Update of B3 lesion guidelines – UK vs Swiss guidance

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B3 guidelines

- Published in the NHS BSP assessment guidance document 2016[1]
- UK B3 Guidelines published in Clinical Radiology – September 2018[2]

[1]NHS Breast Screening Programme Clinical guidance for breast cancer screening assessment NHSBSP publication number 49 Fourth edition November 2016

[2]Pinder SE, Shaaban A, Deb R, Desai A, Gandhi A, Lee AH, Pain S, Wilkinson L, Sharma N. NHS Breast Screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions). Clinical radiology. 2018 May 15.

NHS Breast Screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions)

- Working group consisting of Radiologists, Pathologists and Surgeons.
- Comprehensive review of the literature
- Pathway for managing the different types of B3 lesions was developed.

Swiss Guidelines

- Following presentations of each B3 lesion in detail with an update of the published literature since the first International Consensus Conference, three questions were asked in turn regarding each of the six B3 lesions:

- Q1. If a core-needle biopsy (CNB) returned a B3 lesion on histology, should the lesion be excised?

- Q2. If so, should it be excised using vacuum-assisted biopsy (VAB) or open surgical excision (OE)?

- Q3. If the VAB returned a B3 lesion on histology and if the lesion was completely removed on imaging, is surveillance acceptable or should a repeat VAB or OE be performed?

A panel discussion followed the voting (89participants) and consensus recommendations were agreed for the management of each B3 lesion along with decisions on surveillance.

Key Differences

- UK guidelines: All B3 lesions except for papilloma with atypia, spindle cell lesions and fibroepithelial lesions should be managed with vacuum assisted excision rather than surgery.
- Swiss guidelines: All ADH and phylloides tumour should go for surgical excision

Defining VAB and VAE – UK guidelines

- Vacuum Assisted Biopsy (VAB) is where vacuum biopsy is replacing the conventional 14G core biopsy to make a **DIAGNOSIS.** The aim is to take the minimum amount of tissue to make a diagnosis.

- Vacuum Assisted Excision (VAE) is where vacuum is used to replace the surgical diagnostic biopsy. The aim is to take plentiful tissue. If the lesion is small (≤15mm) then likely to excise the lesion but if >15mm then likely to obtain representative sampling of an area. Aim for about 4G tissue.

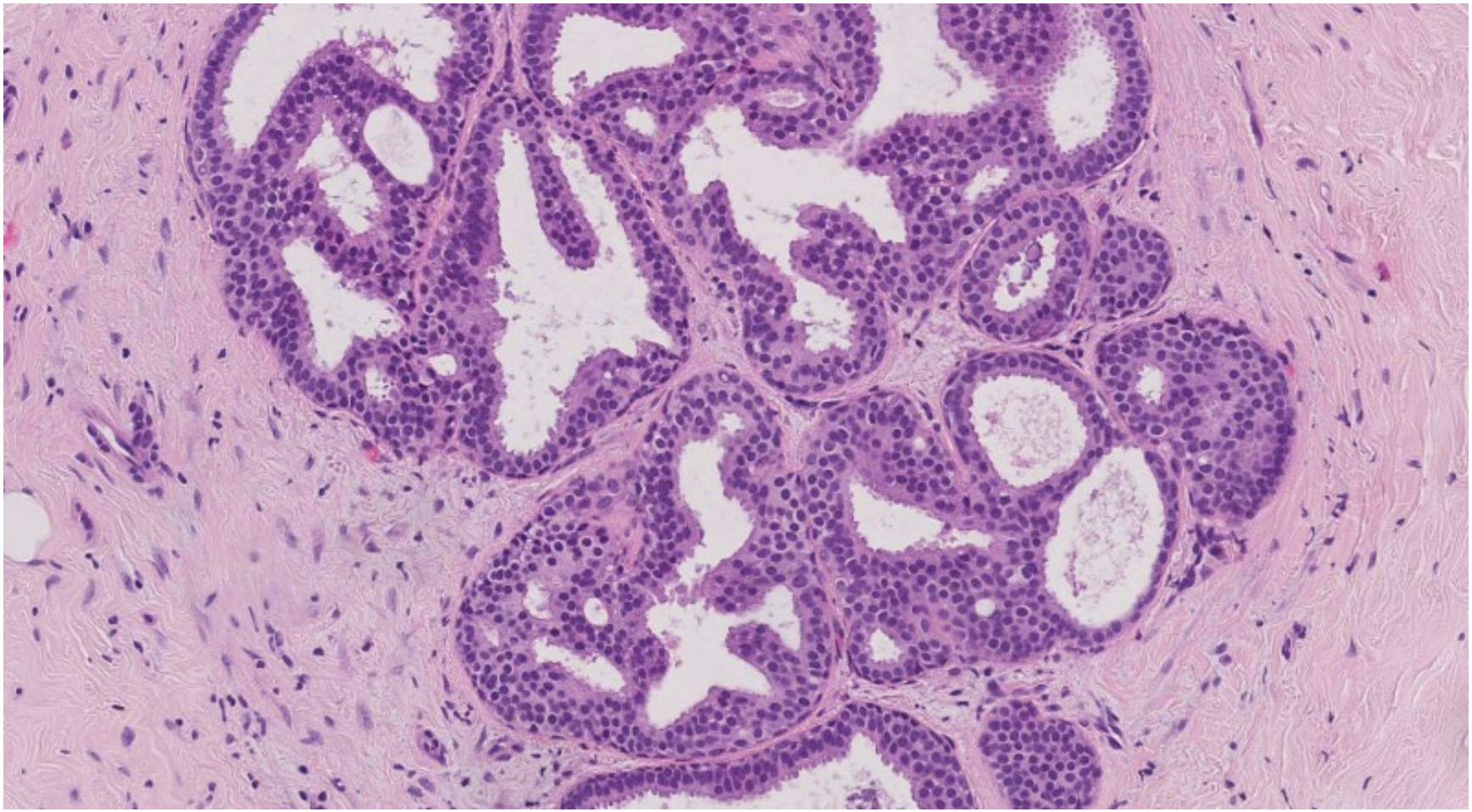
UK guidelines

- Changes in pathology reporting

ADH

- ADH has been used historically when reporting core biopsy or surgical diagnostic biopsy
- The definition of atypical ductal hyperplasia (ADH) is derived from surgical resection specimens and relies on a combination of architectural, cytological and size extent criteria
- ADH is defined as an intraductal epithelial proliferation showing the features of low grade DCIS, but in less than two duct spaces or less than 2 mm in diameter.
- ADH cannot be definitively diagnosed on the limited sampling provided by core biopsy, as the extent of the lesion cannot be determined with accuracy.

