Diagn Interv Radiol 2023; DOI: 10.4274/dir.2022.221790

BREAST IMAGING

ORIGINAL ARTICLE

Outcomes of high-risk breast lesions diagnosed using image-guided core needle biopsy: results from a multicenter retrospective study

Ayşenur Oktay, Özge Aslan, Füsun Taşkın, Nermin Tunçbilek, Selma Gül Esen İçten, Pınar Balcı, Mustafa Erkin Arıbal, Levent Çelik, İhsan Şebnem Örgüç, Figen Başaran Demirkazık, Serap Gültekin, Ayşe Murat Aydın, Emel Durmaz, Sibel Kul, Figen Binokay, Meltem Çetin, Ganime Dilek Emlik, Meltem Gülsün Akpınar, Sadiye Nuray Kadıoğlu Voyvoda, Ahmet Veysel Polat, Işıl Başara Akın, Şeyma Yıldız, Necdet Poyraz, Arzu Özsoy, Pelin Seher Öztekin, Eda Elverici, İlkay Koray Bayrak, Türkan İkizceli, Funda Dinç, Gülten Sezgin, Gökçe Gülşen, Işıl Tunçbilek, Sabiha Rabia Yalçın, Gül Çolakoğlu, Serpil Ağlamış, Ravza Yılmaz, Günay Rona, Gamze Durhan, Davut Can Güner, Fatma Çelik Yabul, Leman Günbey Karabekmez, Burçin Tutar, Muhammet Göktaş, Onur Buğdaycı, Aslı Suner, Necmettin Özdemir

From the Department of Radiology (A.O. ✉ oktay.aysenur@gmail.com, Ö.A.), Ege University Faculty of Medicine, İzmir, Turkey; Department of Radiology (F.T.), Acıbadem MAA University Faculty of Medicine; Acıbadem MAA University Senology Research Institute, Acıbadem Atakent Hospital, İstanbul, Turkey; Department of Radiology (N.T.), Trakya University Faculty of Medicine, Edirne, Turkey; Department of Radiology (S.G.E.İ.), Acıbadem MAA University Faculty of Medicine; Acıbadem MAA University Senology Research Institute, İstanbul, Turkey; Department of Radiology (P.B., I.B.A.), Dokuz Eylül University Faculty of Medicine, İzmir, Turkey; Department of Radiology (M.E.A.), Acıbadem MAA University Faculty of Medicine, İstanbul, Turkey; Department of Radiology (L.Ç., D.C.G.), Maltepe University Faculty of Medicine; İstanbul, Turkey; Department of Radiology (İ.Ş.Ö.), Manisa Celal Bayar University Faculty of Medicine, Manisa, Turkey; Department of Radiology (F.B.D., M.G.A., G.D.), Hacettepe University Faculty of Medicine, Ankara, Turkey; Department of Radiology (S.G.), Gazi University Faculty of Medicine, Ankara, Turkey; Department of Radiology (A.M.A., S.A.), Fırat University Faculty of Medicine, Elazığ, Turkey; Department of Radiology (E.D.), Akdeniz University Faculty of Medicine, Antalya, Turkey; Department of Radiology (S.K.), Karadeniz Techinal University Faculty of Medicine, Trabzon, Turkey; Department of Radiology (F.B.), Çukurova University Faculty of Medicine, Adana, Turkey; Department of Radiology (M.Ç.), Süleyman Demirel University Faculty of Medicine, Isparta, Turkey; Department of Radiology (G.D.E., N.P.), Necmettin Erbakan University Meram Faculty of Medicine, Konya, Turkey; Department of Radiology (S.N.K.V., G.R.), University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Turkey; Department of Radiology (A.V.P., İ.K.B.), Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey; Department of Radiology (Ş.Y., F.Ç.Y.), Bezmialem Vakıf University Faculty of Medicine, İstanbul, Turkey; Department of Radiology (A.Ö., E.E.), University of Health Sciences Turkey, Ankara City Hospital, Ankara, Turkey; Department of Radiology (P.S.Ö.), Ankara Training and Research Hospital, Ankara, Turkey; Department of Radiology (T.İ., G.G.), University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, İstanbul, Turkey; Department of Radiology (F.D.), Muğla Sıtkı Koman University Faculty of Medicine, Muğla Turkey; Department of Radiology (G.S.), İzmir Katip Çelebi University, Atatürk Training and Research Hospital, İzmir, Turkey; Department of Radiology (I.T., S.R.Y.), Medsentez Private Clinic, Ankara, Turkey; Department of Radiology (G.Ç.), University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, İzmir, Turkey; Department of Radiology (R.Y.), İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey; Department of Radiology (L.G.K), Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey; Department of Radiology (B.T.), Acıbadem Maslak Hospital, İstanbul, Turkey; Department of Radiology (M.G.), Ministry of Health Çerkezköy State Hospital, İstanbul, Turkey; Department of Radiology (O.B.), Marmara University Faculty of Medicine, İstanbul, Turkey; Department of Biostatistics and Medical Informatics (A.S.), Ege University Faculty of Medicine, İzmir, Turkey; Department of Medical Pathology (N.Ö.), Ege University Faculty of Medicine, İzmir, Turkey.

Received 25 July 2022; revision requested 05 August 2022; accepted 27 August 2022.

Epub: 09.01.2023

Publication date: 21.07.2023

DOI: 10.4274/dir.2022.221790

You may cite this article as: Oktay A, Aslan Ö, Taşkın F, et al. Outcomes of high-risk breast lesions diagnosed using image-guided core needle biopsy: results from a multicenter retrospective study. *Diagn Interv Radiol.* 2023;29(4):579-587.

PURPOSE

The clinical management of high-risk lesions using image-guided biopsy is challenging. This study aimed to evaluate the rates at which such lesions were upgraded to malignancy and identify possible predictive factors for upgrading high-risk lesions.

METHODS

This retrospective multicenter analysis included 1.343 patients diagnosed with high-risk lesions using an image-guided core needle or vacuum-assisted biopsy (VAB). Only patients managed using an excisional biopsy or with at least one year of documented radiological follow-up were included. For each, the Breast Imaging Reporting and Data System (BI-RADS) category, number of samples, needle thickness, and lesion size were correlated with malignancy upgrade rates in different histologic subtypes. Pearson's chi-squared test, the Fisher–Freeman–Halton test, and Fisher's exact test were used for the statistical analyses.

RESULTS

The overall upgrade rate was 20.6%, with the highest rates in the subtypes of intraductal papilloma (IP) with atypia (44.7%; 55/123), followed by atypical ductal hyperplasia (ADH) (38.4%; 144/375), lobular neoplasia (LN) (12.7%; 7/55), papilloma without atypia (9.4%; 58/611), flat epithelial atypia (FEA) (8.7%; 10/114), and radial scars (RSs) (4.6%; 3/65). There was a significant relationship between the upgrade rate and BI-RADS category, number of samples, and lesion size Lesion size was the most predictive factor for an upgrade in all subtypes.

