Archives of Surgical Research | Review Article

The Grey Zone: A Review Of The Management Of B3 Lesions Of The Breast

Bushra Rehman[1], Huma Majeed Khan[1]

IMPORTANCE With the advent of widespread breast cancer screening programs along with rising public awareness, the number of patients presenting with B3 lesions on core biopsy has also increased. This grey zone consists of heterogeneous pathological entities with variable malignant potential, necessitating excision biopsy for full histological examination. This puts an additional burden on cost, theater time and requiring invasive procedure on the patient. The term 'malignant potential' confers either an increased probability of finding concomitant cancer on excision biopsy, or evolution towards in situ or invasive cancer over a period of time. The risk is not restricted to the breast where the biopsy or excision of the B3 lesion occurred, but anywhere in the same or contralateral breast. Because of management controversies, a multidisciplinary approach is the need of the hour to decrease the over or under diagnosis, and over or under treatment. This review is aimed at giving an overview of morphology and biological significance of B3 entities and current agreement on its management. It also focuses on the ways these internationally agreed protocols can be adopted in our resource constrained country.

KEY WORDS Core needle biopsy, uncertain malignant potential, upgrade to malignancy, identification rate, Vacuum assisted procedures.

HOW TO CITE Rehman B, Khan HM. THE GREY ZONE: A Review Of The Management Of B3 Lesions Of The Breast. *Archives of Surgical Research*. 2021, 2 (2):45-50. https://doi.org/10.48111/2021.02.09.

Review Article

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Huma Majeed Khan, Ittefaq Hospital Trust, Lahore fj2008gs@gmail.com.
https://doi.org/10.48111/2021.02.09

With the advent of widespread breast cancer screening programs along with rising public awareness, the number of patients presenting with B3 lesions on core biopsy has also increased. This grey zone consists of heterogeneous pathological entities with variable malignant potential, necessitating excision biopsy for full histological examination. This puts an additional burden on cost, theater time and requiring invasive procedure on the patient. The term 'malignant potential' confers either an increased probability of finding concomitant cancer on excision biopsy, or evolution towards in situ or invasive cancer over a period of time. The risk is not restricted to the breast where the biopsy or excision of the B3 lesion occurred, but anywhere in the same or contralateral breast. Because of management controversies, a multidisciplinary approach is the need of the hour to decrease the over or under diagnosis, and over or under treatment. This review is aimed at giving an overview of morphology and biological significance of B3 entities and current agreement on its management. It also focuses on the ways these internationally agreed protocols can be adopted in our resource constrained country.

Patients presenting with radiologically or clinically detected breast lesions are subjected to core needle biopsy (CNB). There is a specific B-coding system for CNB result interpretation, which was first established in the European breast-screening programs[1]. Histology results on conventional needle core biopsy or vacuum assisted biopsy are classified as follows:.

B0: Non- diagnostic.
B1: Normal breast tissue.
B2: Benign breast lesion.
B3: Uncertain malignant potential (heterogeneous)
B4: Suspicious for malignancy.
B5: Malignant.

What are B3 Lesions?

These are a heterogeneous category encompassing a number of lesions that includes the following: [2]

- Atypical intraductal epithelial proliferation (AIDEP)
- Flat epithelial atypia (FEA)
- Lobular lesions (ALH, LCIS)
- Papillary lesions (with or without atypia)
- Cellular fibroepithelial lesions (where phyllodes tumour is considered)
- Radial scars (with or without atypia

A combination of the B3 lesions is known to occur particularly in the spectrum of low nuclear grade neoplasia family (FEA, lobular neoplasia, AIDEP).[3] Other less common lesions within this category include apocrine atypia, myofibroblastoma, vascular lesions and bland spindle cell lesions.

How common is it (Identification rate)?

This mainly refers to the CNB results of the mass screening programs in Europe and North America. The B3 identification rate on CNB varies across different studies. In

the UK, the reported rate was 5%[4], 4.5% in Germany[5], 11.9% in Italy[6] and 17% in Switzerland[7]. While study of 5750 needle core biopsies in the USA showed an incidence of 8%.[8] Swiss Minimally Invasive Breast Biopsy group (MIBB) Database presented histology from 31,574 vacuum assisted biopsies (VAB), from 2007 until 2017. Total 6020 cases i.e. 19.1% showed B3 lesions.

