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Are we overtreating intraductal papillomas?

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Abstract

Background—The management of intraductal papillomas (IDPs) diagnosed on core needle biopsy (CNB) remains controversial regarding whether excision is required. We evaluated whether excision of IDPs might be overtreatment based on a consecutive patient population where all IDPs were routinely excised.

Materials and methods—We retrospectively reviewed the records of consecutive patients treated with excision of IDPs at our institution from 2009–2016. We evaluated the rate of upgrade of IDPs on CNB and factors predicting for malignant upgrade.

Results—Of 153 CNB specimens, 136 (88.9%) were IDPs without atypia and 14 (9.2%) showed atypia. The overall upgrade rate on final pathology was 7.3% with 1.3% for invasive cancer, 2.7% for DCIS and 3.3% for ADH. Of the 14 patients with atypia on CNB, 2 of these patients (14.2%) were found to have DCIS. In the absence of atypia on CNB, upgrade rates were 1.5% for invasive

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and 1.5% for in situ carcinoma. Personal history of breast cancer and MRI-guided biopsy predicted for malignant upgrade.

Conclusion—IDPs on CNB have a low chance of harboring an occult malignancy. Given the low probability of upgrade to invasive breast cancer, it is reasonable to consider watchful surveillance in the absence of a prior personal history of breast cancer or atypia on CNB.

Keywords

intraductal papilloma; breast neoplasm; atypia; breast cancer; core needle biopsy

Introduction

Intraductal papillomas (IDPs) are tumors that form in the lactiferous ducts and are characterized as proliferative lesions of epithelium covering a fibrovascular core.[1] Depending on the location where tumors arise, IDPs may be solitary and centrally located or multifocal and peripherally located in the mammary ductal systems.[1] Multiple lesions occurring in the periphery of the breast are referred to as papillomatosis and are associated with a higher incidence of carcinoma.[1] Previous studies have shown that image-guided core needle biopsy (CNB) can correctly diagnose the majority of papillary lesions.[2] Although malignant papillary tumors are uncommon, some IDPs are susceptible to malignant change. Furthermore, there have been studies that classify papillomas with features more worrisome for malignant upgrade.[3,4] According to their pathologic features, papillomas can be potentially classified as benign or can be upgraded to atypical ductal hyperplasia, ductal carcinoma in situ or invasive carcinoma.[4] CNBs yield small specimens that may not correctly characterize the entire lesion. Therefore, it is suggested to surgically excise the papilloma given a wide range of reported upgrade rates ranging from 2.3 to 39%.[5–10] Certain features such as atypical pathology on CNB, large size, palpability of the lesion, and symptomatic nature of IDPs are reasons to excise due to an increased risk of malignancy. However, Jaffer et al.[6] reported that incidental papillomas of a size less than 2 mm do not require excision. It has also been observed that benign IDPs without atypia may not require excision in the absence of a palpable mass or radiology/pathology discordance.[7]

Given that the patient population for this study was the Los Angeles County (LAC) + University of Southern California (USC) Medical Center, an urban safety-net institution, the routine management for IDPs was to excise all papillomas due to concerns regarding whether patients will have access to medical follow-up. The aim of our study was to evaluate whether excision of all IDPs might be overtreatment based on quantifying the rates of upgrade in a population where all IDPs diagnosed on CNB were consecutively excised. We sought to evaluate if routine excision of all IDPs is warranted based on the rate of upgrade to malignancy, and to determine factors predicting for higher risk of malignant upgrade of IDPs.

Materials and methods

Medical records of patients treated for IDP at LAC+USC Medical Center from 2009 to 2016 were retrospectively reviewed. A total of 153 patients who had CNB proven IDPs and

