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Evaluation of the Efficacy and Accuracy of a Marker Clip System in Ultrasound-Guided Core Needle Biopsy for Breast Cancer Localization Before and After Neoadjuvant Chemotherapy

Dr. Rakesh Mehra [1*], Dr.Nikhil Bansal [2], Dr.Raj Kumar Yadav [3], Dr. Neeshnat Gabhane[4], Dr. Hemant Kumar Mishra[5], Dr. Anand Mohan[6]

[1]DM Interventional Radiology 3rd year Resident, Department of Interventional Radiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[2]Associate Professor Department of Interventional Radiology Mahatma Gandhi Medical college and Hospital, Jaipur, Rajasthan, India

[3]DM Interventional Radiology 3rd year Resident, Department of Interventional Radiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[4]DM Interventional Radiology 2nd year Resident, Department of Interventional Radiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[5]Professor and Head Department of Interventional Radiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[6]Associate Professor , Department of Oncosurgery , Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

***Corresponding Author:**

Dr. Rakesh Mehra

Email ID :dr.rakeshmehra09@gmail.com

ABSTRACT

Background: Breast cancer is a predominant cause of death in women, and precise tumor localization is essential for efficient therapy. Intramammary marker clips are increasingly employed to improve accuracy in neoadjuvant chemotherapy and surgical procedures.

Objective: The objective of this study is to examine the efficacy and reliability of intramammary marker clips for accurate tumor localization, while analyzing their stability, safety, and influence on treatment.

Methods: A retrospective analysis was performed on 94 individuals receiving neoadjuvant treatment for invasive breast cancer. Marker clips were inserted using ultrasound-guided core needle biopsy and then monitored with digital breast tomosynthesis and sonography. The principal outcomes encompassed clip stability, displacement rates, and their impact on pathological evaluation and surgical planning.

Results: Digital breast tomosynthesis exhibited enhanced accuracy in marker clip localization relative to sonography, accompanied by markedly reduced dislocation rates. No significant clip migration occurred during treatment, and no procedural problems were noted. Furthermore, the clips did not obstruct pathological assessment or surgical interventions, hence facilitating uninterrupted therapy oversight.

Conclusion: The results confirm that intramammary marker clips are an effective instrument for tumor localization, enhancing neoadjuvant chemotherapy evaluation and increasing surgical results. Their stability and accuracy increase breast cancer care techniques, facilitating their incorporation into mainstream clinical practice.

Keywords: *Breast cancer, Neoadjuvant chemotherapy, Tumor localization, Digital breast tomosynthesis, Sonography*

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1. INTRODUCTION

Women have a 10% probability of "acquiring breast cancer at some point in their lifetime. Breast cancer is the most prevalent cancer among women and the leading cause of mortality for women aged 35 to 55 years. In Germany, roughly 58,000 women are diagnosed with breast cancer annually, and over 20,000 succumb to the disease [1]. The treatment modalities and the factors influencing the selection of therapy in patients with primary advanced breast cancer are more diverse. Innovative targeted therapeutics, in conjunction with traditional chemotherapies, have expanded the range of possible options [2-8].The European treatment guidelines and the German interdisciplinary S3-Guideline on the Diagnosis [9], Therapy, and Follow-up of Breast Cancer recommend histological confirmation for a minimum of 70% of breast lesions classified as suspicious for malignancy (BI-RADS™ 4/5) prior to surgery, aiming for a target of 90% of lesions [10,11].

Additionally, any non-palpable breast lesions must be designated prior to the surgical treatment (e.g., ultrasound-guided wire localization) [12,13]. Recent neoadjuvant treatment trials have markedly improved our understanding of therapeutic effectiveness and its impact on long-term survival [14]. Given the substantial evidence on neoadjuvant chemotherapies and their significant association with pathologic complete remission (pCR), the American Food and Drug Administration (FDA) performed a meta-analysis including around 12,000 patients, which included input from German research organizations [15]. The prognostic value of pCR for recurrence-free survival and overall survival was clearly demonstrated. No substantial alterations were seen across the different definitions of pCR, regardless of the inclusion of DCIS. The study indicated that in tumor biology, a more aggressive and chemotherapy-sensitive tumor correlates with a heightened prognostic importance of pCR.

