HOLOGIC

Reducing ADH underestimation

How vacuum-assisted breast biopsy improves diagnostic accuracy

Summary

- The accurate diagnosis of atypical ductal hyperplasia (ADH) remains a critical challenge for clinicians, with underestimation carrying significant implications.
- Vacuum-assisted breast biopsy (VABB) improves diagnostic accuracy, with a 37 % decreased risk of ADH underestimation compared to core needle biopsy (CNB).
- VABB results in a 22 % decreased risk for repeat biopsy compared to CNB, translating to more efficient use of resources and staff time.
- VABB extracts more representative tissue samples from a single insertion, while reducing patient discomfort.
- VABB contributes to reducing overall healthcare costs with a lower cost per diagnosis compared to CNB.

ADH is one of the most common breast lesions, and one that has uncertain malignant potential – also known as high-risk or B3 lesions – carrying the highest increase in breast cancer risk.[1] Accurately distinguishing ADH from ductal carcinoma *in situ* (DCIS) – a non-invasive cancer – is a recurring challenge for clinicians and pathologists, as biopsies often fail to capture, or underestimate, the severity of the lesion. For this reason, surgery has previously been the preferred strategy for all high-risk lesions, but conservative management is increasingly favoured to reduce overtreatment and its associated costs, and spare patients from unnecessary anxiety.[2] This paper investigates the challenge of diagnosing ADH, and describes how using vacuum-assisted breast biopsy (VABB) can help to reduce ADH underestimation and improve patient outcomes.

The clinical challenge: ADH underestimation

Since their introduction into clinical practice in the early 1990s, percutaneous image-guided breast biopsies have significantly improved the management of patients with lesions of uncertain malignant potential, almost entirely replacing surgical excisions for establishing a diagnosis.[3] The European guidelines for managing B3 lesions recommend using either CNB or VABB[4] over fine-needle aspiration biopsy. However, even using these methods, many cases are still challenging to classify, presenting with similar pathology to DCIS, which results in significant interobserver variation amongst pathologists.[5]

The debate on the management of patients with B3 lesions is centred on the upgrade rate, which is the rate at which percutaneously diagnosed lesions are upgraded to DCIS or invasive cancers following surgical excision or during active imaging surveillance.[1] In clinical practice, this remains highly variable – with between 5 and 50 % of a lesion's severity underestimated at biopsy – and difficult to predict, but it is critical to how each patient is managed.[4] Several previous studies have analysed the relationships between pathological parameters – including the extent of ADH, degree of atypia and presence of necrosis – with the outcome determined from surgical specimens,[6–10] but none of them has been able to predict the requirement for surgery over conservative management.[11]

The World Health Organization defines ADH as an epithelial proliferative lesion with similar cytologic and architectural features to low-grade DCIS, but less developed in their degree and extent.[5] Even though most authorities agree that abnormal cell quantity is one of the most significant distinguishing factors, the science remains inexact,[5] often making it difficult for pathologists to differentiate.

VABB's role in reducing ADH underestimation

While both CNB and VABB remain the preferred methods for preoperative diagnosis of breast lesions, the latter has mounting evidence for reducing underestimation and improving the accuracy of diagnosis. This is due, in part, to the fact that VABB is performed with larger needles compared to CNB, allowing more tissue to be removed – and, with it, a more complete sample of the lesion – which has been shown to reduce the chances of false negative results or underestimation.[12,13] This is highlighted in multiple studies, including:

- Badan *et al*., who found that the underestimation rate for ADH using CNB was 50 %, compared to 25 % with VABB[12];
- Rageth *et al*. returned similar results, with 57 % underestimation for CNB and 33 % for VABB[11];
- Calvo *et al*. concluded that the diagnostic underestimation rate when using CNB is approximately three times that for VABB.[14]

These results corroborate data in the wider literature, implying that the choice of biopsy method directly influences diagnostic accuracy. The ability to analyse larger volumes of lesion tissue with VABB may help to minimise sampling errors, leading to a reduced frequency of underestimation and the need for repeat biopsy.[15]

Hologic commissioned a third party to perform a systematic literature review and meta-analysis to gain detailed insights into the clinical effectiveness of VABB. Of the 959 papers that were identified as relevant, 97 were included in the final analysis based on the PICOS model (Annex 1), with a selection of the results shown below.[16]

- Women having VABB as an initial biopsy for a suspicious finding on imaging have a **37 % decreased risk of ADH underestimation** compared to women having CNB (RR:**0.63** (0.55- 0.72), p<0.01).
- When using stereotactic-guided VABB, the risk of ADH underestimation is **decreased by 47 % compared to CNB (RR: 0.53 (0.42- 0.66), p<0.01) and 67 % compared to stereotactic-guided CNB (RR: 0.33 (0.24-0.46), p<0.01).**
- VABB results in a **22 % decreased risk for repeat biopsy** compared to CNB (RR: **0.78** (0.69- 0.88), p<0.01).
- **Concordance rate is increased by 7 %** when using VABB over CNB (RR: **1.07** (1.04- 1.14), p<0.01).

