Wireless Ultrasound-Guided Vacuum-Assisted Breast Biopsy: experience in clinical practice at European Institute of Oncology

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Key Words:	Breast, Diagnostic Technics and Procedures, Large-Core Needle Biopsy, Histology, Clinical Practice

Wireless Ultrasound-Guided Vacuum-Assisted Breast Biopsy: experience in clinical practice at European Institute of Oncology

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Running Title: Clinical use of Wi-UVAB at IEO

Keywords: Breast; Diagnostic Technics and Procedures; Large-Core Needle Biopsy; Histology; Clinical Practice

Abstract

Background: In the last few years, UltraSound-guided Vacuum Assisted Breast Biopsy (US-VABB) has replaced surgical biopsy due to higher diagnostic accuracy and lower patient discomfort, and, at present, an even greater possibility is represented by the new wireless ultrasound-guided VAB device (Wi-UVAB). The purpose of our study is to determine the diagnostic accuracy of this new device in a sizeable representative number of patients.

Methods: From January 2014 to June 2018, 168 biopsies were performed in our institution using the new Wi-UVAB device. We analyzed sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of biopsies obtained with the new device using surgical results as reference point, following patients for at least one year.

Results: In our cohort, we obtained a complete sensitivity of 97.5%, an absolute sensitivity of 94.3%, a complete specificity of 98% and an absolute specificity of 98%. The positive predictive value of the procedure was 97.5% while the negative predictive value was 98%. The diagnostic accuracy was 98%.

Conclusions: The Wi-UVAB is a safe procedure with high diagnostic accuracy, comparable to that of the traditional Vacuum assisted Breast Biopsy and even higher than that of core needle biopsy (CNB). Moreover, the Wi-UVAB is easy to use and shows low costs as core needle biopsy (CNB).

Introduction

The histological diagnosis of suspicious breast lesions is the first step in the correct management of the patient: in recent years, percutaneous breast biopsy has become an excellent alternative to surgical biopsy [1].

Among the percutaneous biopsies, several studies have shown that Vacuum Assisted Breast Biopsy (VABB), introduced in 1990s, provides lower underestimation rate and disagreement rate in comparison to the core-biopsy [1,2]. US-VABB is used particularly in cases of mismatch between imaging reports and histological diagnosis after core needle biopsy (CNB) and in very small breast lesions (<10 mm) [3,4].

Furthermore US-VABB can be used for the complete removal of benign lesions [5].

On the other hand, the US-VABB has some disadvantages, due to its large equipment, time requested and high cost [6].

Interestingly, a Wireless VAB guided ultrasound device (Wi-UVAB – Mammotome ELITE) has been introduced into current clinical practice [7]. Mammotome ELITE (Devicor Medical products) is easy to manage due to the lack of a connection line, rapid preparation of the equipment, small size of the device and reduced costs [8].

The technical characteristics of the ELITE are shown in Table 1 and in Figures 1 and 2.

Material and Methods

The institutional Review Board of our hospital approved this retrospective study and written informed consent was obtained from all participants.

At the European Institute of Oncology (IEO) between January 2014 to June 2018, 168 biopsies were performed using the Mammotome ELITE by expert radiologists and examined by pathologist, all with at least 10 years' experience in breast diseases.

105 out of 168 biopsies were performed with a 13G needle; the remaining 63 were performed with a 10G needle. BI-RADS range from 3 to 5.

The tissue samples obtained using the US-VABB procedure were examined at the Department of Pathology.

All samples were classified into five micro-histologic group (B1-B5) according to the European Guidelines [5]. Almost all the lesions classified as benign (B2) had been monitored for at least 12 months after VABB by ultrasound, but 12 B2 cases with histo-radiological discordance were submitted to surgical biopsy after multidisciplinary consultation; the same was for all lesions classified as B3. B5 lesions were directly submitted to surgical excision.

After institutional Review Board approval, we compared, retrospectively, the BI-RADS score [9] with biopsy and surgery histological results.