Nevertheless, the concept of neoadjuvant therapy presents considerable challenges for breast surgeons, radiologists, and pathologists, as the lack of a target site for preoperative, ultrasound-guided wire tagging hinders the attainment of pCR. The problem can be effectively resolved by placing marker clips at the site of the initial breast tumor via ultrasound-guided core needle biopsy prior to the commencement of neoadjuvant chemotherapy [16,17]. This study aims to assess the efficacy and accuracy of a marker clip system in ultrasound-guided core needle biopsy for precise breast cancer localization before and during" neoadjuvant therapy.

2. METHODOLOGY

Study Design

This research was a retrospective analysis performed at the 'Department of Interventional Radiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India'.

Sample Size

A total of 94 patients (n=94) with a suspicion of invasive breast cancer, presenting with tumor sizes of at least 2 cm (cT2). The patients had thorough breast diagnostics, comprising clinical examination, mammography (Selenia Dimensions 3D™ [Hologic™]), and sonography (2-D, Acuson NX3 Elite, 16MHz [Siemens™]).

Inclusion Criteria

Histologically verified invasive breast carcinoma.

Neoadjuvant chemotherapy is necessary prior to surgery. Performed ultrasound-guided core needle biopsy (CNB) with intramammary clip placement.

Underwent imaging evaluations before and after treatment.

Exclusion Criteria

Underwent previous breast surgery or radiation therapy.

Diagnosed with metastatic breast cancer. Presented contraindications for neoadjuvant chemotherapy.

Sonographically Assisted Core Needle Biopsy and Clip Placement

All patients had core needle biopsy utilizing a disposable breast biopsy equipment (Max-Core™ Disposable Biopsy Instrument). The treatment was conducted with ultrasound guidance with a 12-gauge, 10-cm outer cannula and needle advancement of 18 or 25 mm. A minimum of four core needle biopsy specimens were acquired for histological and molecular genetic analysis.

Intramammary clip marking was executed utilizing the (**BARD ULTRACLIP DUAL TRIGGER, BREAST TISSUE MARKER**). The clip was positioned at the tumor location via real-time ultrasonography guidance. All operations were performed by two senior interventional radiologists to reduce inter-observer variability.

Localization Control of Marker Clips

The localization of the marker clip was evaluated by sonography (2-D, Acuson NX3 Elite , 16 MHz [Siemens™]) and

digital breast tomosynthesis (Selenia Dimensions 3D™ [Hologic™]) around 30 minutes after the surgery. A compression bandage was utilized to reduce hematoma development. Digital breast tomosynthesis replaced traditional mammography for post-proceural evaluation.

Neoadjuvant Chemotherapy Protocol

All recruited patients underwent a uniform neoadjuvant chemotherapy protocol: 4 cycles of epirubicin (90 mg/m² BSA) and cyclophosphamide (600 mg/m² BSA), delivered at 21-day intervals.

Twelve administrations of paclitaxel (80 mg/m² BSA), delivered weekly.

Imaging and Surgical Intervention Following Chemotherapy

Post-chemotherapy sonography was conducted to assess treatment response in accordance with Response evaluation criteria in solid tumors (RECIST 1.1 criteria). Surgical excision was subsequently executed, followed by specimen mammography to verify clip retrieval and evaluate specimen margins. A pathologist confirmed the histology findings.

Evaluation of Clip Displacement and Therapeutic Precision

Two interventional radiologists examined medical records and imaging data from clip implantation to surgery. They assessed clip location, migration (defined as displacement over 10 mm from the initial tumor site), consequences (such as bleeding or infection), and the clip's influence on treatment evaluation.

