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FULL PAPER

Evaluating the use of vacuum-assisted excisions in the management of B3 breast lesions

[1]CLARE MCLACHLAN, MS, [2]MARCUS JACKSON, SFHEA, PHD and [3]ALEXANDRA VALENCIA, MD

[1]Bristol Breast Care Centre, North Bristol NHS Trust, Beaufort House, Southmead Hospital, Westbury-on-Trym, Bristol, United Kingdom
[2]Diagnostic Radiography Section, Centre for Allied Health, St George's University of London, London, United Kingdom
[3]Bristol Breast Care Centre, North Bristol NHS Trust, Bristol, United Kingdom

Address correspondence to:
Miss Clare McLachlan
E-mail: *claremclachlan1@outlook.com*
Dr Marcus Jackson
E-mail: *mjackson@sgul.ac.uk*

Objective: To evaluate the use of vacuum-assisted excisions (VAEs) in the management of B3 lesions within a single UK breast care centre. Assessment was made by determining the upgrade rates of the different B3 lesions at VAE.
Methods and Materials: The study population comprised all patients who had a B3 result and subsequently underwent a VAE between November 2016 and October 2021. Patients with ipsilateral cancers were excluded. Retrospective biopsy and VAE results were reviewed. Upgrade rates and confidence intervals were calculated, and statistical significance was tested to determine any differences between upgrade rates of the B3 groups.
Results: 480 VAEs for B3 lesions were performed, with 10 excluded. Overall upgrade rate was 5%. 87.5% of upgrades were to non-invasive disease. Atypical intraductal epithelial proliferation (AIDEP) had a 15% upgrade rate, significantly different to lobular neoplasia (2%), papilloma without atypia (0%), and radial scar without atypia (0%). 10% of B3 lesions with atypia were upgraded, significantly different to 0% of B3 lesions without atypia. B3 lesions diagnosed by vacuum-assisted biopsy (VAB) had a significantly higher upgrade rate of 8% compared with 2% for lesions diagnosed by core biopsy (CBX), although this result was impacted by high numbers of AIDEP diagnosed by VAB.
Conclusions: The results suggest using VAE for the management of AIDEP is appropriate. However, they also indicate that by performing VAEs of papillomas and radial scars without atypia, overtreatment may be occurring.
Advances in knowledge: This study adds to the ongoing discussion on the best treatment of B3 breast lesions.

INTRODUCTION

Approximately 7% of breast screening biopsies yield a B3 histopathological result.[1] The management of this group of lesions with 'uncertain malignant potential' has been much debated in the published literature.[1]

The subgroups of B3 lesions have diverse histopathological features and therefore have differing malignant potential.[2] The main subgroups are: Atypical intraductal epithelial proliferation (AIDEP), Lobular neoplasia (LN), Flat epithelial atypia (FEA), Radial Scar (RS) with or without atypia, Papilloma (PL) with or without atypia, Cellular Fibroepithelial Lesions and Mucocele-like lesions (ML) with or without atypia.[3] Breast atypia refers to epithelial cells with irregular or abnormal cytologic changes[4] and the presence of atypia in breast lesions is associated with a higher risk of breast cancer.[5]

The numbers of B3 lesions being detected are rising because of improved imaging, biopsy techniques, and pathology diagnosis.[1] The historical treatment of these lesions was surgical excision to allow complete histological characterisation.[6] With the increasing availability of VAB equipment and the scrutiny, the screening service has received for overdiagnosis and overtreatment of breast disease, a review of the management of these lesions was timely.[7]

The national breast screening service released updated guidelines for the management of B3 breast lesions in November 2016.[3] They recommended VAEs for most B3 lesions diagnosed either by CBX or VAB. Studies have shown VAEs are a safe alternative to surgical excisions with similar upgrade rates.[7,8] There are a few exceptions: surgical excision is still

advised for papillomas with atypia and cellular fibroepithelial lesions, as the pathologist needs the intact lesion.[3]

VAEs are less invasive and less expensive than surgical excisions.[9] They take a large volume of tissue (4g) to extensively sample the area.[1] The aim is to determine if there is a pathological upgrade to malignancy, changing the treatment for the patient.

