.5 year duration of the study, all cases were reviewed during weekly radiology–pathology concordance conferences. Electronic record review of radiology–pathology concordance comments revealed $<1\%$ (3 of 462) cases were disconcordant. All three cases with histologic findings not explained by imaging findings were diagnosed as radial scar on biopsy, and two of the three cases went to excision while the third was lost to follow-up.

Our current institution guidelines include recommendation for excision in the setting of atypical ductal hyperplasia, lobular carcinoma *in situ*, atypical lobular hyperplasia, flat epithelial atypia, and radial scar. More recently, recommendations for excision or surveillance were made on a case-by-case basis after radiology–pathology correlation conference and with patient input.

For the analysis, upgrades were defined as ductal carcinoma *in situ*, pleomorphic lobular carcinoma *in situ*, and invasive mammary carcinoma on excision. Residual high-risk lesions such as atypical ductal hyperplasia, lobular carcinoma *in situ*, atypical lobular hyperplasia, and flat epithelial atypia on excision were not included as upgrades.

For categorical variables, statistical comparisons between groups were made using χ^2 or Fisher's exact test, where appropriate. For normally distributed

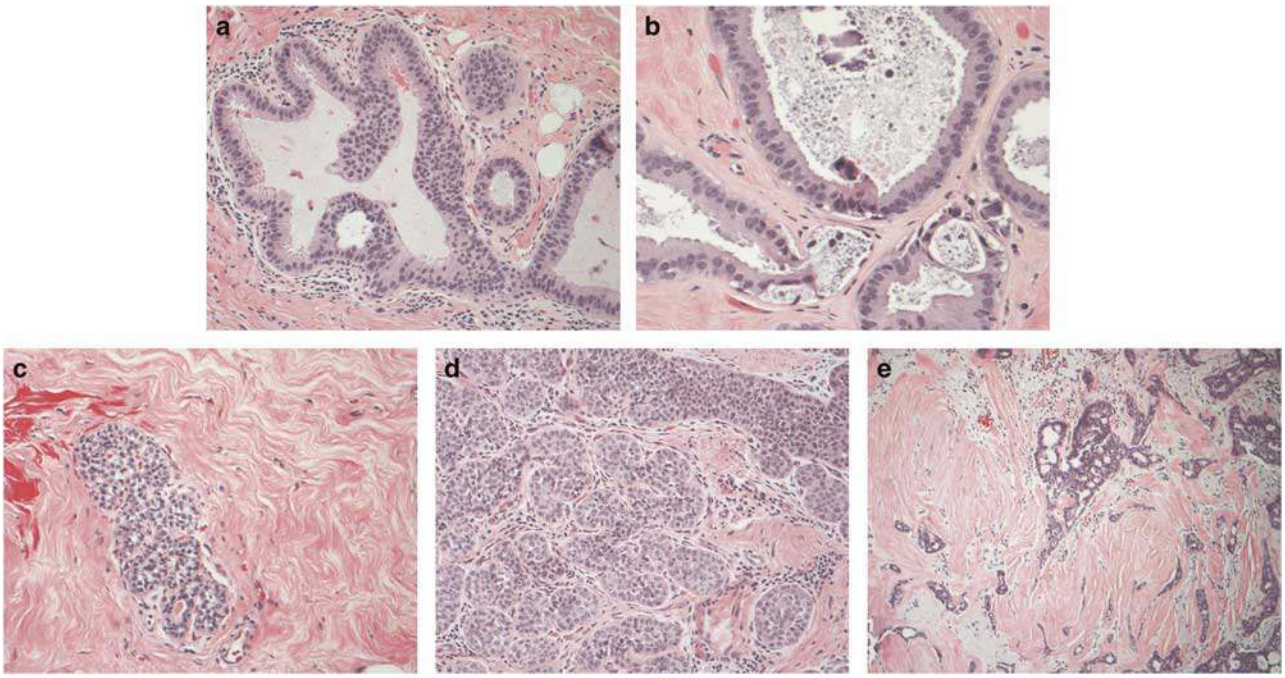

Figure 1 High-risk breast lesions. (**a**) Atypical ductal hyperplasia with low-grade nuclear atypia demonstrating 'roman bridge' and micropapillary architectural complexities. (**b**) Flat epithelial atypia, often detected due to luminal microcalcifications, consists of a monolayer of cytologically low-grade columnar-shaped cells with luminal 'tomb-stone' snouts lining a distended duct. (**c**) Atypical lobular hyperplasia consisting of uniform, dishesive small cells. (**d**) Lobular carcinoma *in situ* with small dishesive cells filling and expanding ductules. (**e**) Radial scar is a stellate lesion with a central elastic stroma and ducts radiating out, entrapped in a background of fibroelastosis, often mimicking a low-grade invasive ductal carcinoma, as seen on this core needle biopsy. (**a**, **c**, **e**: hematoxylin and eosin ×20; **b**, **d**: hematoxylin and eosin ×40)

