Received:
21 December 2017

Revised:
10 February 2018

Accepted:
12 February 2018

<https://doi.org/10.1259/bjr.20180003>

Cite this article as:

Schiaffino S, Massone E, Gristina L, Fregatti P, Rescinito G, Villa A, 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**: 20180003.

FULL PAPER

Vacuum assisted breast biopsy (VAB) excision of subcentimeter microcalcifications as an alternative to open biopsy for atypical ductal hyperplasia

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Objective: Atypical ductal hyperplasia (ADH) is a proliferative lesion associated with a variable increased risk of breast malignancy, but the management of the patients is still not completely defined, with mandatory surgical excision in most cases. To report the results of the conservative management with mammographic checks of patients with ADH diagnosed by vacuum assisted breast biopsy (VAB), without residual calcifications.

Methods: The authors accessed the institutional database of radiological, surgical and pathological anatomy. Inclusion criteria were: ADH diagnosed by VAB on a single group of microcalcifications, without residual post-procedure; follow-up at least of 12 months. Exclusion criteria were the presence of personal history of breast cancer or other high-risk lesions; association with other synchronous lesions, both more and less advanced proliferative lesions.

Results: The 65 included patients were all females, with age range of 40–79 years (mean 54 years). The

maximum diameter range of the groups of microcalcifications was 4–11 mm (mean 6.2 mm), all classified as BI-RADS 4b (Breast Imaging Reporting and Data System 4b) and defined as fine pleomorphic in 29 cases (45%) or amorphous in 36 cases (55%). The range of follow-up length was 12–156 months (mean 67 months). Only one patient developed new microcalcifications, in the same breast, 48 months after and 15 mm from the first VAB, interpreted as low-grade ductal carcinoma *in situ* (DCIS) at surgical excision.

Conclusion: These results could justify the conservative management, in a selected group of patients, being the malignancy rate lower than 2%, considered in the literature as the “probably benign” definition.

Advances in knowledge: Increasing the length of follow-up of selected patients conservatively managed can improve the management of ADH cases.

INTRODUCTION

Atypical ductal hyperplasia (ADH) is an intraductal proliferative lesion associated with a variable increased risk of breast malignancy, with part of cytological and histological features shared with carcinoma *in situ*, but without cellular morphological alteration enough to justify an unequivocal diagnosis of carcinoma *in situ*.¹ The management of the patients with a diagnosis of ADH is still not completely defined, and the surgical excision is mandatory in most cases. A significant group of patients, presented with a group of microcalcifications detected by mammography, are diagnosed by stereotactically-guided vacuum assisted breast biopsy (VAB), with possibility of complete removal of calcifications. In the literature, a few studies^{2–7}

(Table 1) proposed conservative management of this group of patients, with mammographic follow-up and without surgical excision.

Before early 2000s, the need of surgical excision after a diagnosis of ADH at micro-histology was mandatory because of high underestimation rate. The spread of larger needles led to lower underestimation rates, enough to justify the conservative management of selected cases.^{2,8–14}

The hypothesis that the complete removal of the lesion with core needle biopsy could justify conservative management were introduced by some authors, as Renshaw and colleagues¹⁵ in 2001. Sneige¹⁶ and other authors^{2,17–19}

Table 1. Development of malignancy during follow-up in different studies from the literature (search included studies from 2001 to 2016)

Authors	Year of publication	Follow-up: range (months)	Follow-up: median (months)	N	Development of malignancy during follow-up
Jackman <i>et al</i> ²	2002	3–35	21	14	7% (1 of 14)
Plantade <i>et al</i> ³	2004	9–42	–	88	2.3% (2 of 88)
Travade <i>et al</i> ⁴	2006	22–62	35.5	31	0% (0 of 31)
Forgeard <i>et al</i> ⁵	2008	6–72	30	135	3% (4 of 135)
Ancona <i>et al</i> ⁶	2011	6–96	45	79	8% (6 of 79)
Nguyen <i>et al</i> ⁷	2011	29.6–132.9	62.2	19	0% (0 of 19)
Present study	2018	12–156	67	65	1.5% (1 of 65)

reported the absence of ADH upgrades in all lesions completely excised at VAB. Recently McGhan²⁰ observed that patients younger than 50 years old, with focal atypia only, and no residual calcifications post-biopsy might represent a low-risk group who could potentially avoid excisional biopsy.

