

Safety and Efficacy of Tomosynthesis-guided Breast Biopsies in the Prone Position: Mono-centric Study and Review of the Literature.

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Abstract

Purpose: The purpose of this study is to describe the safety and efficacy of 9G needle biopsy under tomosynthesis guidance with the patient in the prone position.

Materials and methods: This is a retrospective observational study conducted on patients with non-palpable breast mass exclusively detectable through tomosynthesis, performed from the 1st January 2018 to the 1st August 2020. The procedures were performed by taking 12 tissue samples from each mass. The evaluated technical success was considered as a conclusive sample for histological diagnosis. We performed a comparison between the procedural data of interventions in patients who have a lesion $\leq 10\text{mm}$ and $> 10\text{mm}$ and between high contrast and low contrast masses. The histological data of the samples were analyzed.

Results: 500 biopsies of the total 1500 performed from the 1st January 2018 to the 1st August 2020 were included in the study; repetitions for inadequate withdrawal occurred 0.4% (3/500). No major complications have ever been observed. Two cases (0.2%) of minor bleeding were observed with self-limited bleeding from the skin breach at 90 minutes without clinical sequelae in an asymptomatic patient. The biopsy samples showed carcinoma in 55.2% (276/500).

Conclusion: Our study suggests that the 9G needle sampling biopsy procedure through tomosynthesis guide with prone patient is a safe and effective procedure for the characterization of indeterminate breast mass.

Introduction

Mammography screening reduces breast cancer mortality to 30% through early detection of breast cancer¹⁻². Prognosis also improves with early diagnosis¹⁻²⁻³. Digital mammography is used in breast cancer prevention screenings, however, due to overlapping of breast tissues, especially in patients with dense glandular parenchyma which can delay a cancer diagnosis. The most frequent mammographic feature of the neoplasm is spiculated tissue, with nearly 90% of such lesions⁴. Five percent of invasive tumors present as areas of glandular distortion with no obvious mass⁴⁻⁵. Digital tomosynthesis of the breast is currently increasingly widespread in the area as it allows to reduce the overlap of the normal breast parenchyma and improves the visibility of the lesion by acquiring images on multiple projections⁶. Therefore, tomosynthesis can improve diagnostic accuracy in the diagnosis of tumors that would otherwise be conventionally occult⁶. In fact, several studies have shown that tomosynthesis increases the cancer detection rate through better visualization of breast masses and architectural distortions. It reduces the recall rate and improves diagnostic accuracy compared to digital mammography¹⁻⁷⁻⁸. The use of tomosynthesis increased for mammography screening and, consequently, tomosynthesis-guided interventional procedures have increased too⁹. Biopsies are performed for parenchymal distortions, calcifications, focal asymmetries and masses that are detectable only with the tomosynthesis method⁹⁻¹⁰. Many studies have shown that tomosynthesis-guided breast biopsies are more technically successful

than mammography-guided stereotaxic biopsies¹¹. Tissue sampling with mammography guidance has largely replaced surgical excision for histological verification¹². Tomosynthesis-guided biopsies can be performed with the patient in an upright position or with the patient prone. Most of the previous studies have evaluated the vertical tomosynthesis biopsy method versus tilted 2D stereotaxic biopsies. There are few studies in the literature that compare the vertical method with the prone method. The purpose of our study is to evaluate the safety and efficacy of the interventional biopsy procedure with prone tomosynthesis guidance on a wide range of interventions.

Materials And Methods

This is a monocentric retrospective observation performed from 1st January 2018 to 1st August 2020, in which we examined the medical records and image storage systems available to the breast radiology of 1500 patients with indeterminate palpable and non-palpable nodular mass of the breast and undergoing subsequent biopsy interventional radiology procedure. Collected data include: age, family history for mammary and gynecological cancers, blood count, coagulation index, anticoagulation and antiplatelet therapy, size and site of the mass, palpable or non-palpable nodule. The study inclusion criteria are: mass greater than 5 mm in maximum diameter, not palpable target lesions, lesions visualized only on tomosynthesis, lesions classified according to ACR BI-RADS with grade 4 and 5, use of 9G needle, execution of 12 standard samples, absence of drug-allergy to anesthetics. No structural features were used to select the tomosynthesis guided biopsy instead of surgical excision. The exclusion criteria are: echo-detectable mass, palpable mass, thrombocytopenia, coagulopathy. Written informed consent on the risks and benefits of the procedure was obtained from all patients prior to the surgery which was performed in accordance with national and European guidelines. The study was approved by the Institutional Review Board. The operators who performed the survey have more than 15 years of experience in interventional breast radiology. The examination is performed on an outpatient basis. Coagulation and platelet counts were monitored for each procedure; SIR-CIRSE guidelines for bleeding risk procedures were followed¹³. The intake of clopidogrel and aspirin was suspended 5 days before the procedure. Anticoagulants were suspended according to drug kinetic and drug dynamic profile. No antibiotics were administered in accordance with current protocols. The tomosynthesis device used for the study was a Giotto plus. Interventional procedures were performed with a standard 9 gauge or petite vacuum breast biopsy device (Eviva; Hologic, Bedford, Massa). In all patients, 12 tissue samples were taken clockwise. The biopsy was performed with a mammograph (Giotto Plus I.M.S.) and a special system to place the patient in the prone position. After positioning the patient, breast compression was applied in the direction that allowed the shortest access to the target lesion (FIG 1-2). The target lesion window of the biopsy was checked by acquiring tomosynthesis scout images. The operator has identified the area of interest within the 3D volume tomosynthesis file. The coordinates were automatically determined by the biopsy software system after that the operator indicated the target location with a cursor (FIG 3). After skin disinfection, deep local anesthesia with 10 mL of lidocaine was performed at the target lesion site. The mechanical guide provides motorized movement for centering the target in the X and Y planes. The Z axis (depth) was adjusted manually. Then a small incision was made with a scalpel

