False negative cases at stereotactic biopsy: our experience

Poster No.: C-2619
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Breast, Mammography, Biopsy, Vacuum assisted biopsy, Cancer, Neoplasia, Pathology
DOI: 10.1594/ecr2015/C-2619

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Learning objectives

To review false-negative cases of breast lesions evaluated with percutaneous stereotactic biopsy using vacuum assisted breast biopsy (VABB) system. To describe the mammographic findings and the false negative cases in our experience.
Background

Diagnostic performance of stereotactic VAB in literature:

Biopsy of breast lesions can be performed using a variety of image-guided techniques. No biopsy method is 100% accurate. Stereotactic VABB is a sampling of non-palpable or indistinct breast lesions using mammographic guidance and a vacuum-assisted device. VABB was first introduced in the mid 90's. It was developed in order to overcome the shortcomings of the fine needle aspiration (FNA) and the core needle biopsy.

The VABB allows the removal of large and multiple tissue samples in a single insertion, in order to acquire more tissue samples and therefore decreasing sampling errors. According to a meta-analysis of 21 VABB-studies, this method has a sensitivity of 98% and a specificity of almost 100%.

According to the literature and our experience, the stereotactic VABB is performed when suspicious mammographic lesions are classified as BI-RADS 4 (suspicious) and BI-RADS 5 (highly suspicious) using the ACR BI-RADS system, and are not clearly visible on the ultrasound (e.g. microcalcifications, asymmetric densities, architectural distortions and some masses). Mendez et al. recommended to perform a biopsy in lesions classified as BI-RADS 3 with microcalcifications due to difficult compliance with short-interval follow-up recommendations. However, a general consensus relating to BI-RADS 3 lesions has not yet been achieved. In our experience, the mammographic lesions subjected to stereotactic VABB are more frequently clusters of microcalcifications, rather than microcalcifications associated to asymmetric density or to architectural distortion and masses with indistinct or microspiculated margins (classified as BI-RADS 3, BI-RADS 4 and BI-RADS 5).

Jackman at al. considered the biopsy result as discordant when the radiologist performing the biopsy, after the consultation with a pathologist, assumed that the histologic findings didn't seem to explain the mammographic appearance of the lesions. The biopsy results were considered discordant also when calcifications were not detected on the radiograph of the samples but they were found at the histologic examination. In cases of the imaging-histology discordancy, a surgical biopsy or the repetition of the stereotactic VABB was recommended.

We retained a biopsy result as discordant when the histology findings didn't seem to match the high level of suspicion of the radiologist performing the biopsy. In these cases we recommend a surgical diagnostic biopsy as an alternative to the adequate follow up (at least for 24 months). The repetition of the stereotactic VABB or the surgical excision...
of the discordant benign lesions with a low level of suspicion was considered when either the patient had a strong family history or was extremely anxious, or there was a concern about the adequate follow up. Before the surgical excision, further investigations (e.g. contrast enhanced MRI) could be considered.

The false-negative rate is the proportion of malignant tumors diagnosed as completely benign (exclusive of high-risk lesions) at the initial biopsy and proved malignant on the histology of the surgical specimen. According to the literature, Jackman et al. reported that in a series of 1280 stereotactic VABB, the false-negative rate was of 1% (five of 508 malignant lesions). The false-negative biopsy findings were related to the gauge of the biopsy probe and to the radiographic findings of the specimen (mostly when microcalcifications were not detected). These rates were not related to the biopsy experience of the radiologist, to the number of specimens obtained per lesion, nor to the lesion type (mass or microcalcifications). The false negative lesions were less common with 11-G probes (0.45% vs. 4.4%; p=0.019) than with a 14-G probes (4.4%, three of 68 lesions). However, there are few studies about differences between 11-G and 14-G VAB false-negative rates and they give conflicting results. Lourenco et al. reported that in a series of 1223 stereotactic VABB there was no statistically significant difference in the histologic underestimation between the 11-G biopsy and the 9-G biopsy.

Many other clinical studies related to stereotactic vacuum-assisted needle biopsy report various methods to reduce the false-negative rate, e.g. the use of 11-gauge needles, a radiologist with more than 15 biopsies experience, a high number of tissue samples, and the presence of microcalcifications on the radiograph of the samples.

