

# Vacuum-Assisted Core Biopsy in Diagnosis and Treatment of Intraductal Papillomas

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## Abstract

**Intraductal breast papilloma is an uncommon benign neoplasm that can be diagnosed and treated with vacuum-assisted core biopsy (VACB), a minimally invasive procedure. If the histopathologic examination shows the lesion to be benign, surgery may be avoided. Intraductal papilloma with atypia requires surgical excision because of a high risk of malignancy. VACB is an interesting alternative to open surgical biopsy.**

**Background:** The aim of this study was to assess the value of mammographically-guided and ultrasonographically-guided vacuum-assisted core biopsy (VACB) in the diagnosis and treatment of intraductal papillomas of breast and to answer the question of whether biopsy with the Mammotome (Mammotome; Cincinnati, OH) allows the avoidance of surgery in these patients. **Patients and Methods:** In the period 2000 to 2010, a total of 1896 vacuum-assisted core biopsies were performed, of which 1183 were ultrasonographically guided and 713 were mammographically guided (stereotaxic). **Results:** In 62 patients (3.2%) histopathologic examination confirmed intraductal papilloma, and in 12 patients (19.4%) atypical lesions were also found. Open surgical biopsy specimens revealed invasive cancer in 2 women these 12 women (false-negative rate, 16.7%; negative predictive value, 83.3%). Biopsy specimens from the remaining 50 patients (80.6%) revealed papilloma without atypia, and further clinical observation and imaging examinations did not show recurrence or malignant transformation of lesions. Hematoma developed in 3 (4.8%) patients as a complication of biopsy; surgical intervention was not required in any of the patients. **Conclusion:** VACB is a minimally invasive and efficient method for diagnosing intraductal papilloma of the breast. If histopathologic examination confirms a benign lesion and corresponds to the clinical presentation, surgery may be avoided. However in all cases, histopathologic diagnosis of papilloma with atypical hyperplasia or a suspected malignant lesion in imaging examinations, despite negative biopsy results, should always be an indication for surgical excision.

*Clinical Breast Cancer*, Vol. 13, No. 2, 129-32 © 2013 Elsevier Inc. All rights reserved.

**Keywords:** Atypical hyperplasia, Intraductal breast papilloma, Mammotome biopsy

## Introduction

An intraductal papilloma is a benign neoplasm that develops inside the breast's milk ducts. It occurs in 2% to 3% of the population, most typically in women between 30 and 55 years of age.<sup>1,2</sup> Intraductal papilloma is a proliferative lesion of epithelium covering a fibrovascular core.<sup>3</sup> Solitary papillomas occur mostly in the subareolar region and more frequently in premenopausal women. Multiple

lesions are usually located peripherally in the breast and are associated with a higher risk of cancer.<sup>3,4</sup> Clinical symptoms of papilloma include greenish, brown, or bloody discharge from the nipple, sometimes accompanied by a palpable breast mass. However they are often asymptomatic and discovered incidentally.<sup>3</sup> Diagnostic examinations include mammography, ultrasonography, galactography, cytologic examination of the nipple discharge, and fine- or core-needle biopsy.

Intraductal breast papillomas are rare, but because no diagnostic and therapeutic standard procedure has been established, they are often problematic for radiologists, surgeons, and pathologists.<sup>2</sup> Most authors believe that the presence of a papilloma in the patient with bloody discharge from the nipple, a palpable lump in the peripheral region of the breast, or a suspected lesion discovered in imaging examinations requires surgical excision of the lesion,<sup>5,6</sup> whereas surgical biopsy should be reserved for the patient with atypia or a malignant process recognized in the biopsy sample.

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Submitted: Jul 11, 2012; Revised: Sep 27, 2012; Accepted: Sep 28, 2012; Epub: Nov 3, 2012

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# VACB for Intraductal Papillomas

**Table 1 Morphologic Features of Intraductal Papillomas in Imaging Examinations**

Examination Type	Morphologic Features	No.	Percentage (%)
Ultrasonography	Solid lesion	37	84.0
	Complex cyst	5	11.4
	Distortion	2	4.6
Mammography	Mass	9	50.0
	Cluster of microcalcifications	7	38.9
	Distorted architecture	2	11.1