The commonest entity among all B3 lesions in two studies (excluding Phyllodes) was found to be ADH or AIDEP.[5, 8]

What is the significance of B3 diagnosis?

These lesions have a low but significant risk, either to harbor a coexisting malignancy or a potential for malignant change in the future, and thus merit excision to establish a diagnosis after complete specimen histology. Diagnosis of in situ or invasive carcinoma on excision of a B3 lesion is called 'upgrading'. Many studies assessed the upgradation rate to in situ or invasive carcinoma (positive predictive value) following the diagnosis of B3. Each study has shown a different overall upgrade rate and of individual B3 entities.

Upgrading to malignancy (Invasive or In-situ):

Although different studies have shown different rates, overall, the association with malignancy is seen in 20–30% of cases.[4, 5], and[10]. Table 1 shows identification and upgrade rate in different studies.

Name of Author	Type of study	Duration	Total number of core biopsies	Identification rate (of B3)	Upgrade rate
Elsayed et al. 2008.[4]	UK East Midlands region	1999–2006	13,452	5%	20%
Ehrenstein et al.[5]	Germany single Institution	2009-2015	8,388	4.5%	26%
Bianchi et al. 2011.[6]	Multiinstitutional Italian series	1998–2009	26,165	11.9%	21.2%
Saladin et al. [7]	Multi institutional in Switzerland	2009 and 2011,	9,153	17.0%	21.5%
Mooney et al. 2016. 8	US single institution	2003–2014	5750	8%	18%
Rakha et al. 2011.9	UK single Institution	2007–2008	3347	4.5%	10%
Nguyen et al. 2011.10	US single institution (MD Anderson Centre)	1997–2009	5383	9.9%	13.2%
Renshaw and Gould 2016.12	US single institution	2000–2004	Not stated	244	34.6%
Mayer et al. 201724	German single institution	2009–2013	Not stated	219	10%

Table 1: Overall upgrade and identification rate of B3 lesions in different studies.

Name of Author	Total no. of core biopsies	Identification Rate (IR of B3)	Upgrade rate of individual B3 entities:
Elsayed et al. 2008.[4] UK East Midlands region (1999–2006)	13,452	5%	AIDEP 32%, LN 30%, RS/CSL with AIDEP or LN 24% RS/CSL without atypia 9%, Papillary lesion with AIDEP or LN 36% Papillary lesion without atypia 4%
Ehrenstein et al.5 Germany single Institution (2009-2015)	8,388	4.5%	ADH 40%, FEA 20.5%, Papillary lesion 13.5%, Radial scar 16.6% LN 0%.
Bianchi et al. 2011.[6] Multi institutional Italian series (1998–2009)	26,165	11.9%	AIDEP 27.3%, FEA 12.7%, LIN 22%, RS 10.6%, PL 13.3%
Saladin et al. [7] Multi institutional in Switzerland 2009-2011	9,153	17.0%	ADH 25.9%, PL 3.1%, FEA 18.3%, LN 26.4%, RS 11.1%
Mooney et al. 2016. [8] US single institution 2003–2014	5750	8%	ADH 18%, FEA 11% Atypical lobular hyperplasia 9% , LCIS 28% , RS16%
Mayer et al. 2017[24] German single institution 2009–2013	Not stated	n=219 (B3)	PL (with atypia) 28.6%, PL(without atypia) 4.7%, B3 (rest of B3 lesions with atypia) 24.0% , B3 (rest of B3 lesions with atypia) 4.8%
Huang et al[25] Single institution Australian 2012–2019	Not stated)	n=299 (B3)	PL (with atypia) 50%, FEA 37.50%, ADH 24.71% LCIS/atypical lobular hyperplasia with calcification 17.65%, PL (without atypia) 4.72%, RS/ classical LCIS (without calcification) 0%

Table 2: Upgrade potential of different lesions in different studies.