at the site of the anesthetic puncture. The " pre-fire " phase consisted of loading the biopsy needle and performing a new scan to document the needle in the appropriate position (FIG 4). The displacement of the target could be caused by the anesthetic. If necessary, the needle position was corrected. Subsequently, the needle was inserted up to the target and two biopsy rotations were performed clockwise. The collected material was placed on a slide for a 2D mammography check in another location to document the sampling performed. All the samples obtained were placed in neutral 10% formalin buffer and sent for pathological analysis. After that, a non-magnetic metal clip was implanted and tomosynthetic control of the same and any hematoma was performed (FIG 5). Manual compression was performed for 15 minutes and steri clips were placed in the site of the skin breach. Thereafter, clinical and ultrasound control was performed at 90 minutes. Tomosynthesis exam was performed after 10 days to evaluate the location of the implanted clips and the evolution of the hematoma (FIG 6-7). The procedural factors evaluated are the following: safety of the procedure by assessing the frequency of vaso-vagal reactions, hematomas, short-term bleeding (up to 10 days). The Evaluated technical success was considered as a conclusive sample for histological diagnosis. Complications were assessed according to the CIRSE Standard for Classification of Complications ¹³. We subsequently evaluated statically significant differences between high-contrast lesions (microcalcifications) and low-contrast lesions (architectural distortions) and between lesions \leq 10 mm and $>$ 10 mm. We also evaluated the average procedural time. Finally, we evaluated the frequency of the obtained histological data and compared them with the existing literature. All statistics were developed in MATLAB® (Mathematics Works, Inc., Natick, Massachusetts, USA). We also performed a comparison between procedural data from interventions in patients with high-contrast lesions (microcalcifications) and low-contrast lesions (architectural distortions) and between lesions \leq 10mm and $>$ 10m: the differences in terms of safety and efficacy were considered statistically significant if p-value $<$ 0.05, using Student's t-test or Wilcoxon signrank test.

Results

Among the 1500 patients examined, 500 patients were enrolled for the safety and efficacy study. Of the 1000 excluded, 870 had performed biopsy interventional procedures under ultrasound guidance, 130 had performed ultrasound-guided FNAC examination. Patients ranged in age from 30 to 89 years (mean, 48 years; median, 46 years). The lesions ranged in size from 6 mm to 10 mm (mean, 7 mm; median, 8 mm). The mean procedure time was 15 min (median 13 min). High-contrast lesions constituted 62% (310/500) while the remaining 48% were low-contrast lesions. There were no complications (hematomas and bleeding) that blocked the execution of the procedure 0% (0/500). Two cases (0.4%) of minor bleeding were observed with self-limited bleeding from the skin breach at 90 minutes without clinical sequelae in an asymptomatic patient. Vaso-vagal reactions did not occur (Table3). Diagnostic failure understood as anatomo-pathological inadequacy of the sample occurred in 0.4% (3/500). Of these 500 women, 93.5% had a biopsy of 1 lesion, 7.5% had biopsy of 2 separate lesions. Tomosynthesis-guided sampling showed carcinoma in 55.2% (276/500). Of these, 20% were ductal carcinoma. Lobular carcinomas were 13%; the frequency of intraepithelial ductal neoplasia was 48% while of intraepitealial lobular neoplasia it was

19% (Table 1-2). All carcinomas underwent surgery which confirmed the biopsy diagnosis. Of the remaining biopsies (224), apocrine metaplasia (25%) and adenosis (22%) were the most frequently found benign lesions. (Table 4). There were no statistically significant differences between the results of biopsies performed on masses ≤ 10 mm and > 10 mm and between high-contrast and low-contrast lesions.