Comparing biopsy techniques: CNB vs VABB

The heterogeneous nature of breast lesions results in varying histological findings from different areas of a mass, suggesting that sampling part but not all of a lesion may miss certain histological components.[17] It is therefore possible for the core of the lesion, which is targeted by CNB, and the surrounding area to differ histologically.[18] As previously mentioned, VABB may help to address this issue by enabling the collection of larger tissue samples, improving the breadth of cell types collected. In addition, VABB offers several key benefits to clinicians and pathologists, including:

- less invasive for the patient as the needle remains in the breast throughout the biopsy, eliminating the need to repeatedly re-target the needle for sampling;
- only one skin puncture is required, making the biopsy more efficient and saving time for both staff and the patient;
- samples can be taken from different sides of the lesion, or the entire lesion can sometimes be removed, with no further surgical procedures required if it is diagnosed as benign;
- the vacuum function prevents the lesion from moving during aspiration, whereas it can sometimes slip during CNB as a result of the puncture;
- vacuum and irrigation also improve the quality of the sample, as blood is aspirated and more tissue can be sampled;
- the overall costs are offset by improved efficiency and reduced need for additional follow-up procedures due to its higher accuracy, helping to alleviate the burden on healthcare resources and staff.

In addition to these clinical benefits, VABB has several advantages for the patient compared to CNB. Firstly, it is a less invasive procedure, with CNB requiring multiple needle insertions – as well as emitting more noise – increasing patient discomfort and anxiety.[18] This is especially relevant when the procedure is performed on more sensitive areas, such as the nipple, the thoracic wall and the axillary region.[19] Despite using lower gauge needles, VABB also results in less pain experienced by women,[20] and is considered a safe and efficient method, with high patient acceptance and comparable rates of minor complications.[21] Additionally, several studies have concluded that VABB is a highly sensitive method (Table 1), with improved diagnostic accuracy resulting in fewer repeat biopsies and follow-up examinations.[22] Grady *et al*. concluded that this contributed to a lower cost per diagnosis, suggesting that VABB can be a more cost-effective solution compared to CNB.[23]

Study	Sensitivity of VABB (%)
Thakkar (Popat) *et al*[24]	96
Safioleas *et al*[25]	98.2
Amorim *et al*[26]	91.7
Yu *et al*[27]	98.1
Kettritz *et al*[28]	99

Table 1: Sensitivity of VABB found in multiple studies.

Conclusion

The accurate diagnosis of ADH remains a critical challenge for clinicians, with underestimation carrying significant implications. The evidence presented in this paper suggests that VABB reduces ADH underestimation, as well as improving diagnostic accuracy and minimising the need for repeat biopsies. This also makes VABB an attractive cost-effective solution, with fewer unnecessary procedures translating to more efficient use of resources and staff time. Finally, the ability of VABB to extract larger, more representative tissue samples from a single insertion, while reducing patient discomfort, strongly advocates its wider adoption as a key tool in clinical practice.

Annex 1

The PICOS model acts as a framework for the eligibility criteria in systematic reviews of literature. In this review, the components listed below were used to search PubMed and Cochrane Library to identify relevant studies.

Components	
Patients / population	**Women with suspected breast cancer** (symptomatic / non-symptomatic: no restriction regarding age or country)
Intervention	Vacuum-assisted breast biopsy
Comparison / control	(i) Core needle biopsy and (ii) fine needle aspiration
Outcomes	• ADH underestimation rate • DCIS underestimation rate • Underestimation rates in general (not clearly assignable to ADH or DCIS underestimation rate) • Repeat biopsy rate • Concordance rate • (Micro)calcification retrieval rate • Sensitivity* • Specificity* • Complications (haematoma, bleeding, infection, pain, ...) • Mortality • Morbidity • Quality of life • Workflow efficacy (time under compression, time period for one biopsy) * Also searched for positive predictive value, negative predicted value, false-negative rate, false-positive rate, area under the curve to collect all data allowing to have a full set of true negatives, true positives, false negatives, and false positives.
Study design(s)	Comparative studies (single-arm studies were excluded)

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