continuous variables, comparisons were made using *t*-test. Multivariate analysis was conducted using stepwise logistic regression. All tests of significance were two-tailed, and significance was set at $P < 0.05$. Statistical analysis was performed with SPSS statistical software (Statistical Package for the Social Sciences, IBM Corp., Version 22.0, Armonk, NY, USA).

Results

Over 14.5 years, 5750 core needle biopsy cases were collected, including 2589 stereotactic, 2913 ultrasound-guided, and 248 MRI-guided biopsies. A total of 462 (8%) high-risk breast lesion core needle biopsy cases were identified, including 249 (4.3%) atypical ductal hyperplasia, 72 (1.3%) flat epithelial atypia, 50 (0.9%) atypical lobular hyperplasia, 37 (0.6%) lobular carcinoma *in situ*, and 54 (0.9%) radial scar. The average patient age in years at index diagnosis was 55.0 for atypical ductal hyperplasia, 52.2 for flat epithelial atypia, 52.6 for atypical lobular hyperplasia, 54.2 for lobular carcinoma *in situ*, and 53.2 for radial scar.

Excision results were available for 333 cases, including 78, 77, 76, 64, and 46% of lobular carcinoma *in situ*, atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia and radial scar cases, respectively (Table 1). No excision results were available for 129 cases, including 22, 23, 24, 36, and 54% of lobular carcinoma *in situ*, atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, and radial scar cases, respectively. Of 129 cases that did not undergo excision, 67 (52%) were lost to follow-up, while 62 (48%) were not excised for other reasons. Many cases lost to follow-up either had no further documentation in the medical record after the biopsy of interest, or had subsequent major illness diagnosed or emergency department visit documented. Cases with no excision that were not lost to follow-up had imaging follow-up at 6 months or later describing no progression of the targeted lesion of concern. Nine of 62 (15%) of no excision cases had surgeon documentation of patient decision to not proceed with excision.

Follow-up results were further analyzed by entity. Of 57 atypical ductal hyperplasia cases that were not excised, 34 (61%) were lost to follow-up, while 23 (40%) were not excised, including 14 cases with imaging follow-up, 7 cases not excised due to patient input, and 2 cases treated with risk-reducing medication. Of 17 flat epithelial atypia cases that were not excised, 8 (47%) were lost to follow-up, while 9 (53%) were not excised including 8 cases with imaging follow-up and 1 case not excised due to patient input. Of 18 atypical lobular hyperplasia

Table 1 Management and excision outcomes of high-risk lesions diagnosed on CNB

CNB	*Incidence (n = 5750)*	*No excision*	*Excision*	*Excision findings*				
				Benign	*High risk*		*Upgrade*	
ADH ($n = 249$)	4.3%	57/249 (23%)	192/249 (77%)	51/192 (26%)	106/192 (55%)	84 ADH 13 LN 8 FEA 1 RS	35/192 (18%)	29 DCIS 6 IDC
FEA ($n = 72$)	1.3%	17/72 (24%)	55/72 (76%)	20/55 (36%)	29/55 (53%)	18 FEA 11 ADH	6/55 (11%)	3 DCIS 2 IDC 1 ITC
ALH ($n = 50$)	0.9%	18/50 (36%)	32/50 (64%)	7/32 (22%)	22/32 (69%)	10 ALH 7 LCIS 3 ADH 2 FEA	3/32 (9%)	2 DCIS 1 ILC
LCIS ($n = 37$)	0.6%	8/37 (22%)	29/37 (78%)	4/29 (14%)	17/29 (59%)	11 LCIS 4 ADH 2 ALH	8/29 (28%)	5 DCIS 1 ILC 1IDC 1 PLCIS
RS ($n = 54$)	0.9%	29/54 (54%)	25/54 (46%)	16/25 (64%)	5/25 (20%)	2 ADH 2 ALH 1 RS	4/25 (16%)	3 DCIS 1 ILC
Cumulative ($n = 462$)	8.0%	129/462 (28%)	333/462 (72%)	98/333 (29%)	179/333 (54%)	104 ADH 45 LN 28 FEA 2 RS	56/333 (17%)	42 DCIS 9 IDC 3 ILC 1 PLCIS 1 ITC