Discussion

Recent scientific indications in the treatment of breast cancer have favored conservative surgery with particular attention to aesthetics. In the past twenty years of breast surgery, one of the most important advances has been the ability to diagnose cancer outside the operating room, using percutaneous biopsy techniques under stereotaxic guidance versus excisional biopsy. The latter often requires repetition of the surgery¹²⁻¹⁴. Cancer diagnosis before surgery can allow for correct pre-operative planning with a reduction in the repetition of operations. In the United States, percutaneous micro-histological biopsy has almost replaced fine needle aspiration (FNA) as the diagnostic method of choice for breast lesions, as it provides histological diagnosis and prognostic markers¹⁵⁻¹⁶. In fact, as described in numerous papers available in the literature, the micro-histological biopsy is superior to the cellular aspirate derived from a fine needle in the diagnosis of the nature of the suspected lesion¹⁷. The thick needle aspiration biopsy provides only the presence or absence of suspected or malignant cells while the micro-histology allows for precise diagnosis of the mass. Percutaneous biopsy with tomosynthetic guidance is the preferred minimally invasive method for the characterization of non-palpable and undetectable areas of the breast (distortions or microcalcifications on ultrasound) as it allows better localization of the lesion through 3D visualization¹⁸. As confirmed by our study, the biopsy, especially if performed with large caliber vacuum needles (caliber 8-10 G), offers a high diagnostic precision which in the literature is between 93% and 100%¹⁸⁻¹⁹, also for the diagnosis of high-risk lesions and tumors in situ. The biopsy gun is used to remove different pieces of tissue and in some cases completely remove the lesion. It is recommended that at least 12 tissue fragments are taken from a single lesion for adequate sampling. Even the size of the tissue fragments is fundamental for the correct diagnosis, in fact, our pathologists have observed that the samples of breast tissue tend to fragment easily, and the analyzes are more complex¹⁸. This consideration is further confirmed by recent scientific studies in which small caliber needles have been used²⁰. Large needles (9 gauge), on the other hand, can deliver lumps of intact breast tissue. Our study confirms that the use of 9 G gauge needles does not increase morbidity and allows diagnosis in most cases compared to the data in the literature. No significant complications occurred in our study. Minor bruises were noted at 10 days. The interventional procedure, although simple to perform, requires a good command of the procedure for calculating the Z axis which corresponds to the depth of the needle. This can be difficult in some cases, especially with low contrast targets, such as non-calcified masses or architectural distortions. All the patients in our study completed the procedure showing a remarkable comfort in accordance with what has already been demonstrated by Schrading et al, who in their paper reported a high tolerance of the patient undergoing breast biopsy guided by tomosynthesis²¹. In fact, in all the patients observed, no discomfort was found, even for those who suffered from back pain or who

had respiratory problems; this may be because we ask before the biopsy for the patient's ability to lie prone for an extended period of time. Among the main advantages of the prone biopsy there is the lack of visualization of the patient's biopsy procedure with reduction of vagal vessel reactions and anxiety crises. Our study suggests that prone tomosynthesis-guided biopsies are technically safe and effective with valid and repeatable clinical performance. Our study suggests that tomosynthesis-guided biopsy may be faster than traditional stereotaxic biopsy²². In fact, the reduced biopsy time is due to a faster targeting and also the confirmation of the clip and the positioning of the needle are easier especially for non-calcified findings or when the complete removal of calcifications is performed. The prone tomosynthetic biopsy has some disadvantages such as the occupation of larger spaces for the bed. The correct characterization of the mass allows an adequate therapeutic choice in fact the histological, imaging and clinical findings must be evaluated together. If the biopsy result is benign and agrees with imaging results, continuous surveillance is acceptable. If the result is indeterminate or discordant from the image, surgical excision is indicated to exclude malignancy. In addition, surgical excision is indicated for biopsies demonstrating atypical hyperplasia (lobular or ductal), lobular carcinoma in situ, or coexisting in situ or invasive ductal carcinoma. Carcinoma in situ can be the cause of potential incorrect sampling²³⁻²⁴. The frequency of ductal carcinoma detected in our study is in agreement with the literature. The frequency of lobular carcinoma also corresponds to the recent literature. The study has several limitations. First of all there is no direct comparison with a group of biopsies performed with a different gauge needle performed by the same operators; moreover the study, being monocentric, has a series of cases limited to a single diagnostic unit. The study suggests that the 9 G needle micro-histological biopsy with tomosynthesis guide with prone patient is a safe and effective technique with a very low complication rate and inadequate samples for diagnosis.

Declarations

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Availability of data, material and code availability: all authors declare that there are availability of data, material and code availability.