CONCLUSION

ADH and atypical IP showed considerable upgrade rates to malignancy, requiring surgical excision. The LN, IP without atypia, pure FEA, and RS subtypes showed lower malignancy rates when the BI-RADS category was lower and in smaller lesions that had been adequately sampled using VAB. After being discussed in a multidisciplinary meeting, these cases could be managed with follow-up instead of excision.

KEYWORDS

Core needle biopsy, B3 lesions, breast cancer, image guided breast biopsy, vacuum assisted biopsy

High-risk breast lesions comprise a heterogeneous group of proliferative lesions that are precursors of breast carcinogenesis and are associated with a higher risk of future breast cancer development.[1,2] These lesions include atypical ductal hyperplasia (ADH), lobular neoplasia (LN) (a term encompassing both atypical lobular hyperplasia [(ALH) and lobular carcinoma in situ (LCIS)], intraductal papilloma (IP) with/without atypia, flat epithelial atypia (FEA), and radial scars (RSs)/complex sclerosing lesions.[3,4] Other terms used in the literature to describe these entities are "lesions of the breast with uncertain malignant potential", "borderline lesions", or "B3 lesions". High-risk lesions are commonly detected due to the increased use of core or vacuum biopsy techniques for screen-detected lesions. High-risk lesions are found in about 3%–9% of cases of percutaneous image-guided breast biopsies performed following a suspicious imaging finding.[5,6]

Percutaneous image-guided needle biopsy has become a standard approach for the tissue diagnosis of suspicious breast lesions. It is performed using either the core needle biopsy (CNB) or vacuum-assisted biopsy (VAB) technique. CNBs are usually performed under ultrasound (US) guidance, while stereotactic system or magnetic resonance imaging (MRI) guidance is used for VABs. When the CNB/VAB detects a high-risk lesion, the possibility of missing the malignant component of the lesion exists; ductal carcinoma in situ (DCIS) and invasive carcinoma can only be detected when surgical excision is performed. The positive predictive value (PPV) for malignancy for CNB/VAB is about 10%–30%.[5,7,8]

The appropriate management of a high-risk lesion following diagnosis using image-guided biopsy is controversial, and recommendations, including surgical excision and follow-up, vary for different lesions.[9] Surgical excision has been used as a general approach to avoid missing an underlying malignancy.[10] However, in recent studies, risk parameters have been identified to upgrade a lesion to suspected malignancy, allowing more conservative approaches in selected cases. To achieve consensus about managing high-risk lesions, the International Consensus Conference was held in Zurich, Switzerland, in 2016 and 2019. This conference introduced second-line VAB as an alternative to open surgical excision in most lesions, and several guidelines were introduced for managing these lesions.[11]

This multicenter study aimed to document the excisional biopsy or follow-up results of high-risk lesions diagnosed on image-guided CNB/VAB and evaluate the clinical, imaging, and histologic features for associated malignancy risk. The possibility of an upgrade related to histologic subtype, tissue sampling, and other variables was also evaluated.

Methods

This retrospective multicenter study included 1.343 patients from 30 centers diagnosed with a high-risk lesion on image-guided CNB or VAB. The ethics committee of the Ege University Faculty of Medicine approved the study (approval number: 20-6T/41; date of approval: June 10, 2020). The study reviewed existing data, so patient consent was not required.

Patients

Radiology records for the 12 years between 2008 and 2020 were reviewed for all image-guided biopsies and pathology reports. Patients diagnosed with ADH, LN (ALH/LCIS), papilloma (with or without atypia), RSs, or FEA on image-guided CNB/VAB were included. The needle biopsy could be performed using either US or stereotactic guidance and tru-cut or vacuum biopsy needles. In addition, patients managed with an excisional biopsy or those with at least one year of documented radiological follow-up after diagnosis with one of the above-mentioned high-risk lesions were included in the study. FEA, seen in conjunction with LN or ADH, was categorized under either LN or ADH as appropriate. Pleomorphic LCIS, fibroepithelial lesions, and mucocele-like tumors were excluded. Further, lesions associated with *in situ* or invasive carcinoma on CNB were excluded.

All patients were discussed at a multidisciplinary meeting, and decisions were made based on biopsy and radiology findings. Histopathologic diagnoses were made according to the current guidelines.[12]

Data analysis

The images used in this study were retrieved from the Picture Archiving and Communication System digital archive, and the results of mammograms, US images, and MRI scans were re-evaluated. The findings were categorized by imaging method, as follows: microcalcifications, a mass/nodular opacity, or suspicious non-mass findings (i.e., architectural distortion and asymmetry) on a mammogram; a mass/nodular lesion or non-mass lesion (i.e., distortion or echogenicity changes) on a US examination; and a mass or non-mass contrast-enhancing lesion on an MRI scan. The patients without imaging findings were also noted. In each case, the lesion's largest diameter was recorded and categorized into two groups: under and above 15 mm. The final Breast Imaging Reporting and Data System (BI-RADS) category on the imaging reports was also documented.

Other data collected from the records included the needle biopsy type and biopsy sampling method. The imaging-guidance modality was chosen based on the findings and visibility of the lesion on imaging. Stereotactic guidance was usually preferred for microcalcifications, while US was used for lesions that were visible on the US. Stereotactically guided biopsies were performed in 182/1.343 (13.6%) patients on a prone table or an add-on unit using a 9 to 12 G directional vacuum-assisted needle. US-guided biopsies were performed in 1.161/1.343 (86.4%) patients with an automated tru-cut system using 14 to 16 G needles with a 2-cm cutting surface. The number of cores used was another analysis point, and this information was categorized as n <4 and n ≥4.

The final pathology reports of the patients who had surgical excision or were stable for at least one year of follow-up were documented. The follow-up period varied between 12 and 180 months (median: 30 months). In total, 929 patients underwent surgical excisional biopsy, and 414 were followed up with at six-month intervals. Recommendations for excision or surveillance were made in a multidisciplinary meeting. The pathological results of excisional biopsies were recorded as either no change in the primary diagnosis by needle biopsy or upgraded to indicate malignancy. The presence of DCIS or invasive carcinoma on histologic examination after an excisional biopsy was regarded as necessitating an upgrade of the high-risk lesion. In follow-up patients, the diagnosis on needle biopsy was considered a compatible result if there was no change in the findings; however, a biopsy was recommended if any suspicious change was observed on follow-up.

