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Investigating the Effectiveness of Using Surgical Clips to Mark Biopsied Breast Masses

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Abstract

Background: The present study was designed with the aim of investigating the effectiveness of using surgical clips to mark biopsied breast masses.

Methods: This study was a semi-experimental study in which the statistical population included all the breast cancer patients who referred to Golestan Hospital for marker testing. A checklist including the variables examined and patient information (such as age, location of lesion, size of lesion, ultrasound findings, mammography findings, history of snake bites, received or not received chemotherapy, response rate to treatment, type of marker used, number of markers used, cabling requirements, operation results) was collected and finally analyzed.

Results: In this study, 42 women with a mean age of 48.29±9.56 years were examined. 22 cases of masses were in the left breast. According to the size results, 35.7% (15) of the masses in the first dimension were between 11 and 20 *mm* and 31.0% (13) were between 21 and 30 *mm* and in the second dimension 45.2% (19) of the masses were between 21-30 *mm* and 28.6% (12) were between 11 and 20 *mm*. In the present study, the results of mammography after surgery showed that all the markers were placed in the correct location, 100% (42) and 71.8% (30) of the markers used were metal and 28.6% (12) were made of titanium metal. One marker was used in 59.5% (25) of the patients and two markers were used in 21.4% (9) of the patients.

Conclusion: This success and effectiveness is due to the innovations used in this study in the shape of the marker and its entry, and it is hoped that the results of this study will be used for better localization of the tumor.

Keywords: Breast neoplasms, Checklist, Female, Humans, Mammography, Snake bites, Surgical instruments, Titanium

Introduction

Breast cancer is the most common malignancy in women in Iran and worldwide and is the leading cause of cancer-related death (1-4). Despite advances in the field of diagnostic and therapeutic treatment of breast cancer, advances in the field of early-stage diagnosis and treatment are still unclear (5,6). According to a review of studies and literature in 2015, it was estimated that the number of deaths from breast cancer was 90,800 in the European Union (EU) and 40,290 in the United States of America (7-9). Several clinical studies show that screening women's breasts using mammography can help detect early signs of breast cancer (10,11). Mammography is important for early detection of the disease, although results are sometimes suspicious or undetectable in patients with early-stage breast cancer or small lesions (12-14). Further investigation includes an imaging breast biopsy with tissue taken from the suspected breast cancer area (lesion). If the area of suspicious lesion is small, the entire lesion can be removed using image-guided sampling. If the pathological results demonstrate malignancy, it is impossible to localize the lesion for surgery. Therefore, to overcome this obstacle, in the final part of the breast biopsy, a metal marker clip (clip) is placed at the site of the suspicious lesion. Placement of a tissue marker after image-guided breast removal has become an important part of clinical procedures, since it allows the radiologist to precisely localize the tumor site preoperatively. Placement of marker clips in the breast is known to be useful for tumor localization during chemotherapy in patients (15,16). The use of a 3 *mm* metal clip as a radiomarker is a common procedure in biopsy procedures so that the lesion can be clearly identified on subsequent imaging examination (17). The use of breast markers is making greater progress in interventional radiology for breast cancer as these clips are inserted under ultrasound guidance (18). Many types of clips and commercial markets are widely available and used before neoadjuvant chemotherapy and surgery. However, these costs are relatively high, prompting researchers to explore lower-cost options such as standard titanium surgical staples, especially for contraindications where treatment costs to patients are high (19). On the other hand, some drugs and medical devices are unaffordable, which leads to scientific research and efforts to realize this diagnostic and therapeutic method. Also, remaining breast masses in patients with known breast cancer who are candidates for chemotherapy may regress following the course of treatment, making them undetectable for potential surgery or follow-up imaging. The anatomical location of the masses is marked with metal markers prior to chemotherapy (18,19). Therefore, this study was conducted with the aim of investigating the effectiveness of using surgical clips to mark biopsied breast masses.

