



Ten years follow-up of histologically benign calcifications in the breast after vacuum-assisted stereotactic biopsy (VASB): Is additional mammographic follow-up warranted?

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ABSTRACT

Objective: This study assessed the short-term and the long-term breast cancer rate in patients with benign histopathologic results after a vacuum-assisted stereotactic biopsy (VASB) for calcifications.

Methods: In a retrospective cohort study, all consecutive patients who had a benign diagnosis after VASB to analyze breast calcifications. Data of breast cancer development at short-term (four years) and long-term follow-up was gathered. Breast cancer rates in our cohort were compared to the breast cancer incidence in the general population.

Results: Of 1376 patients who underwent VASB to analyze breast calcifications, 823 had a benign histopathologic diagnosis. During short-term follow-up, eight patients developed breast cancer. During the mean long-term follow-up period of 9.3 ± 3.1 years, 22 patients were diagnosed with ipsilateral breast cancer. The incidence rate of breast cancer after benign biopsy was comparable to the rate in the general population.

Conclusion: In patients with VASB-confirmed benign calcifications of the breast, we found no excess incidence of ipsilateral breast cancer during ten years follow-up. Therefore, in patients with an increased risk of breast cancer (due to a history of breast cancer or familial risk) annual mammography should be sufficient. Patients with a population-based risk may be monitored via biennial mammography by the national screening program. More frequent screening would provide no benefit.

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1. Introduction

The introduction of full-field digital mammography (FFDM) resulted in an increase in the detection of suspect calcifications compared to conventional screen-film mammography (SFM) [1,2]. The morphologic presentation of calcifications on mammography is not reliable for predicting malignancy. Consequently, these calcifications require histologic evaluation, since they may be the sole indication for the presence of breast cancer [3,4]. Over the years, vacuum-assisted stereotactic biopsy (VASB) has become the standard diagnostic tool for the analysis of clustered calcifications

[5–7].

The majority of these subclinical calcifications are benign on histologic examination [4,6–8] and the management varies from (additional short-term) mammographic follow-up to no additional follow-up at all [9,10]. However, some studies found an association between the presence of calcifications and the development of breast cancer [11–13]. Therefore, the aim of this study was to assess both the short-term and the long-term breast cancer rate in women with a benign VASB histopathologic result for clustered breast calcifications and to compare that rate with the breast cancer incidence in the general population.

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2. Methods

2.1. Study design

The present study was a single center retrospective cohort study of all consecutive patients who presented at a large teaching hospital in the Netherlands between August 2004 and May 2014 for vacuum-assisted stereotactic biopsy (VASB) to analyze breast calcifications, and received a benign diagnosis. The institutional review board approved the study and granted a waiver of informed consent, since data was retrospectively collected and anonymized.

2.2. Patient selection

Patients had been referred via the national screening program or by their general practitioner for breast-related symptoms or familial risk, or they were already in hospital follow-up (Table 2 for specific reasons for follow-up). The diagnostic work-up consisted of physical breast examination, digital mammography, ultrasound examination of the breast and, if necessary, also of the axilla. Diagnostic outcomes of all patients were discussed in a multidisciplinary consultation with a breast surgeon, a plastic surgeon, a radiologist, a pathologist, and an oncologist. The radiologic-pathologic concordance was determined. Management was based on the histopathologic result and the radiologic results.

Patients were included if they had received VASB to analyze breast calcifications, and if the histopathologic result was benign. Patients were excluded if they had a malignant result, a high-risk histopathologic result, or a radiologic-pathologic discordant result. Lesions classified as high-risk based on the histopathologic result included flat epithelial atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, papillary lesions, radial scar or phyllodes tumor. The Radiologic and pathologic findings were considered to be concordant if the pathologic result provided an acceptable explanation for the imaging feature and discordant if they did not.

Patient-related variables were gathered from electronic medical records of our institutional database. All cases were reviewed based on the clinical conclusions.