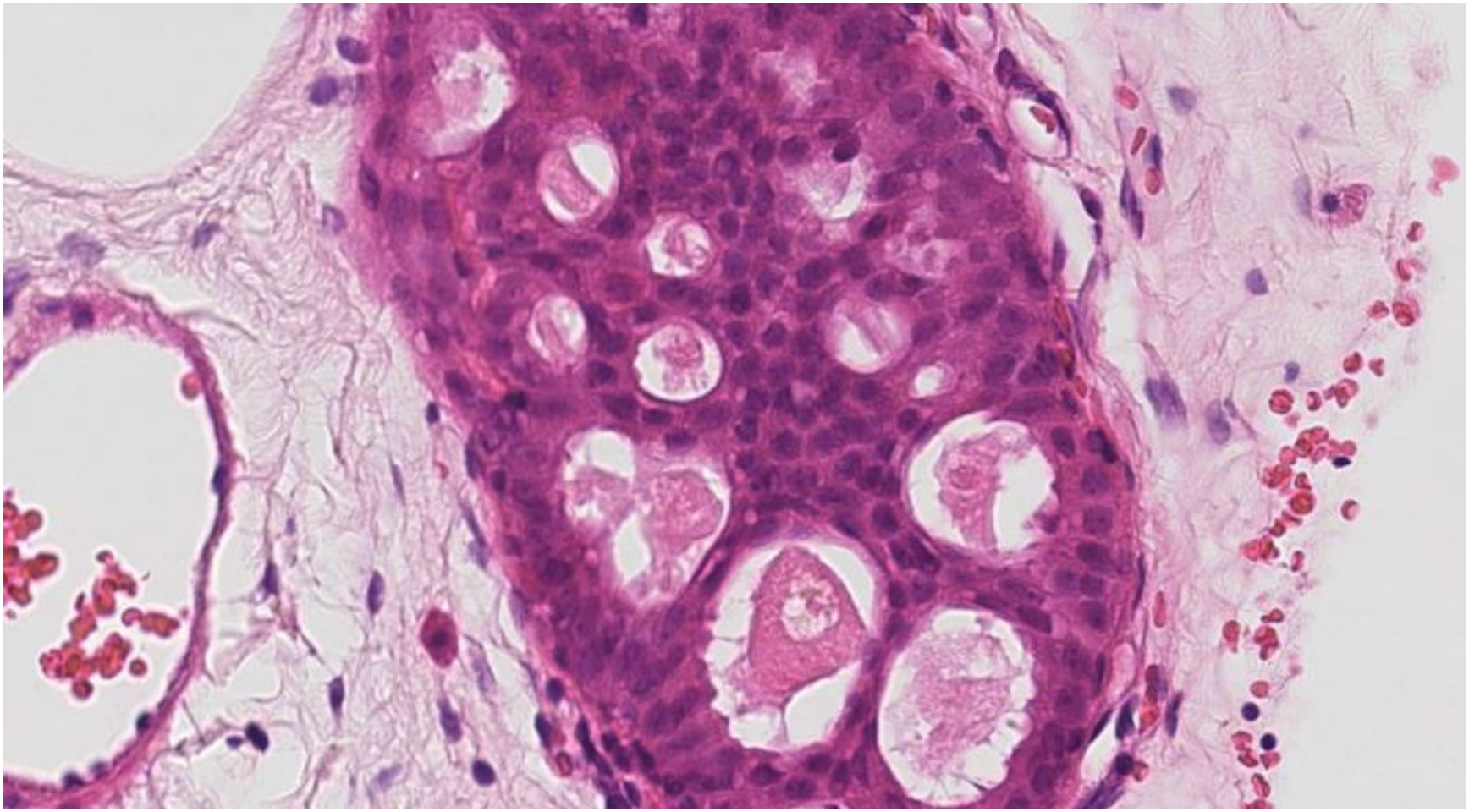
ADH



AIDEP

- Atypical intra ductal epithelial proliferation (AIDEP) is an intraduct epithelial cell proliferation that is partly monomorphic and shows cytological and/or architectural atypia
- Quantitative and qualitative in nature
- Replaced the term atypical ductal proliferation (ADH) when reporting core biopsies

AIDEP



AIDEP

- Clustered microcalcification is the most common radiological abnormality (75%; 137 of 182 cases[1]), with masses and distortions equally comprising the remaining lesions. In other series[2] the proportion of AIDEP presenting with microcalcification is even higher (86%).
- The upgrade rate of AIDEP to malignancy is greater with small samples (e.g., 14 G cores) compared to VAB specimens.
- The upgrade rate for AIDEP varies from 18–87% for 14 G needles compared to 10–39% with 11 or 9 G samples with a pooled positive predictive value of 21% from vacuum-assisted sampling.[3]
- In essence, unsurprisingly, if a greater amount of tissue is provided, there is a lower chance of “missing” a diagnosis of DCIS or invasive cancer.
- This reflects the more extensive sampling that is achieved with VAB in this group of lesions in which there is a moderate chance of co-existing malignancy.