underwent surgical excision were included in this study. The patients' records were reviewed for demographic information, clinical presentation, radiographic features, type of biopsy performed, CNB histology and final excisional pathology. Mammography and ultrasound were performed as routine imaging studies, and magnetic resonance imaging (MRI) was used for lesions with indeterminate radiologic findings or lesions that could not be seen on routine imaging. Palpability of the lesion was determined by the treating breast surgeons and documented in the medical record. The size of the tumor was determined by the single largest dimension given in the radiology report. The location of the lesion on ultrasound was defined as central if the lesion located within 2cm from the nipple and peripheral if it located at a distance greater than 2cm from the nipple. The CNB procedures were performed in the Radiology Department of LAC+USC using a 14-gauge Tru-Cut automated core biopsy needle (Baxter Healthcare, Valencia, CA) or a spring-loaded biopsy gun (Magnum; Bard, Covington, GA) with a 14-gauge biopsy needle. MRI guided core biopsies were performed using a 9-gauge vacuum assisted device (Hologic, Marlborough, MA). Ethics approval for the study was obtained from the Health Sciences Institutional Review Board (IRB) at USC. The IRB granted a waiver of informed consent.

Statistical analyses were carried out using SPSS software version 19.0 (SPSS, Inc., Chicago, IL, USA). We performed univariate analysis to evaluate the association between variables and IDPs without atypia versus IDPs with atypia or malignant upgrade. The association between variables was analyzed using the Chi-square test or the Fisher's exact test for categorical data and the Student's t-test for continuous data. Variables found to be significant on univariate analysis (p-value <0.05) were used for multivariate analysis. Unconditional logistic regression was used to assess odds ratios (ORs) and 95% confidence intervals (CI). All tests were two-sided and a p-value <0.05 was considered to indicate a statistically significant difference.

Results

Patient characteristics are presented in Table 1. The mean age of the patients was 54.8 ± 11.6 years. All patients in this study underwent mammography and ultrasound. Eight patients required MRI for diagnosis and 4 out of 8 required MRI guided biopsy to confirm the diagnosis of papilloma. Among the 4 patients who underwent MRI guided biopsy, 2 patients had bloody nipple discharge without abnormal findings on other diagnostic imaging. The other 2 patients had no clinical symptoms but were found to have architectural distortion on mammography. Common abnormal mammographic findings were mass, architectural distortion and calcification (80.9%, 10.5% and 8.6%, respectively). Among all 153 patients, 127 patients (83%) had their IDPs detected by mammographic imaging. We defined symptomatic patients as those with palpable lesions, nipple discharge, or both and therefore received diagnostic mammograms. Seventy-one patients were asymptomatic and identified by screening mammography. Fifty-four patients (35.3%) presented with a palpable mass. Thirty-seven patients (24.3%) presented with symptoms of nipple discharge. Of these, 16 patients (10.5%) presented with the "classic" bloody nipple discharge and 21 patients (13.8%) presented with clear nipple discharge (Table 1). One hundred thirty-eight lesions (93.9%) were centrally located in the breast. The remaining 15 peripherally located lesions were not associated with malignancy.

Of all 153 lesions, 136 (88.9%) had no atypia and 14 (9.2%) showed atypia on CNB pathology. On final pathology of all surgically excised specimens, 14 (9.2%) showed atypia, 4 (2.6%) showed ductal carcinoma in situ (DCIS) and 2 (1.3%) showed invasive carcinoma. Of the 14 patients (9.2%) found to have atypia on CNB, 2 of these patients (14.2%) were found to have DCIS and 6 patients (42.9%) were found to have atypical ductal hyperplasia (ADH) on final excisional pathology. The overall upgrade rate on final pathology was 7.3% with 1.3% for invasive cancer, 2.7% for DCIS and 3.3% for ADH. In patients with IDPs without atypia on CNB, only 9 patients (6.7%) were upgraded to malignancy or atypia on final excisional pathology. In these patients, the upgrade rate to malignancy was 2.9% with 1.5% (2 patients) for invasive cancer and 1.5% (2 patients) for DCIS.