Main points

- High-risk breast lesions are a heterogeneous group of proliferative lesions that are precursors to breast carcinogenesis and are associated with a higher risk of future breast cancer.
- Clinical management of high-risk lesions using image-guided biopsy is challenging.
- High-risk breast lesions should be managed in a case-based manner after discussion among a multidisciplinary team.

The diagnosis on CNB/VAB and the outcomes were compared, and the upgrade rate and PPV for malignancy [i.e., (number of malignant cases/total number of participants) × 100] were calculated. The association between the parameters described above and the upgrade rate or PPV for malignancy were evaluated.

Statistical analysis

All patient information was anonymously submitted to a medium in an anonymized manner via software from all included centers. Patient characteristics were reported as frequencies and percentages (%) for categorical variables, and descriptive statistics (mean, median, minimum, and maximum values) were calculated for continuous variables. If the variables had a normal distribution, the mean and standard deviation (SD) were given; otherwise, the median and range were given. Pearson's chi-squared test, the Fisher–Freeman–Halton test, and Fisher's exact test were used to analyze the categorical variables in groups. A value of $P < 0.05$ was considered statistically significant. The data were analyzed using the IBM SPSS Statistics version 25.0 statistical software package.

Results

In total, 1.343 patients met our criteria, of which 375 (27.9%) had ADH, 55 (4.1%) had LN (ALH/LCIS), 611 (45.5%) had IP without atypia, 123 (9.2%) had IP with atypia, 114 (8.5%) had FEA, and 65 (4.8%) had RSs. The patients were between 17 and 86 years of age, with a mean age of 47.45 years (SD: 0.459).

In all cases, the upgrade rate to malignancy was 20.6% (Table 1). Of these, 52% (144/277) were cases of ADH. Almost half (47.2%) of all upgrades were to invasive cancer. Upgrades to low-grade DCIS were more common than upgrades to high-grade DCIS (32.9% vs. 19.9%, respectively). According to the pathologic subtypes, IP with atypia was the most common type, with an upgrade rate of 44.7% (55 of 123 cases), followed by ADH (38.4%, 144 of 375 patients). The upgrade rate was 12.7% in LN, 8.7% in FEA, 9.4% in IP without atypia, and 4.6% in RSs. The pathological subtype had a statistically significant relationship with malignant vs. benign diagnosis $P < 0.001$).

In about half the cases (49%), the lesions were categorized as BI-RADS 4A lesions, followed by BI-RADS 4B (26.7%), BI-RADS 4C (13.1%), and BI-RADS 5 (3.3%). These categories were most common in the subtypes ADH and IP with atypia. A biopsy was still recommended in 7.9% of patients, although the lesions were categorized as BI-RADS 3. The malignancy upgrade rate had a statistically significant relationship with the BI-RADS category ($P < 0.05$). In the imaging findings, microcalcifications on mammograms were common in the LN, FEA, and ADH subtypes (70.3%, 64%, and 54.8%, respectively). The mass lesions detected on mammography, US, or MRI were most frequently IPs with or without atypia. Lesions presenting as non-mass lesions on mammography, US, or MRI were seen in all subtypes. There was no statistically significant relationship between the imaging findings and upgrade rates.

Table 2 summarizes the outcomes of biopsy or follow-up and malignancy upgrade rate according to the BI-RADS category, needle size, number of samples, and lesion size. There was no statistically significant relationship between malignancy upgrade rate and needle size ($P > 0.05$). However, the relationship between the malignancy upgrade rate and the number of samples and lesion size was statistically significant ($P = 0.008$ and $P < 0.001$, respectively). Lesion sizes were between 4 and 135 mm (mean: 13.8; median: 10), which was the most predictive factor for an upgrade when all the patients were analyzed together.

The results varied among the lesion subtypes. In the ADH group, a statistically significant change in the upgrade rate was recorded according to BI-RADS category, needle thickness, number of samples, and lesion diameter (Table 3). The malignancy rate was higher in the BI-RADS 4C and 5-category le-

Table 1. Upgrade to malignancy related to subtypes of high-risk lesions

Pathology subtype n (%)	Benign n (%)	Malignant n (%)				Total (n)	*P*
		Low-grade DCIS n (%)	High-grade DCIS n (%)	Invasive carcinoma n (%)	Total n (%)		
ADH	231 (61.6)	42 (11.2)	37 (9.8)	65 (17.3)	144 (38.4)	375	
LN	48 (87.3)	1 (1.8)	2 (3.6)	4 (7.3)	7 (12.7)	55	
RS	62 (95.4)	0 (0)	2 (3.1)	1 (1.5)	3 (4.6)	65	
IP with atypia	68 (55.3)	19 (15.4)	7 (5.7)	29 (23.6)	55 (44.7)	123	<0.001*
FEA	104 (91.2)	4 (3.6)	3 (2.6)	3 (2.6)	10 (8.8)	114	
IP without atypia	553 (90.5)	25 (4.1)	4 (0.6)	29 (4.8)	58 (9.5)	611	
Total	1.066 (79.4)	91 (6.8)	55 (4.1)	131 (9.7)	277 (20.6)	1.343	

Benign, benign and stable on follow-up; *$P < 0.05$. ADH, atypical ductal hyperplasia; LN, lobular neoplasia; RS, radial scar; IP, intraductal papilloma; FEA, flat epithelial atypia; DCIS, ductal carcinoma in situ.

Table 2. Distribution of malignancy upgrade according to BI-RADS category, needle size, number of samples, and lesion size

		Benign n (%)	Malignant n (%)	Total n	*P*
BI-RADS category	BI-RADS 3–4A–B	949 (84.5)	174 (15.5)	1,123	<0.001*
	BI-RADS 4C–5	117 (53.2)	103 (46.8)	220	
Needle thickness	9–12 gauge	152 (84.0)	29 (16.0)	181	0.100
	14–16 gauge	914 (78.7)	248 (21.3)	1.162	
Number of samples	<4	309 (75.0)	103 (25.0)	412	0.008*
	≥4	757 (81.3)	174 (18.7)	931	
Diameter of lesion	≤15 mm	753 (86.0)	123 (14.0)	876	<0.001*
	>15 mm	313 (67.0)	154 (33.0)	467	

Benign, benign and stable on follow-up; *$P < 0.05$. BI-RADS, Breast Imaging Reporting and Data System.

sions. The upgrade rate varied according to needle type, 41% vs. 28% for tru-cut vs. vacuum biopsies. The number of samples and lesion size correlated with upgrade rates, being 49.0% when there were fewer than four samples vs. 34.3% when there were four samples or more, and 29.1% vs. 51.6% for lesions ≤15 mm and >15 mm, respectively. In the multivariate analysis, the lesion diameter and needle size were the most predictive of a lower upgrade rate (20% when 9 to 12 G needles were used for lesions ≤15 mm in size) (Table 4).