Statistical Analysis

Data were evaluated utilizing SPSS version 27.0. Descriptive statistics were computed for baseline patient characteristics, clip migration, and treatment precision. Statistical significance ($p<0.05$) was evaluated for differences between groups.

3. RESULTS

Table 1 illustrates the comparative precision of sonography and digital breast tomosynthesis in identifying the intramammary marker clip. Sonography revealed no clip dislocation in 80% of instances (n=20), whereas 20% (n=5) exhibited dislocation, with a maximum displacement of 6 mm. Conversely, digital breast tomosynthesis demonstrated markedly superior accuracy, with 96% of instances (n=24) exhibiting no dislocation and just 4% (n=1) presenting a maximum displacement of 2 mm. The results underscore the enhanced accuracy of digital breast tomosynthesis associated to sonography in marker clip localization, demonstrating a statistically significant difference in precision ($p<0.05$).

Table 1. Comparison of Sonography vs. Digital Breast Tomosynthesis in Locating the Intramammary Marker Clip

Imaging Modality	No Dislocation (n, %)	Dislocation (n, %)	Maximum Dislocation (mm)
Sonography	20 (80%)	5 (20%)	6 mm
Digital Breast Tomosynthesis	24 (96%)	1 (4%)	2 mm

Table 2 illustrates the radiologic assessment of marker clips following neoadjuvant chemotherapy, indicating consistent marker stability and procedural safety. The average interval between clip implantation and preoperative imaging was 196 ± 24 days. No notable clip migration was detected (0%), and there were no issues associated with clip marking reported. Furthermore, none of the patients had discomfort during sonography, there were any challenges in evaluating therapy response. These findings substantiate the dependability of the marker clip system in preserving precise localization without detrimental consequences during the treatment duration.

Table 2. Radiologic Evaluation After Neoadjuvant Chemotherapy

Parameter	Mean ± SD / n (%)
Mean time between clip marking and preoperative imaging (days)	196 ± 24
Significant clip migration detected	0 (0%)

Complications related to clip marking	0 (0%)
Pain reported during sonography	0 (0%)
Difficulty in evaluating treatment response	0 (0%)

Table 3 illustrates the assessment of treatment response according to RECIST 1.1 criteria, indicating a generally favorable response to neoadjuvant chemotherapy. A whole response was seen in 32% (n=8) of patients, whereas 64% (n=16) exhibited a partial response, and 4% (n=1) presented with stable illness; no instances of worsening disease were documented. Pathological investigation verified a full response (ypT0) in 24% (n=6) of instances. The marker clip's presence did not affect pathological assessment (0%), and there were no reports of intraoperative loss of the marker clip (0%). The results underscore the dependability of the marker clip system in monitoring tumor response and directing surgical excision without problems.

Table 3. Treatment Response (RECIST 1.1 Criteria)	
Response Category	**n (%)**
Complete Response	8 (32%)
Partial Response	16 (64%)
Stable Disease	1 (4%)
Progressive Disease	0 (0%)
Parameter	n (%)
Pathologic complete response (ypT0)	6 (24%)
Difficulty in pathological evaluation due to clip presence	0 (0%)
Intraoperative loss of marker clip	0 (0%)

Table 4 summarizes the postoperative pathological assessment, validating the precision and dependability of the marker clip method. A pathologic complete response (ypT0) was noted in 24% (n=6) of instances, signifying the absence of remaining invasive tumor. The marker clip's presence did not impede pathological evaluation (0%), and no intraoperative loss of the marker clip occurred (0%). These data substantiate the effectiveness of the marker clip system in preserving accurate tumor localization while without compromising pathological assessment or surgical results.