Materials and Methods

The present semi-experimental study was conducted on all breast cancer patients who referred to Golestan Hospital in Ahvaz, southwest of Iran for wire placement. The study was conducted in accordance with the Declaration of Helsinki and the patients enrolled and they were willing to participate and sign a consent form. The use of chemical substances and foreign bodies, the prescription of drugs or new surgical procedures on patients as research with treatment are among the topics covered by national and international codes of ethics in research. Any substance used in the body should not cause physical or mental harm to the patient. Therefore, in clinical trials, the biosafety and toxicology phases of the study should first be completed and then their ease of use should be demonstrated in animals and then in humans. This topic has been considered by researchers since the inception of the idea of the mentioned innovative plan. With regard to biological safety and non-toxicity, as well as the possibility of its use in humans, it should be stated that the same type of clip as described in the literature review is used in various operations and therefore is safe, non-toxic and harmless to humans. It should be mentioned that the markers utilized in this study are well-known surgical clips that have been deformed and have received the required therapeutic approvals. Figure 1 displays images of the clips prior to and following deformation.

Healthy and sick have already been shown. In addition, pregnant patients, prisoners, and patients who are under any kind of pressure were not included in this study. The patients examined were not deprived of the main and gold standard treatment, but this

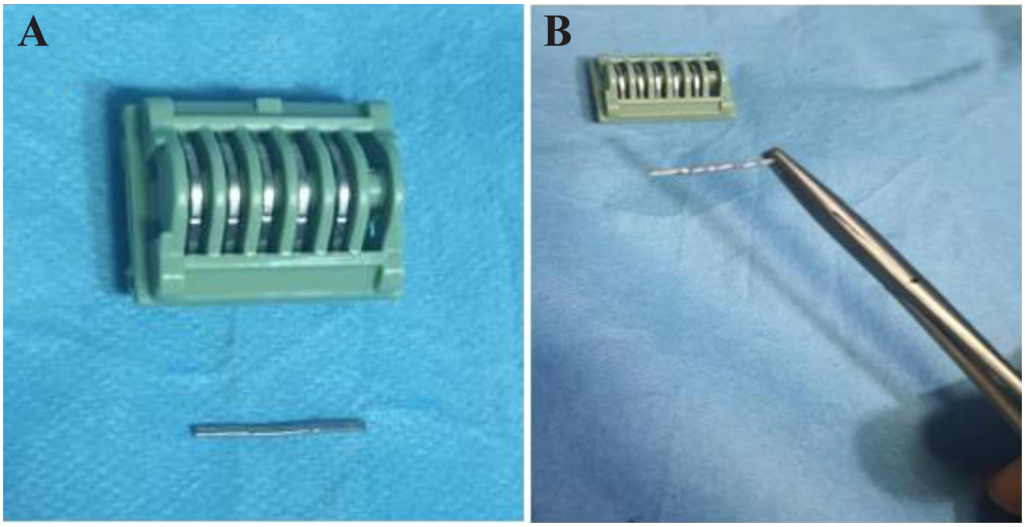

Figure 1. Clips used in the study: (A) prior to deformation, (B) following deformation.

measure was intended to improve the follow-up care and treatment of the patients. The modification stated in the clip was the innovative aspect of this design and it was optimal for the purpose of this study to produce the modified type in terms of physical form which is the product of this research if the claim of this research has proven that the production tool is efficient. Aside from being toxic, harmless and usable in humans, the markers produced by the researcher were used on-site using a completely sterile method. The above clips are the same surgical titanium clips that the researcher initially made as a pilot in several volunteer samples by providing sufficient explanations about the research nature of the work and mentioning the benefits and predictions of the project while obtaining informed consent letter to insert the clips. This was carried out and if, according to the predictions, there are no complications or problems for the patient, this study was carried out on all samples examined. This work has already been done worldwide, with a slight difference in the type of innovation specific to this project for similar patients. This is not possible for most needy patients in the country. If this plan is successful, all patients in the country will be offered the opportunity of easy much cheaper access than the foreign model. In this method, the surgical clip, which is initially curved and has the shape of a number 8, is straightened with a needle holder in the middle and the second needle holder is used to hold both ends and a needle holder around the axis of the clip needle holder. It is rotated again until it takes a spiral shape and, in this way, it becomes better and more accurate to find and see it on ultrasound. To place the marker within the lesion, use a gray angioket (number 16) and insert the angioket into the chest until it reaches the end of the lesion. If the lesion is small, inserted the angioket out of the lesion, then take out its metal part and insert the marker made into the lesion through the plastic part of the angioket and then use the metal part of the angioket to insert the marker into the lesion. Before and after marker placement, mammogram and ultrasound finding of the breast were taken to confirm that all markers were positioned correctly (Figure 2).