The purpose of this retrospective observational study is to report the malignancy rate, defined as the development of new calcifications or other suspicious lesions during the long-term follow-up (over 5 years as a mean length) of patients with ADH diagnosed by VAB without residual calcifications conservatively managed.

METHODS AND MATERIALS

The authors reviewed the clinical-radiological history of patients with a diagnosis of ADH performed by stereotactically-guided VAB, in our Institute, from October 2003 to December 2015. IRB approved this retrospective observational study and the data collection was performed accessing the electronic database of radiological, surgical and pathological anatomy units of the Institute. All mammographies have been performed for opportunistic screening as our Institute is not a population screening center.

For each included patient demographics (Table 2), radiological and histopathological data were recorded.

Inclusion criteria were: ADH diagnosed by VAB performed on a single group of calcifications; absence of residual post-procedure, checked with mammogram performed immediately after the biopsy; follow-up length at least of 12 months. No limits of age were

included among the criteria that drove to the choice of follow-up rather than resection.

Exclusion criteria were: the presence of personal history of breast cancer or other high-risk lesions, as well as the presence of BReast CAncer gene mutations; association with other synchronous lesions, both more and less advanced proliferative lesions, excluded the patient from the study. The presence of multiple foci of hyperplasia or high percentage of hyperplasia were exclusion criteria.

Image analysis

Two different full field digital stereotactic units (Selenia Dimensions Digital Mammography System, Hologic, Bedford, MA; Giotto Image SD Full-Field Digital Mammography Unit, IMS Italy) were used for the images acquisition.

All the mammograms were stored and anonymized by the first author and reviewed on high-resolution digital mammographic screens by two of the authors (BLINDED and BLINDED), radiologists with 25 and 10 years of experience in breast radiology. The two readers were blinded to the clinical history and histological findings of the patients.

Two sets of images were stored, anonymized and dissociated: the first included all the pre-VAB magnified views (Figure 1) and the second all the mammographic checks during the follow-ups.

In the first set the aim was to detect, measure and classify the groups of microcalcifications. In the second the aim was to detect the presence of residual lesions, the appearance of new suspicious microcalcifications or other equivocal/suspicious mammographic signs.

Radiological data included (Table 2): location of the group of microcalcifications, larger diameter of the group, type of microcalcifications and Breast Imaging Reporting and Data System (BI-RADS) classification.²¹

Percutaneous biopsy and histopathological assessment

The patients underwent stereotactically-guided VAB using a 11-gauge directional VAB device (Mammotome, Ethicon

Table 2. Patients' demographics and radiological data

Number of patients.	65 (all females)
Age at ADH diagnosis ^a	40–79 (54) years
BI-RADS 4b (%)	65 (100%)
Diameter of groups of microcalcifications ^a	4–11 (6.2) mm
Type of microcalcifications	Fine pleomorphic 29 cases (45%) Amorphous 36 cases (55%)

ADH, Atypical ductal hyperplasia; BI-RADS, Breast Imaging Reporting and Data System.

^aData are range (mean).

Figure 1. Direct magnification mammography: suspicious group of fine pleomorphic microcalcifications of about 5 mm of extension, classified as BI-RADS 4b. BI-RADS, Breast Imaging Reporting and Data System.

Endo-Surgery, Breast care, Norstedt, Germany) or 9-gauge VAB device (Suros ATEC, Suros Surgical Systems/Hologic, Indianapolis, IN), followed by the insertion of a metallic marker in the site of the biopsy. The presence of the calcifications in the specimens were mammographically checked (Figure 2).