Most problematic is treatment of asymptomatic patients with a core-biopsy diagnosis of intraductal papilloma without atypia.<sup>1,7,8,9</sup> There is a growing number of reports showing the accuracy of vacuum-assisted core biopsy (VACB) in the diagnosis and treatment of intraductal breast papillomas,<sup>1,3,8,10</sup> particularly in patients without clinical and pathologic features indicating a high risk of a malignant process and with agreement between results of the histopathologic and imaging examinations.<sup>11,12</sup>

The aim of this study was to assess the value of mammographically-guided and ultrasonographically-guided VACB in the diagnosis and treatment of intraductal papillomas of the breast. Attempts were made to answer the question of whether biopsy with a Mammotome (Mammotome, Cincinnati, OH) allows surgery to be avoided in this group of patients.

## Patients and Methods

In the period 2000 to 2010, in the Regional Outpatient Clinic of Breast Diseases at the Clinic of General, Oncological, and Gastrointestinal Surgery of the University Hospital in Krakow, a total of 1896 vacuum-assisted core biopsies were performed, of which 1183 were ultrasonographically guided and 713 were mammographically guided (stereotaxic). In 62 patients (3.2%), histopathologic examination confirmed intraductal papilloma.

All patients underwent breast ultrasonographic examination, and women older than 40 years additionally underwent mammography. Patients with focal lesions evidenced in imaging examinations and classified as Breast Imaging Reporting and Data System BI-RADS) 4a, 4b, and 4c qualified for biopsy. The parameters analyzed included size of the lesion as shown in the mammogram or ultrasonogram, a peripheral (lesion situated in the outer third of the breast) or central location, or a lump detected in a physical examination. None of the patients had discharge from the nipple.

Of all 62 biopsies, 44 (71%) were ultrasonographically guided and 18 (39%) had digital mammographic guidance. Morphologically, papillomas were identified by ultrasonography as solid lesions (37%-84.0%), complex cysts (5%-11.4%), and distortions (2%-4.6%). Mammograms revealed mass (9%-50.0%), cluster of microcalcifications (7%-38.9%), and distorted architecture (2%-11.1%) (Table 1).

For the diagnostic examinations, 10-gauge needles (Encor Breast Biopsy System; Bard Biopsy Systems, Tempe, AZ) and 11-gauge needles (Mammotome) were used. All lesions were completely removed and the number of biopsy specimens ranged from 5 to 14 and 7 on average. The patients who did not provide informed consent or

**Table 2 Length of Follow-Up of Patients Without Atypia in VACB**

Length of Follow-Up	Number of Patients	Percentage of Patients (%)
< 2 y	8	16.0
2-5 y	17	34.0
> 5 y	25	50.0
<b>Total</b>	50	100.0

Abbreviation: VACB = vacuum-assisted core biopsy.

had allergy to local anesthetics or active skin infections on the breast were disqualified from biopsy.

Tissue specimens were preserved in 10% formaldehyde solution and sent for histopathologic evaluation to the Pathomorphology Lab of the Jagiellonian University Medical College.

Women who were diagnosed with papilloma without atypia in the histopathologic examination were followed with clinical, mammographic, and ultrasonographic examination 3 and 6 months after the procedure and then annually. The period of observation ranged from 14 months to 10 years and 5 years on average (Table 2). Whenever histopathologic examination of a specimen showed papilloma with atypical hyperplasia, the patients were qualified in the second stage for open surgical biopsy.

## Results

A study group consisted of women aged 18 to 76 years (mean age, 49.6 years) with breast lesions ranging from 4 to 18 mm and 8 mm on average. Clinical and morphologic characteristics of the analyzed parameters—including location in the breast, size of the lesion seen by ultrasonography/mammography, and the result of the histopathologic examination—are shown in Table 3.

In 12 (19.4%) patients, histopathologic examination revealed papillomas with atypia. All these patients qualified for open surgical biopsy. Final histopathologic examination did not detect atypical lesions in 7 patients, it confirmed intraductal atypical hyperplasia excised within a healthy tissue margin in 2 patients, a radial scar was confirmed in 1 patient, and invasive cancer (1 infiltrating ductal cancer, 1 infiltrating lobular cancer) was confirmed in 2 patients. Histologic underestimation occurred in 2 of 12 (16.7%) patients. Clinical and pathologic characteristics of lesions with a final diagnosis after open surgical biopsy are summarized in Table 4.