In terms of postoperative pathology, the masses' pathology remained unchanged before and after marker placement, since the procedures carried out on the study participants only serve to identify the anatomical location of the mass and do not alter the pathology of the lesions. However, in the present study, in terms of pathology, 31 patients (73.8%), 7 patients (16.7%), and 4 patients (9.5%) had invasive ductal breast cancer (IDC), invasive lobular carcinoma (ILC), and ductal carcinoma in situ (DCIS), respectively.

A checklist including the variables examined and patient information such as (age, location of lesion, size of lesion, ultrasound findings, mammography findings, history of snake bites, received or not received chemotherapy, response rate to treatment,

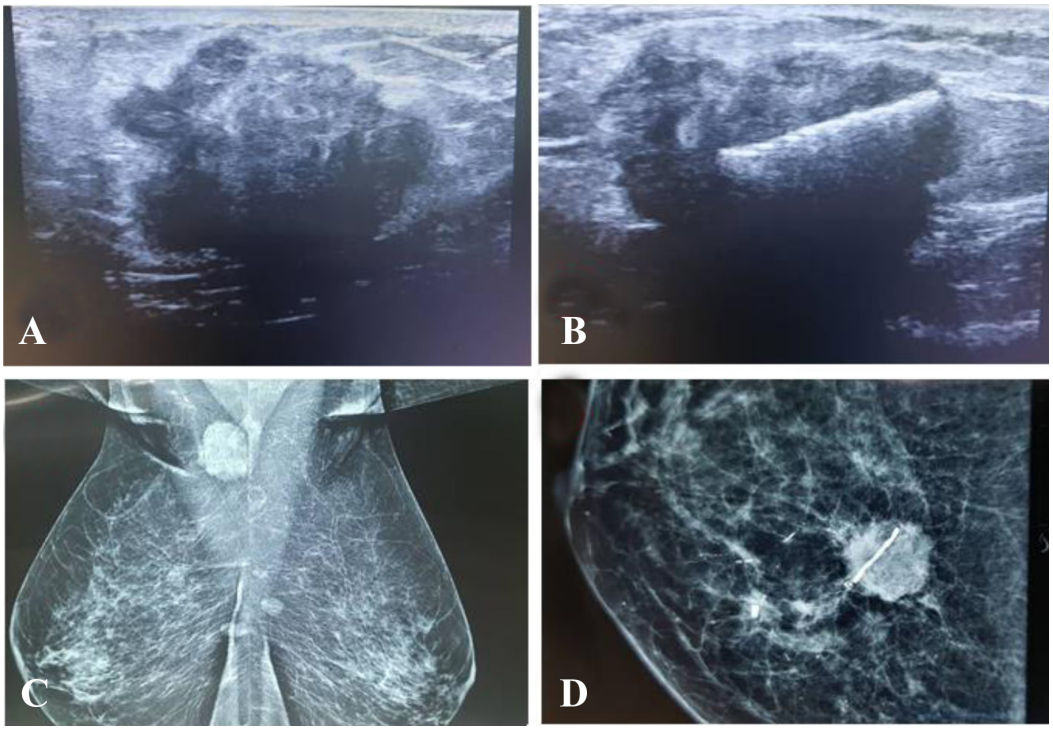

Figure 2. Mammography and ultrasound findings of the breast before and after marker placement. (A) Ultrasound before marker placement, (B) Ultrasound after marker placement, (C) Mammography before marker placement and (D) Mammography after marker placement.

type of marker used, number of markers used, cabling requirements, operation results) was collected and finally analyzed.