An over 20 years experienced pathologist, with special interest in breast pathology, reviewed all the cases, and defined the

Figure 2. Magnification radiograph of VAB specimens, checking the presence of microcalcifications in the specimens. VAB, vacuum assisted breast biopsy.

diagnosis of ADH using the criteria defined by Page et al²², Page and Rogers²³, and Tavassoli and Norris²⁴.

Management of the patients

The management protocol in patients without residual microcalcifications post-VAB included two mammograms with 6-month interval in the first year after biopsy. In the absence of new microcalcifications or other suspicious lesions detected during these checks, the patients returned to the conventional screening program.

Statistical analysis

Continuous variables were expressed as range (mean), while categorical variables were expressed as frequency and percentage.

RESULTS

Between October 2003 and December 2015, among 2642 consecutive VAB, 235 consecutive cases of ADH were detected in our Institute, 65 of which fitting the inclusion and exclusion criteria. All these patients accepted the non-surgical management after clarification and were included in the study. The remaining 170 patients were excluded for different reasons: the presence of associated lesions ($n = 33$), the presence of residual calcifications ($n = 97$) or follow-up <12 months ($n = 40$).

The included patients were all females, with age range of 40–79 years (mean 54 years) (Table 2). The maximum diameter range of the groups of microcalcifications was 4–11 mm (mean 6.2 mm), they were all classified as BI-RADS 4b and defined as fine pleomorphic in 29 cases (45%) or amorphous in 36 cases (55%).

The range of follow-up length was 12–156 months (mean 67 months), but with only 3 patients with 12 months of minimum follow-up length. During the follow-ups, only one patient developed new microcalcifications, in the same breast, 48 months after and 15 mm from the first VAB. The calcifications were stereotactically biopsied, with diagnosis of low-grade ductal carcinoma *in situ* (DCIS), confirmed at surgical excision. In all the other patients, we found no new suspicious microcalcifications or other equivocal/suspicious mammographic signs during the programmed mammographies.

Considering all the patients, we found a malignancy rate of 1.5%, fitting the “probably benign” definition and supporting the hypothesis of conservative management.

DISCUSSION

ADH is a known risk factor for the development of DCIS and invasive carcinoma. Numerous studies have shown that females with ADH have a breast cancer risk or odds ratio of about four times that of the general population.^{25–32} One of the first studies, started in 1978³³ and updated every 10 years,^{34,35} on the effects of long term follow-up of patients with diagnosis of DCIS, found cases of breast carcinoma diagnosed over 15 years after the first biopsy, in the same quadrant and in the same breast from which the original biopsy was taken. We can include in this study ADH lesions, considering that ADH was often diagnosed as DCIS in the 1970s. These results suggest that a long-term follow-up is

needed in these patients, and our results must be confirmed with further studies.

The hypothesis of conservative management of patients with complete removal of the lesion after percutaneous needle biopsy was introduced by Renshaw and colleagues¹⁵ in 2001, using core needle biopsy and shared by the First International Consensus Conference on lesions of uncertain malignant potential in the breast³⁶ recommendations.

However, not all the groups share these conclusions. Jackman's group² excluded the hypothesis of predicting factors feasible for excluding the indication for surgical excision. Even the complete removal of the lesion was excluded as a factor associated with the "probably benign" definition, by Jackman and other authors.^{3,37}

The largest retrospective study³⁸ ever conducted on ADH upgrading rate at surgery identified no subgroups for safe clinical-only follow-up and recommended surgery in all cases of ADH diagnosed by percutaneous breast biopsy. Over a 10-year period, in 13,488 consecutive breast biopsies, ADH was diagnosed in 3.8% of cases. In 422 selected core breast biopsies with primary diagnosis of ADH, the diagnosis was upgraded at surgery in 31.3% of cases. However, a possible limit of the study was that they did not consider the complete removal of microcalcifications as a possible option for safe clinical-only follow-up.