2.3. Imaging and vacuum-assisted stereotactic biopsy

Mammographic lesions were classified based on the Breast Imaging Reporting and Data System (BI-RADS) classification, and ACR-criteria for calcifications were applied, which means that at least five calcifications had to be present within 1 cm of each other [14]. VASB was performed if no accompanying signs were detected that could be used for ultrasound-guided biopsy.

Biopsies were executed with 9G-needles, except for the biopsies taken before January 15, 2008, for which only 10G-needles were available. All stereotactic core biopsies were accomplished with the VACORA vacuum-assisted stereotactic breast device (10G biopsies) or the Hologic Eviva vacuum-assisted stereotactic breast device (9G biopsies). Before core needle biopsy, informed consent had been obtained from and time-out procedure had been performed on each patient. Patients were placed in prone position. Prior to VASB a local field anesthesia with lidocaine was administered. Routinely, six to twelve specimens were obtained with each core biopsy. After each procedure, the presence of calcifications was confirmed with specimen radiographs. If no calcifications were visible in the specimen, additional biopsies were obtained.

All core biopsies were performed by a board-certified breast radiologist (with at least six years of experience) or by a resident under supervision of an experienced board-certified breast radiologist.

2.4. Short- and long-term follow-up of benign breast calcifications after biopsy

All data concerning the development of breast cancer subsequent to VASB was collected from the local institutional database (mammographic follow-up). To prevent overlooking any relevant data, the possible development of breast cancer was also verified until the end of 2018, using data from the national registry of histopathology and cytopathology, which covers data of all hospitals in the Netherlands. In this way, the course subsequent to the time of biopsy could be identified for each patient, even for patients without local treatment or follow-up data. Data concerning contralateral breast cancer was also collected.

The short-term follow-up was defined as the four-years subsequent to biopsy. If ipsilateral breast cancer developed within these four-years subsequent to biopsy, it was conservatively classified as breast cancer related to the lesion that had been originally biopsied. The long-term follow-up was defined as the complete period from the first biopsy until the final check for breast cancer at the end of 2018 or the date of diagnosis of ipsilateral breast cancer. To calculate accurate follow-up time, all patients were checked to be alive at the end of 2018. If patients were deceased, the date of death was used as last follow-up date. If it was not possible to confirm that a patient was alive, the moment of last contact registered in the institutional database was used as the last follow-up date.

2.5. Data analysis

Patient demographics and biopsy variables were analysed using descriptive analyses, presented as means with standard deviation or as numbers with percentages. Differences between patients who developed breast cancer within four years after biopsy and those who did not were identified with univariate analyses using Fisher's exact tests and non-parametric tests for categorical and continuous variables.

The risk for developing breast cancer after a diagnosis of benign calcifications was estimated with a Kaplan-Meier cumulative incidence analysis and compared with the corresponding breast cancer incidence in the general population. The incidence rates of ipsilateral and contralateral breast cancer were calculated for a four-year period subsequent to biopsy. The age-dependent breast cancer incidence in the general population of the Netherlands was calculated based on the incidence rate among women per age category in 2010, which was published on www.cijfersoverkanker.nl (for invasive breast cancer and DCIS). To specify the incidence rate for one breast, the total incidence was divided by two. The increase of age during follow-up was accounted for in the calculation of breast cancer incidence in the general population.

No imputations were made for missing data. Two-sided *p*-values of *p* < 0.05 were considered statistically significant. All statistical analyses were performed using the statistical software of IBM SPSS version 24.

3. Results

3.1. Patient characteristics

In total, 1376 patients were identified who had undergone VASB to analyze breast calcifications, 823 of whom met the inclusion criteria (Fig. 1). The mean age at first presentation was 55.7 ± 10.3 years. In 51% of the included patients, mammography had been performed after recall by the national screening program, in 23% after referral by a general practitioner, and in 26% during hospital follow-up. Overall, 79% of the patients had a BI-RADS 4 mammography, 87% had no history of breast cancer, and 3% were