Abbreviations: ADH, atypical ductal hyperplasia; ALH, atypical ductal hyperplasia; CNB, core needle biopsy; DCIS, ductal carcinoma *in situ*; FEA, flat epithelial atypia; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ITC, isolated tumor cells; LCIS, lobular carcinoma *in situ*; LN, lobular neoplasia; PLCIS, pleomorphic lobular carcinoma *in situ*; RS, radial scar.

Table 2 Characteristics of invasive tumors seen on excision of high-risk lesions diagnosed on CNB

CNB	*Excision*	*Grade*	*ER*	*PR*	*HER2 IHC*	*HER2 FISH*	*Ki67 (%)*
ADH	IDC	2	+	+	−	−	10
ADH	IDC	2	+	+	−	−	25
ADH	IDC	2	+	+	−	−	20
ADH	IDC	2	+	+	−	−	20
ADH	IDC	2	+	+	−	−	5
ADH	IDC	2	+	+	−	−	10
FEA	IDC	2	+	+	−	−	5
FEA	IDC	1	+	−	−	−	< 5
LCIS	IDC	3	−	−	+	+	75
ADH	ILC	1	+	−	−	+	< 5
ALH	ILC	1	+	+	−	−	< 5
RS	ILC	1	+	−	−	+	5

Abbreviations: ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; CNB, core needle biopsy; ER, estrogen receptor; FEA, flat epithelial atypia; FISH, fluorescent *in situ* hybridization; HER2, human epidermal growth factor receptor 2 protein; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LCIS, lobular carcinoma *in situ*; PR, progesterone receptor; RS, radial scar; −, negative; +, positive.

cases that were not excised, 7 (39%) were lost to follow-up, while 11 (61%) were not excised including 10 cases with imaging follow-up and 1 case not excised due to patient input. Of eight lobular carcinoma *in situ* cases that were not excised, 6 (75%) were lost to follow-up, while 2 (25%) were not excised, but had imaging follow-up. Finally, of 29 radial scar cases that did not undergo excision, 12 (41%) were lost to follow-up, while 17 (58%) had documentation of recommendation for imaging surveillance (specifically 6-month follow-up) after radiology-pathology consensus conference.

Univariate analysis was performed overall and by entity to assess for differences between the lost to follow-up and no excision groups and yielded no significant differences in patient age and radiographic features, including needle gauge, BI-RADS score, calcification *vs* mass targeting and lesion size; however, our analysis is limited by low case numbers.

Of 333 excision cases, the diagnosis was benign in 98 (29%), residual high risk in 179 (54%), and upgraded to carcinoma in 56 (17%) (Table 1). Upgraded cases included 42 ductal carcinoma *in situ*, 9 invasive ductal carcinoma, 3 invasive lobular carcinoma, 1 pleomorphic lobular carcinoma *in situ*, and 1 isolated tumor cells. Most invasive tumors had low to intermediate modified Bloom and Richardson grade and scores, estrogen receptor (ER) positive, progesterone receptor (PR) positive, and human epidermal growth factor receptor 2 (HER2) protein negative by immunohistochemistry and/or fluorescent *in situ* hybridization with low proliferation indices (Table 2). By entity, the upgrade rate was 18% (35/192) for atypical ductal hyperplasia, 11% (6/55) for flat epithelial atypia, 9% (3/32) for atypical lobular hyperplasia, 28% (8/29) for lobular carcinoma *in situ*, and 16% (4/25) for radial scar.