The only statistically significant variable in the LN subtype was the BI-RADS category. There was no statistically significant correlation between the needle thickness, number of samples, lesion size, and upgrade at the final diagnosis. In the multivariate analysis, the results did not predict malignancy when larger needle sizes were used in lesions ≤15 mm (Table 4).

In the IP without atypia and FEA subtypes, the upgrade rate changed with the lesion diameter and BI-RADS category (Table 3). In the multivariate analysis, the patients who had IP without atypia, diagnosed using a 9 to 12 G needle and a lesion ≤15 mm, were all in the benign group (n = 34; Table 4). In IP without atypia, the upgrade rate was 6% in patients with lesions ≤15 mm, in whom 14 to 16 G needles were used for sampling, vs. 18% in patients with lesions >15 mm, in whom samples were taken using the same needle size. The difference between these results was statistically significant. The percentage of upgrade to malignancy did not change even when 9 to 12 G needles were used in lesions >15 mm (18%). In the FEA subtype, there was no malignancy at final diagnosis when 14 to 16 G needles were used to sample lesions ≤15 mm in 44 patients; however, the upgrade rate was 20% with the same needle size when the lesion size was >15 mm. The upgrade rate also varied with lesion size when 9 to 12 G needles were used (4% for lesions ≤15 mm, and 17% for lesions >15 mm) ($P = 0.002$; Table 4).

In patients with atypical IP, a statistically significant difference was found between lesion size and an upgrade to malignancy (Table 3). Of the 123 atypical IP lesions, 121 were sampled with 14 to 16 G needles, and the malignancy rate was 38% for lesions ≤15 mm in size and 57% for those >15 mm, which was statistically significant ($P = 0.043$; Table 4).

In the RS subtype, a statistically significant difference was found between needle size and upgrade to malignancy ($P = 0.038$; Table 3). Fourteen to 16 G needles were used for all these lesions, and the 42 lesions that were ≤15 mm in size were all benign at the final diagnosis. The other predictive factor for the upgrade was lesion size, with only one malignant of the 46 RS lesions ≤15 mm (Table 4).

Discussion

This multicenter study reviewed the outcomes of surgical biopsies and long-term follow-up visits of high-risk lesions (B3 lesions) diagnosed using a CNB. More than two-thirds of the patients (n = 929) underwent a surgical biopsy, and 20.6% were found to have a breast malignancy. At final diagnosis, more than half of all malignancies were DCIS (52.8%), and low-grade DCIS was more common than high-grade DCIS (32.9% vs. 19.9%, respectively). In the literature, the PPVs ranged from 9.9% to 35.1% when all subtypes of B3 lesions were included.[7,13,14] Bianchi et al.[7] reviewed 3.107 cases and re-

ported a 21.2% upgrade rate, similar to this study's results. In addition, the number of DCIS cases was higher than that of invasive cancers in studies by Houssami et al.[14] and Strachan et al.[15]

Several variables should be considered when deciding what the next steps should be following a diagnosis of a high-risk lesion of the breast through an image-guided needle biopsy. In this study, upgrades to malignancy were associated with the BI-RADS category, the number of samples taken, and the lesion size. The lesion size was the most predictive factor for an upgrade, the rate being 14% vs. 33% for tumors that were ≤15 mm vs. those that were >15 mm in size, respectively. The underestimation rate was reduced with more sampling, 18.7% for four samples or more and 25% for fewer than four samples. In all lesions, 16.4% were categorized as BI-RADS 4C or 5, and the malignancy rate in this group was 47.2% vs. 15.5% for BI-RADS 3 or 4A–B lesions. These results show the importance of the BI-RADS classification and the radiologic–pathologic concordance of the lesions. There was no statistically significant relationship between radiologic findings (i.e., calcification and mass or non-mass lesion) and upgrade rate.

In managing high-risk lesions, surveys have shown significant variation in the recommendations of radiologists, pathologists, and surgeons.[9,16,17] Surgical excision has traditionally been performed as a safe option to exclude any associated adjacent malignancy that could have been missed when performing a CNB on high-risk lesions. However, high-risk breast lesions comprise a variety of lesion subtypes, showing different radiologic and histologic features and levels of malignancy risk.[11] Malignancy diagnosed at surgical excision is more frequent in lesions with atypia than in those without. In the present study, an associated DCIS or invasive cancer malignancy was most commonly seen in cases of atypical IP (upgrade rate of 44.7%), followed by ADH (38.4%). Accordingly, this study's results indicate that the surgical excision of these two categories of lesions is warranted. Strachan et al.[15], Rakha et al.[18], and de Beça et al.[19] also reported that the underestimation of malignancy is much higher in lesions with atypia than in those without atypia. Moreover, distinguishing ADH from a low-grade DCIS through a pathology review can be difficult. As such, the management of these two lesion types was consistent, with excision still being recommended in the guidelines for both. However, alternatives such as further sampling or surveillance can be considered for lesions without atypia.[11,20]

The reported rates of underlying co-existing malignancy for ADH diagnosed by needle biopsy varied between 4% and 54%, with a pooled median diagnosis upgrade rate of 25%.[1,21] There have been efforts to identify indicators of ADH lesions with a low risk of being upgraded to malignancy. Several histopathologic criteria, including the extent of the ADH and percentage of lesion removal, were found to be predictive factors of the upgrade rate.[22-24] While the present study did not evaluate any histopathologic parameters, the variables of biopsy type, needle size, number of samples, lesion size, and BI-RADS category of the lesion all showed a statistically significant correlation with the upgrade rate. ADH lesions ≤15 mm sampled with larger core needle sizes had a lower upgrade rate. However, this rate was too high to avoid excisional biopsy, which was done in 11 of 56 cases. Schiaffino et al.[25] proposed the conservative management of ADH only in a highly selective group of patients diagnosed using a stereotactic VAB for a single group of microcalcifications, without residual findings, and without a high percentage of hyperplasia at histological assessment.