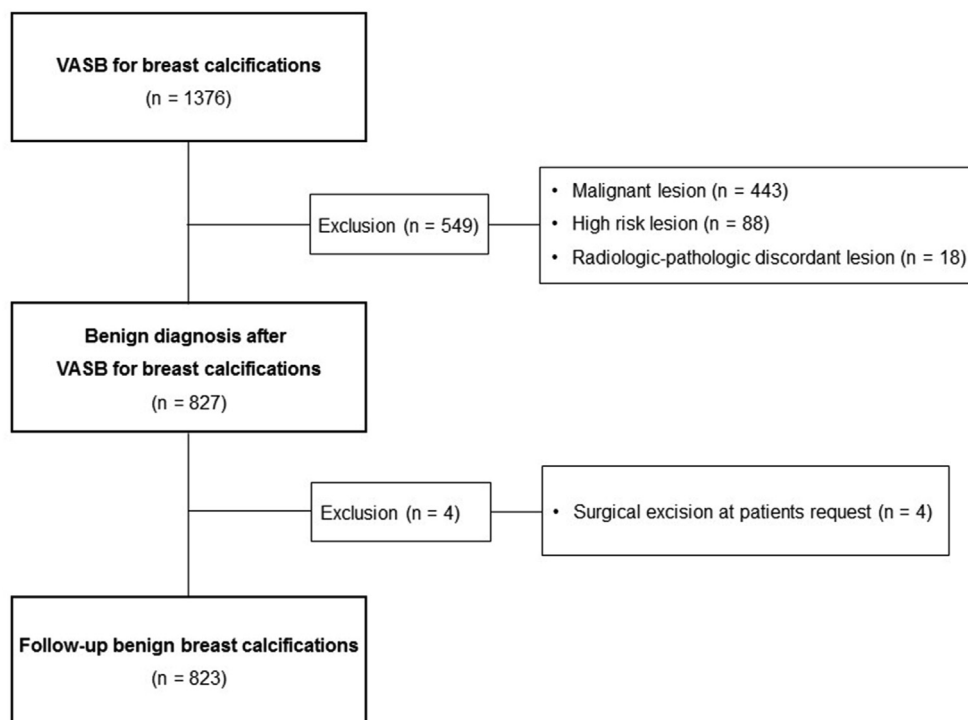


Fig. 1. Patient selection and management flowchart for patients with clustered calcifications. VASB = Vacuum-Assisted Stereotactic biopsy; *High risk lesion* = The histopathologic result included flat epithelial atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, papillary lesions, radial scar or phyllodes tumor; *Radiologic-pathologic discordant lesion* = the pathologic result provided not an acceptable explanation for the imaging feature.

diagnosed with contralateral breast cancer synchronous to the benign calcifications (Table 1).

3.2. Short-term follow-up (possible missed diagnosis)

Within four-years after biopsy, eight of 823 (1%) patients developed ipsilateral breast cancer, the median interval being 2.4 years after biopsy (range 1.1–2.7). In five of these patients, the breast cancer manifested at the biopsy site (i.e., in the same breast quadrant as the initial biopsy). In the other three patients, breast cancer was not located at the biopsy site but in another quadrant of the ipsilateral breast. The mean age at first biopsy was 59.4 ± 10.2 years. Of these eight patients, six (75%) were already in follow-up at the time of VASB due to a medical history of breast cancer. This differed significantly from the patients who did not develop ipsilateral breast cancer within four years after biopsy (See Table 2 for more details).

Fig. 2 compares Kaplan-Meier estimates of breast cancer in the ipsilateral breast after benign biopsy with the background risk of breast cancer in one breast. The cumulative incidence of developing breast cancer in the first four years of follow-up in the study population was 0.0098 and in the general population 0.00704 (Fig. 2).

3.3. Long-term follow-up (late development of breast cancer)

After a mean follow-up period of 9.3 ± 3.1 years, 44 of 823 (5%) patients were identified who had developed invasive breast after a benign histopathologic diagnosis of clustered calcifications.

Of these 44 patients, 22 (3%) were diagnosed with contralateral breast cancer after a median interval of 8.5 (range 1.9–13.7) years. The other 22 (3%) developed breast cancer ipsilateral to the biopsy site after a median interval of 6.1 years after biopsy (range 1.1–12.4) (See Table 3 and Table 4 for more details).