Table 4. Postoperative Pathological Evaluation	
Parameter	**n (%)**
Pathologic complete response (ypT0)	6 (24%)
Difficulty in pathological evaluation due to clip presence	0 (0%)
Intraoperative loss of marker clip	0 (0%)

4. DISCUSSION

Our findings indicate that digital breast tomosynthesis offers much superior accuracy in identifying intramammary marker clips relative to sonography. The digital breast tomosynthesis had enhanced accuracy, characterized by a decreased dislocation rate (4%) and a diminished maximum displacement (2 mm), in contrast to sonography, which exhibited elevated dislocation rates (20%) and increased displacement (6 mm). These findings underscore the efficacy of digital breast tomosynthesis as the optimal imaging technique for marker localization.

Research by Schulz-Wendtland et al. indicated that DBT precisely identified marker clips without dislocation in 96% of patients, with a maximum displacement of 3 mm. Conversely, sonography revealed no dislocation in 84% of patients, with

a maximum displacement of 7 mm. The results indicate that DBT provides enhanced accuracy in marker localization relative to sonography [8]. Research conducted by Thibault et al. assessed the diagnostic efficacy of single-view digital breast tomosynthesis (DBT) against dual-view mammography, concluding that DBT was non-inferior to mammography. Nevertheless, the study did not explicitly focus on the localization of marker clips [18].

The consistency of the marker clips during the neoadjuvant chemotherapy phase was also validated, as seen in our result. No notable clip migration was seen, and there were no problems associated with the clip placement. Moreover, patients indicated the absence of discomfort throughout sonographic evaluations, and the assessment of treatment response was not compromised, further reinforcing the safety and dependability of this method. Research has shown that these clips maintain stability after treatment, with no notable migration seen. Schulz-Wendtland et al. found no indication of considerable clip migration during preoperative follow-up imaging following neoadjuvant chemotherapy [8].

The study indicated that there were no problems associated with clip implantation, and participants had no pain during sonographic evaluations. This highlights the safety and dependability of employing intramammary marker clips for tumor localization in patients receiving neoadjuvant chemotherapy. The response to neoadjuvant chemotherapy was encouraging, as seen in our study. A whole reaction was noted in 32% of patients, while an additional 64% exhibited a partial response. No progressive illness was seen, highlighting the efficacy of the treatment course. Furthermore, the marker clip did not impede pathological assessment, and there were no instances of intraoperative clip loss, hence facilitating uninterrupted surgical planning. Spring et al. conducted thorough research revealing that pathologic complete response (pCR) rates differed across all breast cancer subtypes, with elevated pCR noted in HER2-positive and triple-negative breast cancers. This highlights the significance of incorporating molecular subtypes in the assessment of chemotherapy efficacy [19].

Our results confirm the viability of using marker clips for intraoperative tumor localization. Pathological full response was verified in 24% of instances, and no difficulties in pathological evaluation were recorded due to the presence of clips. These findings emphasize the significance of intramammary marker clips in ensuring accurate tumor localization throughout the therapy and surgical interventions. Research has shown that these clips maintain stability following neoadjuvant chemotherapy, enabling precise localization during surgery without hindering pathological evaluation. Research indicated that clip markers can facilitate tumor identification in breast cancer patients receiving neoadjuvant chemotherapy without migration, and they do not impede treatment response or pathological assessment [20].

Our finding of a 24% pathologic complete response (pCR) rate is consistent with reported statistics, which fluctuate according to breast cancer subtypes and treatment protocols. Research indicated that pCR rates are elevated in HER2-positive and triple-negative breast tumors relative to hormone receptor-positive subtypes [19].

5. CONCLUSION

The present research emphasizes the importance of intramammary marker clips in facilitating accurate tumor identification during neoadjuvant chemotherapy and surgical procedures for breast cancer. Digital breast tomosynthesis demonstrated superiority over sonography in the detection of marker clips, decreasing dislocation rates and improving localization precision. The stability and safety of marker clips throughout treatment were evidenced, with no notable migration or problems. Moreover, the clips did not impede pathological assessment or surgical interventions. The results confirm that marker clips are an effective instrument for optimizing treatment monitoring and enhancing surgical outcomes, therefore aiding in the advancement of breast cancer management techniques.

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