Authors' contributions: All authors participated in the creation of the paper.

Ethics approval: The paper is approved.

Consent to participate : all authors declare that there are consent to participate

Consent for publication : all authors declare that there are consent for publication.

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Tables

Table 1

Ductal intraepithelial neoplasia	Frequency
DIN I a	6%
DIN I b	26%
DIN I c	6%
DIN II	5%
DIN III	5%

Table 2

Lobular intraepithelial neoplasia	Frequency
LIN I	12%
LIN II	4%
LIN III	3%

Table 3

Complications	Frequency
Major bleeding	0%
Minor bleeding	0.2%
Vaso-vagal reaction	0%
Hematomas detected after 10 days	4%

Table 4

Breast lesions in follow-up	Frequency
Apocrine metaplasia	25%
Adenosis	22%
Ordinary ductal hyperplasia	14%
Fibrosclerosis	10%
Necrosis	7%
Radial scar	9%
Complex sclerosing	13%

Figures

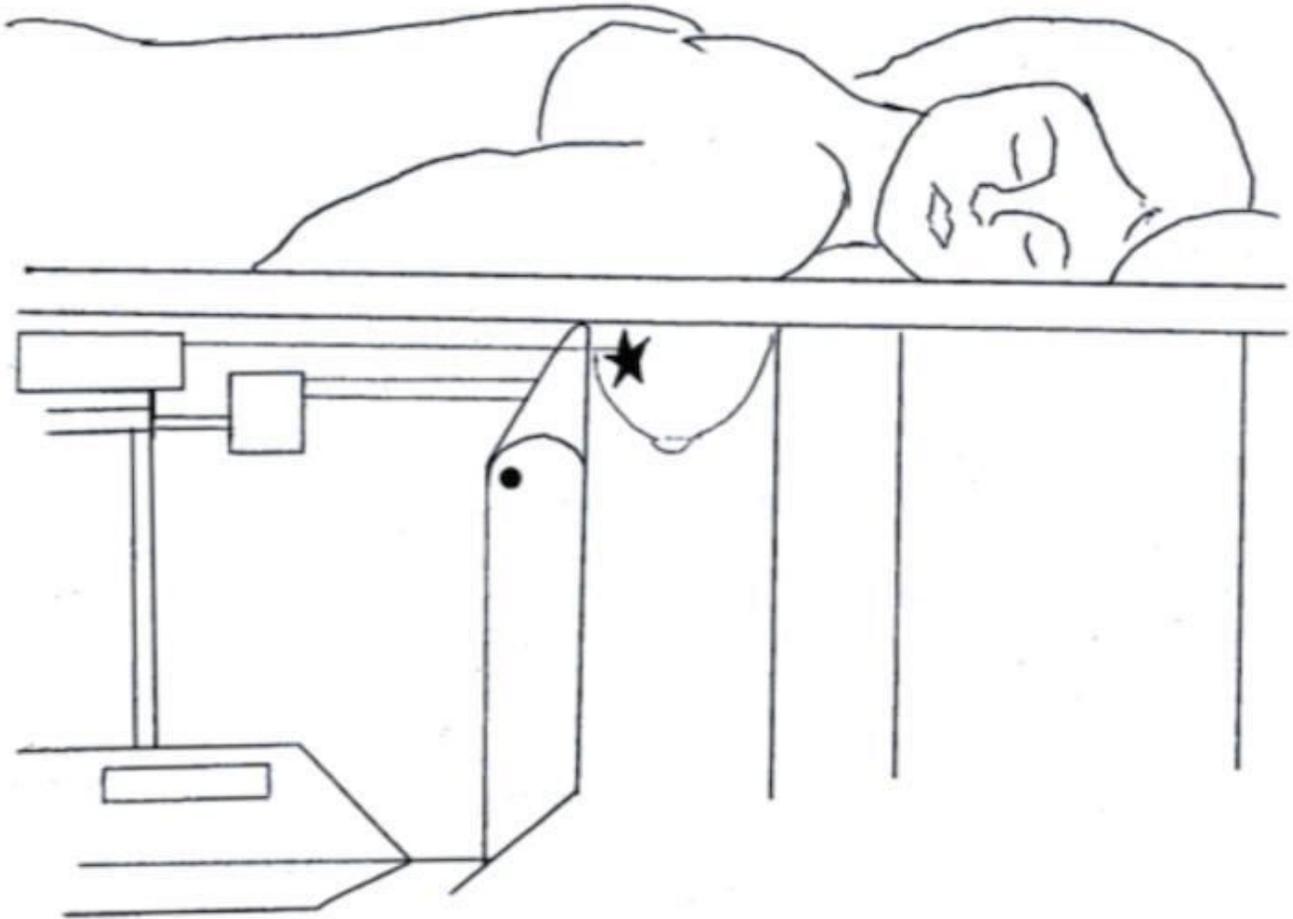


Figure 1

After positioning the patient, breast compression was applied in the direction that allowed the shortest access to the target lesion