In the current study, the upgrade rate within the subtype of LN was 12.7%. Pleomorphic types and variants of LCIS were excluded from this study, as there is already a consensus that excision is necessary for such types to ensure no underlying cancer is missed.[26] The BI-RADS score, lesion size, and needle type predicted an upgrade to LN carcinoma. Lesions measuring ≤15 mm and sampled with 9 to 12 G VAB needles were benign at surgical excision; however, the upgrade rate was 10% when 14 to 16 G needles were used for the same lesion sizes. The malignancy rate for lesions >15 mm also changed depending on the needle type, 40% for vacuum and 20% for core biopsy needles. Although the upgrade rate in LN has been reported to range between 0% and 50% in the literature.[4,27-29] Recent studies have shown that the upgrade rates decrease significantly when the BI-RADS score and pathologic results are concordant.[30-33] Mooney et al.[6] reported a 5% upgrade rate upon excision for LN diagnosed incidentally vs. a 39% upgrade rate for targeted lesions. Therefore, routine excision is no longer required in all ALH or LCIS cases.[34]

In the current study, the upgrade rate for IP with atypia was 44.7%, and for IP without atypia, 9.4%. A meta-analysis demonstrated a 15.7% pooled underestimation for non-malignant papillary breast lesions, with higher rates among atypical lesions (i.e., 36.9% for atypical lesions vs. 7% for benign IPs).[35] Therefore, there is no debate that surgical excision should be done after diagnosing atypical papillary breast lesions on core biopsy. However, there is no consensus on how best to manage benign IPs. In the current study, the lesion diameter and BI-RADS score correlated with an upgrade to malignancy in IPs without atypia. No malignancy was found in lesions ≤15 mm, sampled with larger needle sizes. When sampling lesions of the same size with 14 to 16 G needles, the upgrade rate was 6.1%. It has previously been demonstrated that lesions >15 mm in a peripheral location, with image-pathology discordance, are associated with a significant risk of upgrade to malignancy.[36]

Recent studies have suggested that imaging follow-up may be reasonable in selected cases, including radiologically concordant or incidentally detected benign IPs of ≤15 mm diagnosed using large-gauge core biopsy needles.[37-39] Pareja et al.[40] found an upgrade rate of 2.3% in their evaluation of 171 radiologic–pathologic concordant IPs without atypia. In a study by Menes et al.[41], upgrades to cancer occurred in 2% of asymptomatic women diagnosed with a benign papillary lesion using a needle biopsy following a mammogram showing a lesion classified as BI-RADS 4. From these results, imaging follow-up seems reasonable for benign papillomas found to be small upon core biopsy, adequately sampled, and radiologically concordant.

For the pure FEA subtype, the reported malignancy upgrade rates vary widely; most published studies have recommended excision. However, in several recent studies, imaging follow-up has been proposed for patients without residual calcifications.[42,43] In the present study, these upgrade rates were statistically significantly correlated with lesion diameter and BI-RADS score. The rate was 1.5% for lesions ≤15 mm. In relation to needle sizes, the upgrade rate was 0% (0/44 cases) for 14 to 16 G and 4% (1/23 cases) for 9 to 12 G needle sizes. A sampling error may have caused the only positive case in this study. In a recent systematic review and meta-analysis including 2.482 cases across 42 studies, this rate was 5%; however, when more than 90% of the calcifications were removed, no cancer was found at excision, and close imaging follow-up was recommended for such patients.[44] Schiaffino et al.[45] found a malignancy rate of less than 2% in patients

Table 3. Distribution of malignancy upgrade in different subtypes of high-risk lesions according to various variables

		ADH (n = 375)			IP without atypia (n = 611)			RS (n = 65)		
		Malignant n (%)	Benign n (%)	*P*	Malignant n (%)	Benign n (%)	*P*	Malignant n (%)	Benign n (%)	*P*
Mammography finding	**Microcalcification**	57 (40.4)	84 (59.6)	0.473	11 (15.7)	59 (84.3)	0.784	1 (11.1)	8 (88.9)	1.000
	Mass	31 (48.4)	33 (51.6)		18 (12.5)	126 (87.5)		0 (0)	5 (100)	
	Non mass	20 (38.5)	32 (61.5)		7 (12.3)	50 (87.7)		1 (5.9)	16 (94.1)	
Microcalcification morphology	**Amorphous**	14 (37.8)	23 (62,2)	0.330	4 (12.5)	28 (87.5)	0.782	1 (14.3)	6(85,7)	1.000
	Coarse heterogeneous	7 (41.2)	10 (58.8)		2 (20.0)	8 (80.0)		0 (0)	1 (100)	
	Newly identified suspect	3 (21.4)	11 (78.6)		0 (0)	2 (100)		0 (0)	0 (0)	
	Fine linear	10 (58.8)	7 (41.2)		1 (25.0)	3 (75.0)		0 (0)	0 (0)	
	Fine pleomorphic	23 (41.1)	33 (58.9)		4 (18.2)	18 (81.8)		0 (0)	1 (100)	
Ultrasonography finding	**Mass**	72 (39.3)	111 (60.7)	0.290	49 (9.7)	457 (90.3)	<0.001*	0 (0)	29 (100)	0.493
	Non mass	55 (45.5)	66 (54.5)		88 (10.1)	71 (89.9)		2 (6.3)	30 (93.8)	
MRI finding	**Mass**	29 (36,7)	50 (63.3)	0.368	27 (13.0)	180 (87.0)	<0.001*	0 (0)	14 (100)	0.224
	Non mass	48 (44.0)	61 (56.0)		31 (32.6)	64 (67.4)		3(20.0)	12 (80.0)	
Lesion diameter	**≤1.5 cm**	64 (29.1)	156 (70.9)	<0.001*	24 (5.6)	403 (94.4)	<0.001*	1 (2.2)	45 (97.8)	0.202
	>1.5 cm	80 (51.6)	75 (48.4)		34 (18.5)	150(81,5)		2 (10.5)	17 (89.5)	
BI-RADS	**3, 4A, 4B**	82 (31.1)	182 (68.9)	<0.001*	43 (7.7)	519 (92.3)	<0.001*	2 (3.4)	56 (96.6)	0.294
	4C–5	62 (55.9)	49 (44.1)		15 (30.6)	34 (69.4)		1 (14.3)	6 (85.7)	
Needle thickness	**9–12 G**	20 (27.8)	52 (72.2)	0.039*	2 (4.4)	43 (95.6)	0.298	2 (25.0)	6 (75.0)	0.038*
	14–16 G	124 (40.9)	179 (59.1)		56 (9.9)	510 (90.1)		1 (1.8)	56 (98.2)	
Number of samples	**<4**	51 (49.0)	53 (51.0)	0.009*	26 (12.3)	186 (87.7)	0.088	1 (5.9)	16 (94.1)	1.000
	≥4	93 (34.3)	178 (65.7)		32 (8.0)	367 (92.0)		2 (4.2)	46 (95.8)	

Benign, benign and stable on follow-up; *$P < 0.05$. ADH, atypical ductal hyperplasia; LN, lobular neoplasia; RS, radial scar; IP, intraductal papilloma; FEA, flat epithelial atypia.
MRI, magnetic resonance imaging; BI-RADS, Breast Imaging Reporting and Data System.

diagnosed using VAB with no residual microcalcifications in concordant findings. The World Health Organization Working Group proposed observation as an acceptable management strategy for radiological–pathological correlated pure FEA.[46]

The upgrade rate was 4.6% for RSs in this study. When the lesion was ≤15 mm, the rate of associated malignancy at surgical excision was 2.2% (1/46 cases). There are variable results in the literature, ranging between 0% and 40%.[47] In a meta-analysis of 49 studies, including 3.163 RS cases with surgical outcomes, the pooled upgrade rate was 7%; yet in the subtype assessed with an 8 to 11 G VAB needle and lacking atypia, this rate was 1%.[48] Li et al.[49] and Conlon et al.[50] found 0.9% and 2% upgrade rates in patients without atypia. Accordingly, imaging surveillance seems to be a reasonable option for selected patients.