Then we considered sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of the histological results obtained with the Mammotome ELITE.

We chose surgical results and negative follow-up (of at least one year) as gold standard.

Statistical analysis

Continuous data are reported as median and ranges. Categorical data are reported as counts and percentages.

In the comparison between radiology BI-RADS and micro-histology BI-RADS (Mammotome ELITE), Mammotome was considered the gold standard.

In the comparison between micro-histology BI-RADS (Mammotome ELITE) and surgery BI-RADS, surgery evaluation was considered the gold standard.

Exact confidence intervals were calculated for sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

All analyses were performed with the statistical software SAS 9.4 (SAS Institute).

Results

The clinico-radiological characteristics are showed in Table 2.

Patients' average age was 55 years (range 33 - 75 years). The menopausal status is available in 48% of the patients. The most frequent parenchyma density class is ACR C [10]. The diameter of the biopsied lesion was between 5 and 15 mm (average 9.5, median 9). The number of biopsy cores obtained was between 3 and 10 (average 7.13; median 7). Only 7 patients (4%) had peri-procedural complication, represented by clinically significant hematoma.

The radiological and micro-histological correlation is shown in Tables 3, 3a and 3b.

Overall, 92 out of 168 patients underwent surgery while the remaining 76 were followed-up for 12 months and none of them developed breast cancer.

Radiological diagnoses were 1 BIRADS 2 (0,5%) 73 BIRADS 3 (43,4%) 12 BIRADS 4a (7,1 %), 21 BIRADS 4b (12,5 %), 54 BIRADS 4c (32,1%) and 7 BIRADS 5 (4,1%).

By considering histological results using VABB procedure, we observed that 83 patients were classified as B2, 5 patients as B3 and 80 patients as B5.

Among the 83 patients classified as B2, we registered the single case with BI-RADS 2, 71 out of 73 patients with BI-RADS 3, 9 out of 12 with BI-RADS 4a and 2 out of 54 patients with BI-RADS 4c.

Moreover, among the 83 patients classified as B2, 12 of them underwent surgery due to their personal medical history and confirmed negative (see Table 4). None of the remaining 71 out of 83 patients developed breast cancer during the follow up.

The correlation between the micro-histology results obtained by VABB and the BI-RADS classification of the lesions confirmed that the radiological method is accurate: with a complete sensitivity of 97.5%, absolute sensitivity of 84.1%, complete specificity of 95.6% and absolute specificity of 97.8%. The positive predictive value was 95.2% and the negative predictive value was 97.7%. The diagnostic accuracy was 96.7%.

The correlation between the micro-histology outcome and surgery is shown in Tables 4, 4a and 4b.

As we have already said, all patients (5) classified as B3 underwent surgery, among them we observed that 2 patients were upgraded to carcinoma in situ (B5a) on surgical excision while the remaining 3 patients were negative at surgery and subsequent follow-up.

All patients classified as B5 (80) underwent surgery and among them, we observed that 11 patients (13.7%) showed carcinoma in situ while the remaining 69 (86.3%) patients showed invasive carcinoma on surgical excision.

To resume, a totality of 6 cases were upgraded on surgical specimen, in detail: 2 cases were classified as B3 at micro-histology and upgraded to carcinoma in situ at surgery while 4 cases were classified as B5a (carcinoma in situ) at micro-histology and upgraded to invasive carcinoma at surgery.

Examples of tissue cores are shown in Figure 3.

Table 5 shows the correlation between the radiological BI-RADS and the surgical results, coding the last as BI-RADS.

We obtained a complete sensitivity of 97.5%, an absolute sensitivity of 94.3%, a complete specificity of 98% and an absolute specificity of 98%.

The positive predictive value of the procedure was 97.5% while the negative predictive value was 98%. The diagnostic accuracy was 98%.

Conclusion

Core biopsies of large lesions obtained by fine needle have some limits, leading to a potential doubtful histological diagnosis. Pathologists generally prefer larger samples by using VABB methodology in order to observe the lesion as much as possible. Indeed, literature data show an average underestimation rate when considering TRU-CUT of about 30%, while the average of false negative results is around 9% [11,12].