In total, 152 (18%) patients did not return for local follow-up. All events of developing breast cancer of all 823 patients were checked in the national histopathologic database. Of the 22 patients diagnosed with ipsilateral breast cancer, two patients diagnosed in another hospital. In one patient breast cancer was detected after 4.0 years and in one patient breast cancer was detected after 6.4 years after the diagnosis of benign clustered calcifications.

4. Discussion

To our knowledge, this is the first study that focused on the long-term follow-up after histopathologic proven benign breast calcifications after VASB without any loss to follow-up. When reviewing the literature on VASB of calcifications of the breast, follow-up time ranged from 3 to 67 months [4,6,10,15–20]. Furthermore, studies show included lesions other than benign calcifications, a large heterogeneity of the outcome measures, and a considerable loss to follow-up (Table 5 [4,15,21–27]). The current study showed that during short-term follow-up 8 patients (1%) were diagnosed with breast cancer, after a median interval between biopsy and diagnosis of 2.4 years. During 10 years of follow-up, ipsilateral breast cancer was diagnosed in 22 (3%) patients, after a median interval to diagnosis of 8.3 years. The majority of these patients (14 out of 22) were already in annual hospital follow-up at the time of benign VASB result for breast calcifications.

Multiple studies have shown that there would be no benefit of follow-up within a year after benign ultrasonic, radiographic and MRI-guided breast biopsies [10,16,17,19,20,28]. Present analysis is focused solely on VASB breast calcifications. Our results are consistent with the previously published results on biopsy with VASB of breast lesions in general. The median interval to diagnosis of breast cancer was 6.1 years. No breast cancers were detected in the first year of follow-up. After two years post-biopsy, breast

Table 1
Patient characteristics of 823 patients with benign histology after VASB of clustered calcifications.

	Number of patients (n)	Percentage (%)	Mean ± std
Age at first presentation, in years	823		55.7 ± 10.3
Referral			
National screening program	416	50.5	
General practitioner	188	22.8	
Follow-up	215	26.1	
Biopsy for other hospital	4	0.5	
In case of referral by follow-up, specification of reason for follow-up			
History of breast cancer	96	11.7	
History or analysis of other malignancy than breast cancer	7	0.9	
Family history of breast cancer	42	5.1	
Benign breast lesion	65	7.9	
Hormonal drug therapy	4	0.5	
Preoperative screening	1	0.1	
History of breast cancer			
No	719	87.4	
Yes	97	11.8	
Missing	7	0.9	
In case of history of breast cancer, side of cancer compared to calcifications			
Ipsilateral	41	5.0	
Contralateral	56	6.8	
BI-RADS classification at the moment of VASB			
BI-RADS 3	166	20.2	
BI-RADS 4	649	78.9	
BI-RADS 5	1	0.2	
Missing	6	0.7	
Breast with clustered calcifications			
Left	431	52.4	
Right	392	47.6	
Histopathologic findings			
Breast tissue without abnormalities	223	27.1	
Mastopathy	287	34.9	
Fibroadenoma	73	8.9	
Fibrosis/fibrocystic breast changes	75	9.1	
(Sclerosing) Adenosis or sclerosis	34	4.1	
Hyperplasia	27	3.3	
Apocrine metaplasia	19	2.3	
Inflammation/necrosis	19	2.3	
Epitheliosis or epithelial proliferation	11	1.3	
Lactational changes	3	0.4	
Combination of different benign pathologic findings	23	2.8	
In case of a combination of different benign pathologic findings, specification			
Fibroadenoma + adenosis	1	0.1	
Fibroadenoma + fibrosis	1	0.1	
Fibroadenoma + mastopathy	12	1.5	
Mastopathy ^a + mucocele like lesion	1	0.1	
Mastopathy + inflammation	3	0.4	
Mastopathy + PASH ^b	1	0.1	
Inflammation + epitheliosis/fibrosis	2	0.2	
Radiation therapy induced changes + fibrosis + necrosis	1	0.1	
Synchronous contralateral breast malignancy			
No	779	97.1	
Yes	24	2.9	
Follow up, in years	823		9.3 ± 3.1
Development of breast cancer over complete follow-up period			
No	779	94.7	
Yes, ipsilateral to clustered calcifications	22	2.7	
Yes, contralateral to clustered calcifications	22	2.7	

^a Mastopathy = combination of (sclerosing) adenosis, epitheliosis, and or apocrine metaplasia.