The large sample size of high-risk lesions in each subtype and the multicenter design are major strengths of the current study. This makes the statistical analysis more valuable. However, this study has several limitations, including its retrospective design, which could have resulted in missing data, and the potential differences in the clinical practices used for selecting and managing patients in different centers. Last, this study did not look at long-term follow-up results for the participants.

In conclusion, high-risk lesions identified by needle biopsy do not follow similar

Table 3. Continued

		FEA (n = 114)			LN (n = 35)			IP with atypia (n = 123)		
		Malignant n (%)	Benign n (%)	*P*	Malignant n (%)	Benign n (%)	*P*	Malignant n (%)	Benign n (%)	*P*
Mammography finding	**Microcalcification**	8	40 (83.3)	0.230	2 (10.5)	17 (89.5)	1.000	6 (66.7)	3 (33.3)	0.245
	Mass	1	12 (92.3)		0 (0)	2 (100)		21 (47.7)	23 (52.3)	
	Non mass	0(0)	14(100)		1 (16.7)	5 (83.3)		13 (68.4)	6 (31.6)	
Microcalcification morphology	**Amorphous**	3 (10.7)	25 (89.3)	0.269	1 (12.5)	7 (87.5)	1.000	2 (50.0)	2 (50.0)	0.600
	Coarse heterogeneous	1 (33.3)	2 (66.7)		0 (0)	0 (0)		2 (100)	0 (0)	
	Newly identified suspect	0 (0)	4 (100)		1 (20.0)	4 (80.0)		0 (0)	0 (0)	
	Fine linear	1 (33.3)	2 (66.7)		0 (0)	1 (100)		1 (100)	0 (0)	
	Fine pleomorphic	3 (30.0)	7 (70.0)		0 (0)	5 (100)		1 (33.3)	2 (66.7)	
Ultrasonography finding	**Mass**	0 (0)	44 (100)	0.003*	4 (19.0)	17 (81.0)	0.355	48 (42.9)	64 (57. 1)	0.077
	Non mass	7 (18.4)	31 (81.6)		1 (5.9)	16 (94.1)		7 (77.8)	2 (22.2)	
MRI finding	**Mass**	0 (0)	25 (100)	0.030*	2 (22.2)	7 (77.8)	1.000	15 (37.5)	25 (62.5)	0.084
	Non mass	6 (18.8)	26 (81.3)		4 (19.0)	17 (81.0)		7 (70.0)	3 (30.0)	
Lesion diameter	**≤1.5 cm**	1 (1.5)	67 (98.5)	0.001*	2 (5.7)	33 (94.3)	0.086	31 (38.3)	50 (61.7)	0.046*
	>1.5 cm	9 (19.6)	37 (80.4)		5 (25.0)	15 (75.0)		24 (57.1)	18 (42.9)	
BI-RADS	**3, 4A, 4B**	1 (1.1)	93 (98.9)	<0.001*	3 (6.4)	44 (93.6)	0.006*	43 (43.9)	55 (56.1)	0.711
	4C–5	9 (45.0)	11 (55.0)		4 (50.0)	4 (50.0)		12 (48.0)	13 (52.0)	
Needle thickness	**9–12 G**	3 (8.6)	32 (91.4)	1.000	2 (10.0)	18 (90.0)	1.000	1 (50.0)	1 (50.0)	1.000
	14–16 G	7 (8.9)	72 (91.1)		5 (14.3)	30 (85.7)		54 (44.6)	67 (55.4)	
Number of samples	**<4**	4 (16.0)	21 (84.0)	0.222	2 (18.2)	9 (81.8)	0.617	19 (44.2)	24 (55.8)	0.931
	≥4	6 (6.7)	83 (93.3)		5 (11.4)	39 (88.6)		36 (45.0)	44 (55.0)	

patterns; routine excision is unnecessary for every lesion. This study's upgrade rates to malignancy were related to the subtype, presence of atypia, and other variables, such as the BI-RADS score, lesion size, biopsy method used, and sampling adequacy. Because of these variables, there cannot be a general recommendation for all high-risk lesions of the breast. Clinical, radiologic, and pathologic features should all be reviewed before deciding whether surgical excision or close follow-up is most appropriate for a lesion. For ADH, although current guidelines recommend surveillance for small-volume lesions that are entirely removed through core biopsy, the recommendation remains typical management of surgical excision. IP with atypia also requires excision following CNB/VAB because of the high rate of associated malignancy. For LN, IP without atypia, pure FEA and RSs, underestimation rates were related to the BI-RADS score and, therefore, to radiology–pathology concordance, sampling adequacy, and lesion size. The upgrade rates increased with higher BI-RADS scores and lesion size in conjunction with insufficient tissue sampling. Boateng et al.[10] reported lower rates when large core needles (i.e., 9 to 11 G) were used and higher rates when 14 G needles were used. Therefore, all cases should be managed case-wise after a multidisciplinary team discussion.

Table 4. Multivariate analysis of malignancy upgrade in different subtypes of high-risk lesions according to needle thickness and lesion diameter

Pathologic subtype	Needle thickness	Lesion diameter	Benign n (%)	Malignant n (%)	Total n	*P*
ADH (n = 375)	9–12 G	≤15 mm	45 (80)	11 (20)	56	0.009*
		>15 mm	7 (44)	9 (56)	16	
	14–16 G	≤15 mm	111 (68)	53 (32)	164	0.001*
		>15 mm	68 (49)	71 (51)	139	
IP without atypia (n = 611)	9–12 G	≤15 mm	34 (100)	0 (0)	34	0.056
		>15 mm	9 (82)	2 (18)	11	
	14–16 G	≤15 mm	369 (94)	24 (6)	393	<0.001*
		>15 mm	141 (82)	32 (18)	173	
Lobular neoplasia (n = 35)	9–12 G	≤15 mm	15 (100)	0 (0)	15	0.053
		>15 mm	3 (60)	2 (40)	5	
	14–16 G	≤15 mm	18 (90)	2 (10)	20	0.631
		>15 mm	12 (80)	3 (20)	15	
Radial scar (n = 65)	9–12 G	≤15 mm	3 (75)	1 (25)	4	1.000
		>15 mm	3 (100)	0 (0)	3	
	14–16 G	≤15 mm	42 (100)	0 (0)	42	
		>15 mm	14 (87)	2 (13)	16	0.073
FEA (n = 79)	9–12 G	≤15 mm	22 (96)	1 (4)	23	0.266
		>15 mm	10 (83)	2 (17)	12	
	14–16 G	≤15 mm	44 (100)	0 (0)	44	0.002*
		>15 mm	28 (80)	7 (20)	35	
Atypical IP (n = 123)	9–12 G	≤15 mm	1(50)	1 (50)	2	-
		>15 mm	0 (0)	0 (0)	-	
	14–16 G	≤15 mm	49 (62)	30 (38)	79	0.043*
		>15 mm	18 (43)	24 (57)	42	