Compared to TRU-CUT methodology, VABB allows a single needle insertion, permitting multiple samples, reducing patient's discomfort, and increasing diagnostic accuracy [13]. However, VABB requires challenging devices and a higher procedure cost [14].

The Wi-UVAB compared to VABB is more manageable, less expensive and accuracy overlaps that of classical VABB. Wi-UVAB does not require additional time to prepare and set up the vacuum device, allowing biopsy to be promptly performed in a short time [15]. According to some authors, the Wi-UVAB would also be associated with minor complications compared to the traditional VABB [16].

By using ELITE, the purpose is to obtain more accurate diagnosis of suspicious breast lesions while decreasing insufficient or inconclusive diagnoses, particularly in small size lesion (<1cm), especially in comparison to TRU-CUT procedure [16].

In our experience, by using Wi-UVAB, 6 out of 168 (3.5%) cases where underestimated but these data are comparable to those reported in the literature on VABB [17]. Moreover, in 5 cases associated with diagnostic underestimation, the average size of the lesion was 10.5 mm, while the average number of cores was 6.9: data similar to the cases study. The main difference is related to the higher percentage of haemorrhagic frustules.

In conclusion the WI-UVAB is a safe procedure with high diagnostic accuracy, comparable to that of the traditional VABB and higher than that of the TRU-CUT. Additionally, the peculiar advantages of the Wi-UVAB are represented by easier handling, single insertion and large tissue samples easier to collect.

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Tables

Table 1. Technical characteristics of the ELITE

	MAMMOTOME ELITE
PROBE WEIGHT	250 G
NEEDLE POINT	Surgical disposable scalpel (B-BRAUN)
Vacuum Pump	Internal 21mmhg
Vacuum	Mainly axial (only 10%lateral)
Core transport	Internal vacuum; automatic transport and collection
PROBE COLLECTOR	Single collector
AVG core weight	60mmhg

Table 2. Patients' characteristics (N=168)

Variable	**Level**	**Overall (N=168)**
Age at ELITE biopsy, median (min-max)		55 (33-75)
Needle diameter, N (%)	10 G	63 (37.5)
	13 G	105 (62.5)
Lesion diameter (mm), median (min-max)		9 (4-21)
Number of diagnostic cores, median (min-max)		7 (3-10)
Complete removal, N (%)	No	105 (62.5)
	Yes	63 (37.5)
Radiology BI-RADS, N (%)	2	1 (0.6)
	3	73 (43.5)
	4a	12 (7.1)
	4b	21 (12.5)
	4c	54 (32.1)
	5	7 (4.2)
Micro-histology BI-RADS (Mammotome ELITE), N (%)	B2	83 (49.4)
	B3 (ADH)	1 (0.6)
	B3 (ALH)	3 (1.8)
	B3 (RS)	1 (0.6)
	B5a	11 (6.5)

	B5b	69 (41.1)
Surgery BI-RADS, N (%)	*	76 (45.2)
	B2	12 (7.1)
	B5a	9 (5.4)
	B5b	71 (42.3)

*These patients did not undergo surgery. They were followed up for 12 months and none of them developed breast cancer. In the analyses they were considered as B2 surgery BI-RADS

ADH: Atypical Duct Hyperplasia; ALH: Atypical Lobular Hyperplasia; RS: Radial Scar

Table 3. Radiology BI-RADS and Micro-histology BI-RADS (Mammotome ELITE)

Radiology BI-RADS	**Micro-histology BI-RADS**						
	B2	**B3 (ADH e PL)**	**B3 (ALH)**	**B3 (RS)**	**B5a**	**B5b**	**Total**
2	1	0	0	0	0	0	1
3	71	0	1	1	0	0	73
4a	9	0	1	0	2	0	12
4b	0	1	1	0	6	13	21
4c	2	0	0	0	3	49	54
5	0	0	0	0	0	7	7
Total	83	1	3	1	11	69	168