^b PASH = pseudoangiomatous stromal hyperplasia.

cancer was detected in two patients. Thus, in our cohort, a short observation period less than two years would not have detected a false negative case. When calcifications are due to a low-grade intraductal carcinoma, they may be falsely diagnosed as benign. The follow-up within a year may identify false negative cases due to sampling error or procedural failure. However, breast calcifications without the presence of a mass or architectural distortion progress

slowly over a longer period [29]. So follow-up with a frequency of annual or biennial screening would be appropriate to observe false negative lesions over time. When imaging features change over time at the biopsy site, a biopsy needs to be performed regardless of the finding and the timing.

The current study showed a relatively low breast ipsilateral cancer rate at short-term follow-up (1%) and at long-term follow-

Table 2

Short-term follow-up; Patients who did not develop breast cancer ipsilateral to the biopsy site (n = 815) compared to patients who did develop breast cancer ipsilateral to the biopsy site (n = 8).

	No breast cancer subsequent to biopsy (n = 815)	Breast cancer subsequent to biopsy (n = 8)	p-value
Mean age ± sd, in years, at moment of first biopsy	55.7 ± 10.3	59.4 ± 10.2	0.243
Referrer			0.004
National screening program	416 (51.0%)		
General practitioner	186 (22.8%)	2 (25.0%)	
Follow up	209 (25.6%)	6 (75.0%)	
Biopsy for other hospital	4 (0.5%)		
In case of referral by follow-up, specification reason for follow-up			0.129
History of breast cancer	90 (11.0%)	6 (75.0%)	
History/analysis of other malignancy than breast cancer	7 (0.9%)		
Family history of breast cancer	42 (5.1%)		
Detected benign lesion	65 (8.0%)		
Hormonal drug therapy	4 (0.5%)		
Preoperative screening	1 (0.1%)		
History of breast cancer			<0.001
No	717 (88.0%)	2 (25.0%)	
Yes	91 (11.2%)	6 (75.0%)	
Missing	7 (0.9%)		
In case of history of breast cancer, side cancer compared to calcifications			1.000
Ipsilateral	39 (4.9%)	2 (25.0%)	
Contralateral	52 (6.4%)	4 (50.0%)	
Median time to diagnosis, in years		2.4 (1.1–2.7)	
Spatial relationship between future development of ipsilateral breast cancer and previous biopsy site			
Biopsy site (biopsied quadrant)		5 (62.5%)	
Other quadrant		3 (37.5%)	