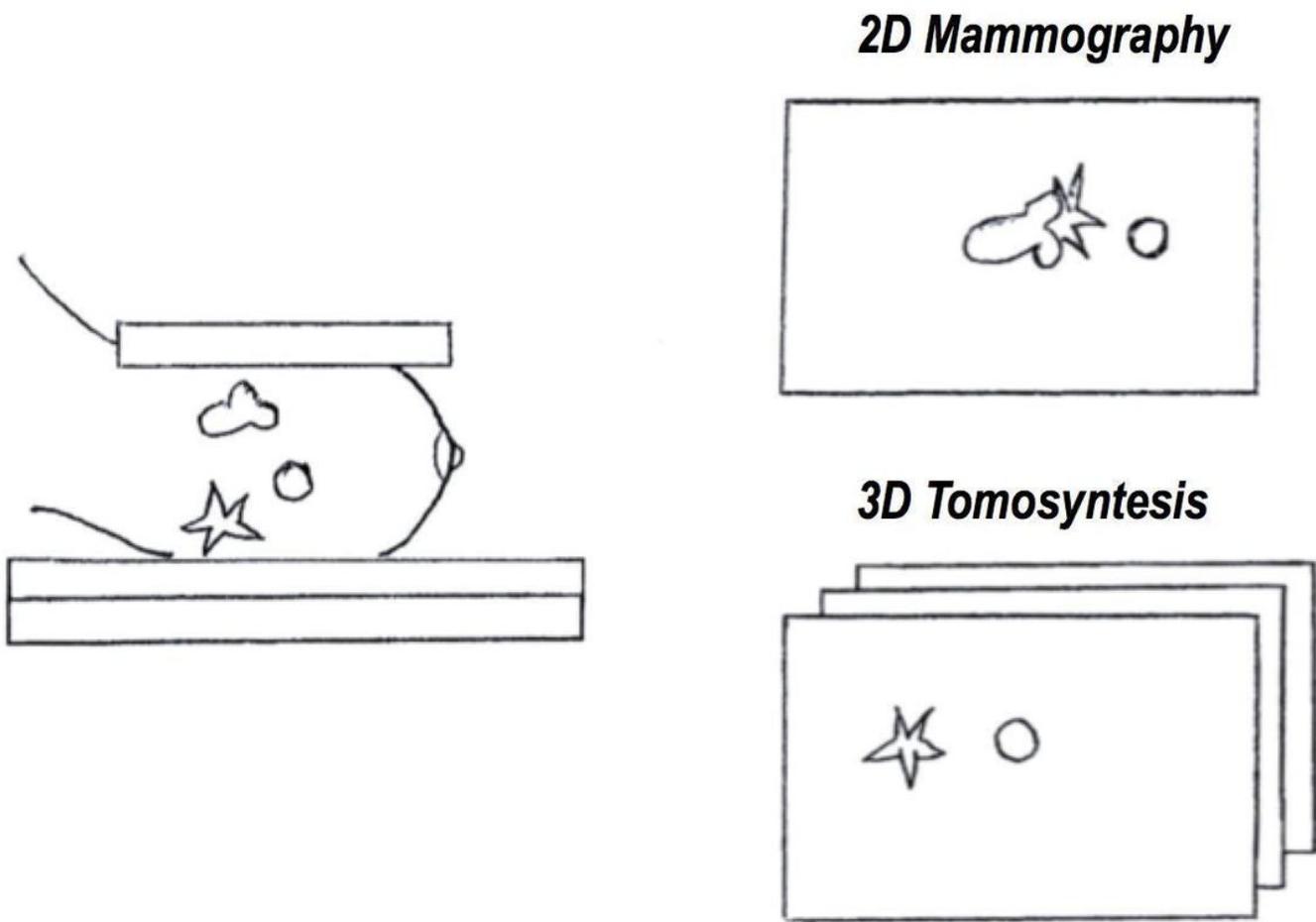


Figure 2

2D mammography and tomosynthesis image acquisition modalities.



Figure 3

Lesion localization phase: microcalcification and distortion (circle) in CC projection was identified.