In 50 (80.6%) patients, histopathologic examination of VACB specimens revealed papilloma without atypia. In the follow-up imaging examinations in this group, there were no cases of papilloma recurrence or malignant transformation. All these patients underwent clinical and ultrasonographic examinations in the first 24 hours after VACB. Hematomas (9, 12, and 27 mm in diameter) developed in the biopsy site in 3 (4.8%) of them. None of the hematomas required surgical intervention.

## Discussion

Diagnostic procedures and therapeutic standards used in patients with intraductal papilloma of the breast have changed over time. At the beginning of the 20th century, mastectomy was performed as a

**Table 3** Clinical and Morphologic Characteristics of Breast Lesions

Features of Biopsied Lesions	Number of Patients	Percentage of Patients (%)
Right Breast	28	45.1
Left Breast	34	54.9
Superior Lateral Quadrant	21	33.9
Superior Medial Quadrant	18	29.0
Inferior Lateral Quadrant	14	22.6
Inferior Medial Quadrant	9	14.5
Size of Lesion < 10 mm	36	58.0
Longest Size on Ultrasonography/Mammography $\geq$ 10 mm	26	42.0
Impalpable Lesion	59	95.1
Palpable Lesion	3	4.9
Lesion Localized Centrally	45	72.5
Lesion in the Periphery	17	27.5
Discharge from the Nipple	0	0
No Discharge from the Nipple	62	100.0

rule in patients with suspected papilloma and bloody discharge from the nipple.<sup>10,13</sup> In 1922, Bloodgood recommended local papilloma excision or isolated resection of the affected duct, which has been standard ever since.<sup>13,14</sup> Surgery remains a golden rule in all cases with the diagnosis of papilloma with atypia or a coexisting malignant process. It is controversial, however, in women with benign papillomas.<sup>14</sup> Many authors believe that surgery can be avoided in cases of benign papilloma confirmed by a Mammotome biopsy.<sup>3,4,15</sup> It should be emphasized that the variety of benign and malignant papilloma-type growths in the breast may pose a diagnostic problem. A fine-needle aspiration biopsy is a minimally invasive technique, yet it is not very efficient in recognizing intraductal papillomas of the breast.<sup>13</sup> Conversely, open surgical biopsy is much more accurate as a diagnostic tool, but it is a more invasive procedure and involves excision of a fragment of the breast parenchyma. It may lead to breast deformation and leave a scar. The development of minimally invasive techniques, including VACB, made it an interesting alternative to open surgical biopsy in the diagnosis and treatment of focal lesions of the breast, as well as papillomas.<sup>5,16,17</sup> It is well tolerated by patients, is efficient, and is associated with a low number of complications. Its accuracy ranges between 98% and 100%<sup>18</sup> and is comparable to that of open surgical biopsy.

Histopathologic diagnosis of a papilloma with atypia is always an indication for open surgical biopsy because of the high risk of a malignant process. According to different authors, the risk ranges from 3% to 100% and on average 30%.<sup>9,13,17,19-21</sup> Chang et al analyzed a group of 60 patients with papilloma diagnosed by biopsy. Of this group, 49 patients had benign lesions and 11 patients were also diagnosed with atypia. All the patients underwent open surgical biopsy. In the first group there were no malignant lesions, whereas in the other group there were 2 cases of preinvasive ductal cancer (underestimation of 18.2%). Statistically, cancer occurred more fre-

quently in patients whose lesions were classified as BI-RADS 4b.<sup>5</sup> In our biopsy specimens from 12 patients with atypical papillomas, there were 2 cases of invasive cancer (underestimation of 16.7%) classified before biopsy as BI-RADS 4c. This observation confirms that open surgical biopsy is necessary when the histopathologic diagnosis is inconsistent with clinical manifestations.

In our study, all women diagnosed with benign papilloma from biopsy results were followed for several months. The mean observation time was 5 years. None of the patients experienced recurrent papilloma or malignant transformation of the lesion, which confirms that further verification of the biopsy site by open surgical biopsy was not necessary in this group.<sup>18,22</sup> In his study, Maxwell analyzed 26 cases of benign papillomas excised during core biopsies and found no recurrence of papilloma or malignant process in 23 patients under observation (mean observation time, 31 months).<sup>3</sup> The remaining 3 patients with recurrence in the biopsy site qualified for open surgical biopsy. Histopathologic examination confirmed the benign character of the lesions. Similar results were reported by Dennis et al, Renshaw et al, and Carder et al who demonstrated that surgery might be avoided in patients with papilloma without atypia excised during a VACB.<sup>10,19,21</sup> The risk of papilloma recurrence may be associated with incomplete excision of the lesion during biopsy. Bonaventure analyzed 13 cases of benign papilloma and reported 2 recurrences in the examinations performed 22 and 26 months after biopsy,<sup>4</sup> which is the indication for regular follow-up of patients undergoing core biopsy excision.