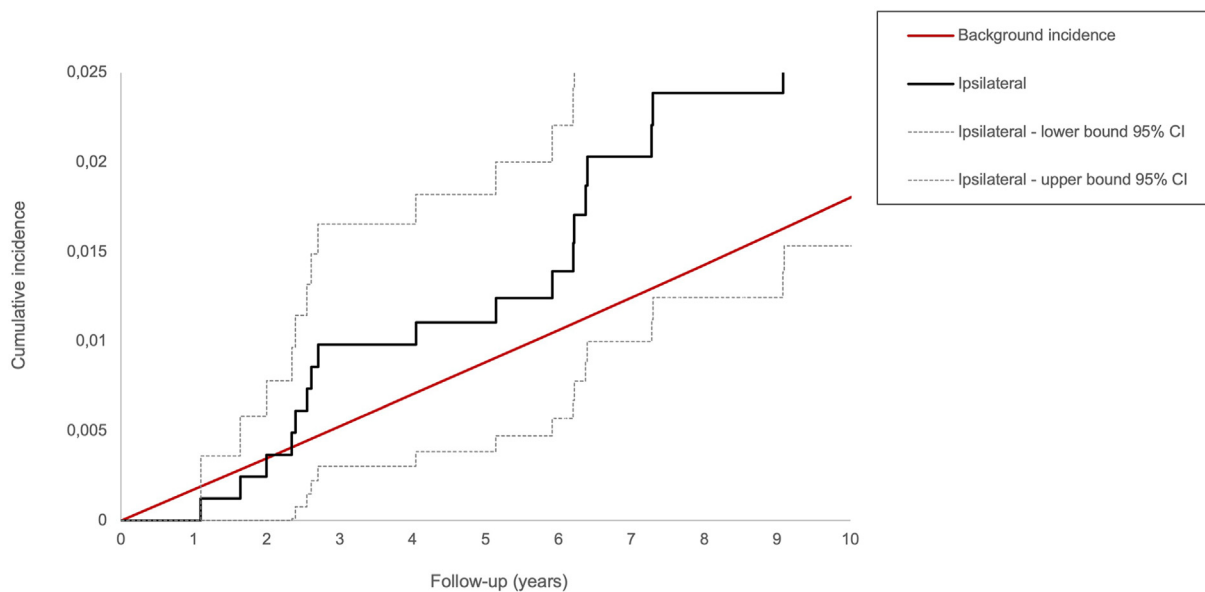


Fig. 2. Cumulative incidence of the development of ipsilateral breast cancer with 95% confidence intervals compared to the general background risk in ten years subsequent to biopsy.

up (3%). Our survival analysis indicated that the risk for breast cancer in our cohort following biopsy is comparable to the risk in the general population. However, it is important to bear in mind that breast cancer is the most frequently detected malignancy in women; in the general population one out of eight women develop breast cancer, and the risk for breast cancer increases with age [30]. In the present study, majority of patients who developed ipsilateral breast cancer were already in hospital follow-up (6 out of 8 at

short-term follow-up, and 14 out of 22 at long-term follow-up; see Table 2 for reasons for follow-up). At short-term follow-up, none of the patients who had been recalled by the national screening program had developed ipsilateral breast cancer after a benign histopathologic result.

The risk for developing breast cancer in our patient population appeared not statistically different to the general background risk. Therefore, there seems no need for additional mammography after

Table 3
Long-term follow-up: Interval from biopsy to diagnosis of ipsilateral breast cancer.

	No breast cancer subsequent to biopsy	Diagnosis of breast cancer subsequent to biopsy	Median interval to diagnosis of ipsilateral breast cancer, in years (minimum, maximum)
Complete study cohort	801	22	6.1 (1.1–12.4)
Primary referral			
National screening program	410	6	8.3 (5.9–12.4)
General practitioner	186	2	2.3 (2.3–2.4)
Follow-up	201	14 ^a	4.6 (1.1–9.1)
Biopsy for other hospital	4		

^a 9 patients with a history of breast cancer, 3 patients with a family history of breast cancer and 2 patients with a benign lesion which required follow-up.

Table 4
Characteristics post-biopsy ipsilateral breast cancer (n = 22).