This service evaluation determined the upgrade rates at VAE of B3 lesions in a single breast care centre in the UK, which is a large and busy breast screening and symptomatic service with approximately 1000 cancers and 100–150 B3 lesions detected per year.

METHODS AND MATERIALS

Patient population and ethical approval

The service evaluation used retrospective secondary data and did not alter patient care, so HRA ethical approval was not required.[10] However, permission was given to access that data by the Research and Development Department and the Departmental Clinical Leads.

All screening and symptomatic patients who underwent a VAE for a B3 result during the 5-year period between November 2016 to October 2021 were included in the study unless they had an ipsilateral cancer.

Initial biopsies were either 14G ultrasound-guided biopsies, with at least three samples taken or X-ray-guided 10G VAB, with standard practice of 12 samples. For VAEs 12 7G/8 G samples were taken.

Patients with a B3 lesion with atypia and no upgrade at VAE were given 5 years of annual surveillance mammograms.[11] B3 lesions without atypia needed no surveillance. Upgraded lesions routinely proceeded to surgical management.

Data collection

Data were collected from the Trust's database. The histology at the initial ultrasound-guided CBX or X-ray-guided VAB was recorded, as well as the VAE histology. X-ray-guided and ultrasound-guided VAEs were collected separately.

Histological categorisation

The B3 lesions were divided into the subgroups according to their histopathology: AIDEP, FEA, LN, papilloma no atypia, radial scar with atypia, radial scar no atypia, mucocele-like lesion, mixed B3 lesions, and other B3 lesions. The category of 'other' B3 lesions included rarer lesions such as spindle cell lesions and angiolipomas. Papillomas with atypia and cellular fibroepithelial lesions not suitable for surgery and other non-specified B3 lesions were also included.

Upgrade rates

Upgrade rates were calculated for each subgroup of B3 lesion. Confidence intervals (CIs) were calculated to establish the reliability of the upgrade rates.

Statistical analysis

Pearson's chi-squared tests (5% sig level) were used to determine if there were differences in the upgrade rates between the subgroups. They were also used to determine if there were significant differences between the upgrade rates of B3 lesions with and without atypia and between 14G diagnosed and VAB diagnosed B3 lesions. Chi-squared tests were not valid when the expected count was less than 5. Fisher's exact tests (5% sig level) were then used instead.

RESULTS

480 VAEs for B3 lesions were performed between November 2016 and October 2021. These were made up of 296 screening cases and 184 symptomatic cases. 305 X-ray-guided VAEs and 175 ultrasound-guided VAEs were performed. 10 cases were excluded because of known ipsilateral cancers. The radiological appearances of the lesions were 206 calcifications, 176 masses, 51 distortions, and 37 miscellaneous. 224 lesions measured 10 mm or less, 118 were 10–20 mm, 51 between 20–30 mm, and 61 were greater than 30 mm. 16 had an unknown size.

An overall upgrade rate of 5% was found. There was variation across the numbers and upgrade rates of each B3 subgroup (Figure 1). Upgrade rates ranged from 0 to 17% and sample sizes from 6 to 145 (Table 1). The most common B3 lesion that underwent VAE was papilloma with no atypia. None of the 145 VAEs performed for this were upgraded to malignancy. The second most common B3 lesion seen was AIDEP. 102 VAEs were performed for AIDEP, 15 of these (15%) were upgraded to malignancy. Other B3 lesions seen in good numbers were radial scars without atypia and LN. None of the 76 radial scars without atypia were upgraded and only one of the 58 VAEs for LN was upgraded (2%).

Mucocele-like lesions had the highest upgrade rate of 17% but only six cases were seen: not statistically reliable, as per the CI of 0.4 to 64.1%. FEA and radial scars with atypia were also not seen in high enough numbers for the results to be reliable.

