







COMMENTARY

The reassurance of the diagnosis benign calcifications after vacuum-assisted stereotactic breast biopsy

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The introduction of breast screening programs resulted in an increase of the detection of nonpalpable breast calcifications.¹ Since calcifications may be the sole presence of breast cancer, suspect breast calcifications require histopathologic evaluation.^{2,3} In current practice, vacuum-assisted stereotactic biopsy (VASB) is the standard diagnostic in the evaluation of calcifications.⁴⁻⁶ Although VASB has been studied frequently, studies have not been specified on breast calcifications specifically.^{4,7-10} We determined the diagnostic performance of VASB specified for breast calcifications in current daily practice.

We conducted a retrospective cohort study of all consecutive patients who underwent VASB to analyze breast calcifications. Histopathologic results were categorized into three groups based on reported pathologic conclusion: (1) malignant lesions, (2) lesions with inconclusive results, and (3) benign lesions. Malignant lesions concerned lesions with ductal carcinoma in situ (DCIS) and/or invasive breast cancer. Inconclusive radiologic-pathologic results included high-risk lesions (including flat epithelial atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, papillary lesions, radial scar, and phyllodes tumor), unrepresentative biopsies, and lesions with discrepancies between radiologic and pathologic findings (determined at multidisciplinary consultation). In case of follow-up for a benign lesion or an inconclusive radiologic-pathologic result, the possible development of breast cancer was verified using data from the local institutional database and the national registry of histopathology and cytopathology, which covers all hospitals in the Netherlands. If ipsilateral breast cancer developed within a period of four years after biopsy, it was classified as breast cancer related to the lesion that had been originally biopsied.

All statistical analyses were performed using the statistical software of IBM SPSS version 24. Patient demographics and biopsy variables were analyzed using descriptive analyses, presented as means with standard deviation or numbers with percentages. The diagnostic accuracy included sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). In this analysis, all malignant lesions classified as true-positive test results. Benign lesions were classified as true-negative test result, unless patients developed ipsilateral breast cancer. Benign lesions with a negative pathologic result based on the surgical specimen were classified as true-negative test result. Patients with inconclusive radiologic-pathologic results who had received a diagnostic surgical excision were classified as positive test result. However, if the final pathology report showed a benign lesion, this was classified as false-positive test. Lesions were classified as false-negative test result if ipsilateral breast cancer had developed during the follow-up after biopsy (without surgical excision). In case no remainder of the primary lesion was detected in the surgical specimen, it was assumed that the complete lesion was present in the biopsy. In these cases, diagnosis was based on the biopsy specimen.

Binomial proportion confidence intervals of the test characteristics were calculated with the Agresti-Coull method. No imputations were made for missing data. Two-sided *p*-values of <0.05 were considered statistically significant.

During the inclusion period, 1533 patients had a lesion on mammography or ultrasound which necessitated VASB. In 1376 patients, VASB was performed to analyze breast calcifications. Of these patients, 827 (60%) patients had a biopsy with benign histology, 443

	Surgical excision or follow-up positive	Surgical excision or follow-up Negative	Total
VASB positive*	n = 456 (443 [§] + 13 [#])	n = 36 [#]	492
VASB negative**	n = 10 (8 ^{§§} + 2 ^{##})	n = 874 (815 ^{§§} + 55 ^{##} + 4 [§])	884
Total	466	910	1376

TABLE 1 Contingency table of 1376 VASB results with results of surgical excision or follow-up

*Histopathologic ductal carcinoma in situ and/or invasive carcinoma[§]; or inconclusive radiologic-pathologic result[#] which required surgical excision. Histopathologic benign clustered calcifications[§] which received surgical excision at patient's request.

**Histopathologic benign clustered calcifications^{§§}; or inconclusive radiologic-pathologic result^{##} which required follow-up.

Surgical excision or follow-up positive = histopathologic ductal carcinoma in situ and/or invasive carcinoma in surgical specimen; or development of ductal carcinoma in situ and/or invasive carcinoma during follow-up.

Surgical excision or follow-up negative = histopathologic benign result of surgical specimen; or no development of ductal carcinoma in situ and/or invasive carcinoma during follow-up.

