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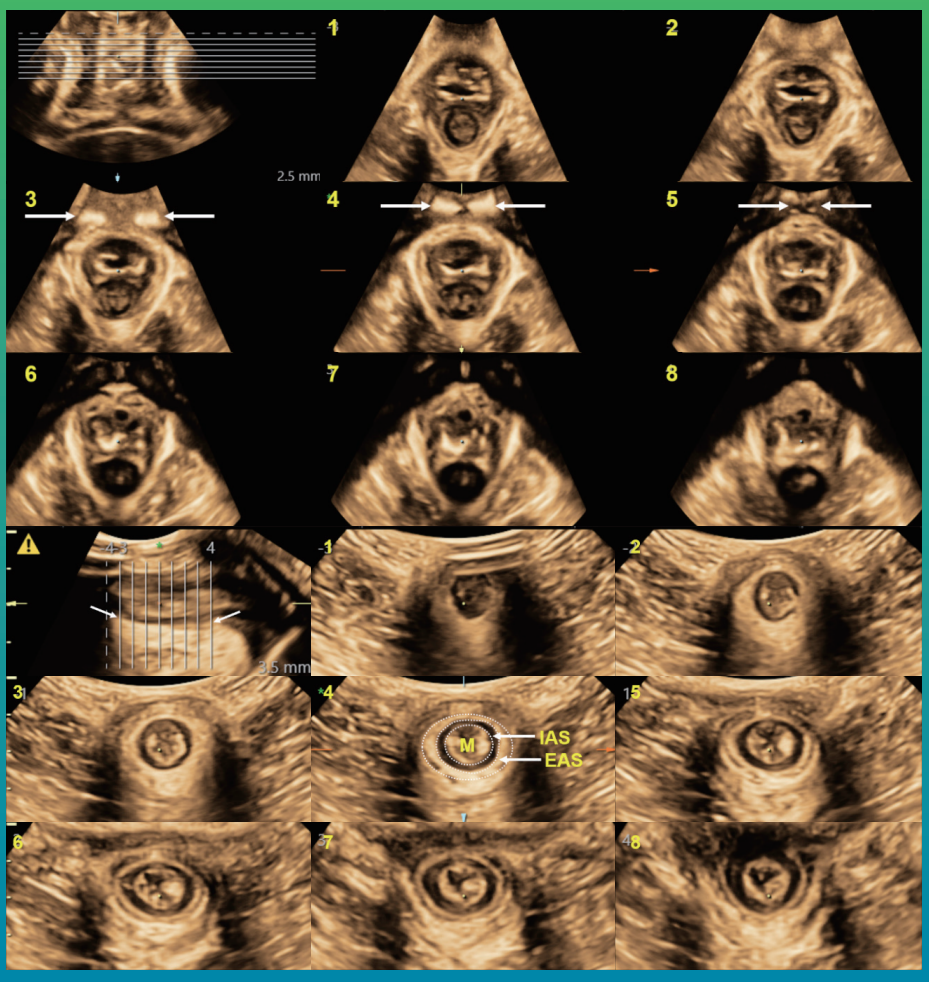

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ORIGINAL RESEARCH

Localization of Nonpalpable Breast Lumps by Ultrasound Local Coordinates and Skin Inking: A Randomized Controlled Trial

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Background and Purpose: Surgery of ultrasound-detected non-palpable breast lesions should be guided by ultrasound. Commonly radiologists localize the lesion under ultrasound preoperatively, which necessitates the availability of a localization device and may involve a substantial cost. We performed a study to prospectively assess the feasibility of ultrasound-guided localization without any special device.

Methods: Women with non-palpable benign breast masses were assigned to the "guide wire insertion" (GWI) or the "local coordinates and skin inking" (LOCSI) groups. In both groups, the tumor was marked as a shadow on the skin by the radiologist under ultrasound. In the GWI group, a guidewire was inserted, and in the LOCSI group, the local coordinates of the lesion relative to the skin and the nipple as well as its clockwise placement were reported.