The 'Other' group included four fibroepithelial lesions, one papilloma with atypia, four dystrophic calcifications, an angiolipoma, a nipple adenoma, and two lesions with atypical cells. One of the dystrophic calcifications was upgraded to IM DCIS. The rest were not upgraded.

Proportion of invasive and non-invasive upgrades at VAE

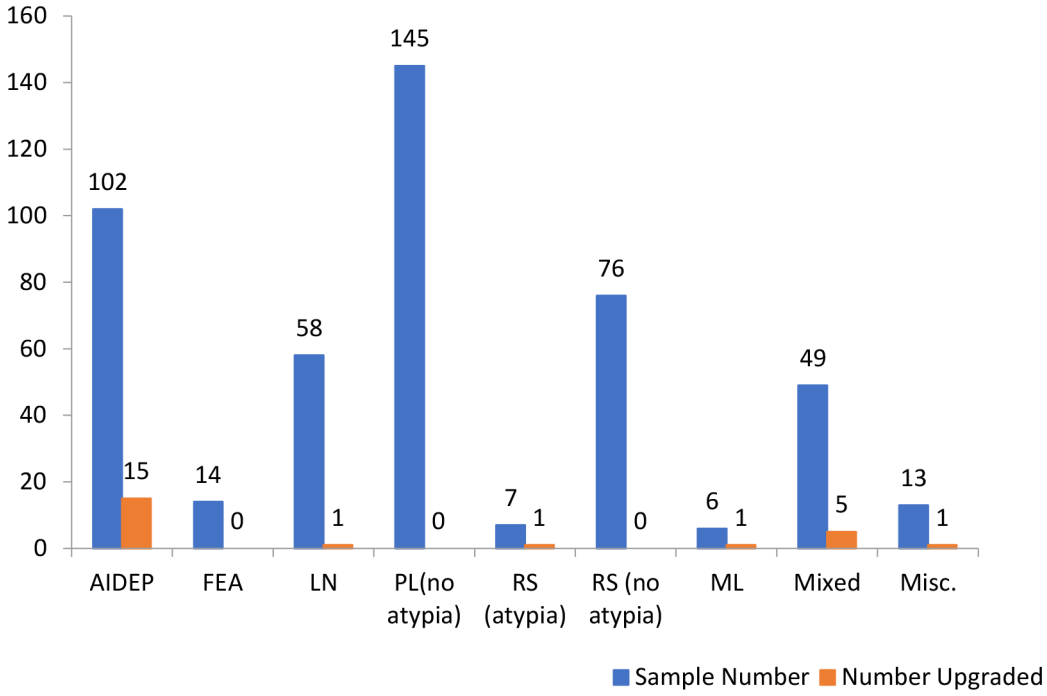
Out of 470 VAEs performed, 24 showed an upgrade to malignancy. 21 were upgraded to non-invasive disease: 20 to DCIS and 1 to Pleomorphic LCIS. Three were upgraded to invasive disease: two to small Grade 1 invasive ductal carcinomas and one to a 1 mm Grade 2 invasive lobular carcinoma (Figure 2).

Statistical differences between the upgrade rates of the B3 subgroups

Each subgroup was compared individually with the other subgroups to see if there was a significantly different upgrade rate to each group (Table 2A and B).

Chi-squared tests showed that the upgrade rate of AIDEP was significantly different to those of LN (p = 0.009), papillomas

Figure 1. Number of VAEs performed for each B3 subgroup and number upgraded.



without atypia (p = 0.000), and radial scars without atypia (p = 0.000). No significant difference was seen between AIDEP and the mixed B3 lesions (p = 0.445).