Results

In this study, 42 women with a mean age of 48.29±9.56 years were examined. 22 cases of masses were in the left breast. According to the size results, 35.7% (15) of the masses in the first dimension were between 11 and 20 *mm* and 31.0% (13) were between 21 and 30 *mm* and in the second dimension, 45.2% (19) of the masses were between 21 and 30 *mm* and 28.6% (12) were between 11 and 20 *mm* (Table 1). In the present study, the results of mammography after surgery showed that all markers were placed in the correct location. Also, all the markers used were made of titanium metal.

One marker was used in 59.5% (25) of the patients and two markers were used in 21.4% (9) of the patients. In all cases, control mammography was performed and the markers were in the right place. Also, there is no previous history of marking in all the cases. 59.5% (25 patients) used one marker, followed by 21.4% (9) of the patients, with two markers. All cases received

Table 1. Frequency and percentage frequency of lesion size in the first and second dimensions

Variable	Size of the lesion *(mm)*	Frequency (percent)
The size of the lesion 1 (*mm*)		
	11-20	15(35.7)
	21-30	13(31)
	31-40	8(19)
	41-50	4(9.5)
	51-60	1(2.4)
	61-70	1(2.4)
The size of the lesion 2 (*mm*)		
	11-20	12(28.6)
	21-30	19(45.2)
	31-40	6(14.3)
	41-50	3(7.1)
	51-60	2(4.8)
	61-70	12(28.6)

* Also, more than one marker was used due to the large number of tumors or the large size of the tumor.

chemotherapy and in all cases the results of surgery were 100% successful and all who used the marker had successful results. Regarding the need for wiring, the results showed that 19 patients (45.2%) needed it and 23 patients (54.8%) did not need it. According to the ultrasound findings, most of the lesions (30, 62.5%) had a hypoechoic area with an irregular border (Table 2).

Discussion

Breast cancer is the most commonly diagnosed malignancy and the second leading cause of cancer-related death in women worldwide (20). Despite recent advances in mammographic screening, locally advanced breast cancer remains a challenging clinical problem 21, affecting 50–70% of breast cancer patients (20,21). Breast markers are becoming increasingly important as they help identify the tumor bed, especially in cases with complete radiographic response. Markers can be removed from a cancerous lesion or left in place after surgery without serious complications (22,23).

In this study, 42 women with a mean age of 48.29± 9.56 years were examined. 22 cases of masses were

Table 2. Frequency and percentage frequency of patient information such as location of lesion, ultrasound findings, mammography findings, received chemotherapy, response rate to treatment, type of marker used, number of markers used, cabling requirements, and operation results

		Frequency (percent)
Markers used (number)	1	25(59.5)
	2	9(21.4)
	3	4(9.5)
	4	3(7.1)
	5	1(2.4)
The type of marker	Titanium metallic	42(100)
Need for wiring	No	23(54.8)
	Yes	19(45.2)
Location of the lesion (clock) *	Between 12 o'clock and 3 o'clock on the right breast	3(7.14)
	Between 3 o'clock and 6 o'clock on the right breast	3(7.14)
	Between 6 o'clock and 9 o'clock on the right breast	6(14.56)
	Between 9 o'clock and 12 o'clock on the right breast	7(16.66)
	Retroareolar area of the right breast	1(2.3)
	Between 12 o'clock and 3 o'clock on the left breast	8(19)
	Between 3 o'clock and 6 o'clock on the left breast	4(9.5)
	Between 6 o'clock and 9 o'clock on the left breast	4(9.5)
	Between 9 o'clock and 12 o'clock on the left breast	5(11.9)
	Retroareolar area of the left breast	1(2.3)
Ultrasound findings (pathological)	A hyperechoic area with irregular borders	30(62.5)
	A hyperechoic area with lobules	11(22.9)
	A hypoechoic area with lobular borders and containing microcalcifications	3(6.25)
	A hypoechoic area with irregular borders and containing microcalcifications	4(8.35)