AIDEP/ADH

- Recognised that upgraded to low grade DCIS
- Swiss guidelines: concerned that this may represent the periphery of a lesion or from a larger area of LG DCIS
  - Overall underestimation rates should not exceed 5% for invasive cancer and 10% for DCIS.
- UK guidelines: recognise upgrade rate is higher. Improve the preoperative upgrade of AIDEP to LGDCIS and support LORIS trial

Leeds Audit on Ductal Atypias

268990 women were screened from April 2009 to March 2016, of which 12434 were recalled to assessment (4.6%).

5582 biopsies were performed of which 688 were B3 lesions (12.3%).

Ductal atypias (FEA and AIDP) (excluding papilloma and radial scars with ductal atypias) accounted for 39.8% of the biopsies.

Results

- 69% (190/274) were managed with vacuum assisted excision (VAE) and annual mammographic follow-up or routine screening surveillance. 3% (7/190) developed a cancer during surveillance period, of which 4 were in the same quadrant.
- 13% (35/274) were upgraded to malignancy following VAE and were treated with therapeutic surgery. 2 developed further cancer on surveillance in the same breast.
- 8% (21/274) had a vacuum excision and a surgical biopsy due to radiological or pathological concern and 14/21 was benign and 7/21 upgraded to malignancy. One case developed cancer in the contralateral breast on cancer follow up.

Results

- 8% (22/274) had a surgical diagnostic biopsy instead of vacuum excision and 13/22 were benign and 9/22 were upgraded to malignancy.
- 2% (6/274) did not go on to have either vacuum excision or surgery due to co-morbidities. 2 developed cancer on surveillance.
- 12/274 (4%) developed malignancy during surveillance period of which 8/274 were in the same breast.

Conclusion

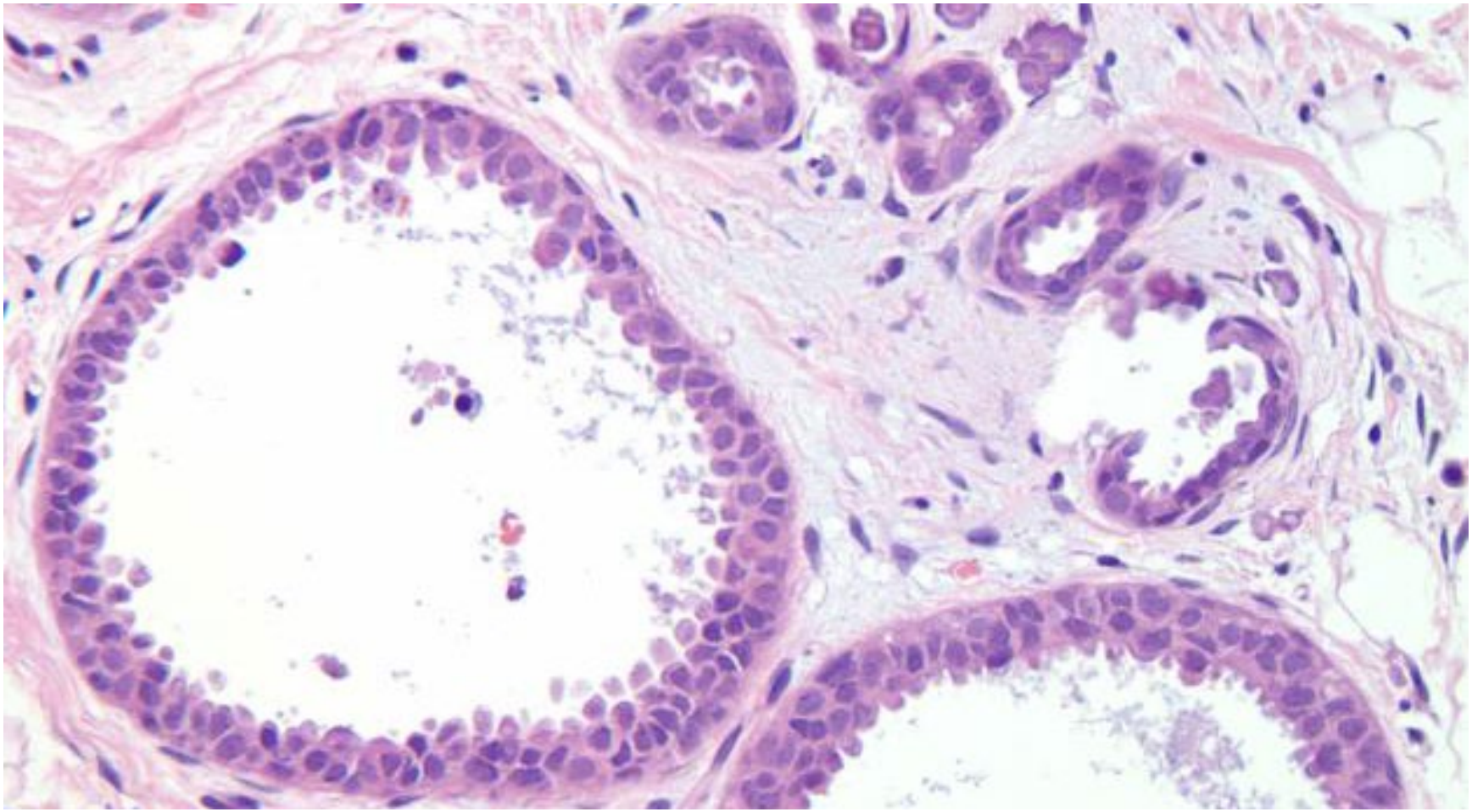
Our study shows that managing ductal atypia with vacuum assisted excision (VAE) is a safe alternative to surgical excision as a primary intervention but multidisciplinary review is important to determine if further surgery is required. Vacuum excision allowed 13% of our women to have a therapeutic surgery as preoperative diagnosis of malignancy was made and 69% avoided surgery altogether.