Usually upgrading is to low grade malignancy:

The rate of progression to malignancy is slow and occurs over a long period of time. Cancers that develop in a small proportion of B3 lesions are often of the low-grade hormone receptor–positive type or in-situ cancer.[11, 12, 13]

Upgrade potential of different lesions:

Different B3 categories have different malignant potential that mainly depends on presence of atypia. Following table (table: 2) shows that malignant potential greatly varies among studies, however on average, the greatest malignant potential is for ADH, FEA and PL with atypia.
Forester et al conducted a meta-analysis (129 studies from 1980 and 2015) that included 11,423 lesions with upgrade rate of 17%. The presence of atypia was associated with significant upgrade potential compared to the same lesion without atypia. For Papillary lesions (PL), upgrade rate to malignancy was 7% without atypia compared to 32% with atypia ($p < 0.01$), similarly for radial scars, upgrade rate to malignancy was 6% without atypia compared to 18% with atypia ($p < 0.034$)[14].

Acceptable rates for the risk of underestimation:

Overall, underestimation rates should not exceed 5% for Invasive cancer and 10% for DCIS[15] acc. to the Second International Consensus Conference on B3 lesions.

CURRENT GUIDELINES FOR THE MANAGEMENT OF B3 LESIONS

Traditionally, B3 lesions were managed by surgical excision. However, current recommendations are in favor of the use of VAE (Vacuum assisted excision) for the management of B3 lesions with no atypia[15]. The B3 lesions with atypia and Fibro-epithelial lesions are, however, still managed with diagnostic surgical excision. The second International Consensus Conference on lesions of uncertain malignant potential in the breast recommended VAE as the gold standard for managing the majority of these lesions.[15, 16.]

Follow-up Following a B3 Diagnosis: The International Consensus recommends surveillance following a B3 diagnosis.[15] The current UK guidelines recommend annual mammographic follow-up for 5 years followed by return to the 3 yearly routine breast cancer screening.

IMPORTANT ASPECTS:

The correlations of Histology with the type of mammographic lesion: Concordance between radiological and histological findings is very important. For discordant lesions (e.g. histological findings do not explain a mass lesion or calcification not identified), a repeat VAB (vacuum assisted biopsy) and or a diagnostic excision may be required. Discussion In the multidisciplinary meeting with careful planning and documentation are therefore important.[15, 17]

However, in one study, the morphological type of mammographic lesion does not appear to be correlated with cancer risk.[18]

Diagnostic Vacuum–Assisted Biopsy (VAB): Vacuum-assisted biopsy (VAB) is done with a vacuum biopsy needle (usually 12-9G) for diagnostic purposes only (larger amount of tissue compared with conventional needle core biopsy (CNB) which is 14G. VAB gives a larger sample for the pathologist to assess and and reduces chances of missing concomitant cancer. This helps in avoiding unnecessary surgeries.[11]

Vacuum-Assisted Excision (VAE): Vacuum-assisted excision (**VAE**) is used in place of a surgical excisional biopsy by a larger needle (7G or 8G). VAE is recommended for further sampling of all B3 lesions diagnosed on conventional CNB or VAB in all categories except: Papillary lesions (PL) with atypia, cellular fibroepithelial lesions (PT), B3 spindle cell lesions, vascular lesions and other rare lesions such as myofibroblastoma and apocrine adenosis.

Open surgical excision is regarded as overtreatment within the breast-screening program because the majority of B3 patients show a final benign diagnosis. Small lesions, typically less than 15 mm, may be completely excised by VAE.19 Patients can therefore avoid the complications of surgery such as anesthetic complications, scarring and difficult follow-up mammographic surveillance due to post-surgical changes. It can help in reducing theater time and overall cost of the procedure.

The NHS Breast Screening Program is keen to minimize overtreatment in the context of B3 lesions and have created a new KPI (key performance indicator) where all appropriate B3 lesions should be managed with VAE and < 25% of B3 lesions should be managed with surgery.

Marker Clips: It is important to insert marker clip when sampling calcification or very small lesions. If more than one area is sampled, then a different clip type per area should be used.

Reporting of Atypia: The diagnosis of B3 lesions should always include a comment on the presence/absence of atypia. Atypia is associated with a higher risk of upgrade to in situ/invasive carcinoma among all B3 lesions, [25] thus altering the management plans. For example, benign papillary lesions without atypia are managed by VAE whereas those with atypia require diagnostic surgical excisions

Adequacy of Excision: Due to the piecemeal nature of the vacuum biopsies, it is not possible for pathologists to comment on the adequacy of excision. Decisions on adequate excision in these instances will depend on the radiological impression. Biopsies of microcalcifications should be x-rayed to make sure that the sampling is adequate.