It is important to draw a sufficient amount of tissue during biopsy. In the present study, 10-gauge and 11-gauge needles were used, and according to most authors this diameter is sufficient to obtain an appropriate amount of tissue. Undoubtedly, the experience of the physician taking the specimen is also an important factor affecting the efficiency of the biopsy.<sup>4</sup>

The only complication found in the analyzed group of patients was hematoma in the biopsy site found in 3 (4.8%) patients. None of these patients required surgical intervention, which confirms that VACB is a safe and well-tolerated method.<sup>23</sup>

## Conclusion

VACB is a minimally invasive and efficient method used to diagnose intraductal papilloma of the breast. If microscopic examination reveals a benign lesion that corresponds to the clinical presentation, surgery may be avoided. In all cases of histopathologically confirmed papilloma with atypical hyperplasia or when clinical features are different from the obtained microscopic findings, surgical excision should always be performed.

## Clinical Practice Points

- Breast papilloma is an uncommon benign neoplasm that occurs in 2% to 3% of the population.
- In many cases, papillomas are diagnosed incidentally during screening mammography or ultrasonography. Clinical symptoms are rare and include brown or bloody discharge from the nipple and sometimes a palpable mass.
- Until now no diagnostic and therapeutic standard procedure for breast papillomas has been established. The conventional management is surgical excision.

**Table 4** Histopathologic Examinations of Open Surgical Biopsy Specimens Initially Diagnosed as Papilloma with Atypia

No.	Mammography	Ultrasonography	Dimensions (mm)	BI-RADS Classification	Core Biopsy Findings	Open Surgical Biopsy Findings
1	No Lesions	Lump	7 × 5	4a	Papilloma with atypia	Papillomatosis
2	No Lesions	Lump	10 × 8	4a	Papilloma with atypia	Papillomatosis
3	No Lesions	Lump	12 × 7	4a	Papilloma with atypia	Papillomatosis
4	No Lesions	Cyst	9 × 5	4a	Papilloma with atypia	Hyperplasia without atypia
5	Cluster of microcalcifications	No lesions	7 × 4	4a	Papilloma with atypia	Hyperplasia without atypia
6	Mass	No lesions	8 × 5	4a	Papilloma with atypia	Hyperplasia without atypia
7	Cluster of microcalcifications	No lesions	11 × 6 mm	4a	Papilloma with atypia	Hyperplasia without atypia
8	Distorted architecture	No lesions	8 × 4	4b	Papilloma with atypia	Radial scar
9	Distorted architecture	No lesions	10 × 7	4b	Papilloma with atypia	Atypical hyperplasia
10	Cluster of microcalcifications	No lesions	8 × 4	4a	Papilloma with atypia	Atypical hyperplasia
11	No lesions	Lump	9 × 6	4c	Papilloma with atypia	Infiltrating lobular cancer
12	Cluster of microcalcifications	No lesions	8 × 4	4c	Papilloma with atypia	Infiltrating ductal cancer

Abbreviation: BI-RADS = Breast Imaging Reporting and Data System.

- The development of ultrasonographically- or mammographically-guided VACB, (stereotaxic), makes minimally invasive diagnosis and treatment possible in these patients.
- Surgical excision can be avoided in cases of benign papilloma confirmed by a Mamotome biopsy; however all histopathologically confirmed papillomas with atypia are always an indication for an open surgical biopsy because of the high risk of a malignant process.
- Upgrade to malignancy is associated with the presence of atypical ductal hyperplasia in the specimen and lesions classified as BI-RADS category 4 or 5.
- Results obtained confirm that VACB is a highly efficient and safe method with a low complication rate. VACB should be a standard and the method of choice in diagnosing breast papillomas.

## Acknowledgments

We are in debt to the patients who participated in this study.

## Disclosures

The authors have stated that they have no conflicts of interest.

## Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.clbc.2012.09.018>.

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