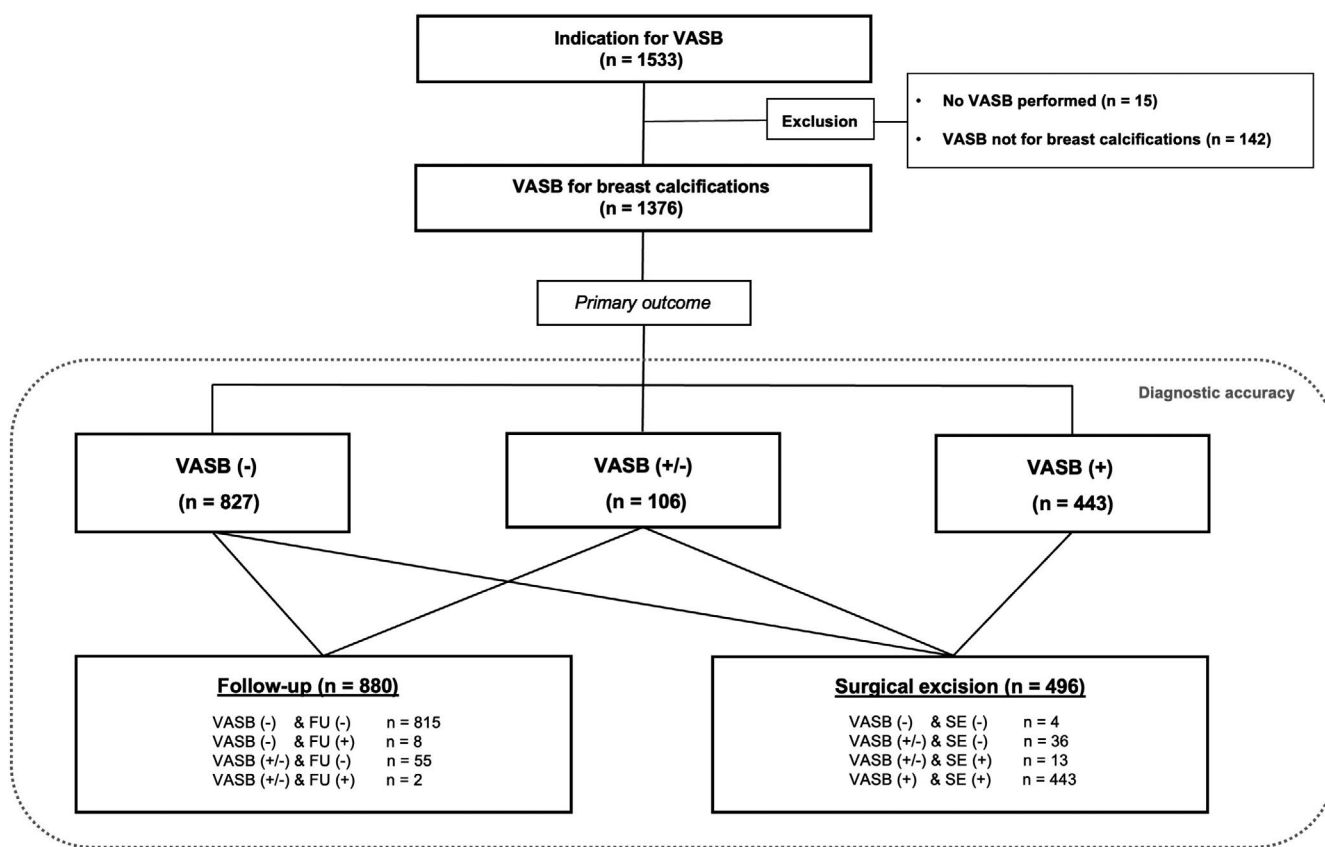


FIGURE 1 Patient selection and management flowchart for patients with breast calcifications. VASB (-) = histopathologically benign calcifications; VASB (+/-) = inconclusive radiologic-pathologic result; VASB (+) = histopathological ductal carcinoma in situ and/or invasive carcinoma. FU (-) = no development of ductal carcinoma in situ and/or invasive carcinoma during follow-up; FU (+) = development of ductal carcinoma in situ and/or invasive carcinoma during follow-up. SE (-) = histopathologically benign result of surgical specimen; SE (+) = histopathologic ductal carcinoma in situ and/or invasive carcinoma in surgical specimen

(32%) patients had a malignant histology, and 106 (8%) patients had an inconclusive radiologic-pathologic result resulting in follow-up or surgical excision. The mean age at first presentation was 56.3 ± 10.1 years, 740 patients (54%) were referred by the national

screening program, and the majority (79%) were diagnosed with a BI-RADS IV lesion.

Of 492 (36%) patients with a positive histopathologic result after VASB or an inconclusive radiologic-pathologic result which required

surgical excision. Of these 492 patients with a positive test result, 456 (33%) patients had breast cancer in the surgical specimen and 36 (3%) did not.

Of 884 (64%) patients with a negative histopathologic result after VASB or an inconclusive radiologic-pathologic result which required follow-up, 10 (1%) patients developed breast cancer during the follow-up period of four years. Of these patients who developed breast cancer during follow-up, 8 patients had a negative histopathologic result after VASB and 2 had inconclusive radiologic-pathologic result. Based on these numbers, VASB for calcifications has a sensitivity of 98% (95% CI 96.0 – 98.9), a specificity of 96% (95% CI 94.6 – 97.1), a PPV of 93% (95% CI 90.1 – 94.6) and a NPV of 99% (95% CI 97.9 – 99.4) (Table 1). Of the patients with a false-negative result the mean age was 57.3 ± 10.2 years, 6 patients (60%) had a history of breast cancer.

In conclusion, VASB for breast calcifications is a diagnostic tool with a very high accuracy. The histopathologic result after VASB for breast calcifications can be considered as an effective and an assured decision tool.

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