Benign, benign and stable on follow-up; *$P < 0.05$. ADH, atypical ductal hyperplasia; IP, intraductal papilloma; FEA, flat epithelial atypia.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Falomo E, Adejumo C, Carson KA, Harvey S, Mullen L, Myers K. Variability in the management recommendations given for high-risk breast lesions detected on image-guided core needle biopsy at U.S. Academic Institutions. *Curr Probl Diagn Radiol.* 2019;48(5):462-466. [CrossRef]
2. Thomas PS. Diagnosis and management of high-risk breast lesions. *J Natl Compr Canc Netw.* 2018;16(11):1391-1396. [CrossRef]
3. Gulla S, Lancaster R, De Los Santos J. High-risk breast lesions and current management. *Semin Roentgenol.* 2018;53(4):252-260. [CrossRef]
4. Nakhlis F. How do we approach benign proliferative lesions? *Curr Oncol Rep.* 2018;20(4):34. [CrossRef]
5. Bick U, Trimboli RM, Athanasiou A, et al. Image-guided breast biopsy and localisation: recommendations for information to women and referring physicians by the European Society of Breast Imaging. *Insights Imaging.* 2020;11(1):12. [CrossRef]
6. Mooney KL, Bassett LW, Apple SK. Upgrade rates of high-risk breast lesions diagnosed on core needle biopsy: a single-institution experience and literature review. *Mod Pathol.* 2016;29(12):1471-1484. [CrossRef]
7. Bianchi S, Caini S, Renne G, et al. Positive predictive value for malignancy on surgical excision of breast lesions of uncertain malignant potential (B3) diagnosed by stereotactic vacuum-assisted needle core biopsy (VANCB): a large multi-institutional study in Italy. *Breast.* 2011;20(3):264-270. [CrossRef]
8. Lucioni M, Rossi C, Lomoro P, et al. Positive predictive value for malignancy of uncertain malignant potential (B3) breast lesions diagnosed on vacuum-assisted biopsy (VAB): is surgical excision still recommended? *Eur Radiol.* 2021;31(2):920-927. [CrossRef]
9. Nizri E, Schneebaum S, Klausner JM, Menes TS. Current management practice of breast borderline lesions-need for further research and guidelines. *Am J Surg.* 2012;203(6):721-725. [CrossRef]
10. Boateng S, Tirada N, Khorjekar G, Richards S, Ioffe O. Excision or observation: the dilemma of managing high-risk breast lesions. *Curr Probl Diagn Radiol.* 2020;49(2):124-132. [CrossRef]
11. Pinder SE, Shaaban A, Deb R, et al. NHS breast screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions). *Clin Radiol.* 2018;73(8):682-692. [CrossRef]
12. Wells CAAI, Apostolikas N, Bellocq JP. Quality assurance guidelines for pathology. In: Perry NMBM, de Wolf C, editors. EC working group on breast screening pathology: Quality assurance guidelines for pathology in mammography screening – open biopsy and resection specimens European guidelines for quality assurance in mammography screening. 4th ed. Luxembourg: Office for Official Publications of the European Communities; 2006:219-256. [CrossRef]
13. Shaaban AM, Sharma N. Management of B3 lesions-practical issues. *Current Breast Cancer Reports.* 2019;11(2):83-88. [CrossRef]
14. 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(8):1253-1257. [CrossRef]
15. Strachan C, Horgan K, Millican-Slater RA, Shaaban AM, Sharma N. Outcome of a new patient pathway for managing B3 breast lesions by vacuum-assisted biopsy: time to

change current UK practice? *J Clin Pathol.* 2016;69(3):248-254. [CrossRef]