### METHODS TO REDUCE THE FALSE-NEGATIVE RATE

<table>
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<th>Method</th>
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<td>use of 11-gauge needles</td>
<td>radiologist with more than 15 biopsies experience</td>
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<tr>
<td>high number of tissue samples</td>
<td>microcalcifications on the radiograph of the samples</td>
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Moreover many studies are concordant about the increasing of the false-negative rate with the increasing mammographic size of the biopsy target.

**Stereotactic VABB: How is it performed?**

The stereotactic devices may have different imaging modalities (analog vs digital), as well as the different modalities of the calculation of the coordinates (manual or digital).
In our department we use a full-field digital mammography (FFDM) with digital modality calculation of coordinates.

**Preliminary phase:** 2 complementary mammograms (cranio-caudal and medio-lateral) are acquired in order to assess precise lesion localization and appropriate biopsy approach. The position of the patient can be prone, sitting, semi-reclining lateral or upright. In our department the VABB is performed in patients in prone position on dedicated prone table unit. The breast is then compressed using a dedicated fenestrated compression plate (fenestration of 5x5 cm), the lesion is identified and placed in its center (Figure 1). Once the lesion is highlighted in the first mammogram at 0 degrees and in two additional projections at +15 and -15 degrees, the center of the lesion is marked and the spatial coordinates are calculated.

**Biopsy:** in our department we use 11-G, 12-G and rarely 10-G needles. The procedure begins with a biopsy needle positioned on the driver, with the tip of the needle touching the skin (Figure 2). Then local anesthesia is performed (Figure 3). After a control image is acquired, a small skin incision (3-4 mm) is made by a lancet to facilitate the introduction of the needle. The pre-fire image is acquired to verify the correct targeting (Figure 4). Then the needle is introduced into the lesion and the post-fire image is acquired to assure that the window of the needle is placed near the lesion (Figure 4). Eventually the sampling is performed using the automated vacuum assisted device. All withdrawn samples are placed on a radio-transparent plate in clockwise direction and labeled to be x-rayed in order to verify the presence of microcalcifications (Figure 5). At the end a radiographic marker is deposited to the biopsy site to identify the area. This marker is visible under x-ray, ultrasound and MRI, and can be useful in the follow-up or the subsequent breast surgery.

**After the procedure:** the needle is pulled out of the breast, the patient is released, the wound is covered with a sterile-strip and the breast is compressed. Two complementary mammograms (CC and MLO) are acquired to verify the clip position (Figure 6). Ice is placed on the breast.
Fig. 1: The breast is compressed using a dedicated compression plate.

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Fig. 2: The tip of the needle is touching the skin.

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Fig. 3: Local anesthesia performance.

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**Fig. 4:** The pre-fire and the post-fire radiographs.

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Fig. 5: The radiograph of the samples.

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**Fig. 6:** 2 complementary views (CC and MLO) of the right breast show the clip positioned at the end of the biopsy (red circles).

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Findings and procedure details

The stereotactic biopsies of 233 women performed at our department from January 2011 to December 2013, were reviewed. We also reviewed the histopathological reports, the records, the clinical and radiological follow-up data. Ten women were excluded due to no clinical or radiological follow-up data availability. After further data analysis another 39 women were excluded. The initial needle biopsy yielded histology consistent of malignant lesion in 67 cases, high-risk lesion in 2 cases and benign/normal breast tissue in 2 cases out of 71 lesions diagnosed as malignant at the final histological examination of the surgical specimen.

The mammographic features of the lesions that were subjected to stereotactic VABB were:

a) Microcalcifications

 o Mostly clustered:
   - Fine heterogeneous microcalcifications (Figure 7).
   - Fine linear microcalcifications (Figure 8).
   - Amorphous microcalcifications (Figure 9).

 o Less commonly:
   - Amorphous microcalcifications with segmental (Figure 10) and linear distribution (Figure 11).
   - Microcalcifications associated to asymmetric density (Figure 12).
   - Microcalcifications associated to architectural distortion (Figure 13).

b) Masses with indistinct or microspiculated margins (Figure 14).

The histological outcome of 184 performed stereotactic biopsies was: 67 malignant lesions, 9 high-risk lesions, 101 benign lesions and 7 normal breast tissue.