Several studies tried to predict malignancy, to avoid surgical excision in selected cases. Some authors proposed^{39–42} a score to predict the risk of malignancy, with low success. In 2012 Bendifallah et al⁴³ tested the statistical performance of the Ko scoring system against an external independent multicenter population. They concluded that the scoring system was not

sufficiently accurate to safely define a subset of patients who would be eligible for follow-up only and no additional treatment. Their results demonstrate a lack of reproducibility in an external population. They proposed a multidisciplinary approach that correlates clinical-pathological and mammographic features for the management of these patients.

The pathological criteria were introduced by different authors,^{5,13–17,44,45} shared by Forgeard and colleagues, but only partially considered in our study.

Like other authors,^{4,7} in our cohort we found a malignancy rate of 1.5%, that could justify a conservative management without the need of surgical excision. However, the study presents some limitations: first, this is a single center study, so we cannot exclude bias derived from the center, and the mammographies have been performed for opportunistic screening. Second, the upgrading rate is based only on imaging findings, without a histological validation, so we cannot consider a real underestimation rate. Third, part of the follow-up of some patients included in the study were previously published in another study.⁴⁶ Fourth, we present a mean follow-up length of 5 years, but, in our opinion, this is still not enough to completely confirm the hypothesis of conservative management.

CONCLUSIONS

The results of this paper could justify the conservative management of ADH, but only in a highly selected group of patients, with a stereotactical VAB diagnosis of ADH, on a single group of microcalcifications, without residual post-procedure and without the presence of multiple foci of hyperplasia or high percentage of hyperplasia at histological assessment.

REFERENCES

- Hartmann LC, Radisky DC, Frost MH, Santen RJ, Vierkant RA, Benetti LL, et al. Understanding the premalignant potential of atypical hyperplasia through its natural history: a longitudinal cohort study. *Cancer Prev Res* 2014; **7**: 211–7. doi: <https://doi.org/10.1158/1940-6207.CAPR-13-0222>
- Jackman RJ, Birdwell RL, Ikeda DM. Atypical ductal hyperplasia: can some lesions be defined as probably benign after stereotactic 11-gauge vacuum-assisted biopsy, eliminating the recommendation for surgical excision? *Radiology* 2002; **224**: 548–54. doi: <https://doi.org/10.1148/radiol.2242011528>
- Plantade R, Hammou JC, Fighiera M, Aubanel D, Scotto A, Gueret S. Underestimation of breast carcinoma with 11-gauge stereotactically guided directional vacuum-assisted biopsy. *J Radiol* 2004; **85**: 4 Pt 1: 391–401.
- Travade A, Isnard A, Bouchet F, Bagard C. Non-palpable breast lesions and core needle biopsy with mammotome 11G: is surgery required in patients with atypical ductal hyperplasia? *J Radiol* 2006; **87**: 307–10.
- Forgeard C, Benchaib M, Guerin N, Thiesse P, Mignotte H, Faure C, et al. Is surgical biopsy mandatory in case of atypical ductal hyperplasia on 11-gauge core needle biopsy? A retrospective study of 300 patients. *Am J Surg* 2008; **196**: 339–45. doi: <https://doi.org/10.1016/j.amjsurg.2007.07.038>
- Ancona A, Capodiceci M, Galiano A, Mangieri F, Lorusso V, Gatta G. Vacuum-assisted biopsy diagnosis of atypical ductal hyperplasia and patient management. *Radiol Med* 2011; **116**: 276–91. doi: <https://doi.org/10.1007/s11547-011-0626-9>
- 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**: 752–61. doi: <https://doi.org/10.1245/s10434-010-1127-8>
- Zhao L, Freimanis R, Bergman S, Shen P, Perrier ND, Lesko N, et al. Biopsy needle technique and the accuracy of diagnosis of atypical ductal hyperplasia for mammographic abnormalities. *Am Surg* 2003; **69**: 757–62.
- Burak WE, Owens KE, Tighe MB, Kemp L, Dinges SA, Hitchcock CL, et al. Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. *Arch Surg* 2000; **135**: 700–3.
- Cangiarella J, Waisman J, Symmans WF, Gross J, Cohen JM, Wu H, et al. Mamotome core biopsy for mammary microcalcification: analysis of 160 biopsies from 142 women with surgical and radiologic followup. *Cancer* 2001; **91**: 173–7.