Table 3 Comparison of cases based on excision status and excision diagnosis

	Excision, n = *333,* n *(%)*	*No excision,* n = *129,* n *(%)*	P-*value*	*Upgrade,* n = *56,* n *(%)*	*No upgrade,* n = *277,* n *(%)*	P-*value*	*Benign,* n = *98,* n *(%)*	*Not benign,* n = *235,* n *(%)*	P-*value*
CNB dx									
ADH	192 (58%)	57 (44%)	< 0.001[a]	35 (63%)	157 (56%)	0.242	51 (52%)	141 (60%)	< 0.001[a]
ALH	32 (10%)	18 (14%)		3 (4%)	29 (11%)		7 (7%)	25 (11%)	
FEA	55 (17%)	17 (13%)		6 (11%)	49 (18%)		20 (20%)	35 (15%)	
LCIS	29 (9%)	8 (6%)		8 (14%)	21 (8%)		4 (4%)	25 (11%)	
RS	25 (8%)	29 (22%)		4 (7%)	21 (8%)		16 (16%)	9 (4%)	
Age (years)			0.140						
< 50	142 (43%)	45 (35%)		26 (46%)	116 (42%)	0.464	42 (43%)	100 (43%)	0.904
≥ 50	191 (57%)	84 (65%)		30 (54%)	161 (58%)		56 (57%)	135 (58%)	
BI-RADS			0.219						
< 4B	130 (39%)	61 (47%)		21 (38%)	109 (39%)	0.908	44 (45%)	86 (58%)	0.120
≥ 4B	190 (57%)	62 (48%)		33 (59%)	156 (57%)		53 (54%)	136 (58%)	
Calc targeting			0.072						
No	75 (23%)	40 (31%)		16 (29%)	59 (21%)	0.297	29 (30%)	46 (20%)	0.062
Yes	258 (77%)	89 (69%)		40 (71%)	218 (79%)		69 (70%)	189 (80%)	
Residual calc			0.122						
No	52 (20%)	13 (15%)		5 (13%)	46 (21%)	0.284	9 (13%)	42 (22%)	0.013[b]
Yes	64 (25%)	22 (25%)		15 (38%)	49 (22%)		12 (17%)	52 (27%)	
Mass targeting			0.106						
No	266 (80%)	94 (73%)		43 (77%)	223 (80%)	0.588	75 (77%)	191 (81%)	0.372
Yes	67 (20%)	35 (25%)		13 (23%)	54 (20%)		23 (24%)	44 (19%)	
Mass size (cm)			0.274						
< 1	41 (61%)	23 (65%)		6 (46%)	35 (67%)	0.359	19 (82%)	22 (50%)	0.001[b]
≥ 1	26 (55%)	12 (34%)		7 (54%)	19 (35%)		4 (17%)	22 (50%)	
Needle gauge			0.685						
9G	275 (83%)	104 (81%)		46 (82%)	229 (83%)	1.000	81 (83%)	194 (83%)	1.000
11G-14G	58 (17%)	25 (19%)		10 (18%)	48 (17%)		17 (17%)	41 (18%)	

Abbreviations: ADH, atypical ductal hyperplasia; ALH, atypical ductal hyperplasia; BI-RADS, Breast Imaging Reporting and Data System score; Calc, calcifications; CNB, core needle biopsy; dx, diagnosis; FEA, flat epithelial atypia; LCIS, lobular carcinoma in situ; RS, radial scar.
Note: Percentage sums may not equal 100% due to incompletely available data. Mass size and residual calcification reported as percent of total cases with mass and calcification targeting, respectively.
[a]Compared to ADH, lesions diagnosed as RS on CNB were less likely to be excised (OR = 0.26, $P < 0.0001$, CI = 0.14–0.47) and less likely to high risk or carcinoma on excision (OR = 0.29, $P = 0.014$, CI = 0.11–0.77) on multivariate logistic regression analysis.
[b]On *post hoc* subgroup analysis, ADH seen in CNB cases targeting smaller masses (< 1 cm) were more likely to be benign (*vs* not benign) (80% *vs* 42%, $P = 0.025$). No other differences within other CNB entity subgroups were significant.

Univariate analysis was utilized to elaborate on differences in age and radiological features based on excision status (excision *vs* no excision) for the 462 high-risk lesion cases, and excision diagnosis (upgrade *vs* no upgrade, and benign *vs* not benign) for the 333 cases that went to excision (Table 3).

Core needle biopsy diagnosis was the only significantly different variable between patients who received excision and patients with no excision ($P < 0.001$) (Table 3, left). On multivariable logistic regression analysis, compared with atypical ductal hyperplasia, lesions diagnosed as radial scar on core needle biopsy were less likely to be excised (OR = 0.26, $P < 0.0001$, CI = 0.14–0.47). A trend towards younger patients (< 50 years old) with more concerning imaging (BI-RADS score ≥ 4B) and targeting of calcifications or larger masses (≥1 cm), with residual calcifications after biopsy was noted among cases that went to excision. However, patient age, BI-RADS score, calcification targeting, mass targeting, and needle gauge were not statistically significant predictors of surgical management (excision *vs* no excision). Variables with excessive missing values (calcification span, residual calcification on mammogram post-core needle biopsy, and mass size) were excluded from regression models.