	History of breast cancer	Years to detection breast cancer	Surgical treatment	Tumor size (mm)	Histopathologic result	Receptor status	Nodal status
1	Yes	2.55	Mastectomy	30	Invasive lobular carcinoma grade 2	ER+, PR+, Her2Neu-	N0
2	Yes	2.61	BCS	No tumor found in surgical specimen	DCIS grade 2	–	Nx
3	Yes	1.63	Mastectomy	50	DCIS grade 3	ER+, PR-, Her2Neu-	Nx
4	No	2.39	Mastectomy	20	Invasive ductal carcinoma grade 2	ER+, PR-, Her2Neu-	N1
5	No	2.34	Mastectomy	16	Invasive ductal carcinoma grade 3	ER-, PR-, Her2Neu-	N1
6	Yes	1.09	Mastectomy	20	DCIS grade 3	–	Nx
7	Yes	2.0	Mastectomy	20	DCIS grade 3	–	N0
8	Yes	2.68	Mastectomy	4	Invasive ductal carcinoma	ER+, PR+, Her2Neu-	N0
9	No	7.29	Mastectomy	25	Invasive ductal carcinoma grade 1 + DCIS	ER+, PR+, Her 2+	N0
10	No	6.39	BCS	11	Invasive ductal carcinoma grade 2	ER+, PR+, Her2Neu-	N0
11	No	5.91	BCS	6	DCIS grade 3	–	N0
12	No	9.08	Mastectomy	10	DCIS grade 2	–	Nx
13	No	6.20	Mastectomy	38	Invasive ductal carcinoma grade 3	ER+, PR-, Her2Neu+	N0
14	No	7.28	BCS	11	Invasive ductal carcinoma grade 1	ER+, PR+, Her2Neu-	N1
15	No	10.28	BCS	17	Invasive ductal carcinoma grade 1 + DCIS	ER+, PR+, Her2Neu-	N0
16	No	6.21	Mastectomy	9	Invasive ductal carcinoma grade 1	ER+, PR+, Her2Neu-	N0
17	Yes	9.10	M+, no surgical treatment				
18	Yes	5.14	Mastectomy	12	Invasive ductal carcinoma grade 1	ER+, PR-, Her2Neu-	N0
19	No	12.43	Mastectomy	11	Invasive ductal carcinoma grade 3 + DCIS	ER-, PR-, Her2Neu-	N0
20	No	12.11					
21	No	6.37	BCS	26	Invasive ductal carcinoma grade 2	ER+, PR+, Her2Neu-	N1
22	Yes	4.04	Mastectomy	39	Invasive ductal carcinoma grade 3	ER-, PR-, Her2Neu-	N1

DCIS = ductal carcinoma in situ; Nx = all cases were DCIS.

* In case of multiple tumors, the tumor with the biggest diameter is noted.

just six months or one year. So, patients with a population-based risk may be monitored via biennial mammography by the national screening programs. For patients with an increased familial breast cancer risk or for patients who were previously treated for breast cancer, the applicable annual mammographic follow-up seems to be sufficient to cover the risk for developing a breast malignancy.

The strengths of our study are the breast lesion location characteristics, the relatively large sample size, and the complete and long-term follow-up as compared to other publications. Because of the access to the national histopathologic archives, there was no loss to follow-up. However, a limitation was that our study may have been limited by its retrospective design. Also, due to the small

number of events, the study was underpowered for the reliable analysis of potential predictors for the development of breast cancer.

5. Conclusion

In patients with VASB-confirmed benign calcifications of the breast, we found no excess incidence of ipsilateral breast cancer during ten years follow-up. Therefore, in patients with an increased risk of breast cancer (due to a history of breast cancer or familial risk) annual mammography should be sufficient. Patients with a population-based risk may be monitored via biennial mammography by the national screening program. More frequent screening

Table 5
Literature overview of articles concerning benign calcifications of the breast.