Columnar cell hyperplasia: With increasing identification of microcalcifications on screening mammograms and subsequent biopsies, this histology is more frequently reported in association with micro-calcifications. Columnar cell change or columnar cell hyperplasia is regarded as a benign lesion (B2). Therefore, if there is no discordance with the radiological/clinical features, diagnostic surgical excision or further VAE is not required.

However, when cytological atypia is present, the lesion is reported as FEA (B3), which is believed to be the earliest morphologically identifiable precursor of low grade breast carcinomas. Similarly, if there is architectural atypia then cores should be categorized according to the extent and degree of this and ADH may be reported.[20]

B3 ENTITIES: Characteristics and recommendation (according to the second international consensus)

1. Atypical intraductal epithelial proliferation (AIDEP/ADH): Histologically, the term 'AIDEP' (Atypical intraductal epithelial proliferation or Atypical epithelial proliferation of ductal type) is recommended for describing atypical ductal hyperplasia (ADH) diagnosed on core biopsy and/or diagnostic VAB. The 'ADH' is quantitative term and can only be used after thorough sampling of excision specimen and the extent of the lesion confirmed to be less than 2 mm on final excision.[15, 21] Lesions larger than 2 mm are labelled as ductal carcinoma in situ (DCIS).

Surgical excision is recommended even if the lesion seems to be completely excised by VAB, followed by surveillance.

2. Flat epithelial atypia (FEA): FEA consists of a few layers of neoplastic columnar type cells with low-grade (monomorphic) atypia without any secondary architecture (flat architecture). The immune-phenotype of a FEA lesion is identical to that of a low-grade DCIS. These are often associated with micro-calcifications. It is believed that columnar cell change actually progresses to FEA. FEA should undergo **VAE** along with yearly surveillance for 5 years.

3. Classical lobular neoplasia: Lobular neoplasia (LN) includes a large spectrum of atypical intra-lobular proliferations, consisting of non-cohesive proliferating cells. Under the term "Classical Lobular Neoplasia," two lesions are defined by the WHO classification as classical lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH). In case of LCIS, these cells expand more than 50% of the acini in a terminal duct-lobular unit (TDLU), while in ALH this affects less than 50%.[22]

ALH/LCIS has to be considered as both a risk factor and a non-obligate precursor of invasive breast carcinoma conferring an 8 to 10 times relative risk compared to the general population. The risk is bilateral with ipsilateral predominance.[21, 23]

A lesion containing classical LN, which 'is visible on imaging', should undergo excision with VAB. Thereafter surveillance is justified if there is no pathological–radiological discordance and no residual lesion. In contrast, morphologic variants of LN (LIN 3, pleomorphic LCIS, and florid LCIS), which are reported as B5a lesions should undergo Open excision.

4. Papillary lesions (PL): Histology demonstrates a papillary proliferation as the basis with a central fibro-vascular core arranged in an inner myoepithelial and outer epithelial layer.

In the current WHO classification of breast tumors, papillary lesions are divided into

(a) Papillomas

(b) Papillomas with atypia (ADH or classical LN), both belonging to the B3 category

(c) Papillomas with DCIS or papillomas completely involved by more extended DCIS (encapsulated papillary carcinoma)

(d) Solid papillary carcinoma belonging to B4 or B5a category.

A PL lesion, which 'is visible on imaging', should undergo excision with VAB. If lesions are large and cannot be completely removed by VAB then open excision should be done. Later, surveillance with mammogram should continue.is important to insert marker clip when sampling calcification or very small lesions. If more than one area is sampled, then a different clip type per area should be used.

5. Phyllodes Tumor (PT): Benign and borderline phyllodes tumors are B3 lesions; a malignant PT is a B5b lesion. Only up to 20% of all PT tumors are borderline or malignant.

Surgical excision is required, with free margins in borderline and wider margins in malignant PTs

6. Radial scar/ complex sclerosing lesion (CSL): RS is characterized by a central area mimicking a scar, with a pseudo infiltrative growth pattern. It consists of a central fibro-elastic zone from which radiate out tubular structures They are seen radiologically as stellate lesions, classically with a more lucent centre but may be indistinguishable from carcinomas. There is general agreement that RS alone is a benign lesion, but RS can be occasionally associated with carcinoma[25].Presence or absence of atypia should be

particularly recorded on CNB or VAB[2] [8].RS/CSL should undergo vacuum assisted excision (VAE). Thereafter, follow-up with mammogram is carried out.