11. Winchester DJ, Bernstein JR, Jeske JM, Nicholson MH, Hahn EA, Goldschmidt RA, et al. Upstaging of atypical ductal hyperplasia after vacuum-assisted 11-gauge stereotactic core needle biopsy. *Arch Surg* 2003; **138**: 619–22. doi: <https://doi.org/10.1001/archsurg.138.6.619>
12. Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. *Radiology* 1997; **202**: 843–7. doi: <https://doi.org/10.1148/radiology.202.3.9051043>
13. Jacobs TW, Connolly JL, Schnitt SJ. Nonmalignant lesions in breast core needle biopsies: to excise or not to excise? *Am J Surg Pathol* 2002; **26**: 1095–110.
14. Darling ML, Smith DN, Lester SC, Kaelin C, Selland DL, Denison CM, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. *AJR Am J Roentgenol* 2000; **175**: 1341–6. doi: <https://doi.org/10.2214/ajr.175.5.1751341>
15. Renshaw AA, Cartagena N, Schenkman RH, Derhagopian RP, Gould EW. Atypical ductal hyperplasia in breast core needle biopsies. Correlation of size of the lesion, complete removal of the lesion, and the incidence of carcinoma in follow-up biopsies. *Am J Clin Pathol* 2001; **116**: 92–6. doi: <https://doi.org/10.1309/61HM-89TD-0M3L-JAHH>
16. Sneige N, Lim SC, Whitman GJ, Krishnamurthy S, Sahin AA, Smith TL, et al. Atypical ductal hyperplasia diagnosis by directional vacuum-assisted stereotactic biopsy of breast microcalcifications. Considerations for surgical excision. *Am J Clin Pathol* 2003; **119**: 248–53. doi: <https://doi.org/10.1309/0GYV4F2LLJAV4GFN>
17. Adrales G, Turk P, Wallace T, Bird R, Norton HJ, Greene F. Is surgical excision necessary for atypical ductal hyperplasia of the breast diagnosed by mammotome? *Am J Surg* 2000; **180**: 313–5. doi: [https://doi.org/10.1016/S0002-9610\(00\)00451-7](https://doi.org/10.1016/S0002-9610(00)00451-7)
18. Philpotts LE, Lee CH, Horvath LJ, Lange RC, Carter D, Tocino I. Underestimation of breast cancer with 11-gauge vacuum suction biopsy. *AJR Am J Roentgenol* 2000; **175**: 1047–50. doi: <https://doi.org/10.2214/ajr.175.4.1751047>
19. Liberman L, Kaplan JB, Morris EA, Abramson AF, Menell JH, Dershaw DD. To excise or to sample the mammographic target: what is the goal of stereotactic 11-gauge vacuum-assisted breast biopsy? *AJR Am J Roentgenol* 2002; **179**: 679–83. doi: <https://doi.org/10.2214/ajr.179.3.1790679>
20. McGhan LJ, Pockaj BA, Wasif N, Giurescu ME, McCullough AE, Gray RJ. Atypical ductal hyperplasia on core biopsy: an automatic trigger for excisional biopsy? *Ann Surg Oncol* 2012; **19**: 3264–9. doi: <https://doi.org/10.1245/s10434-012-2575-0>
21. American College of Radiology, Bi-Rads Committee. *ACR BI-RADS atlas: breast imaging reporting and data system*. Reston, VA: American College of Radiology; 2013.
22. Page DL, Dupont WD, Rogers LW, Rados MS. Atypical hyperplastic lesions of the female breast. A long-term follow-up study. *Cancer* 1985; **55**: 2698–708. doi: [https://doi.org/10.1002/1097-0142\(19850601\)55:11<2698::AID-CNCR2820551127>3.0.CO;2-A](https://doi.org/10.1002/1097-0142(19850601)55:11<2698::AID-CNCR2820551127>3.0.CO;2-A)
23. Page DL, Rogers LW. Combined histologic and cytologic criteria for the diagnosis of mammary atypical ductal hyperplasia. *Hum Pathol* 1992; **23**: 1095–7. doi: [https://doi.org/10.1016/0046-8177\(92\)90026-Y](https://doi.org/10.1016/0046-8177(92)90026-Y)
24. Tavassoli FA, Norris HJ. A comparison of the results of long-term follow-up for atypical intraductal hyperplasia and intraductal hyperplasia of the breast. *Cancer* 1990; **65**: 518–29. doi: [https://doi.org/10.1002/1097-0142\(19900201\)65:3<518::AID-CNCR2820650324>3.0.CO;2-O](https://doi.org/10.1002/1097-0142(19900201)65:3<518::AID-CNCR2820650324>3.0.CO;2-O)
25. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, et al. Benign breast disease and the risk of breast cancer. *N Engl J Med* 2005; **353**: 229–37. doi: <https://doi.org/10.1056/NEJMoa044383>
26. Degnim AC, Visscher DW, Berman HK, Frost MH, Sellers TA, Vierkant RA, et al. Stratification of breast cancer risk in women with atypia: a Mayo cohort study. *J Clin Oncol* 2007; **25**: 2671–7. doi: <https://doi.org/10.1200/JCO.2006.09.0217>
27. Page DL, Dupont WD, Rogers LW, Rados MS. Atypical hyperplastic lesions of the female breast. A long-term follow-up study. *Cancer* 1985; **55**: 2698–708. doi: [https://doi.org/10.1002/1097-0142\(19850601\)55:11<2698::AID-CNCR2820551127>3.0.CO;2-A](https://doi.org/10.1002/1097-0142(19850601)55:11<2698::AID-CNCR2820551127>3.0.CO;2-A)
28. Collins LC, Baer HJ, Tamimi RM, Connolly JL, Colditz GA, Schnitt SJ. Magnitude and laterality of breast cancer risk according to histologic type of atypical hyperplasia: results from the Nurses' Health Study. *Cancer* 2007; **109**: 180–7. doi: <https://doi.org/10.1002/cncr.22408>
29. Marshall LM, Hunter DJ, Connolly JL, Schnitt SJ, Byrne C, London SJ, et al. Risk of breast cancer associated with atypical hyperplasia of lobular and ductal types. *Cancer Epidemiol Biomarkers Prev* 1997; **6**: 297–301.
30. Zhou WB, Xue DQ, Liu XA, Ding Q, Wang S. The influence of family history and histological stratification on breast cancer risk in women with benign breast disease: a meta-analysis. *J Cancer Res Clin Oncol* 2011; **137**: 1053–60. doi: <https://doi.org/10.1007/s00432-011-0979-z>
31. 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**: 25–9. doi: <https://doi.org/10.1016/j.pathol.2015.11.015>
32. Latronico A, Nicosia L, Faggian A, Abbate F, Penco S, Bozzini A, et al. Atypical ductal hyperplasia: our experience in the management and long term clinical follow-up in 71 patients. *Breast* 2018; **37**: 1–5. doi: <https://doi.org/10.1016/j.breast.2017.10.003>
33. Betsill WL, Rosen PP, Lieberman PH, Robbins GF. Intraductal carcinoma. Long-term follow-up after treatment by biopsy alone. *JAMA* 1978; **239**: 1863–7.
34. Sanders ME, Schuyler PA, Dupont WD, Page DL. The natural history of low-grade ductal carcinoma in situ of the breast in women treated by biopsy only revealed over 30 years of long-term follow-up. *Cancer* 2005; **103**: 2481–4. doi: <https://doi.org/10.1002/cncr.21069>
35. Sanders ME, Schuyler PA, Simpson JF, Page DL, Dupont WD. Continued observation of the natural history of low-grade ductal carcinoma in situ reaffirms proclivity for local recurrence even after more than 30 years of follow-up. *Mod Pathol* 2015; **28**: 662–9. doi: <https://doi.org/10.1038/modpathol.2014.141>
36. Rageth CJ, O'Flynn EA, Comstock C, Kurtz C, Kubik R, Madjar H, et al. First international consensus conference on lesions of uncertain malignant potential in the breast (B3 lesions). *Breast Cancer Res Treat* 2016; **159**: 203–13. doi: <https://doi.org/10.1007/s10549-016-3935-4>
37. Penco S, Rizzo S, Bozzini AC, Latronico A, Menna S, Cassano E, et al. Stereotactic vacuum-assisted breast biopsy is not a therapeutic procedure even when all mammographically found calcifications are removed: analysis of 4,086 procedures. *AJR Am J Roentgenol* 2010; **195**: 1255–60. doi: <https://doi.org/10.2214/AJR.10.4208>
38. Deshaies I, Provencher L, Jacob S, Côté G, Robert J, Desbiens C, et al. Factors associated with upgrading to malignancy at surgery of atypical ductal hyperplasia diagnosed on core biopsy. *Breast* 2011; **20**: 50–5. doi: <https://doi.org/10.1016/j.breast.2010.06.004>
39. Ko E, Han W, Lee JW, Cho J, Kim EK, Jung SY, et al. Scoring system for predicting

