Underestimation of breast carcinoma in B3 lesions diagnosed through core needle biopsy (cnb) or vacuum assisted biopsy (vad) and potential role of MRI.

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Purpose

The use of Core Needle Biopsy (CNB) and Vacuum-assisted Biopsy (VAB) for the histological characterization of mammary lesions as an alternative to the surgical biopsy is limited by the frequent borderline microhistological findings (B3 lesions = lesions of uncertain malignant potential) obtained through these percutaneous biopsy techniques.

The B3 category includes extremely heterogeneous lesions in terms of both pathological and prognostic features.

The greatest challenge in the clinical management of these lesions is represented by the meaningful histological underestimation of malignancy obtained through the percutaneous biopsy techniques (about 25% of these lesions resulted to be malignant at the definitive histological examination).

Until now none of the examined clinical, radiological and histological features of B3 category seemed to be able to define a subgroup of borderline lesions characterized by an underestimation of malignancy <2%.

According to the American College of Radiology guidelines this latter category of lesions could be managed through clinical-radiological follow up instead of surgical excision. Nowadays the largest part of patients with B3 lesions undergo surgical intervention, therefore defining the above-mentioned subgroup could have a significant impact on Health Service costs and patients’ psychological wellness.

Aims of our study were to evaluate the confidence of Core Needle Biopsy (CNB) and Vacuum-assisted Biopsy (VAB) techniques in the diagnosis and management of lesions of uncertain malignant potential (B3) and to analyze the potential role of MRI in the identification of malignant lesions.
Methods and Materials

A retrospective analysis was performed on 655 patients who presented different types of abnormalities with various grade of malignancy suspicion at the imaging investigations (mammography or ultrasound) undergoing CNB with 14G needle (496 patients) and VAB with 11G needle (159 patients) in a period of 18 months.

Only those patients affected by B3 lesions were considered (41/655 patients, 6.3%, 33 diagnosed through VAB and 8 through CNB). The histological examination of these 41 B3 lesions showed: 22 cases of atypical ductal hyperplasia (ADH), 13 cases of lobular intraepithelial neoplasia (LIN), 4 radial scars, 1 case of papillary lesion and 1 phylloides tumour.

In the subgroup of patients who underwent surgical intervention, with available histological exam on surgical specimen (30/41 patients, 73.2%), results were compared to the microhistological diagnosis obtained through the percutaneous biopsy (24 VAB e 6 CNB; ADH = 15 lesions, LIN = 10 lesions, Radial Scar = 3 lesions, papillary lesion = 1 lesion and phylloides tumour = 1 lesion).

Ten patients were also submitted to presurgical MRI (Signa Tomographer GE Healthcare 1.5 T) and the findings compared to the final histological results.

Considering the subgroup of patients who were not immediately submitted to surgically intervention (10/41), 7 were subjected to a clinical-radiological follow up, 1 is actually waiting for the surgical intervention and 2 have not referred to our Service anymore.
Results

The histological examination on surgical specimen showed that 13/30 lesions were tumors (false negatives), including 9 intraductal in situ carcinomas (5 ADH, 2 LIN and 2 Radial Scars; 8 of these lesions were diagnosed through VAB and 1 of them through CNB) and 4 infiltrating ductal carcinomas (3 ADH and 1 LIN; 3 identified through CNB and 1 through VAB). The other 17/30 cases were benign lesions (true negatives), with a concordance between biotical and histological specimens of 57% (34% for CNB and 62.5% for VAB) (Fig. 3 on page 7). According to these results, the overall PPV and PNV values of the two biopsy techniques were 43.3% and 56.7% respectively, with a total malignancy underestimation of 43%, 66.6% for NBC and 37.5% for VAB.

In the group of 10 patients who were studied through MRI (5 ADH, 3 LIN, 2 Radial Scars) the definitive histological examination showed 1 infiltrating ductal carcinoma (ADH) and 3 intraductal in situ carcinomas (1 ADH and 2 Radial Scars). In two of these cases (1 infiltrating ductal carcinoma and 1 intraductal in situ carcinoma), MRI did not identify any pathological abnormalities (lack of enhancement or poor enhancement with derived T/I curves type 1). In the rest of them (2 intraductal in situ carcinomas) MRI showed suspicious enhancement features of the lesions (derived T/I curves type 3), in agreement with the definitive histological diagnosis (Fig. 4 on page 8). No pathological MRI findings (lack of enhancement) were found in the six patients with a definitive benign histological examination. MRI showed a SB of 50%, a SP of 100% and a PNV of 80%, with an overall underestimation of malignancy of 20%.