Fisher's exact test showed that the upgrade rate of papillomas without atypia was significantly different from mucocele-like lesions (p = 0.040) and the mixed group (p = 0.001). The upgrade rate of radial scars without atypia was shown to be significantly different from the mixed group (p = 0.008)

Statistical difference between the upgrade rates of B3 lesions with atypia and without atypia

The B3 lesions with atypia had a 10% upgrade rate at VAE compared with 0% for the B3 lesions without atypia (Figure 3). A significant difference was seen between the two groups using chi-squared (p = 0.000). Three dystrophic B3 lesions, including one cancer, could not be classified as having atypia or no atypia, so were excluded from this test.

Statistical differences in the upgrade rates of B3 lesions diagnosed by 14g CBX and VAB

Figure 4 shows the difference between initial biopsy method and upgrade rate. 209 14G US CBXs were performed and 4 of these were upgraded at VAE (2%), compared with 237 stereotactic core VABs performed, of which 20 were upgraded at VAE (8%).

Table 3 shows that there is a significant difference between the overall upgrade rates of B3 lesions diagnosed by either 14G CBX or VAB when tested with chi-squared. However, no

Table 1. Upgrade Rates with 95% Confidence Intervals.

B3 Subgroup:	Sample Number:	Number Upgraded:	Upgrade Rate:(%)	95% CI:(%)
AIDEP	102	15	15	8.5–23.1
FEA	14	0	0	0–23.2
LN	58	1	2	0–9.2
PL no atypia	145	0	0	0–2.5
RS with atypia	7	1	14	0.4–57.9
RS no atypia	76	0	0	0–4.7
ML	6	1	17	0.4–64.1
Mixed	49	5	10	3.4–22.2
Other	13	1	8	0.2–36
Overall	470	24	5	3.3–7.5

Figure 2. Percentage of Invasive and Non-invasive Upgrades at VAE.

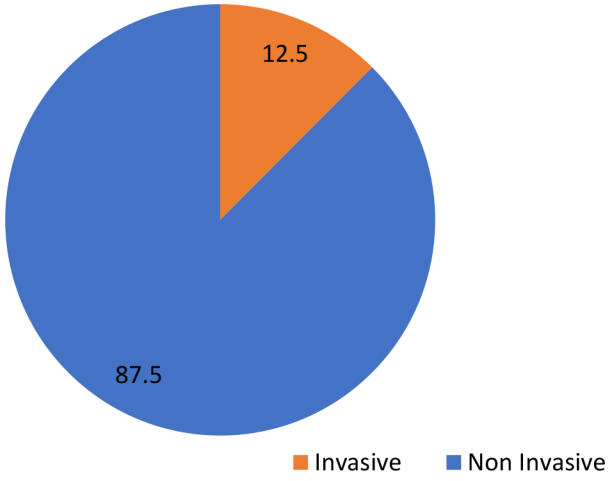
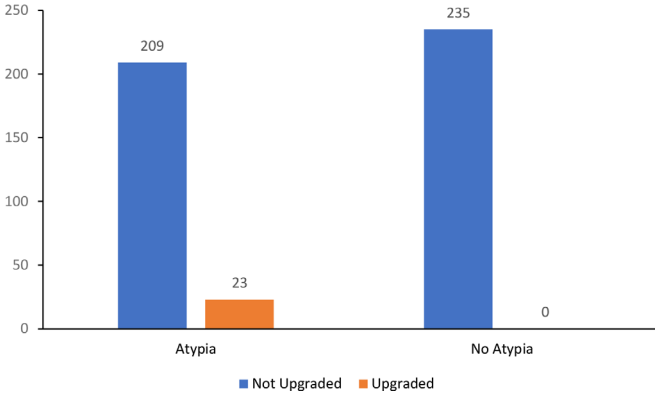


Figure 3. VAE outcomes split according to whether the initial biopsy result showed atypia or no atypia.



significant difference was seen when each B3 subgroup was tested individually using Fisher's exact test.