Comparing upgrade *vs* no upgrade (high-risk or benign) groups yielded no significantly different variables (Table 3, middle). A trend towards larger mass size (≥1 cm) and presence of residual calcification was appreciated among upgraded cases. BI-RADS scores and patient age were similar between the upgrade and no upgrade groups.

The data were reorganized to evaluate differences between benign *vs* not benign (high risk or upgrade) groups (Table 3, right). Based on logistic regression

Table 4 Incidental lobular neoplasia is less likely to upgrade on excision

	Incidental (n = *38*)	*Targeted* (n = *23*)	P-*value*
Upgrade	2 (5%)	9 (39%)	0.002
No upgrade	36 (95%)	14 (60%)	

modeling, radial scar was less likely (*vs* atypical ductal hyperplasia) to be high risk or carcinoma on excision (OR = 0.29, $P = 0.014$, CI = 0.11–0.77). Cases that were not benign on excision (*vs* benign) were more likely to have residual calcifications (27% *vs* 17%, $P = 0.013$), and mass size greater than 1 cm (50% *vs* 17%, $P = 0.001$). On *post hoc* subgroup analysis, atypical ductal hyperplasia cases that were high risk or upgrade (*vs* benign) on excision were more likely to have larger masses (≥1 cm) ($P = 0.025$). No other significant difference was found between benign and not benign groups within the separate atypical ductal hyperplasia, flat epithelial atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, or radial scar subgroups on *post hoc* subgroup analysis. However, among cases that were benign on excision, there was a trend towards lower BI-RADS scores (< 4B), smaller mass sizes (< 1 cm), and no targeting of calcifications or residual calcifications.

Of note, the upgrade rate was highest for lobular carcinoma *in situ* (28%), but this rate decreased to 7% (1/14) for incidental lobular carcinoma *in situ*, and lobular neoplasia (lobular carcinoma *in situ* or atypical lobular hyperplasia) diagnosed incidentally (*vs* targeted) on core needle biopsy was significantly less likely to upgrade on excision (5% *vs* 39%, $P = 0.002$) (Table 4).

Discussion

Optimal management for high-risk breast lesions diagnosed on core needle biopsy remains controversial. Institutional differences in excision rates underscore the lack of consensus.[22–24] The wide range of published upgrade rates to ductal carcinoma *in situ* and/or invasive mammary carcinoma on excision partly contributes to the problem. Here we present the most comprehensive literature review of reported upgrade rates for atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma *in situ*, flat epithelial atypia, and radial scar, along with a summary of the key findings from our statistical analysis with management recommendations (Tables 5–8).

The estimated rate of atypical ductal hyperplasia diagnosis on core needle biopsy has been reported at 3%, and atypical ductal hyperplasia was diagnosed in 4.3% of core needle biopsy cases at our institution.[25] On literature review, 23% of atypical ductal hyperplasia cases were upgraded on average, with a range of 0–62% (Table 5).[12,13,17,19,22,24,26–60] In our study, the upgrade rate for patients with atypical ductal hyperplasia diagnosis on core needle biopsy was 18%. No significant decrease in frequency of upgrade for atypical ductal hyperplasia was seen when a larger needle was used for biopsy. Consistent with published findings, atypical ductal hyperplasia lesions associated with a smaller targeted mass (< 1 cm) in our study were statistically more likely to be benign on excision.[34] However, 17% (4/23) of atypical ductal hyperplasia core needle biopsy cases involving targeting of smaller masses (< 1 cm) still upgraded to carcinoma. In agreement with generally accepted practice guidelines, we conclude that atypical ductal hyperplasia seen on core needle biopsy merits surgical excision.