CLASSIFICATION 1:
Radiology BI-RADS “Positive” if equal to 4c or 5
Micro-histology B “Positive” if equal to B5b

Table 3a. Radiology BI-RADS and Micro-histology BI-RADS (Mammotome ELITE)

Radiology BI-RADS	**Micro-histology BI-RADS**		
	Negative	**Positive**	**Total**
Negative	94	13	107
Positive	5	56	61
Total	99	69	168

	Estimate	95% exact CI
Sensitivity	0.81	0.70-0.90
Specificity	0.95	0.89-0.98
Positive Predictive Value	0.92	0.82-0.97
Negative Predictive Value	0.88	0.80-0.93
Accuracy	0.89	0.84-0.94

CLASSIFICATION 2:
Radiology BI-RADS "Positive" if equal to 4b, 4c or 5
Micro-histology B "Positive" if equal to B5a or B5b

Table 3b. Radiology BI-RADS and Micro-histology BI-RADS (Mammotome ELITE)

Radiology BI-RADS	Micro-histology BI-RADS		
	Negative	**Positive**	**Total**
Negative	84	2	86
Positive	4	78	82
Total	88	80	168

	Estimate	95% exact CI
Sensitivity	0.98	0.91-1.00
Specificity	0.95	0.89-0.99
Positive Predictive Value	0.95	0.88-0.99
Negative Predictive Value	0.98	0.92-1.00
Accuracy	0.96	0.92-0.99

Table 4. Micro histology B (Mammotome ELITE) and Surgery B

Micro histology B	Surgery B			
	B2	**B5a**	**B5b**	**Total**
B2	83	0	0	83
B3 (ADH e PL)	0	1	0	1
B3 (ALH)	2	1	0	3

B3 (RS)	1	0	0	1
B5a	1	6	4	11
B5b	1	1	67	69
Total	88	9	71	168

CLASSIFICATION 1:
Micro histology B "Positive" if equal to B5b
Surgery B "Positive" if equal to B5b

Table 4a. Micro histology B (Mammotome ELITE) and Surgery B

Micro histology B	**Surgery B**		
	Negative	**Positive**	**Total**
Negative	95	4	99
Positive	2	67	69
Total	97	71	168

	Estimate	**95% exact CI**
Sensitivity	0.94	0.86-0.98
Specificity	0.98	0.93-1.00
Positive Predictive Value	0.97	0.90-1.00
Negative Predictive Value	0.96	0.90-0.99
Accuracy	0.96	0.92-0.99

CLASSIFICATION 2:
Micro histology B "Positive" if equal to B5a or B5b
Surgery B "Positive" if equal to B5a or B5b

Table 4b. Micro histology B (Mammotome ELITE) and Surgery B

Micro histology BI RADS	**Surgery BI RADS**		
	Negative	**Positive**	**Total**
Negative	86	2	88
Positive	2	78	80

Total	88	80	168

	Estimate	95% exact CI
Sensitivity	0.98	0.91-1.00
Specificity	0.98	0.92-1.00
Positive Predictive Value	0.98	0.91-1.00
Negative Predictive Value	0.98	0.92-1.00
Accuracy	0.98	0.94-0.99

Table 5. Radiology BI-RADS and surgery BI-RADS

Radiology BI-RADS	**Surgery BI-RADS**			
	B2	**B5a**	**B5b**	**Total**
2	1	0	0	1
3	73	0	0	73
4a	10	2	0	12
4b	1	4	16	21
4c	3	3	48	54
5	0	0	7	7
Total	88	9	71	168

Figure legends and Tables

Figure legends

Figure 1a: Mammotome ELITE at the beginning of a procedure

Figure 1b: Ultrasound image of Mammotome ELITE during an ultrasound guided biopsy

Figure 2: 900 rpm means the power of the inside trocar. The 18,4mm is the aperture. The 10mm is the dead space. The 136mm is the length of the probe.