Pure B3 histology	*N*	With subsequent OE	Total upgrade	Upgrade to DCIS OR pleomorphic LN	Upgrade to IC	No upgrade
ADH	**943**	**591 (62.7%)**	**149 (25.2%)**	**119 (20.1%)**	**30 (5.1%)**	**408 (69.0%)**
FEA	994	249 (25.1%)	40 (16.1%)	22 (8.8%)	18 (7.2%)	181 (72.7%)
LN	701	268 (38.2%)	68 (25.4%)	35 (13.1%)	33 (12.3%)	178 (66.4%)
PL	1251	272 (21.7%)	21 (7.7%)	16 (5.9%)	5 (1.8%)	217 (79.8%)
PT	35	4 (11.4%)	0	0	0	4 (100%)
RS	415	75 (18.1%)	6 (8%)	5 (6.7%)	1 (1.3%)	60 (80.0%)

Flat Epithelial Atypia - FEA

- This refers to dilatation of terminal duct lobular unit lined by rounded to cuboidal cell showing cytological atypia.
- The cells retain the columnar cell phenotype and often show apical snouts and secretion.
- Nuclear stratification, without associated architectural complexity, can be seen.
- Luminal secretion and calcification are common.
- It is important to note that FEA definition does not include high grade nuclear atypia. If the latter is present, the lesion should be classified as high grade flat/clinging DCIS.

FEA on Vacuum biopsy



FEA

- The upgrade rate for FEA remains somewhat unclear, as this entity has not been recognised and reported for many decades and has during this time undergone several changes in nomenclature.
- FEA not infrequently co-exists with AIDEP and the upgrade rate in this setting is higher than FEA alone.[4]
- Although initial reports indicated a high risk of associated malignancy, later series note that this is not as prevalent as some of the earlier reports suggest.
- Overall, Verschuur-Maes *et al.*,[4] in a systematic review including 390 of 668 (58%) where patients had a diagnosis of columnar cell atypia (i.e., FEA) and then surgical excision (within 4 months of the core biopsy specimen) reported that 57 (17%) had associated carcinoma in the subsequent excision (37 DCIS, 10%; 20 invasive carcinoma, 4%).
- This is essentially similar to UK data from the West Midlands and South Central regions within the NHS BSP where a positive predictive value of 20.8% for FEA was reported[2] and with a series from Italy where the upgrade was 12.7% following VAB sampling.[1]

UK and Swiss guidelines

- Consensus – should be managed with VAE

ISLN

- Associated with increased risk of development of invasive cancer in either breast
- Associated with an upgrade with co-existing or adjacent DCIS and/or invasive carcinoma
- Upgrade rate is about 27%
- Ensure radiological and pathological concordance

ISLN

- On core biopsy spectrum of lesions from ALH to LCIS
- Often incidental finding in 0.3% - 3.8% of breast biopsies
- Recent study
  - 299 cases of pure lobular neoplasia
    - Excluded pleomorphic and necrotic forms
  - Constituted 2.1% of biopsies performed (352/16945)
  - Follow up in 275 patients
  - 27 cancers (9.8%)
    - 3 in same quadrant previously biopsied
    - 24 elsewhere in the breast.
  - Conclusion: Low risk forms do not need to be removed surgically provide radiological and pathological concordance.

UK vs Swiss Guidelines

- Consensus – A core biopsy showing lobular neoplasia should undergo VAE and surveillance provided no pathological and radiological discordance

Traditional management

- B3 lesions on core biopsy warranted further sampling
- Traditionally managed with surgical excision
- Day case procedure
- Wire localisation
- General anaesthetic
- Surgical scar
- If upgrade to cancer then second operation required as unable to assess margins