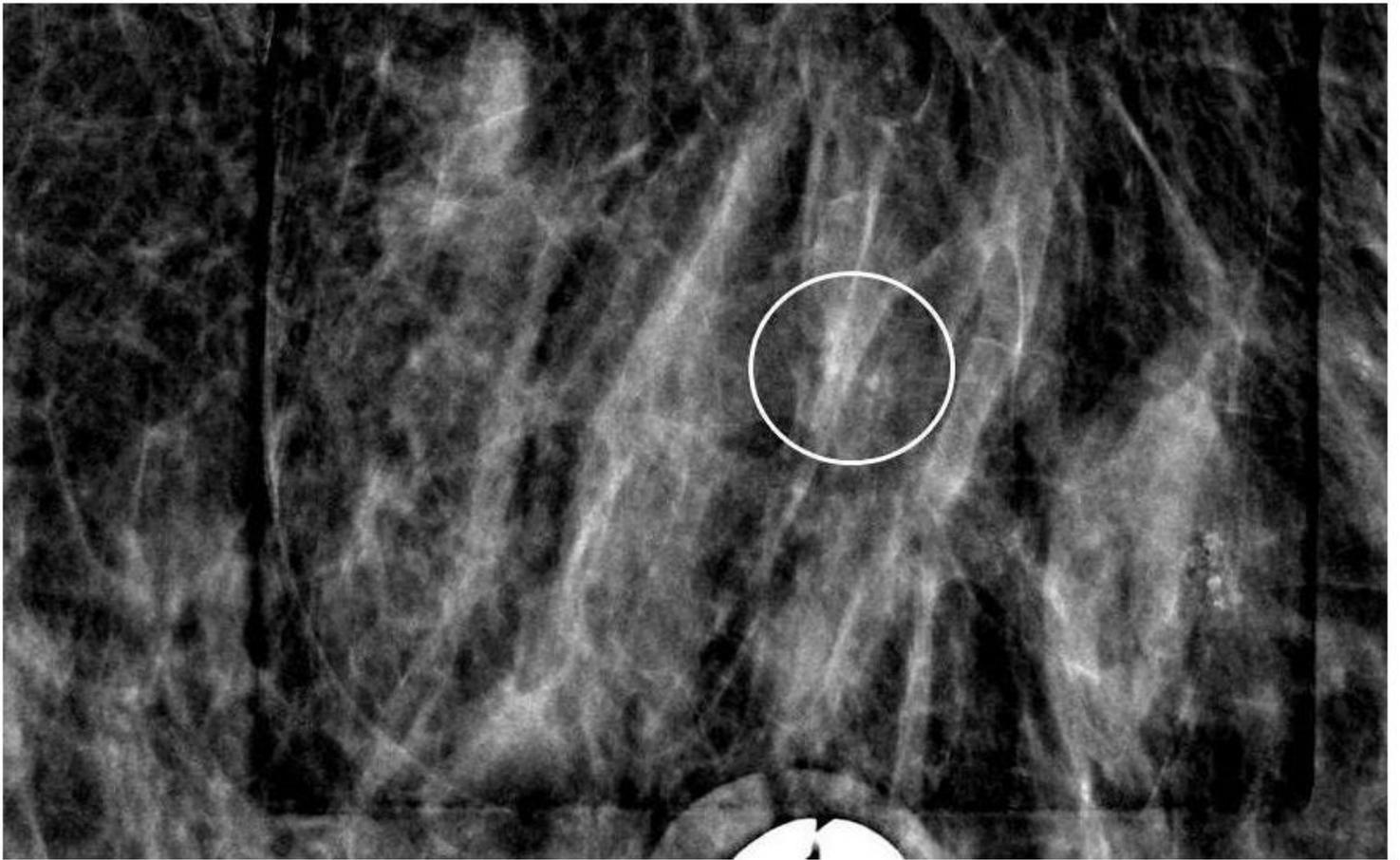


Figure 4

The " pre-fire " phase: consisted of loading the biopsy needle and performing a new scan to document the needle in the appropriate position of the target (circle).