The estimated rates of lobular neoplasia diagnosis on core needle biopsy have been reported at approximately 1%.[25] Our institutional diagnosis rate was 0.9% for atypical lobular hyperplasia and 0.6% for lobular carcinoma *in situ*. Literature review yielded a 9% mean upgrade rate for atypical lobular hyperplasia (range 0–67%), and an 18% mean upgrade rate for lobular carcinoma *in situ* (range 0–60%) (Table 6).[13,14,18,19,21,28,61–83] At our institution, the upgrade rate for atypical lobular hyperplasia was 9%, and the upgrade rate for lobular carcinoma *in situ* was 24%. Recent studies examining incidentally diagnosed lobular neoplasia reported rates below 2%.[78,82] In agreement with these findings, radiology–pathology correlation analysis of our excised lobular neoplasia cases revealed that incidental atypical lobular hyperplasia and lobular carcinoma *in situ* had an upgrade rate of 5%, significantly lower than the 39% upgrade rate for targeted lobular neoplasia ($P = 0.002$). Larger needle size in the setting of lobular neoplasia did not decrease upgrade frequency. Similar to the National Comprehensive Cancer Network 2015 Guidelines, we support surgical excision when atypical lobular hyperplasia and lobular carcinoma *in situ* are diagnosed on core needle biopsy.[84]

In our study, the rate of pure flat epithelial atypia diagnosis on core needle biopsy was 1.3% with an upgrade rate of 11%. On literature review, approximately 8% of pure flat epithelial atypia diagnosed on core needle biopsy was upgraded to carcinoma, with a range of 0–21% (Table 7).[19,20,22,24,30,85–104] In our study, no statistically significant radiologic differences were seen between upgraded and not upgraded flat epithelial atypia core needle biopsy groups; however, residual calcification after biopsy was associated with upgrade. For pure flat epithelial atypia, as stated in the World Health Organization Working Group, careful radiological–pathological correlation is necessary, and in the absence of residual calcifications or other indications for excision, surveillance may be acceptable.[105]

The estimated rate of radial scar diagnosis on core needle biopsy has been reported at 1–2%, and our rate was 0.9%.[25] On literature review, a 7% average

Table 5 Literature review of upgrade rates of ADH diagnosed on CNB

	Upgrade rate (%)	*Excision* (n)	*Upgrade* (n)	*DCIS* (n)	*IMC* (n)
Menes *et al*	18	685	123	101	22
Bianchi *et al*	27	275	75	NR	NR
Saladin *et al*	26	266	69	NR	NR
Rakha *et al*	51	261	133	95	38
Khoury *et al*	28	203	57	47	10
Wagoner *et al*	18	123	22	22	0
Nguyen *et al*	13	121	16	14	2
Forgeard *et al*	25	116	29	26	3
McGhan *et al*	18	114	20	15	5
Eby *et al*	17	105	18	14	4
Kohr *et al*	20	101	20	17	3
McLaughlin *et al*	13	101	13	11	2
Khoury *et al*	15	100	15	12	3
Bonnett *et al*	9	90	8	NR	NR
Darling *et al*	19	86	16	11	5
Sohn *et al*	18	78	14	9	5
Ko *et al*	46	74	34	23	11
Lourenco *et al*	29	73	21	18	3
Allison *et al*	11	72	8	5	3
Winchester *et al*	17	65	11	6	5
Andrales *et al*	15	62	9	7	2
Teng-Swan *et al*	23	61	14	14	0
Doren *et al*	33	51	17	9	8
Ely *et al*	36	47	17	15	2
Burak *et al*	13	46	6	2	4
Mesurolle *et al*	62	45	28	13	15
Arpino *et al*	29	45	13	11	2
Chae *et al*	22	45	10	8	2
Sneige *et al*	7	42	3	3	0
Lee *et al*	32	41	13	7	6
Liberman *et al*	54	37	20	13	7
Plantade *et al*	27	37	10	7	3
Pandelidis *et al*	14	37	5	4	1
Yeh *et al*	8	36	3	NR	NR
Maganini *et al*	13	32	4	3	4
Travade *et al*	19	31	6	NR	NR
Philpotts *et al*	23	26	6	5	1
Lourenco *et al*	32	19	6	4	2
Bedei *et al*	12	17	2	2	0
Brem *et al*	25	16	4	2	2
Burbank *et al*	0	8	0	0	0
Our data	18	192	35	29	6
Mean	23				

Abbreviations: ADH, atypical ductal hyperplasia; CNB, core needle biopsy; DCIS, ductal carcinoma in situ; IMC, invasive mammary carcinoma; NR, not reported.

upgrade rate was reported with a range of 0–16% when radial scar was diagnosed on core needle biopsy (Table 8).[2,3,15,16,19,23,24,44,106–118] Our institutional upgrade rate of 16% was higher than the reported average, likely due to our small case volume ($n = 25$). No statistically significant radiologic differences were seen between upgraded and not upgraded radial scar core needle biopsy groups in our study. Previous research has shown that incidental and small radial scar lesions (< 5 mm) were less likely to be upgraded on excision.[16,110,115] There is no consensus for the management of radial scar without atypia. It may be prudent to recommend conservative excision for radial scar without atypia with radial scar size greater > 5 mm. After careful radiological–pathological correlation, watchful surveillance may be acceptable for incidental and small radial scar seen on core needle biopsy. Radial scar with atypia should be excised.