On univariate analysis, the patients with personal history of breast cancer, age over 55 years and MRI guided biopsy were associated with overall upgrade of IDPs to either atypia or malignancy ($p = 0.005$, $p = 0.044$ and $p = 0.028$, respectively) (Table 2). However, personal history of breast cancer and age over 55 years were the only two patient characteristics that were significantly associated with malignant upgrade to invasive or in situ carcinoma ($p = 0.027$ and $p = 0.029$, respectively) (Table 3). Among the 19 patients with a personal history of breast cancer, a total of 5 patients were upgraded to malignancy or atypia with an upgrade rate of 26.3%. This differs to patients without a personal history of breast cancer whose upgrade rate was 2.6% (6 out of 131). In patients with a personal history of breast cancer, 3 out of 19 were upgraded to invasive cancer (2 patients) or DCIS (1 patient), with total of 15.8% upgraded to malignancy. While only 3 out of 131 patients without a personal history of breast cancer were upgraded to DCIS equaling a 2.3% upgrade rate to malignancy. Among 4 patients who underwent MRI guided biopsy, the total upgrade rate was 50% – one patient was upgraded to ADH and one patient was upgraded to DCIS. Because there were some IDPs diagnosed as atypia on the final pathology without upgrade, we performed a separate analysis for predictive factors for malignancy or atypia regardless of upgrade status. We found that personal history of breast cancer and age >55 were significantly associated with a final diagnosis of malignancy or atypia on final excisional pathology on univariate analysis regardless of upgraded or found on CNB ($p < 0.001$ and $p = 0.034$, respectively) (Table 4). Tumor size, palpability and the other clinical factors were not associated with a significant upgrade rate. On multivariate analysis, personal history of breast cancer and MRI guided biopsy were shown to be independent predictive factors of overall upgrade to either atypia or malignancy of IDPs (OR = 6.23, $p = 0.013$ and OR = 14.25 and $p = 0.024$, respectively). Only a patient's personal history of breast cancer was a predictive factor of malignant upgrade to invasive or in situ carcinoma of IDPs in our analysis (OR = 7.99 and $p = 0.018$) (Table 5).

Discussion

The surgical excision of IDPs with atypia has been well established in the literature.[1] Although excision of IDPs without atypia is controversial, it is generally acceptable to excise all IDPs because of the potential to upgrade to malignant tumor or atypia on final surgical pathology. Given our safety-net patient population, we routinely surgically excised all IDPs at LAC+USC Medical Center since our patients may not be able to undergo watchful surveillance. The aim of our study was to evaluate if excision of all IDPs regardless

of atypia was, in fact, overtreatment. A strength of this study was that this was a consecutive and relatively large cohort. In our series, 6.7% of the patients diagnosed with IDPs without atypia on CNB were upgraded to malignant tumor or atypia on final excisional pathology and 14.2% of the patients diagnosed with IDPs with atypia on CNB were upgraded to DCIS. Upon surgical excision, the overall upgrade rate of IDPs to malignant tumor or atypia was 7.5%. This is similar to the results of previous studies, in which the upgrade rates of IDPs ranged from 2.3% to 39%.[5–10] Our results are also consistent with previous studies that showed higher upgrade rates in IDPs with atypia than that of IDPs without atypia on CNB.[7,8,11]

There is no controversy regarding excision of IDPs with atypia, but there is still debate about the best treatment of IDPs in the absence of atypia. Several investigators have contended that all IDPs should be excised[12,13] because of malignant risk and the possibility of under-diagnosis using CNB. CNB of breast disease has been established as a gold standard diagnostic method with an accuracy of 93.2%.[14] However, under-diagnosis of IDPs can occur in a CNB because only a small portion of the tumor is included in the CNB specimen. Malignant tumors adjacent to the IDPs or malignancy in only a portion of the IDP can be missed with a CNB. Also, the presence of a normal myoepithelial layer, which is an important histologic feature to distinguish benign IDPs from papillary carcinoma in situ,[15] cannot be visible in a small CNB specimen. Furthermore, because an atypical papilloma can be diagnosed depending on the percentage of atypical epithelial proliferation, proper sampling is vital to classifying IDPs correctly.[15] Even with advanced biopsy techniques such as vacuum assisted biopsy, the lesion may be under-sampled and there is a possibility of leaving atypia or even malignancy behind.[12] A recent study by Shiino et al.[13] revealed that IDPs on CNB could potentially be upgraded to malignancy on subsequent excisional biopsy regardless of the presence or absence of atypical features. In this regard, excision of all IDPs may be acceptable to reduce the risk of breast cancer. However, our results showed only an upgrade rate of 2.9% for IDPs without atypia to malignancy and therefore excision of all IDPs without atypia may be overtreatment. Several investigators have described that IDPs without atypia can be managed with imaging follow-up rather than surgical excision.[7,11,15] Regardless, patients with papillary lesions have an elevated risk of subsequent breast cancer diagnosis and those with atypia should be counseled regarding chemoprevention.[16,17]