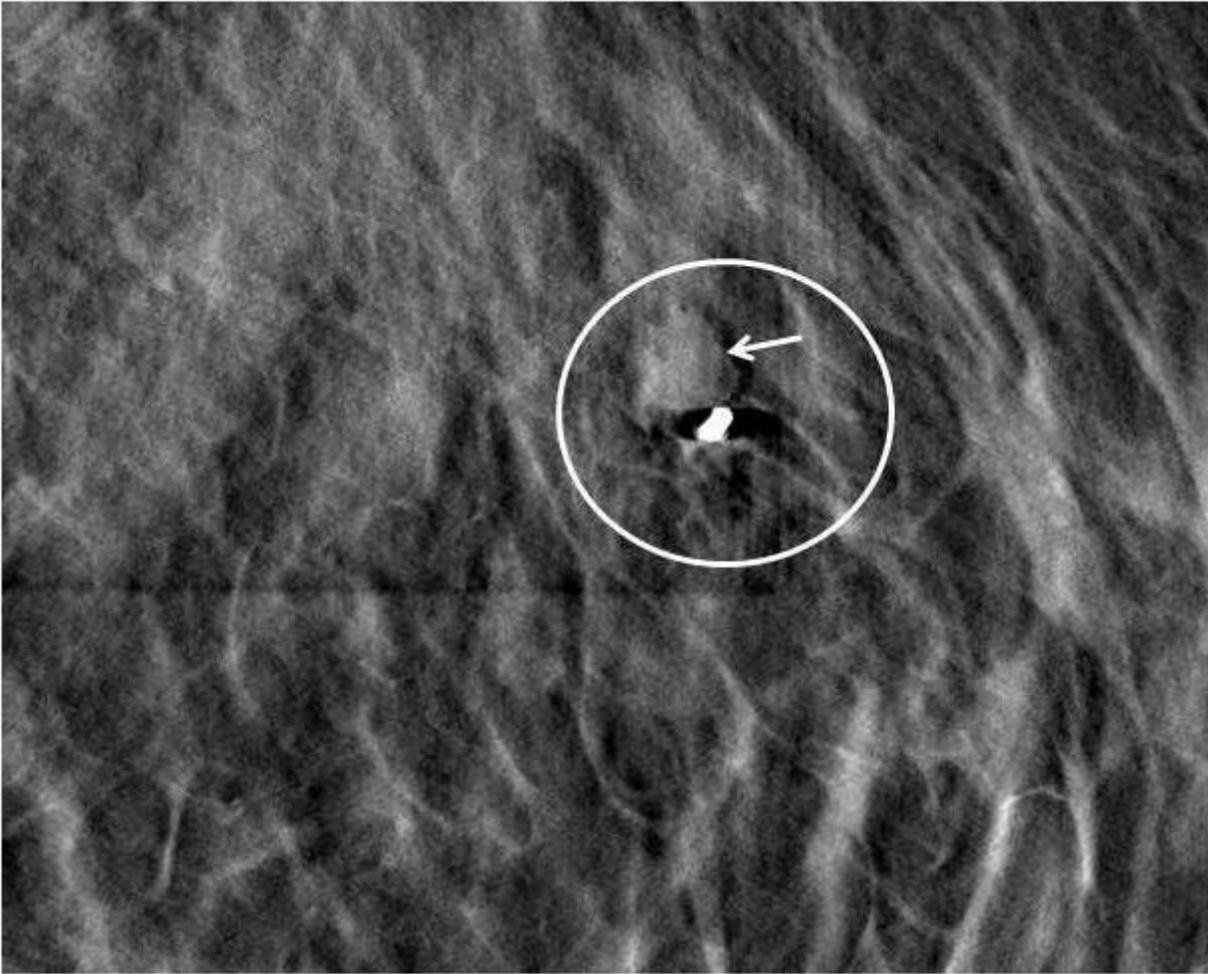


Figure 5

The post biopsy phase (circle): the implantation of the non-magnetic metal clip and any hematomas (arrow) was checked.