With the exception of mass size ≥ 1 cm for atypical ductal hyperplasia, no other variables, including BI-RADS score, target lesion (mass *vs* calcification), mass size, calcification span, needle gauge, or residual calcification seen on mammogram post-core needle biopsy were predictive of upgrade to carcinoma excision for any other entity in our study. However, our analysis carries biases inherent to retrospective reviews, including insufficient case numbers to power statistical regression analysis, and incompletely available data. Heterogeneity in study design, including variations in size, inclusion and exclusion criteria, imaging modality, biopsy

Table 6 Literature review of upgrade rates of lobular neoplasia diagnosed on CNB

	ALH						*LCIS*				
	Upgrade rate (%)	*Excision* (n)	*Upgrade* (n)	*DCIS* (n)	*IMC* (n)		*Upgrade rate (%)*	*Excision* (n)	*Upgrade* (n)	*DCIS* (n)	*IMC* (n)
Zhao *et al*	3	163	5	4	1	Neill *et al*	4	104	4	1	4
Brem *et al*	22	97	21	15	6	Zhao *et al*	8	74	6	3	3
Shah-Khan *et al*	1	81	1	1	0	Brem *et al*	25	67	17	7	10
Subhawong *et al*	0	56	0	0	0	Destounis *et al*	33	63	21	14	7
Karabakhtsian *et al*	10	52	5	3	2	D'Alfonoso *et al*	8	61	5	1	4
Hwang *et al*	2	48	1	1	0	Renshaw *et al*	4	52	2	1	1
Rendi *et al*	4	48	2	NR	NR	Gao *et al*	16	49	8	4	4
Renshaw *et al*	3	40	1	0	1	Ibrahim *et al*	39	49	19	8	11
Ibrahim *et al*	28	40	11	7	4	Hwang *et al*	15	39	6	2	4
Rakha *et al*	24	33	8	3	5	Heller *et al*	27	30	8	4	4
Neill *et al*	9	22	2	2	0	Karabakhtsian *et al*	20	25	5	2	3
Foster *et al*	10	20	2	2	0	Cangiarrella *et al*	10	20	2	1	1
Elsheikh *et al*	25	20	5	4	1	Londero *et al*	60	20	12	5	7
Sohn *et al*	0	19	0	0	0	Rakha *et al*	15	20	3	1	2
Cangiarrella *et al*	6	18	1	0	1	Rendi *et al*	5	20	1	NR	NR
Arpino *et al*	6	17	1	1	0	Shah-Khan *et al*	5	20	1	0	1
Allen *et al*	19	16	3	0	3	Khoury *et al*	29	17	5	1	4
Mahoney *et al*	7	15	1	0	1	Foster *et al*	27	15	4	2	2
Heller *et al*	13	15	2	0	2	O'Neil *et al*	29	14	4	1	3
O'Neil *et al*	8	13	1	0	1	Crisi *et al*	15	13	2	0	2
Khoury *et al*	25	12	3	2	1	Subhawong *et al*	33	12	4	1	3
Londero *et al*	13	8	1	1	0	Elsheikh *et al*	27	11	3	0	3
Middleton *et al*	67	6	4	0	4	Mahoney *et al*	40	10	4	2	2
Shin *et al*	0	5	0	0	0	Middleton *et al*	22	9	2	0	2
Crisi *et al*	0	3	0	0	0	Shin *et al*	13	8	1	1	1
Our data	9	32	3	2	1	Liberman *et al*	0	5	0	0	0
						Arpino *et al*	50	4	2	0	2
						Sohn *et al*	0	2	0	0	0
						Our data	24	29	7	5	2
Mean	9					Mean	18				

Abbreviations: ALH, lobular carcinoma *in situ*; CNB, core needle biopsy; DCIS, ductal carcinoma *in situ*; IMC, invasive mammary carcinoma; LCIS, lobular carcinoma *in situ*; NR, not reported.