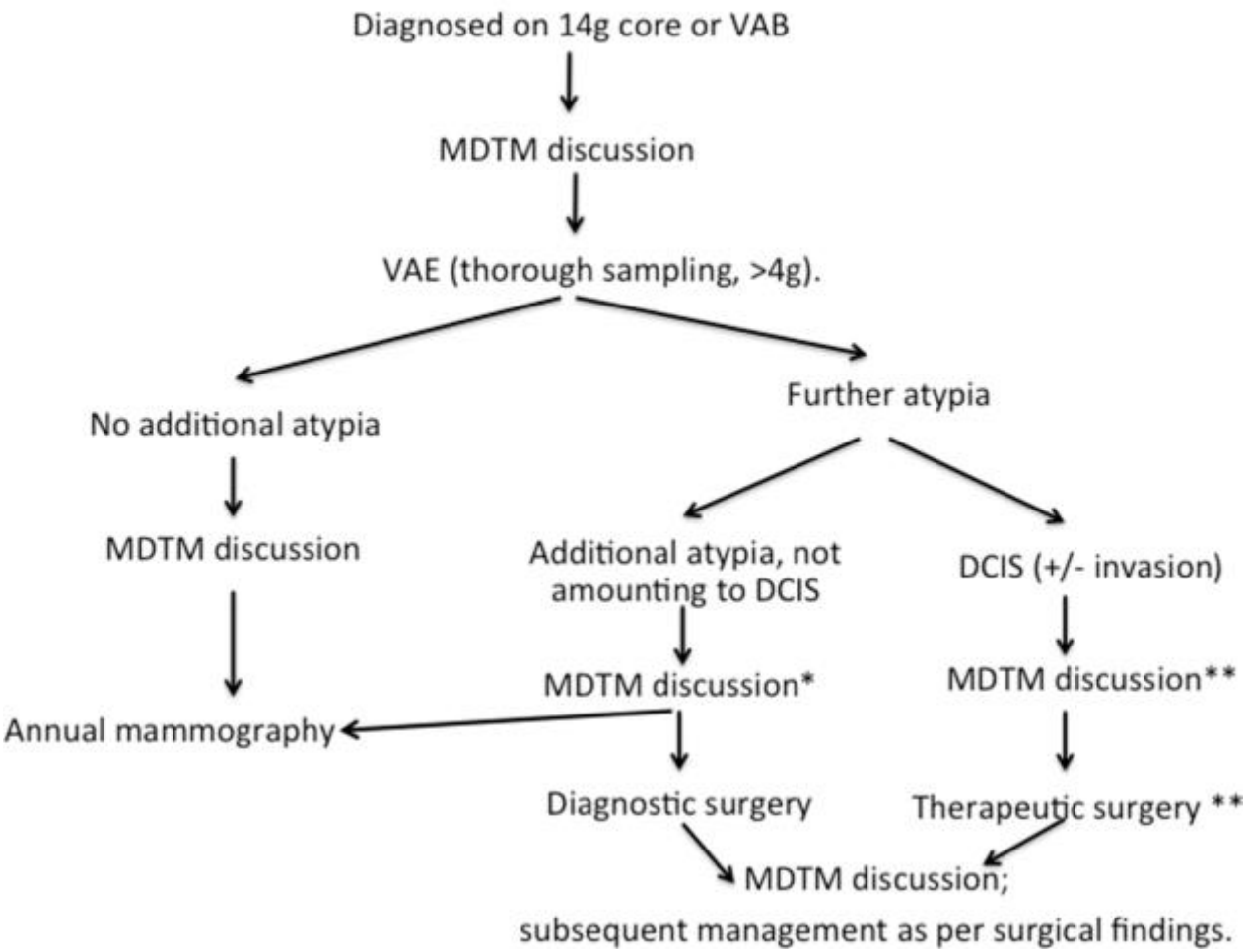
New pathway

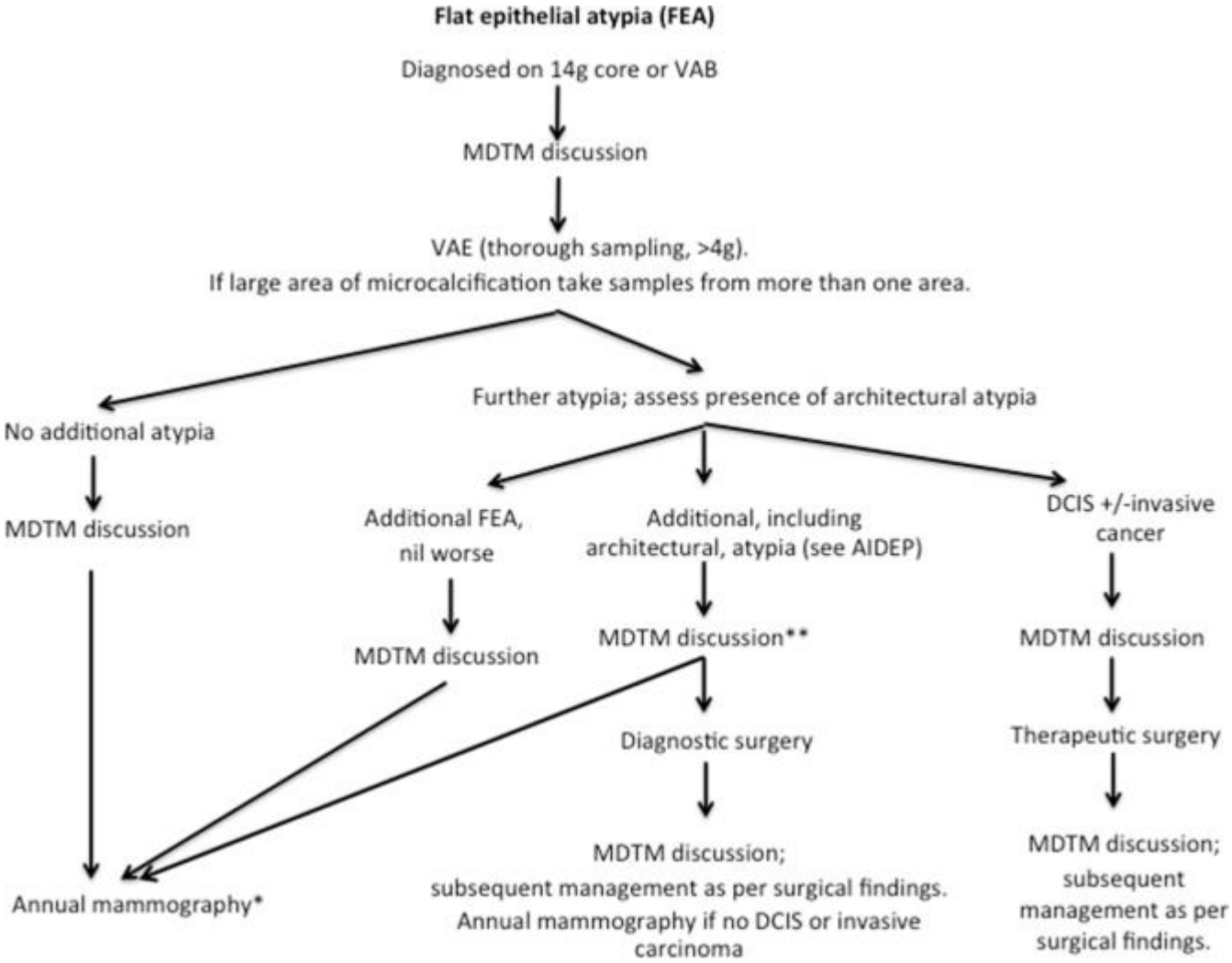
- Initial biopsy can be 14G or VAB 9-14G
- If B3 diagnosis discussion at MDM
  - Suitable for VAE
- VAE
  - Aim to remove 4g of tissue.
  - X-ray sample if for calcification
  - Clip placement advised
  - Post biopsy mammogram