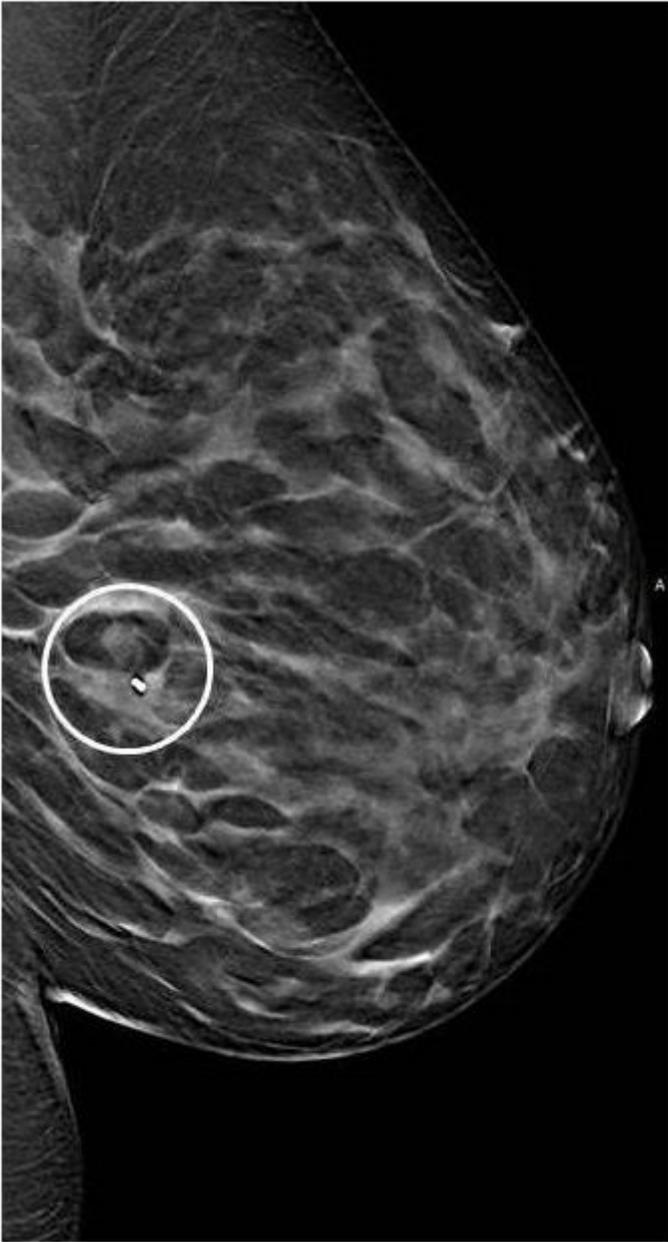


Figure 6

Tomosynthesis exam MLO projection: exam performed 10 days after biopsy showing clip and small hematoma (circle).

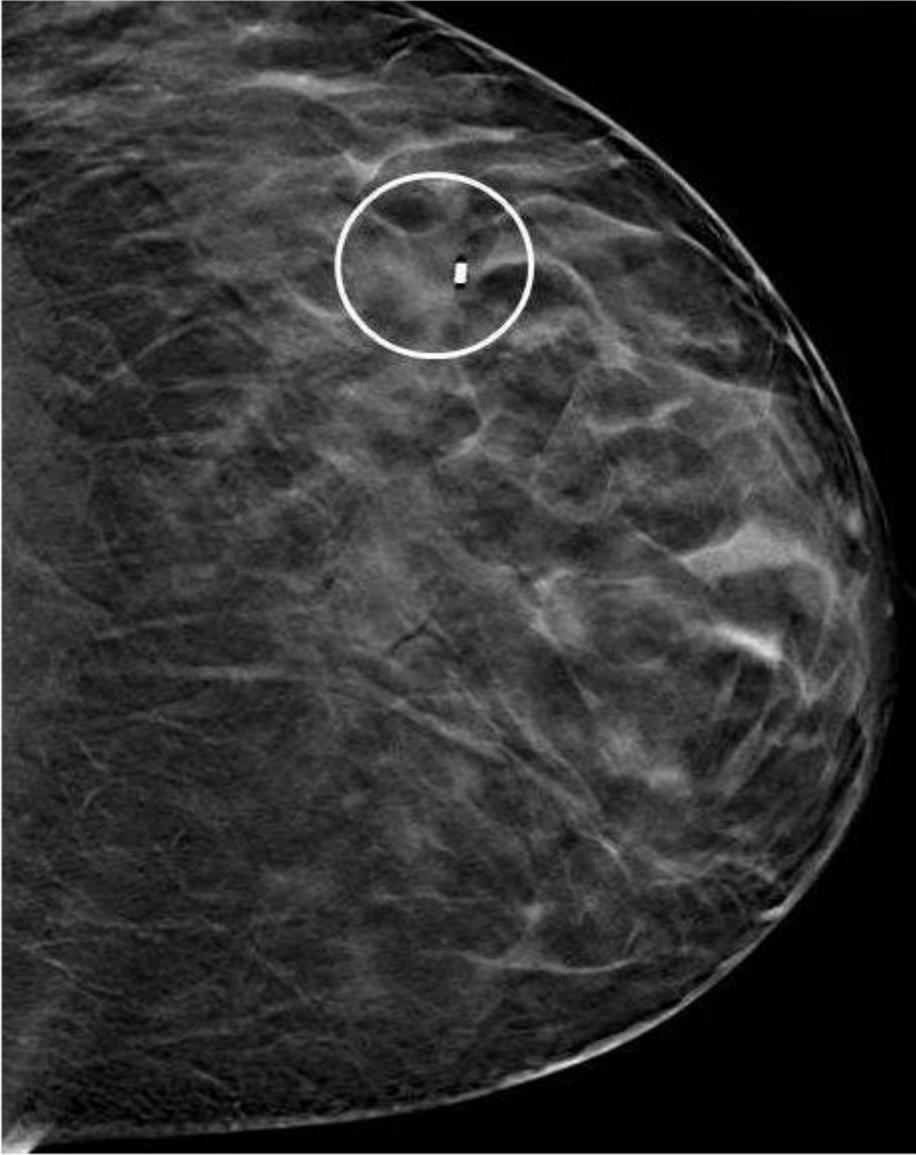


Figure 7

Tomosynthesis exam CC projection: exam performed 10 days after biopsy showing clip and small hematoma (circle).