In recent years, many studies have investigated the factors predictive of malignant upgrade of IDPs,[5,8,18–21] but results were inconsistent. Shouhed et al. showed that a clinically palpable mass was the only significant predictor of upstaging to malignancy[5] while Hong et al. revealed that age >54 years and lesion size >1 cm were significantly associated with upgrade to malignancy.[8] Laval et al. described that age, menopausal status, lesions peripheral to the nipple and atypia on core needle biopsy were predictors of malignancy.[18] Conversely, several studies found no clinical, radiologic or histologic features to be helpful in predicting the possibility of histologic upgrade of CNB-diagnosed IDPs.[19,20] In our analysis, we aimed to find characteristics associated with the upstaging of IDPs. We found that personal history of breast cancer and MRI guided biopsy were the only two significant predictors of upgrade in IDPs. Nipple discharge (including bloody nipple discharge) and the size of IDPs were not associated with upgrade. Given these results, we propose that active

surveillance of CNB proven IDPs without atypia in patients without a personal history of breast cancer or MRI guided biopsy is a reasonable alternative to surgical excision.

Our study has several limitations. First, this was a retrospective study with single cohort and a comparative analysis for a non-excision group was not included. However, CNB and surgical management of all consecutively treated IDPs were performed in single institution with a uniform policy of excising all IDPs, which reduces the potential for selection bias. Second, the population of the study was relatively small given that this was a single institutional study and because IDP is not a particularly common lesion. Nevertheless, our study showed similar upgrade rates compared to the published literature. Table 6 compares our results with those of previously published series of greater than 100 patients with surgically excised IDPs.[8–11,19,21–30] Upgrade rates of IDPs without atypia to DCIS ranged from 1.2 to 5.8% and 0.0 to 2.6% for upgrade to invasive cancer in these studies.[8,10,21,23,25,28,29] Conversely, the older studies quoted for papillary lesions in the American Society of Breast Surgeons consensus guidelines were summarized in Table 7 showing higher upgrade rates compared to recent studies which may be secondary to a selection bias.[31–34]

Currently, there are two ongoing clinical trials comparing the safety of active surveillance alone versus standard surgical excision and/or adjuvant therapies for patients with low risk DCIS diagnosed by vacuum-assisted biopsy or core-needle biopsy.[35,36] As with IDPs, the natural history of progression from low grade DCIS to invasive carcinoma is uncertain.[37] Given the current thinking about possible overdiagnosis and overtreatment of DCIS, it is timely to apply this logic to the contemporary management of IDP. The low upgrade rates observed in our large series of excised IDPs allows the opportunity to follow these patients with serial breast imaging with mammography and ultrasound as an alternative to mandatory surgical excision. Our study is congruent with contemporary large published series in the finding that the vast majority of patients do not benefit from excision of IDP.

Conclusions

To evaluate whether excision of all IDPs might be overtreatment, we analyzed the rates of upgrade to atypia or malignancy for a series of consecutive IDPs diagnosed on CNB which were excised regardless of atypia status per our institutional policy. We found that the overall upgrade rate of IDPs diagnosed on CNB was low at 7.3%. Of note, the upgrade rate of IDPs with atypia on CNB was higher than that of IDPs without associated atypia on CNB. For lesions with atypia, the risk of DCIS was 14.2%, but for lesions without atypia, the risk of either DCIS or invasive carcinoma was only 1.5% for each. Therefore, all IDPs found on CNB have a defined but low risk of harboring an occult malignancy and excision of IDPs associated with atypia on CNB is reasonable.