* More than one lesion was observed in some patients. Also, more than one marker was used due to the large number of tumors or the large size of the tumor.

in the left breast. Nafisi *et al's* study 4 in which breast cancer was most common in the age group of 40 to 59 years. However, Mir *et al* 8 reported in their epidemiological study that the highest incidence of breast cancer occurred between the ages of 45 and 49 years. In the study by Ji *et al* in 2019, the average age of the patients was 46.60 years and most masses were observed in the left breast (51.3%) (24), which is consistent with the results of the present study. In the study conducted by Perkins *et al* in 2004, breast cancer was diagnosed about 5% more often in the left breast than in the right side (25).

According to the size results, 35.7% (15) of the masses in the first dimension are between 11 and 20 *mm* and 31.0% 13 are between 21 and 30 *mm* and in the second dimension 45.2% (19) of the masses are between 21 and 30 *mm* and 28.6% (12) are between 11 and 20 *mm*. In the study by Ji *et al* in 2019, 53.1% of the tumors were smaller than 20 *mm* 24. In the study carried out by Croman *et al* in 2003, 52.4% of the masses were smaller than 20 *mm* 26. In the study by Liu *et al* in 2021, the size of 56.7% of masses was between 11 and 20 *mm* 27, which is consistent with the results of the present study.

In the current study, the results of mammography after surgery showed that all the markers were 100% placed in the correct location. Yoon *et al* reported in their 2015 study that there was no mammographic evidence of clip displacement during postoperative follow-up, final preoperative follow-up, and in surgical specimens 28. It was reported that there was no evidence of significant clip displacement at preoperative follow-up after neoadjuvant chemotherapy (29). In a study by Abdul Fatah *et al* from 2022 entitled "Evaluation of cost-effective placement of surgical metal clips for tumor localization in BIRDAS-VI breast cancer patients undergoing neoadjuvant chemotherapy", a positive marker shift was reported in 2 patients (5.3%) (30).

In a study titled "Ultrasound-guided surgical clip placement for tumor localization in patients undergoing neoadjuvant chemotherapy for breast cancer", Yoren *et al* reported that surgical clips can replace commercial tissue markers for tumor localization in breast cancer patients undergoing NAC without displacement. Surgical clips are well tolerated and safe for the patient, readily visible on imaging, do not affect response to treatment, and are affordable 28. Abdul Fatih *et al* stated in their study that the use of breast markers before NAC is mandatory when surgical clips can safely replace tumor localization, since they are effective, safe, well tolerated and lightweight. They are visible on imaging and do not interfere with the assessment of the disorder. The therapeutic response is uneventful and the cost is low compared to commercially available breast clamps (30). In 2019, Al-Din Shalabi *et al* reported in a study entitled "Localization of malignant breast masses with clips and wires in patients undergoing neoadjuvant chemotherapy and breast conserving treatment" that clip markers can be used for tumor localization in patients with breast cancer undergoing neoadjuvant chemotherapy without deferment. Clips are patient-friendly and safe, easy to visualize on imaging, do not affect treatment response, and are cost-effective. Even if the tumor cannot be felt, it serves as a guide for the localization of chemotherapy after neoadjuvant therapy (31). The results of all these studies are consistent with the present study.

In this study, 71.8% (30) of the markers used were metal and 28.6% (12) were titanium, and 59.5% (25) of the patients used a marker and 21.4% (9) of the patients used two markers. Yoren *et al* reported that most markers used were metal (28). In the study by Abdul Fatih *et al*, all the markers used were made of metal 30, which is consistent with the present study.

Conclusion

The results of the present study showed that marking was successful in all the 42 patients and no clip migration was observed, and that the type and shape of the breast tissue marker had an influence on its visibility on ultrasound, which in turn had an impact on the localization method. This success and effectiveness is due to the innovations used in this study in the shape of the marker and its entry, and it is hoped that the results of this study will be used for better localization of the tumor.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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