B3 LESIONS IN PAKISTAN

In our part of the world, screening programs are non-existent, so mostly symptomatic patients present to the clinicians. Commonest symptoms are feelings of a lump or mastalgia. In addition, biopsies are taken only by conventional CNBs (not VAB) meaning lesser tissue available to the pathologists and relatively higher probability of reporting a B3 lesion only and missing out on coexisting upgraded pathologies. Another issue is the lack of a national database to know the exact B3 lesion identification rate in all core biopsies performed (symptomatic patients usually).

At Ittefaq Hospital (Trust) breast surgery department, about 5% of all breast biopsies (including palpable and impalpable lesions) were found to be B3 lesions. Pathology facilities are relatively better across the country, so that is not a point of concern. However, the awareness of B3 management according to recent guidelines is still very poor among clinicians that may result in, either, avoidable over-treatment or an under-treatment and subsequent risk of missing a malignancy. Also, because of unavailability of vacuum assisted excision, all B3 lesions may mandate open excision. Breast surgery units are recommended to include vacuum assisted biopsy and vacuum assisted excision facilities. In future, screening programs on either a national or a local level, for at least high risk population, will help in reducing mortality, improving survival, conserving breast and cutting treatment costs.

Declaration of conflict of interest: none'. Also, this article has not been published previously.

ARTICLE INFORMATION Accepted for Publication: March 15, 2021 Published Online: June 29, 2021.
https://doi.org/10.48111/2021.02.09

Author Affiliations: 1. Ittefaq Hospital Trust, Lahore

Financial Support and Sponsorship: Nil.