Study	Number of patients	Study design	Lesions	Modality (X-ray guided, stereotactic, US)	Management of benign result after VASB	Development malignancy after biopsy without surgery	duration follow-up	lost-to-follow-up	Main conclusion
Cangiarella et al., 2000 [21].	142 (160 biopsies whereof 132 benign)	retrospective	Mammographic calcifications	Stereotactic VASB biopsy; 11G	Surgical excision or mammographic follow-up	0	6–36 months (mean 20,5 months)	40 (34%)	A diagnosis of atypia on Mammotome biopsy warranted excision of the atypical area, yet the underestimation rate for the presence of carcinoma remained low. The likelihood of an invasive component at excision was low for microcalcification diagnosed as DCIS on Mammotome biopsy. Mammotome biopsy proved to be an accurate technique for the sampling and diagnosis of mammary microcalcification.
M. Kikruchi et al., 2007 [22].	51	Retrospective study	calcifications on mammogram	stereotactic guided vacuum-assisted breast biopsy; 11G	n/a	n/a	n/a	n/a	Attention should be paid to prevent unnecessary MMT procedures. Heterogeneity in the density and size of calcifications is a reliable criterion for clinical decision-making.
V. Kumaroswamy et al., 2008 [23].	100 (benign + without excision = 17)	Retrospective;	microcalcifications	Stereotactic biopsy; 11G	Excision or follow-up	n/a	n/a	n/a	MMT biopsy is particularly useful for further assessment of an inadequate (B1) or suspicious (B4) CNB diagnosis. Diagnostic surgical excision remains the method of choice for managing atypical/uncertain lesions (B3).
B. Sigal-Zafrani et al., 2008 [15].	1009 (529 = benign)	Retrospective study	ACR IV-V microcalcifications	Stereotactic biopsy; 11G	Benign result = Surveillance (95%)	n/a for benign lesions	n/a for benign lesions	n/a for benign lesions	VLNB constitutes an alternative to surgical biopsy. This procedure avoids surgery for most benign lesions and reduces the number of surgical procedures in malignant lesions
N. Cho et al., 2009 [24].	75 (benign = 45)	prospectively evaluated	suspicious calcifications on screening mammography	US-guided VASB	n/a	n/a	n/a	n/a	US-guided 11-G vacuum-assisted biopsy retrieved calcifications from 71% (53/75) of lesions. Successful calcification retrieval was found to be related to the visibility of associated masses or dilated ducts by US, and to lesion depth,

(continued on next page)

Table 5 (continued)

Study	Number of patients	Study design	Lesions	Modality (X-ray guided, stereotactic, US)	Management of benign result after VASB	Development malignancy after biopsy without surgery	duration follow-up	lost-to-follow-up	Main conclusion
K. Suzuki et al., 2009 [25].	39 (lesions)	Retrospective study	segmental calcifications	MMT biopsy with screen-film mammography system	FU of lesion using mammography and ultrasonography	n/a	n/a	n/a	size, and distribution, and level of suspicion at mammography Lesions with heterogeneous calcifications are frequently malignant, and biopsy should be considered.
S. Bae et al., 2015 [26].	406	Retrospective review	BI-RADS 4,5 lesions - only microcalcification	US-CNB, US-VAB, S-VAB	Mammographic follow-up	0	1173.8 days (range, 385 –1924 days).	15 (4%)	Ultrasonography-guided vacuum-assisted biopsy is more accurate than US-CNB when suspicious microcalcifications are detected on US. Calcifications with malignant pathology are significantly more visible on US than benign lesions VASB should be the standard method of choice for BI-RADS 4 microcalcifications. This method obviates the need for a surgical procedure in 73% of BI-RADS 4 microcalcification-only patients.
M.M. Atasoy et al., 2015 [4].	63 patients (66 lesions whereof 51 benign)	Retrospective study	BI-RADS 4 microcalcifications-only lesions	Stereotactic vacuum-assisted core needle breast biopsy; 10G	follow-up - first FU at 6th month after biopsy	0	mean = 21.2 months (at least 10 months)	3 (6%)	VASB should be the standard method of choice for BI-RADS 4 microcalcifications. This method obviates the need for a surgical procedure in 73% of BI-RADS 4 microcalcification-only patients.
R. Yonekura et al., 2019 [27].	594 (371 = benign)	Retrospective study	breast calcifications	SVAB procedure; 11 G	annual follow with mammography, US and examination	4	71.5 months (range 5.6 –119.3 months)	63 patients (17%)	When SVAB results in non-malignant, patients may be followed by annual screening, while re-biopsy needs to be performed for the patients with a discordant result of SVAB and with changes in an imaging finding during a follow-up

VASB = Vacuum-Assisted Stereotactic Biopsy; G = Gauge; VB = vacuum biopsy; VLNB = Vacuum-assisted large-core needle biopsy; FU = follow-up; US = ultrasound; FEA = flat epithelial atypia; VABB = vacuum-assisted breast biopsy; ADH = Atypical ductal hyperplasia; MMT = mammatome; CNB = Core Needles Biopsy; SIFU = Short-Interval Follow-Up; RTAS = Return To Annual Screening.

would provide no benefit.

Declaration competing interest

None.

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