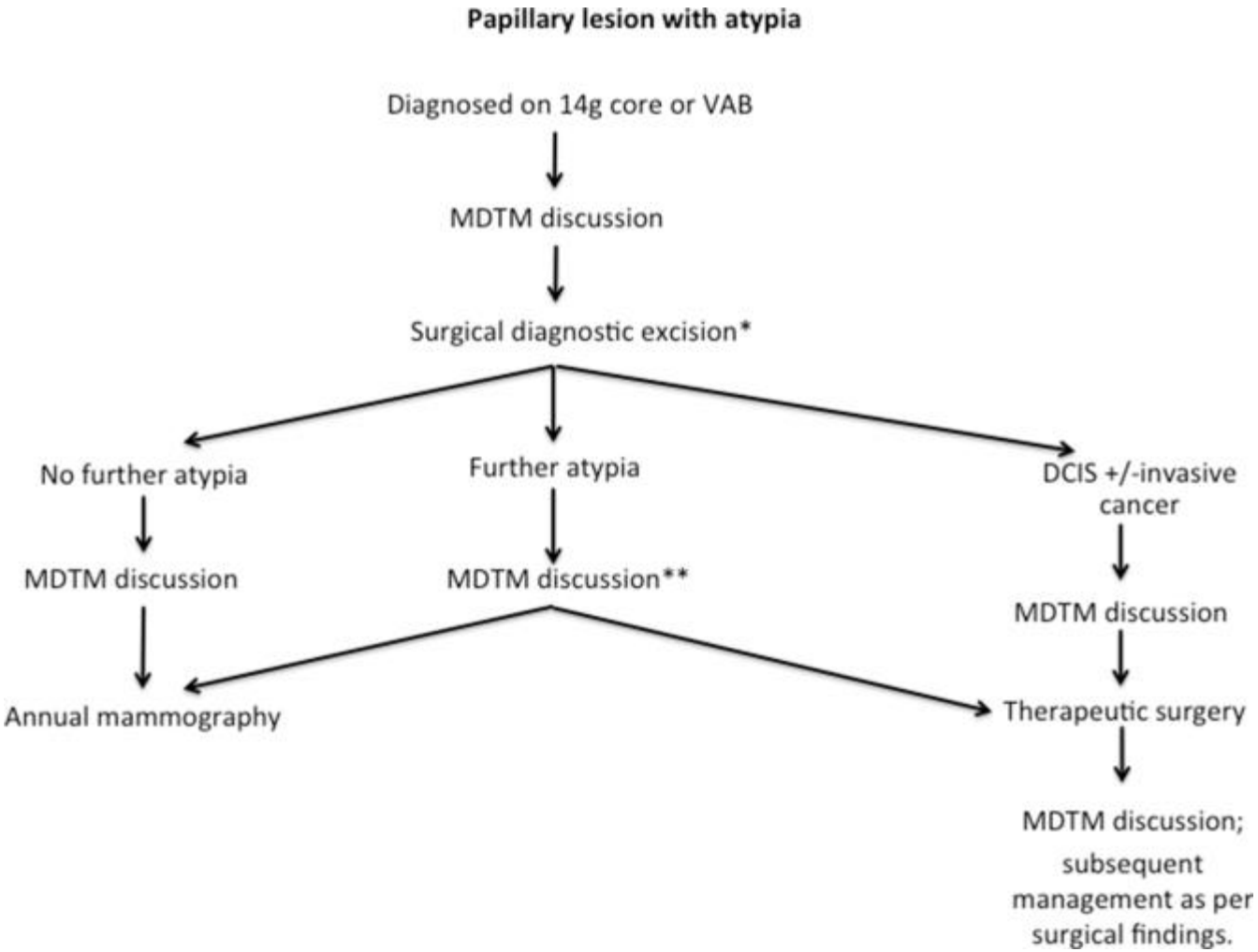
New pathway

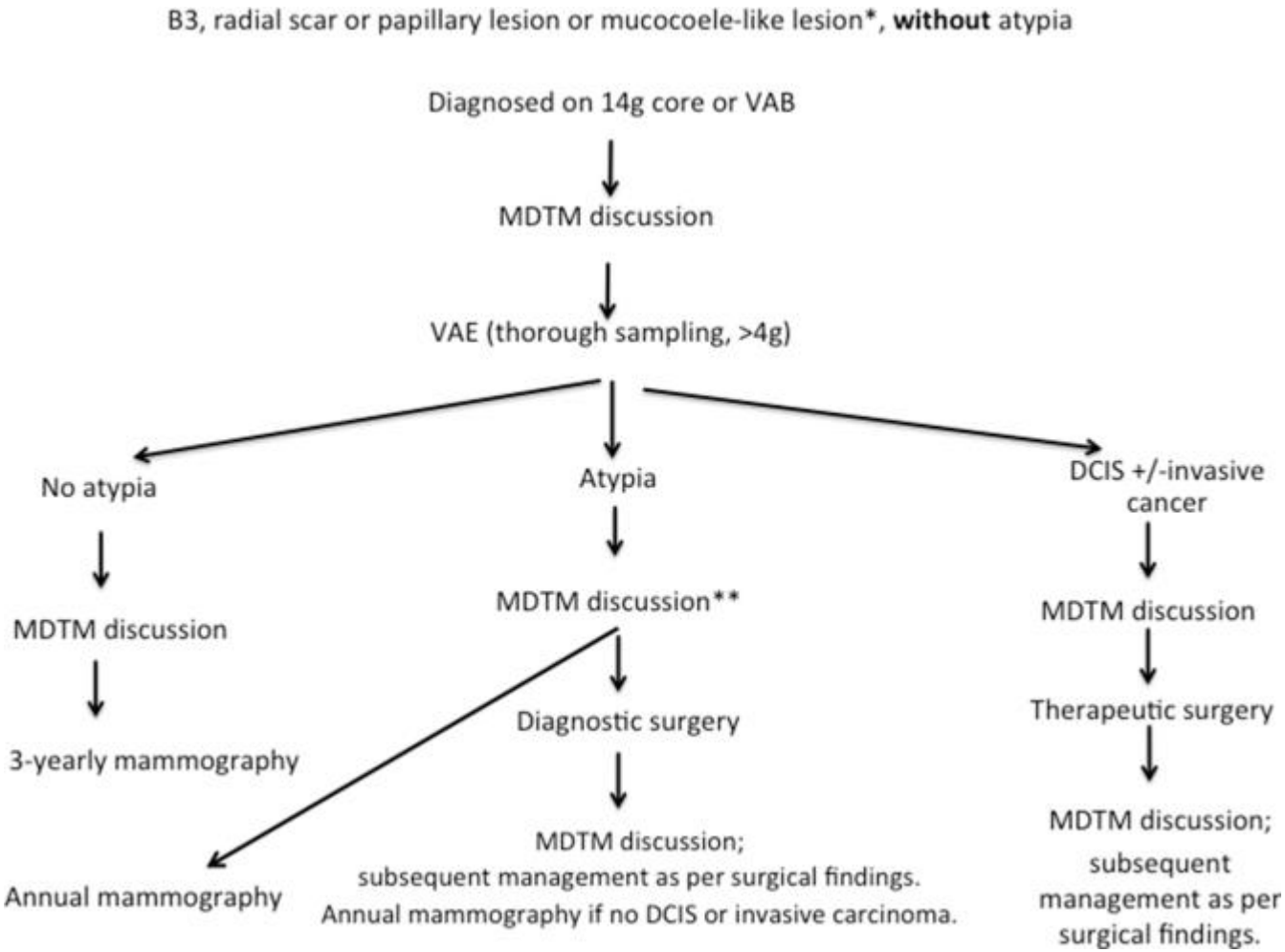
- Radiology report needs to state the needle gauge and number of cores and number of cores with calcifications
- Adequacy of sampling
- MDM discussion
- Follow discussion