In our series, patients requiring MRI guided biopsy of their IDP or those having a personal history of breast cancer were found to be independent factors associated with an increased risk of upgrade. None of the other clinical characteristics such as lesion size, location, palpability or nipple discharge, which have previously been reported as predictive factors, were found to be associated with upgrade in this study. Because of this, we concluded that

active surveillance in patients without a personal history of breast cancer or requiring MRI guided biopsy is a safe alternative to surgical excision for IDPs without atypia found on CNB. In these patients, IDPs can be managed by regular follow-up with standard imaging studies (mammogram and ultrasound). Lesions requiring MRI guided biopsy generally cannot be visualized by mammogram or ultrasound, which is an uncommon circumstance.

The concern about overtreatment of high risk lesions is pervasive in the literature. Just as the natural progression of low risk DCIS to invasive carcinoma has yet to be defined, the same can be said for IDPs with or without atypia. Therefore, we propose that not all IDPs need to be surgically excised, as the majority of the patients do not benefit from surgical excision.

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Table 1

Patient and tumor characteristics

Variables	Values
Mean Age, years	54.8 ± 11. 6
Race, n (%)	
Hispanic	117 (76.5%)
African American	12 (7.8%)
Caucasian	1 (0.7%)
Asian	23 (15.0%)
Positive Family History, n (%)	27 (18.0%)
Mean duration of follow-up, months	26.3 ± 80.4
Mean lesion size, cm	1.5 ± 1.1
≤ 1cm, n (%)	61 (39.9%)
> 1cm, n (%)	92 (60.1%)
Core Needle Biopsy Histology, n (%)	
No atypia	136 (88.9%)
Atypia	14 (9.2%)
Not specified	3 (2.0%)
Final Excisional Pathology, n (%)	
Benign	133 (86.9%)
Atypical ductal hyperplasia	14 (9.2%)
Ductal Carcinoma in situ	4 (2.6%)
Invasive carcinoma	2 (1.3%)
Imaging Method of Detection, n (%)	
MMG	127 (83.0%)
US	18 (11.8%)
MRI	8 (5.2%)
BIRADS score, n (%)	
2	1 (0.7)
3	4 (2.6)
4a	124 (81.0)
4b	18 (11.8)
4c	6 (3.9)
Method of Biopsy, n (%)	
Stereotactic Biopsy	11 (7.4%)
US guided biopsy	134 (89.9%)
MRI biopsy	4 (2.7%)

Variables	Values
Nipple Discharge, n (%)	37 (24.3%)
Bloody	16 (10.5%)
Clear	21 (13.8%)
None	115 (75.7%)
Palpable Mass, n (%)	54 (35.3%)
Location of Mass, n (%)	
Central Mass	138 (93.9%)
Peripheral Mass	9 (6.1%)

MMG, mammography; US, ultrasound; MRI, magnetic resonance imaging; BIRADS, Breast Imaging Reporting and Data System

Table 2

Characteristics of the intraductal papillomas associated with overall upgrade rate to atypia or malignancy on the final excisional pathology (univariate analysis).

Factors	No upgrade	Upgrade	*p* - value
Age, mean (years)	54.4 ± 11.7	61.0 ± 7.6	0.068
Age ≥ 55 years, n (%)	70 (50.4)	9 (81.8)	0.044
Personal history of breast cancer, n (%)	14 (10.1)	5 (45.5)	0.005
Family history of breast cancer, n (%)	25 (18.4)	2 (18.2)	0.99
Oral contraceptives use, n (%)	21 (15.9)	3 (33.3)	0.18
Hormone replacement therapy, n (%)	1 (0.8)	0 (0.0)	1.00
Lymphadenopathy, n (%)	4 (2.9)	0 (0.0)	1.00
Nipple Discharge, n (%)	33 (23.9)	3 (27.3)	0.73
Bloody Nipple Discharge, n (%)	14 (10.1)	1 (9.1)	1.00
Clear Nipple Discharge, n (%)	19 (13.8)	2 (18.2)	0.66
Palpable Mass, n (%)	50 (36.0)	3 (27.3)	0.75
BIRADS score ≥ 4b, n (%)	22 (15.8%)	2 (18.2)	0.69
Size of tumor > 1cm, n (%)	85 (61.2)	6 (54.5)	0.75
Size of tumor > 2cm, n (%)	27 (19.4)	3 (27.3)	0.46
Central Location of IDP, n (%)	126 (94.0)	10 (100.0)	1.00
Stereotactic Biopsy, n (%)	10 (7.4)	1 (9.1)	0.59
US biopsy, n (%)	124 (91.2)	8 (72.7)	0.086
MRI Biopsy, n (%)	2 (1.5)	2 (18.2)	0.028

BIRADS, Breast Imaging Reporting and Data System; IDP, Intraductal papilloma; US, ultrasound; MRI, magnetic resonance imaging

Table 3

Characteristics of the intraductal papillomas associated with the upgrade rate to malignancy only (invasive or in situ carcinoma) on the final excisional pathology (univariate analysis).