16. Georgian-Smith D, Lawton TJ. Variations in physician recommendations for surgery after diagnosis of a high-risk lesion on breast core needle biopsy. *AJR Am J Roentgenol.* 2012;198(2):256-263. [CrossRef]
17. Lawton TJ, Georgian-Smith D. Excision of high-risk breast lesions on needle biopsy: is there a standard of core? *AJR Am J Roentgenol.* 2009;192(5):W268. [CrossRef]
18. Rakha EA, Lee AH, Jenkins JA, Murphy AE, Hamilton LJ, Ellis IO. Characterization and outcome of breast needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening. *Int J Cancer.* 2011;129(6):1417-1424. [CrossRef]
19. de Beça FF, Rasteiro C, Correia A, Costa S, Amendoeira I. Improved malignancy prediction by B3 breast lesions subclassification. *Ann Diagn Pathol.* 2013;17(5):434-436. [CrossRef]
20. Falomo E, Adejumo C, Carson KA, Harvey S, Mullen L, Myers K. Variability in the management recommendations given for high-risk breast lesions detected on image-guided core needle biopsy at U.S. Academic Institutions. *Curr Probl Diagn Radiol.* 2019;48(5):462-466. [CrossRef]
21. Co M, Kwong A, Shek T. Factors affecting the under-diagnosis of atypical ductal hyperplasia diagnosed by core needle biopsies - A 10-year retrospective study and review of the literature. *Int J Surg.* 2018;49:27-31. [CrossRef]
22. Nguyen CV, Albarracin CT, Whitman GJ, Lopez A, Sneige N. Atypical ductal hyperplasia in directional vacuum-assisted biopsy of breast microcalcifications: considerations for surgical excision. *Ann Surg Oncol.* 2011;18(3):752-761. [CrossRef]
23. Peña A, Shah SS, Fazzio RT, et al. Multivariate model to identify women at low risk of cancer upgrade after a core needle biopsy diagnosis of atypical ductal hyperplasia. *Breast Cancer Res Treat.* 2017;164(2):295-304. [CrossRef]
24. Caplain A, Drouet Y, Peyron M, et al. Management of patients diagnosed with atypical ductal hyperplasia by vacuum-assisted core biopsy: a prospective assessment of the guidelines used at our institution. *Am J Surg.* 2014;208(2):260-267. [CrossRef]
25. Schiaffino S, Massone E, Gristina L, et al. Vacuum assisted breast biopsy (VaB) excision of subcentimeter microcalcifications as an alternative to open biopsy for atypical ductal hyperplasia. *Br J Radiol.* 2018;91(1085):20180003. [CrossRef]
26. Krishnamurthy S, Bevers T, Kuerer H, Yang WT. Multidisciplinary considerations in the management of high-disk breast lesions. *AJR Am J Roentgenol.* 2012;198(2):W132-W140. [CrossRef]
27. Brem RF, Lechner MC, Jackman RJ, et al. Lobular neoplasia at percutaneous breast biopsy: variables associated with carcinoma at surgical excision. *AJR Am J Roentgenol.* 2008;190(3):637-641. [CrossRef]
28. Cohen MA. Cancer upgrades at excisional biopsy after diagnosis of atypical lobular hyperplasia or lobular carcinoma in situ at core needle biopsy: some reasons why. *Radiology.* 2004;231(3):617-621. [CrossRef]
29. Hussain M, Cunnick GH. Management of lobular carcinoma in-situ and atypical lobular hyperplasia of the breast--a review. *Eur J Surg Oncol.* 2011;37(4):279-289. [CrossRef]
30. Chaudhary S, Lawrence L, McGinty G, Kostroff K, Bhuiya T. Classic lobular neoplasia on core biopsy: a clinical and radio-pathologic correlation study with follow-up excision biopsy. *Mod Pathol.* 2013;26(6):762-771. [CrossRef]
31. Murray MP, Luedtke C, Liberman L, Nehhozina T, Akram M, Brogi E. Classic lobular carcinoma in situ and atypical lobular hyperplasia at percutaneous breast core biopsy: outcomes of prospective excision. *Cancer.* 2013;119(5):1073-1079. [CrossRef]
32. Nakhlis F, Gilmore L, Gelman R, et al. Incidence of adjacent synchronous invasive carcinoma and/or ductal carcinoma in-situ in patients with lobular neoplasia on core biopsy: results from a prospective multi-institutional registry (TBCRC 020). *Ann Surg Oncol.* 2016;23(3):722-728. [CrossRef]
33. Hwang H, Barke LD, Mendelson EB, Susnik B. Atypical lobular hyperplasia and classic lobular carcinoma in situ in core biopsy specimens: routine excision is not necessary. *Mod Pathol.* 2008;21(10):1208-1216. [CrossRef]
34. Morrow M, Schnitt SJ, Norton L. Current management of lesions associated with an increased risk of breast cancer. *Nat Rev Clin Oncol.* 2015;12(4):227-238. [CrossRef]
35. Wen X, Cheng W. Nonmalignant breast papillary lesions at core-needle biopsy: a meta-analysis of underestimation and influencing factors. *Ann Surg Oncol.* 2013;20(1):94-101. [CrossRef]
36. Ahn Sk, Han W, Moon HG, et al. Management of benign papilloma without atypia diagnosed at ultrasound guided core needle biopsy: Scoring system for predicting malignancy. *Eur J Surg.* 2018;44(1):53-58. [CrossRef]
37. Zaleskia M, Chenb YA, Chetlenc AL, et al. Should we excise? Are there any clinical or histologic features that predict upgrade in papillomas, incidental or non-incidental? *Ann Diagn Pathol.* 2018;35:62-68. [CrossRef]
38. Mosier AD, Keylock J, Smith DV. Benign papillomas diagnosed on large gauge vacuum assisted core needle biopsy which span <1.5 cm do not need surgical excision. *Breast J.* 2013;19(6);611-617. [CrossRef]
39. Ko D, Kang E, Park SY, et al. The management strategy of benign solitary intraductal papilloma on breast core biopsy. *Clin Breast Cancer.* 2017;17(5):367-372. [CrossRef]
40. Pareja F, Corben A, Brennan S, et al. Breast intraductal papillomas without atypia in radiologic-pathologic concordant core needle biopsies: Rate of upgrade to carcinoma at excision. *Cancer.* 2016;122(18):2819-2827. [CrossRef]
41. Menes TS, Rosenberg R, Balch S, Jaffer S, Kerlikowske K, Miglioretti DL. Upgrade of high-risk breast lesions detected on mammography in the Breast Cancer Surveillance Consortium. *Am J Surg.* 2014;207(1):24-31. [CrossRef]
42. Piubello Q, Parisi A, Eccher A, Barbazeni G, Franchini Z, Iannucci A. Flat epithelial atypia on core needle biopsy: which is the right management? *Am J Surg Pathol.* 2009;33(7): 1078-1084. [CrossRef]
43. Villa A, Chiesa F, Massa T, et al. Flat epithelial atypia: comparison between 9-gauge and 11-gauge devices. *Clin Breast Cancer.* 2013;13(6):450-454. [CrossRef]
44. Wahab RA, Lee SJ, Mulligan ME, Zhang B, Mahoney MC. Upgrade rate of pure flat epithelial atypia diagnosed at core needle biopsy: a systematic review and meta-analysis. *Radiol Imaging Cancer.* 2021;3(1):e200116. [CrossRef]
45. Schiaffino S, Gristina L, Villa A, et al. Flat epithelial atypia: conservative management of patients without residual microcalcifications post-vacuum-assisted breast biopsy. *Br J Radiol.* 2018;91(1081):20170484. [CrossRef]
46. Verschuur-Maes AH, van Deurzen CH, Monninkhof EM, van Diest PJ. Columnar cell lesions on breast needle biopsies: is surgical excision necessary? A systematic review. *Ann Surg.* 2012;255(2):259-265. [CrossRef]
47. Linda A, Zuiani C, Furlan A, et al. Radial scars without atypia diagnosed at imaging-guided needle biopsy: How often Is associated malignancy found at subsequent surgical excision, and do mammography and sonography predict which lesions are malignant? *AJR Am J Roentgenol.* 2010;194(4):1146-1151. [CrossRef]
48. Farshid G, Buckley E. Meta-analysis of upgrade rates in 3163 radial scars excised after needle core biopsy diagnosis. *Breast Cancer Res Treat.* 2019;174(1):165-177. [CrossRef]
49. Li Z, Ranade A, Zhao C. Pathologic findings of follow-up surgical excision for radial scar on breast core needle biopsy. *Hum Pathol.* 2016;48;76-80. [CrossRef]
50. Conlon N, D'Arcy C, Kaplan JB, et al. Radial scar at image-guided needle biopsy: is excision necessary? *Am J Surg Pathol.* 2015;39(6):779-785. [CrossRef]