  - Surgical diagnostic biopsy
  - Beast screening
  - 5 year mammographic follow up
  - Take into account family history and risk

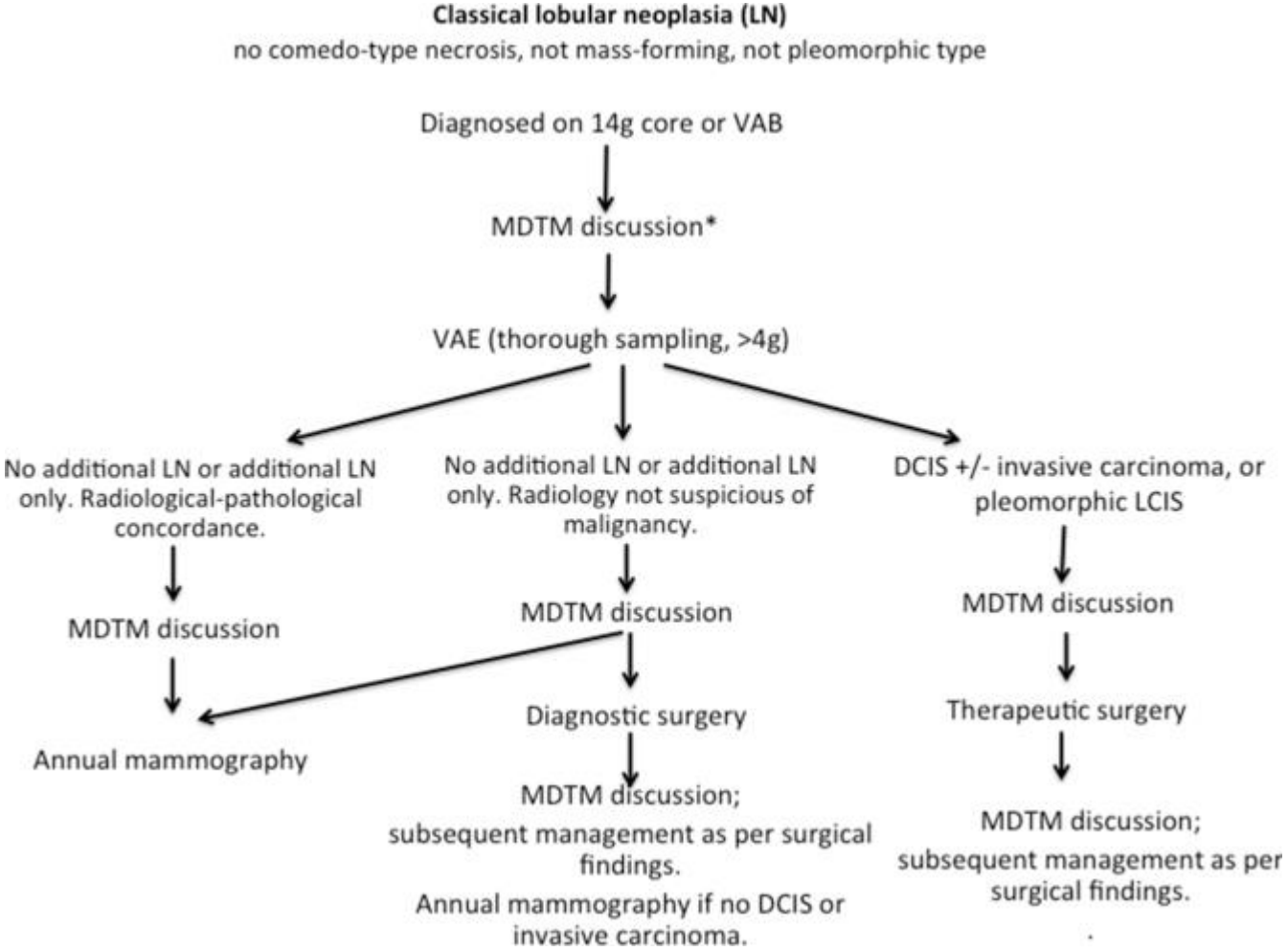
Atypical Intraductal Epithelial Proliferation (AIDEP) or radial scar/CSL with atypia