According to our results, VAB shows lower values of malignancy underestimation than CNB, due to the larger volumes of tissue for histopathological evaluation provided by the first technique, which allow a better sampling of the lesions. In our study more than a third of the lesions, primarily classified as borderline, appeared to be malignant at the definitive histological examination. However we noticed important variations between the PPV values obtained for every single subgroup of lesions. In agreement with other studies ADH (15/30, 50% of B3) and LIN (10/30, 33% of B3) were the most frequent lesions at the histological analysis.

These two categories together (83.3%) form the group with the highest lesion-specific risk of malignancy (histological underestimation of malignancy of 44%; VPP of ADH=53.3% and VPP of LIN=30%) and reasonably require a surgical approach.

The high percentage of underestimation obtained for the Radial Scar category (2/3=66.6) has to be analyzed apart. The limited number of patients of our study should explain the discrepancy between our percentage and the values reported in Medical Literature (underestimation taxes included between 8 and 20%). Furthermore it is correct to remind that in both these cases, which resulted to be intraductal in situ carcinomas, the surgical specimen demonstrated the association with epithelial atypia (ADH-LIN), which is known to imply and increased risk of associated neoplasia.
Fig. 1: Histological underestimation at 11-g VAB. (A) Craniocaudal (magnification view) of right breast shows cluster of heterogeneous calcifications with no associated mass, with a maximum extension of 10 mm (BI-RADS R3). (B,C,D) 11-g VAB (magnification view of specimens with calcifications and of breast excision specimen with microcalcifications and microclip) revealed breast tissue with atypical ductal hyperplasia (ADH). (E,F) Dynamic Contrast-enhanced MRI showed a focal area of enhancement, measuring 9 mm, with an early washout pattern (T-SI curve type 3). Final histological examination resulted in a diagnosis of ductal carcinoma in situ (DCIS).

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Fig. 2: Example of False-Negative diagnosis at percutaneous biopsy (VAB) and at MRI. (A) Craniocaudal (magnification view) of right breast demonstrates a cluster of pleomorphic microcalcifications with no associated mass, with extension of 6 mm (BI-RADS R4). (B) 11-g VAB (magnification view of specimens with calcifications) revealed lobular neoplasias (ALH and LCIS). (C,D) Dynamic contrast-enhanced MR image showed diffuse and symmetrical non-masslike enhancement, with benign features. Surgical excision yielded invasive ductal carcinoma.

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**Fig. 3:** Example of True-Negative diagnosis at percutaneous biopsy (VAB). (A) Craniocaudal (magnification view) of left breast shows cluster of heterogeneous calcifications with no associated mass, with a maximum extension of 8 mm (BI-RADS R3). Stereotactic 11-g VAB revealed breast tissue with lobular intraepithelial neoplasia (LIN 1-2). (B, C) Dynamic Contrast-enhanced MRI showed no enhancement at all. Final histological examination confirmed the benign nature of the lesion.

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Fig. 4: Example of a False-Negative diagnosis at percutaneous biopsy (CNB). (A) Standard craniocaudal mammogram of left breast demonstrate a focal area of architectural distortion with spiculation. An ultrasound guided biopsy resulted in a diagnosis of radial scar without malignancy. (B, C,D) Dynamic Contrast-enhanced MRI showed, in left breast, a focal area of enhancement with irregular margins (B). Kinetic analysis demonstrated rapid enhancement in the early dynamic phase and washout pattern (T-SI curve type 3), with suspicious features (C,D). At surgical excision the lesion was upgraded to radial scar associated with DCIS G2-G3.
Conclusion

The B3 category management (surgery vs follow up) should be planned within a multidisciplinary team. This process can not be separated from the analysis of a series of variables as the histological subgroup, the radiological features, the type of sampling procedure, the quality and quantity of the sample, the pathologist’s experience, the patient's age and anamnestic data. Thus, in order to guarantee the patient's best choice in terms of efficacy and to minimize as much as possible surgery for benign disease.

MRI could play an important role in a new approach to B3 lesions; even with the limitations connected to the low number of patients, our study shows high values of PNV (80%) and SP (100%) which suggest a potential role of this radiological method in excluding the presence of malignancy. This may allow only a clinical-radiological follow-up to patients with not suspicious MRI features (lack of enhancement of the lesions or benign findings).
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