DISCUSSION

This study evaluating the use of VAEs in the management of B3 lesions was performed to establish if the departmental upgrade rates aligned with the published literature and whether the current practice is supported by the findings. The upgrade rates found in this study were lower than the rates found in similar published UK studies. For example this study's overall upgrade rate was 5%, compared with 16.6%, 19%, and 8.6% in the published literature.[5,7,12] Possible reasons for this lower upgrade rate could be pathologist variability, departmental practice variability or population variability.[1,2] Pinder et al mentions sampling using larger needles and better image guidance for the decrease in upgrade rates seen in the more recent literature.[1] Standard departmental practice is first line VAB for calcifications and 12 10G cores are routinely taken, giving a large volume of tissue, which may explain the lower upgrade rate.

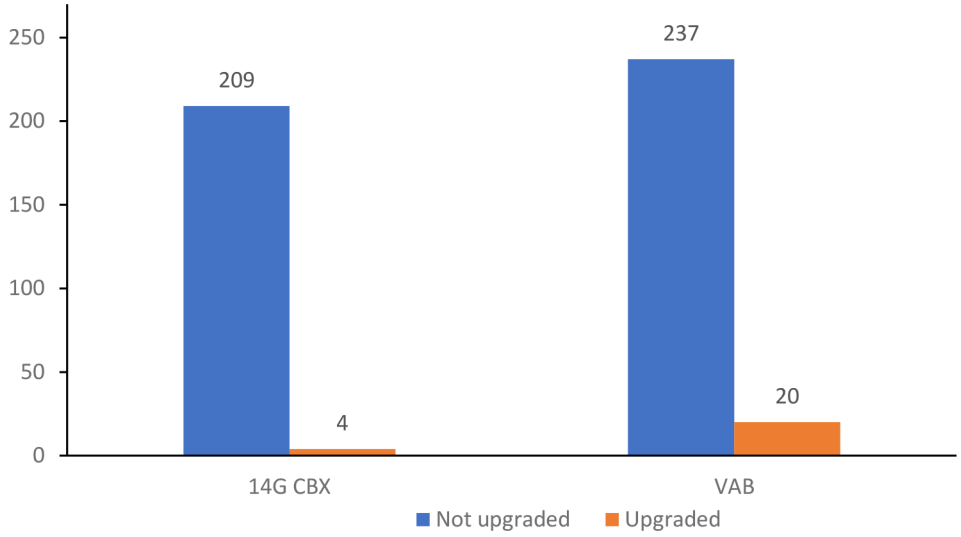
AIDEP had an upgrade rate of 15%. This aligns with the literature in being the most upgraded lesion.[2] 15 out of the 24 (62.5%) lesions that were upgraded at VAE showed AIDEP on their initial biopsy. Also, four out of the five of the mixed B3 lesions that were upgraded had AIDEP as one of the lesions. AIDEP was therefore present in 79% of the upgraded lesions. AIDEP had a significantly similar upgrade rate to the mixed group, as expected due to AIDEP being seen frequently in this group. AIDEP had a significantly different upgrade rate when compared with LN, papillomas without atypia and radial scars without atypia, which was not unexpected due to the very low upgrade rates in these lesions.

No cases of papillomas without atypia and radial scars without atypia were upgraded at VAE. These results suggest that the disadvantages of a costly and invasive procedure are not being

Table 2. Significant Results

	FEA	LN	PL No atypia	RS Atypia	RS No atypia	ML	MIXED	OTHER
A Significant Results according to Chi-squared								
AIDEP	NA	Yes $p = 0.009$	Yes $p = 0.000$	NA	Yes $p = 0.000$	NA	No $p = 0.445$	NA
B Significant Results according to Fishers								
AIDEP	No	Yes $p = 0.011$	Yes $p = 0.000$	No	Yes $p = 0.000$	No	No $p = 0.609$	No
FEA		No	NA (Both 0%)	No	NA (Both 0%)	No	No	No
LN			No	No	No	No	No	No
PL No atypia					NA (Both 0%)	Yes $p = 0.040$	Yes $p = 0.001$	No
RS Atypia					No	No	No	No
RSW No atypia						No	Yes $p = 0.008$	No
ML							No	No
MIXED								No

Figure 4. Bar chart showing VAE outcomes split according to initial biopsy method.



outweighed by the benefits of upgrading these lesions and therefore a change in patient management.