Reluctance to change

- Lack of national guidance – now present
- Upgrade to malignancy

Upgrade to malignancy

- Fear of missing cancer prompts surgical excision
- Upgrade rate varies from 9.9%-35.1%

B3 lesions upgrade to invasive

	Grade 1	Grade 2	Grade 3	Not assessable	Unknown	Total invasive with B3
2001/02	60%	23%	4%	8%	5%	78
2002/03	56%	28%	7%	4%	5%	82
2003/04	56%	33%	5%	4%	2%	102
2004/05	55%	32%	4%	5%	3%	96
2005/06	50%	37%	4%	6%	3%	108
2006/07	55%	37%	2%	2%	4%	101
2007/08	39%	46%	7%	2%	6%	89
2008/09	54%	43%	1%	3%	0%	112
2009/10	54%	41%	3%	1%	1%	93
2010/11	48%	41%	4%	4%	4%	85
2011/12	51%	36%	4%	6%	4%	108
2012/13	49%	40%	5%	5%	1%	81
2013/14	51%	39%	4%	4%	1%	67
2014/15	45%	46%	3%	5%	1%	74

B3 upgraded to B5a

	Low	Intermediate	High	Not assessable	Unknown	Total non invasive with B3
2001/02	60%		18%	6%	15%	177
2002/03	63%		15%	6%	17%	199
2003/04	66%		20%	6%	8%	206
2004/05	73%		15%	7%	5%	292
2005/06	63%		21%	8%	8%	336
2006/07	31%	24%	20%	19%	6%	322
2007/08	32%	21%	20%	9%	18%	317
2008/09	28%	29%	14%	14%	16%	309
2009/10	29%	27%	15%	13%	16%	300
2010/11	28%	27%	15%	29%	1%	323
2011/12	23%	26%	16%	34%	0%	353
2012/13	28%	23%	13%	34%	3%	373
2013/14	26%	25%	13%	34%	1%	370
2014/15	29%	27%	12%	32%	0%	297

Upgrade to malignancy

- When the malignant biopsies are reviewed it can be seen that 79% of the B3 lesions are upgraded to DCIS and 20% to invasive cancers.
- 56% of the cases are LG or IG DCIS, with HGDCIS accounting for 12%. In 32% it was not assessable – likely because the grade was not stated in the pathology report or too small to grade.
- 66% belong to the excellent or good prognostic group.
- Upgrade rate highest with AIDEP
- VAE allows pre-operative diagnosis of cancer
- Allows women the option of entering LORIS trial (trial comparing surgery with active monitoring for low-risk DCIS) and avoiding surgery

Changes to NBSS

- New field to document VAE
- Pathology will not provide a code for VAE
- Either E2 benign or E5 malignant
- If VAE and B3 lesion then coded as E2
- If VAE and cancer then coded as E5
- If VAE LCIS then coded as E5 = B5a = surgical biopsy

New codes

- The full list of Epithelial Proliferation codes is:
- ENP – Not present
- EPW – Present without atypia
- EAD – Present with atypia (ductal)
- EAF – Present with atypia (FEA)
- EAL – Present with atypia (lobular)
-

Benign codes for VAE and Surgery

- BBP – Borderline Phyllodes Tumour
- BCC – Columnar cell change
- BCF – Cellular Fibroepithelial Lesion/Benign Phyllodes
- BCR – Complex sclerosing lesion/radial scar
- BDE – Periductal mastitis/duct ectasia
- BFA – Fibroadenoma
- BFC – Fibrocystic change
- BML – Mucocele-like Lesion
- BPM – Multiple papilloma
- BPS – Solitary papilloma
- BSA – Sclerosing adenosis
- BSC – Solitary cyst
- BST – Stromal lesion of uncertain significance
- BXX – Other

ABS surgical audit

- Radiology KPI
- <25% of women should have surgery for the management of B3 lesions
- Codes have now been addressed and mandatory field
- Separate entry for VAB, VAE and surgery and this will allow for robust data collection

Radiology KPI

- Of 1,618 B3 cases without atypia, eligible for VAE
  - 1,167 (72.1) had VAE only
  - 451 (27.9%) had surgery
    - 83 (5.1%) were upgraded to malignancy
- Of 1,494 B3 cases with atypia
  - 1,017 (68.1%) had VAE only
  - 477 (31.9%) had surgery
    - 69 (11.3%) were upgraded to malignancy

Radiology KPI

- This is a new KPI introduced this year but the data has to be interpreted with caution.
- The assessment guidance document was published November 2016 and therefore not all units will have implemented the new guidance regarding management of B3 lesions
- The terms vacuum assisted excision (VAE) and vacuum assisted biopsy (VAB) have been used interchangeably and changes have been made to NBSS to ensure more accurate recording regarding VAB and VAE

Surveillance

- Insufficient evidence to determine the optimal follow up
- Currently many units are doing 5 year annual mammographic follow up for B3 lesions with atypia and then they return to routine screening

In summary

- UK is leading the way with regards to management of B3 lesions
- NHS BSP guidelines on the management of B3 lesions
- Radiology KPI on B3 for ABS surgical audit data - <25% of B3 cases should be managed surgically
- Ensure robust data collection by modernising the codes, updating NBSS and making the fields mandatory
- Support **SLOANE** by submitting atypia cases

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