Factors	No upgrade	Upgrade	*p* - value
Age, mean (years)	54.6 ± 11.7	62.3 ± 5.9	0.11
Age ≥ 55 years, n (%)	73 (50.7)	6 (100.0)	0.029
Personal history of breast cancer, n (%)	16 (11.1)	3 (50.0)	0.027
Family history of breast cancer, n (%)	115 (81.6)	5 (83.3)	1.00
Oral contraceptives use, n (%)	23 (16.8)	1 (25.0)	0.53
Hormone replacement therapy, n (%)	1 (0.7)	0 (0.0)	1.00
Lymphadenopathy, n (%)	140 (97.2)	6 (100.0)	1.00
Nipple Discharge, n (%)	34 (23.8)	2 (33.3)	0.63
Bloody Nipple Discharge, n (%)	14 (9.8)	1 (16.7)	0.48
Clear Nipple Discharge, n (%)	20 (14.0)	1 (16.7)	1.00
Palpable Mass, n (%)	93 (64.6)	4 (66.7)	1.00
BIRADS score ≥ 4b, n (%)	22 (15.3)	2 (33.3)	0.25
Size of tumor > 1cm, n (%)	87 (60.4)	4 (66.7)	1.00
Size of tumor > 2cm, n (%)	28 (19.4)	2 (33.3)	0.35
Central Location of IDP, n (%)	130 (94.2)	6 (100.0)	1.00
Stereotactic Biopsy, n (%)	11 (7.8)	0 (0.0)	1.00
US biopsy, n (%)	127 (90.1)	5 (83.3)	0.482
MRI Biopsy, n (%)	3 (2.1)	1 (16.7)	0.16

BIRADS, Breast Imaging Reporting and Data System; IDP, Intraductal papilloma; US, ultrasound; MRI, magnetic resonance imaging

Table 4

Characteristics of the intraductal papillomas associated with final diagnosis of malignancy or atypia on final excisional pathology (regardless of upgraded or found on CNB) in the univariate analysis

Factors	Benign	Malignancy or atypia	*p*- value
Age, mean (years)	54.0 ± 11.5	60.4± 10.8	0.02
Age ≥ 55 years, n (%)	66 (49.6)	15 (75.0)	0.034
Personal history of breast cancer, n (%)	11 (8.3)	9 (45.0)	< 0.001
Family history of breast cancer, n (%)	25 (19.2)	2 (10.0)	0.53
Oral contraceptives use, n (%)	21 (16.7)	3 (16.7)	1.00
Hormone replacement therapy, n (%)	1 (0.8)	0 (0.0)	1.00
Lymphadenopathy, n (%)	3 (2.3)	1 (5.0)	0.43
Nipple Discharge, n (%)	31 (23.5)	6 (30.0)	0.58
Bloody Nipple Discharge, n (%)	13 (9.8)	3 (15.0)	0.45
Clear Nipple Discharge, n (%)	18 (13.6)	3 (15.0)	1.00
Palpable Mass, n (%)	48 (36.1)	6 (30.0)	0.6
BIRADS score ≥ 4b, n (%)	22 (16.5)	2 (10.0))	0.74
Size of tumor > 1cm, n (%)	80 (60.2)	12 (60.0)	0.99
Size of tumor > 2cm, n (%)	26 (19.5)	4 (20.0)	1.00
Central Location of IDP, n (%)	120 (93.8)	18 (94.7)	1.00
Stereotactic Biopsy, n (%)	10 (7.7)	1 (5.3)	1.00
US biopsy, n (%)	118 (88.1)	16 (84.2)	0.41
MRI Biopsy, n (%)	2 (1.5)	2 (10.5)	0.079