Table 7 Literature review of upgrade rates of FEA diagnosed on CNB

	Upgrade rate (%)	*Excision* (n)	*Upgrade* (n)	*DCIS* (n)	*IMC* (n)
Becker *et al*	4	239	10	8	2
Bianchi *et al*	9	190	18	NR	NR
Villa *et al*	6	121	7	NR	NR
Ozoaru *et al*	3	95	3	1	2
Peres *et al*	10	94	9	5	4
Khoumais *et al*	11	94	10	5	5
Saladin *et al*	18	82	15	NR	NR
Calhoun *et al*	7	73	5	3	2
Lavoué *et al*	13	60	8	6	2
Ceugnart *et al*	6	52	3	3	0
Biggar *et al*	6	51	3	2	1
David *et al*	18	40	7	3	4
Senetta *et al*	0	36	0	0	0
Chivukula *et al*	14	35	5	3	2
Noske *et al*	7	30	2	2	0
Dailani *et al*	3	29	1	1	0
Solorzano *et al*	14	28	4	3	1
Rakha *et al*	21	24	5	4	1
Prowler *et al*	0	24	0	0	0
Piubello *et al*	0	20	0	0	0
Menes *et al*	0	16	0	0	0
Ingegnoli *et al*	20	15	3	3	2
Kunju *et al*	21	14	3	NR	NR
Lee *et al*	14	7	1	1	0
Martel *et al*	0	5	0	0	0
Our data	11	55	6	3	3
Mean	8				

Abbreviations: CNB, core needle biopsy; DCIS, ductal carcinoma *in situ*; FEA, flat epithelial atypia; IMC, invasive mammary carcinoma; NR, not reported.

Table 8 Literature review of upgrade rates of radial scar without atypia diagnosed on CNB

	Upgrade rate (%)	*Excision* (n)	*Upgrade* (n)	*DCIS* (n)	*IMC* (n)
Rakha *et al*	9	278	25	14	11
El-Sayed *et al*	12	156	19	10	9
Miller *et al*	2	102	2	1	1
Matrai *et al*	0	77	0	0	0
Brenner *et al*	7	73	5	3	2
Andacoglu *et al*	6	67	4	NR	NR
Linda *et al*	8	62	5	3	2
Bianchi *et al*	8	49	4	3	1
Conlon *et al*	2	48	1	1	0
Lieske *et al*	9	43	4	NR	NR
Hayes *et al*	10	42	4	4	0
Dillon *et al*	5	41	2	2	0
Rakha *et al*	3	39	1	1	0
López-Medina *et al*	16	38	6	1	5
Kirwan et al	0	34	0	0	0
Cawson *et al*	0	27	0	0	0
Lee *et al*	4	23	1	1	0
Rajan *et al*	5	22	1	1	0
Saladin *et al*	11	18	2	NR	NR
Resetkova *et al*	0	10	0	0	0
Philpotts *et al*	0	6	0	0	0
Our data	16	25	4	3	1
Mean	7				

Abbreviations: DCIS, ductal carcinoma *in situ*; CNB, core needle biopsy; IMC, invasive mammary carcinoma; NR, not reported.

technology, outcome metrics and inclusion of other histopathology in the samples studied, precluded combination of the studies collected into an effective meta-analysis.

This is the largest single-institution analysis of a variety of high-risk breast lesions diagnosed on core needle biopsy, including management recommendations for atypical ductal hyperplasia, flat epithelial

atypia, atypical lobular hyperplasia, lobular carcinoma *in situ*, and radial scar. For years teams have published upgrade analyses of high-risk breast lesions diagnosed on core needle biopsy in an effort to prevent over- or undertreatment, and management remains problematic. We agree with the general opinion in the literature that a multicenter controlled study evaluating high-risk breast lesions is needed.[25,119–121] Research in molecular differences between groups of high-risk lesions may offer further risk stratification. Because ductal carcinoma *in situ* is being considered for a 'downgrade' to the diagnosis 'borderline breast lesion' with approved trials randomizing patients to active monitoring and standard treatment, similar studies could be performed with high-risk breast lesions such as atypical ductal hyperplasia and lobular carcinoma *in situ*.[122] Long-term studies will be important to better characterize the risks and benefits of excision.

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Disclosure/conflict of interest

The authors declare no conflict of interest.

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