Conflicts of Interest: There are no conflicts of interest

REFERENCES

1. Ellis O, Humphreys S, Michell M, Pinder SE, Wells CA, Zakhour HD. Guidelines for non-operative diagnostic procedures and reporting in cancer screening. *NHSBSP Publications*. 2001;50:35–40.
2. Brian D Hayes, Cecily M Quinn. Pathology of B3 lesions of the breast. *Diagnostic Histopathology*. 2009;15(10):459-469.
3. Abdel-Fatah TM, Powe DG, Hodi Z, Reis-Filho JS, Lee AH, Ellis IO. Morphologic and molecular evolutionary pathways of low nuclear grade invasive breast cancers and their putative precursor lesions: further evidence to support the concept of low nuclear grade breast neoplasia family. *Am J Surg Pathol*. 2008;32(4):513–23.
4. El-Sayed ME, Rakha EA, Reed J, Lee AH, Evans AJ, Ellis IO. Predictive value of needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening. *Histopathology*. 2008;53(6):650–7
5. Richter-Ehrenstein C, Maak K, Roger S, Ehrenstein T. Lesions of "uncertain malignant potential" in the breast (B3) identified with mammography screening. *BMC Cancer*. 2018;18(1):829
6. Bianchi S, Caini S, Renne G, Cassano E, Ambrogetti D, Cattani MG, 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):264–70.
7. Saladin C, Haueisen H, Kampmann G, Oelschlegel C, Seifert B, Rageth L, et al. Lesions with unclear malignant potential (B3) after minimally invasive breast biopsy: evaluation of vacuum
8. biopsies performed in Switzerland and recommended further management. *Acta Radiol*. 2016;57(7):815–21.
9. 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):1471–84
10. Rakha EA, Ahmed MA, Aleskandarany MA, Hodi Z, Lee AH, Pinder SE, et al. Diagnostic concordance of breast pathologists: lessons from the National Health Service Breast Screening Programme Pathology External Quality Assurance Scheme. *Histopathology*. 2017;70(4):632–42.
11. 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):752–61
12. 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
13. Renshaw AA, Gould EW. Long term clinical follow-up of atypical ductal hyperplasia and lobular carcinoma in situ in breast core needle biopsies. *Pathology*. 2016;48(1):25–29
14. Houssami N, Ciatto S, Ellis I, Ambrogetti D. Underestimation of malignancy of breast core-needle biopsy: concepts and precise overall and category-specific estimates. *Cancer*. 2007;109(3):487–495
15. Forester ND , Lowes S, Mitchell E ,Twiddy M. High risk (B3) breast lesions: What is the incidence of malignancy for individual lesion subtypes? A systematic review and meta-analysis. *EJSO*. 2019;45:519-527
16. Rageth CJ, O'Flynn EAM, Pinker K, Kubik-Huch RA, Mundinger A, Decker T, et al. Second International Consensus Conference on lesions of uncertain malignant potential in the breast(B3 lesions). *Breast cancer research and treatment*. 2018
17. Lucioni M, Rossi C, Lomoro P, Ballati F,Fanizza M, Ferrari A, Garcia-Etienne CA, Boveri E, Meloni G, Sommaruga MG, Ferraris E, Lasagna A, Bonzano E, Paulli M, Sgarella A, Di Giulio. Positive predictive value for malignancy of uncertain malignant potential (B3) breast lesions diagnosed on vacuum-assisted biopsy (VAB): is surgical excision still recommended? *G.Eur Radiol*. 2021 Feb;31(2):920-927.
18. Santucci D,Faiella E, Calabrese A, Favale L ,Zobel BB, Carlo de Felice. Our Radiological Experience on B3 Lesions: Correlation Between Mammographic and MRI Findings With Histologic Definitive Result. *Clin Breast Cancer*. 2019;19(5):643-e653.
19. Hoffmann.O,Stamatis GA,Bittner AK,Arnold J,Schnabel R,Krüger K,Kimmig R, Heubner M. B3-lesions of the breast and cancer risk - an analysis of mammography screening of patients. *Mol Clin Oncol*. 2016; 4(5): 705–708.
20. Pinder SE, Shaaban A, Deb R, Desai A, Gandhi A, Lee AHS, 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
21. Pinder SE and Reis-Filho JS. Non-operative breast pathology: columnar cell lesions. *J Clin Pathol*. 2007; 60(12): 1307–1312.
22. Perry N, Broeders M, de Wolf C, Törnberg S, Holland R, von Karsa L (eds) European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition/ Supplements. *European Commission, Office for Official Publications of the European Union, Luxembourg*, 73–120
23. Dabbs DJ, Schnitt SJ, Geyer FC, Weigelt B,

Baehner FL, Decker T, Eusebi V, Fox SB, Ichihara S, Lakhani SR et al (2013) Lobular neoplasia of the breast revisited with emphasis on the role of E-cadherin immunohistochemistry. *Am J Surg Pathol*. 2013;37(7):1-11

24. Fisher ER, Land SR, Fisher B, Mamounas E, Gilarski L, Wolmark N. Pathologic findings from the National Surgical Adjuvant Breast and Bowel Project: twelve-year observations concerning lobular carcinoma in situ. *Cancer*.2004;100(2):238–244
25. Chuba PJ, Hamre MR, Yap J, Severson RK, Lucas D, Shamsa F, Aref A. Bilateral risk for subsequent breast cancer after lobular carcinoma-in-situ: analysis of surveillance, epidemiology, and end results data. *J Clin Oncol* 2005;23(24):5534–5541
26. I O Ellis, S Humphreys, M Michell, S E Pinder, C A Wells, H D Zakhour. Guidelines for breast needle core biopsy handling and reporting in breast screening assessment. *J Clin Pathol* 2004;57:897–902.
27. Mayer S, Kayser G, Rucker G, Bogner D, Hirschfeld M, Hug C, et al. Absence of epithelial atypia in B3-lesions of the breast is associated with decreased risk for malignancy. *Breast*. 2017;31: 144–9.
28. Y. Y. Huang,H. Park, S. McLaren, P. Thirunavukkarasu, J. T. W. Lin, R. Rajakaruna, R. Dhillon, A. K. Ponniah. B3 lesion upgrade rates in a tertiary Australian breast centre: a 8-year experience. *ANZ journal of Surgery*. 2020;90(12):2521-2526
29. Kalife ET, Lourenco AP, Baird GL, Wang Y Clinical and radiologic follow-up study for biopsy diagnosis of radial scar/radial sclerosing lesion without other atypia. *Breast J*. 2016;22(6):637–644.