- malignancy in patients diagnosed with atypical ductal hyperplasia at ultrasound-guided core needle biopsy. *Breast Cancer Res Treat* 2008; **112**: 189–95. doi: <https://doi.org/10.1007/s10549-007-9824-0>
40. Boughey JC, Hartmann LC, Anderson SS, Degnim AC, Vierkant RA, Reynolds CA, et al. Evaluation of the Tyrer-Cuzick (International Breast Cancer Intervention Study) model for breast cancer risk prediction in women with atypical hyperplasia. *J Clin Oncol* 2010; **28**: 3591–6. doi: <https://doi.org/10.1200/JCO.2010.28.0784>
 41. Pankratz VS, Hartmann LC, Degnim AC, Vierkant RA, Ghosh K, Vachon CM, et al. Assessment of the accuracy of the Gail model in women with atypical hyperplasia. *J Clin Oncol* 2008; **26**: 5374–9. doi: <https://doi.org/10.1200/JCO.2007.14.8833>
 42. M T, A P, F G, D S, S Z, M S. Positive predictive value of breast lesions of uncertain malignant potential (B3): can we identify high risk patients? The value of a multidisciplinary team and implications in the surgical treatment. *Surg Oncol* 2016; **25**: 119–22. doi: <https://doi.org/10.1016/j.suronc.2016.04.002>
 43. Bendifallah S, Defert S, Chabbert-Buffet N, Maurin N, Chopier J, Antoine M, et al. Scoring to predict the possibility of upgrades to malignancy in atypical ductal hyperplasia diagnosed by an 11-gauge vacuum-assisted biopsy device: an external validation study. *Eur J Cancer* 2012; **48**: 30–6. doi: <https://doi.org/10.1016/j.ejca.2011.08.011>
 44. Ely KA, Carter BA, Jensen RA, Simpson JF, Page DL. Core biopsy of the breast with atypical ductal hyperplasia: a probabilistic approach to reporting. *Am J Surg Pathol* 2001; **25**: 1017–21.
 45. Allison KH, Eby PR, Kohr J, DeMartini WB, Lehman CD. Atypical ductal hyperplasia on vacuum-assisted breast biopsy: suspicion for ductal carcinoma in situ can stratify patients at high risk for upgrade. *Hum Pathol* 2011; **42**: 41–50. doi: <https://doi.org/10.1016/j.humpath.2010.06.011>
 46. Villa A, Tagliafico A, Chiesa F, Chiaramondia M, Friedman D, Calabrese M. Atypical ductal hyperplasia diagnosed at 11-gauge vacuum-assisted breast biopsy performed on suspicious clustered microcalcifications: could patients without residual microcalcifications be managed conservatively? *AJR Am J Roentgenol* 2011; **197**: 1012–8. doi: <https://doi.org/10.2214/AJR.11.6588>