BIRADS, Breast Imaging Reporting and Data System; IDP, Intraductal papilloma; US, ultrasound; MRI, magnetic resonance imaging; CNB, core needle biopsy

Table 5

Factors associated with the overall upgrade (atypia, invasive or in situ carcinoma) or malignant upgrade (invasive or in situ carcinoma) of intraductal papillomas on the final excisional pathology in the multivariate analysis

Factors	Overall upgrade			Malignant upgrade		
	Odds Ratio	95% CI	*p*-value	Odds Ratio	95% CI	*p*-value
Age ≥ 55 years	2.72	0.51–14.39	0.24	0.025	0.00–4.66	0.17
Personal history of breast cancer	6.23	1.48–26.22	0.013	7.99	1.42–44.98	0.018
MRI guided biopsy	14.25	1.41–143.76	0.024	8.00	0.56–115.19	0.13

CI, confidence interval; MRI, magnetic resonance imaging

Table 6

Summary of the rates of malignant upgrade after final surgical excision of intraductal papillomas on core needle biopsy from the literature

Study	Year	Number of excised IDPs	Number of IDP with atypia on CNB (%)	% upgrade to DCIS	% upgrade to invasive cancer
Ahn et al. [20]	2017	299	49 (16.4)	8.7	3.7
Khan et al. [11]	2017	147	45 (30.6)	6.1	8.2
Ko et al. [19]	2017	346	0	2.3	0.0
Hong et al. [8]	2016	234	0	3.8	2.1
Pareja et al. [10]	2016	171	0	1.2	1.2
Kim et al. [21]	2016	230	0	1.7	0.9
Foley et al. [22]	2015	238	50 (21.0)	12.2	6.7
Glenn et al. [9]	2015	169	23 (13.6)	0.0	7.1
Li et al. [23]	2012	370	0	1.6	0.3
Fu et al. [17]	2012	268	65 (24.3)	6.7	1.5
Rizzo et al. [24]	2012	276	26 (9.4)	11.9	1.4
Kim et al. [25]	2011	146	15 (10.3)	6.8	4.8
Youk et al. [26]	2011	160	0	3.8	1.3
Jaffer et al. [27]	2009	104	0	5.8	2.6
Rizzo et al. [28]	2008	124	23 (18.5)	10.5	0.0
Kiran et al. (this study)	2017	153	14 (9.2)	2.7	1.3

IDP, Intraductal papilloma; CNB, core needle biopsy; DCIS, ductal carcinoma in situ

Table 7

Summary of the rates of malignant upgrade after final surgical excision of intraductal papillomas on core needle biopsy from the studies quoted for papillary lesions in the American Society of Breast Surgeons consensus guidelines

Study	Study year	Method of identifying patients (year)	Number of IDPs diagnosed on CNB[a]	Number of excised IDPs	Number of IDP with atypia on CNB, n (%)	Upgrade to DCIS, n (%)	Upgrade to invasive cancer, n (%)	Overall upgrade rate to malignancy, n (%)	Upgrade from atypia to malignancy, n (%)
Renshaw et al.[31]	2004	Retrospective review of core needle biopsy (1996–2003)	62	40	20 (52.6)*	12 (30)	3 (7.5)	15 (37.5)	14 (36.8)*
Agoff et al.[32]	2004	Retrospective review of pathologic files (1995–2003)	51	45	25 (55.6)	10 (22.2)	2 (4.4)	12 (26.7)	12 (48)
Sohn et al.[33]	2007	Retrospective review of core needle biopsy (1994–2005)	215	59	26 (12.1)	NA	NA	18 (30.5)	5 (26)
Sydnor et al.[34]	2007	Mammographic database review (1994–2003)	63	38	15 (23.8)	9 (23.7)	5 (13.2)	14 (36.8)	10 (67)

*The rate was calculated by the number of cases out of 38 IDPs, which was available for slide review except unavailable 2 IDPs with atypia on original CNB.

IDP, Intraductal papilloma; CNB, core needle biopsy; DCIS, ductal carcinoma in situ; NA, not available