The patients with apparently concordant imaging-histology benign lesions underwent a 12-month post-biopsy mammographic follow up. A surgical excision was recommended in patients with malignant and high-risk lesions diagnosed on the stereotactic biopsy. Twelve lesions underwent surgical diagnostic biopsy due to a highly discordant level of
imaging suspicion to the initial histological outcome of the VABB. Two of these lesions turned out to be malignant at the final histological examination of the surgical specimen and therefore considered as false-negative lesions at the stereotactic biopsy (Figure 15, 16A, 16B and 17). The False negative diagnoses were made using two different needle sizes (11-G and 12-G). Twelve and twenty-four samples were acquired and in both cases, there were microcalcifications detected on the radiograph of the specimens but only in a few tissue samples. In one of the following case examples the lesion size was 40 mm, and this could increase the probability of missing the malignant growth. As described in the literature, false negative cases can occur even when the lesions have increased dimensions and when microcalcifications are present on the radiograph of the samples.

In one of the twelve discordant benign lesions subjected to the surgical diagnostic biopsy, the final histological outcome was a pre-cancerous condition Lobular Carcinoma in Situ (LCIS).

Now we describe two false negative cases.

CASE 1 (Figure 15, 16A and 16B):

50 year old woman was recalled from the regional screening program due to the presence of fine heterogeneous microcalcifications associated to an asymmetric density in the internal quadrants of the right breast. The microcalcifications were classified as suspicious (BI-RADS 4). A sampling was performed using a 12-G needle obtaining 24 tissue samples. The radiograph of the samples confirmed presence of microcalcifications in 3 samples out of 24. The histological result of the stereotactic biopsy specimen was normal breast tissue that later turned out to be Invasive Ductal Carcinoma (IDC) at the histological examination of the surgical specimen.

CASE 2 (Figure 17):

52 year old woman was recalled from the regional screening program due to the presence of fine heterogeneous microcalcifications, with the extension of approximately 4 cm, in the external quadrants of the left breast. The microcalcifications were classified as suspicious (BI-RADS 4). A sampling was performed using a 11-G needle obtaining 12 tissue samples. The radiograph of the samples confirmed presence of microcalcifications in 4 samples out of 12. The histological result of the stereotactic biopsy specimen was fibrocystic mastopathy that later turned out to be Ductal Carcinoma in Situ (DCIS) at the histological examination of the surgical specimen.
**Fig. 7:** The left CC view shows the cluster of fine heterogeneous microcalcifications (red arrow).

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Fig. 8: The left MLO view shows the cluster of fine linear microcalcifications (red arrow).

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**Fig. 9:** The left MLO view shows the cluster of amorphous microcalcifications (red arrow).

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Fig. 10: The right CC view shows amorphous microcalcifications with segmental distribution (red arrow).

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Fig. 11: The right MLO view shows amorphous microcalcifications with linear distribution (red arrow).

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Fig. 12: The left MLO view shows microcalcifications associated to an asymmetric density (red arrow).

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**Fig. 13:** The left CC view shows microcalcifications associated to an architectural distortion.

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**Fig. 14:** The right CC view shows the mass with indistinct margins (red circle).

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Fig. 15: The MLO view of the right breast shows the cluster of fine heterogeneous microcalcifications associated to an asymmetric density which were classified as suspicious (BI-RADS 4). The histological result of the stereotactic biopsy specimen was normal breast tissue that later turned out to be Invasive Ductal Carcinoma (IDC) at the histological examination of the surgical specimen.

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Fig. 16: Image 16A: the CC view of the right breast (performed immediately after the stereotactic VABB) shows the clip that has been positioned after the biopsy. Image 16B: the CC view of the right breast shows the guide wire that has been positioned on the site of microcalcifications associated to an asymmetric density, before the surgical diagnostic biopsy.

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**Fig. 17:** The CC view of left the breast shows fine heterogeneous microcalcifications (red circle), with the extension of approximately 4 cm, in the external quadrants of the left breast which were classified as suspicious (BI-RADS 4). The histological result of the stereotactic biopsy specimen was fibrocystic mastopathy that later turned out to be Ductal Carcinoma in Situ (DCIS) at the histological examination of the surgical specimen.

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Conclusion

In our experience, the diagnostic surgical biopsy should be performed as an alternative to a follow-up (at least for 24 months) when: there is a high level of suspicion on the mammography, the stereotactic biopsy turns out to be negative or benign and the histological outcome is considered discordant by a radiologist. The lesion size, the presence of microcalcifications, the radiograph of the samples, and the size of the needle probe could be important causes of the false negative findings on the stereotactic VABB.
Personal information

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References