Lesions with atypia had a 10% upgrade rate compared with 0% for lesions without atypia. These results are similar to a study by Giannotti et al of 15.5%[12] versus 0%, but much lower than Sharma et al's study of 29.1%[5] versus 13.3%. This result suggests that atypia is a risk factor for upgrade and that we may be overtreating the B3 lesions without atypia. It needs to be noted that AIDEP is an atypical B3 lesion and so the large number of AIDEP upgraded compared to the other B3 lesions could have impacted on this result.

Only 3 of the 24 lesions (12.5%) were upgraded to an invasive cancer. Two small Grade 1 cancers and a 1.2 mm Grade 2 cancer were found at VAE but no residual invasive cancer was seen at surgery. The other 21 lesions were upgraded to *in situ* cancers that were mostly a mixture of high-grade and intermediate-grade DCIS. Again, this aligns with the published literature.[5] High-grade and intermediate-grade DCIS have a high probability of progressing to an invasive cancer within several years if left untreated,[13] so VAEs offer an important opportunity to identify and treat these lesions in the hope of avoiding biologically more aggressive disease in the future.

The overall upgrade rate was higher for VAB diagnosed B3 lesions, compared with 14G CBX diagnosed B3 lesions (8% 'v' 2%), and this was significantly different. This goes against the trend seen in some of the literature,[1,12] where a higher upgrade rate was seen in the 14G CBXs, thought to be due to the smaller sample size. This anomaly can be explained by the fact that the lesion with the highest upgrade rate: AIDEP, is mostly diagnosed from X-ray-guided VABs of calcification and this may have skewed the results. When Fisher's exact tests were performed comparing the difference between the 14G CBX and VAB for each subgroup, no significant difference was found for any group. This suggests that the site providing the data for this study is using the correct biopsy method, according to imaging presentation, otherwise some differences might be expected.

Table 3. Differences in the upgrade rates of B3 lesions diagnosed by 14G CBX and VAB

	14G Number	14G Upgrade Rate %	VAB Number	VAB Upgrade Rate %	Sig. difference? (5% Sig)
AIDEP	19	16	83	14	No $p = 1.0$ FET
FEA	4	0	10	0	NA
LN	10	0	48	2	No $p = 1.0$ FET
PL no atypia	131	0	14	0	NA
RS atypia	4	0	3	33	No $p = 0.43$ FET
RS no atypia	34	0	42	0	NA
ML	3	0	3	33	No $p = 1.0$ FET
Mixed	4	25	45	9	No $p = 0.36$ FET
Other	4	0	9	11	No $p = 1.0$ FET
Overall	213	2	257	8	Yes $p = 0.004$ PCS

FET: Fisher's Exact Test. PCS: Pearson's Chi-squared Test

The study was limited due to the low numbers in some of the subgroups and further research with a larger study population is required to determine reliable upgrade rates for all B3 lesions. The results of this study can only be applied to this department, so recommendations to broader practice cannot be made. However, the results can add to the ongoing discussion and highlights the importance of knowing each department's figures, as they can vary from the literature.

CONCLUSIONS

Low upgrade rates were found in this one-unit study and the results demonstrate that the different subtypes of B3 lesions have varying rates of upgrade to malignancy. The figure of only 24 out of the 470 VAEs performed being upgraded, suggests that considerable time and resource is spent performing an invasive procedure that is unlikely to change management. This suggests that different management strategies could be used for the different B3 lesions to ensure cancers are still diagnosed but overtreatment of low-risk lesions is minimalised. For example, it may not be necessary to perform a VAE for patients with papillomas and radial scars without atypia. AIDEP, however, has a statistically significant upgrade rate and is, therefore, appropriately managed by VAE.

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