Figure 3: Fresh breast tissue cylinders measuring about 15 mm.

Tables

Table 1: Technical characteristics of the ELITE

Table 2: Patients' characteristics (N=168)

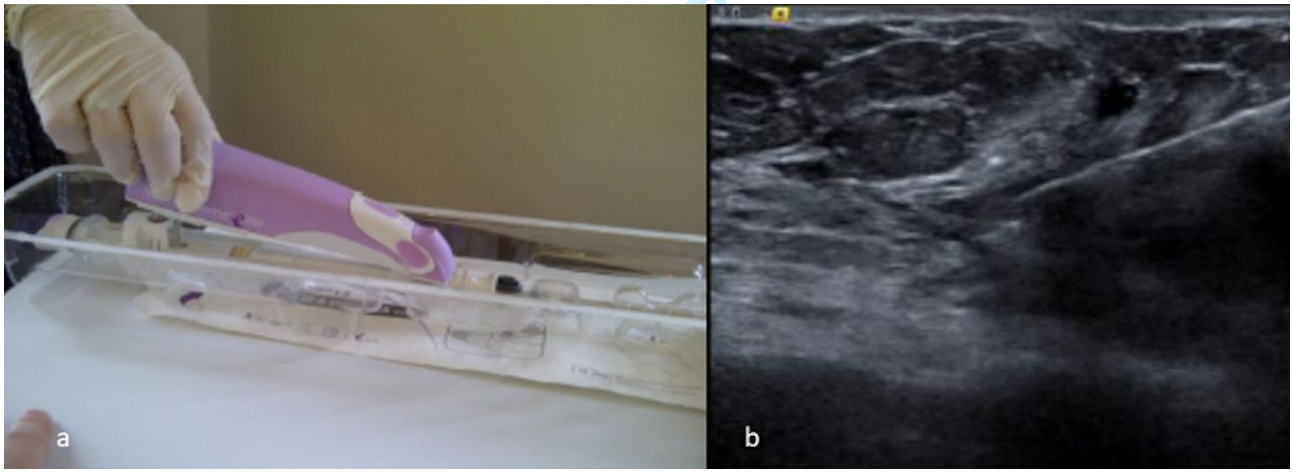
Table 3: Radiology BI-RADS and Micro-histology BI-RADS (Mammotome ELITE)

Table 4: Micro-histology B (Mammotome ELITE) and Surgery B

Table 5: Radiology BI-RADS and surgery BI-RADS

Figures

Figure 1: Example of ELITE Device



Figures 2: Technical dimensions of 13 Gauge Mammotome ELITE Probe

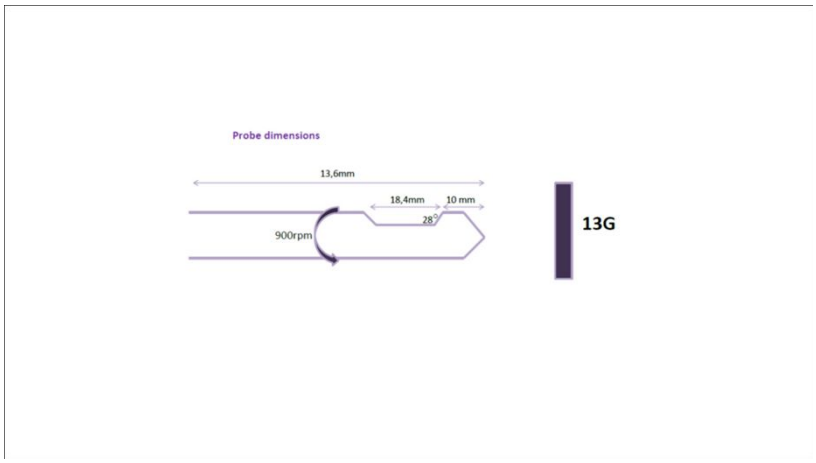


Figure 3: Core specimens obtained after breast biopsy performed with ELITE.