Results: Overall, 29 cases were included in the study, 11 in the GWI and 18 in the LOCSI groups. In all cases, the specimen was correctly excised. The weights of the resected specimens were significantly higher with GWI; LOCSI prevented excessive tissue extraction. Clinicians reported LOCSI as "very easy" more frequently, and surgery took less time.

Conclusions: Overall, our study showed that LOCSI was feasible and can be a suitable method in areas with limited resources. We propose similar studies with a larger sample size, inclusion of malignant cases for margin assessment, and estimation of the cost-effectiveness of the technique.

Key words: Breast ultrasound; Image-guided; Non-palpable breast lesions; Preoperative localization; Guide wire

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Surgical excision of breast lesions that are not palpable but are detected by ultrasound (US) exam should be assisted by a US-guided localization procedure. If the equipment is available in the operating room and the surgeon is expert in breast US, this can be done under direct US [1]. However, more commonly the lesion should be localized under US by a radiologist, before the surgery. There are several methods of localization, which successfully locate the lesion most of the time. These include, among many old and novel methods, the use of a wire, a magnetic or radioactive seed, a radiofrequency device, a non-radioactive radar, or an isotope compound to localize the lesion [2-5]. Therefore, they are dependent on the availability of a localization device or material and comprise a substantial cost.

The standard and most common technique is guide

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wire insertion (GWI) under US [3], where a wire is placed in the tumor by the radiologist, and the surgeon excises the whole breast tissue around the wire up to a diameter consistent with the US size of the lesion, plus an extra margin as needed. Two main disadvantages of this technique among others are the necessity to schedule the patient for wire insertion in the radiology suite at a short interval before the operation [2], and the possibility of wire dislocation if the interval is long; in addition, the wire and insertion needle must be available.

In the sanction era in Iran, we had times when wires were barely available, and considering their escalating price, they were hardly affordable for many patients; also, isotope or magnetic beads are not available in Iran. A method that is used in some centers in Iran and elsewhere is localization via intralesional injection of methylene blue under US and then excision of the blue lesion [6,7]. However, this method needs rapid transfer of the patient to the operating room and initiating the surgery soon enough so that the marker is not spread around or absorbed; consequently, it does not permit any time interval between the localization procedure and the surgery [6,7].

Considering all these facts, we presumed that if a localization method did not require any equipment other than the US device, could be scheduled without strict time limits, and could accurately localize the lesion; it would save an extra time for the patient and the radiologist, ease the scheduling, and allow resection of non-palpable lesions even in hard circumstances, when equipment was scarce. Since the location of any fixed object in any space can be defined by recording its coordinates in three directions relative to a constant point, we assumed that breast lesions also could be localized by defining their distance from constant points on the breast under US guidance: the nipple and the skin for two dimensions, and the clockwise situation for the third. In addition, the localization process could be supported by designing the shadow of the lesion on the skin at the same time, as is commonly done for patients who undergo US-guided GWI in our institute.

Therefore, we performed a study to assess the feasibility of finding non-palpable breast masses using these local coordinates and skin inking (LOCSI); and compare the results with the GWI method.

Methods

This study has been approved by the Institutional Research Board and the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (Proposal Code: 97-03-218-40390 and Ethics Approval ID: IR.TUMS.VCR.REC.1397.874). Also, the study has been registered and approved in the Iranian Registry of Clinical Trials at 2019-04-06, the trial registration reference is IRCT20100706004329N8. All the participants were aware of the research protocol and signed an informed consent.

The study population consisted of women attending the Breast Clinic of Arash Women's Hospital. Inclusion criteria were female sex, age between 18 to 70 years, non-palpable benign breast masses requiring surgical excision due to clinical or histological indications, and consent to participate in the study. Exclusion criteria consisted of bra cup size above DD, very pendulous breasts, and a highly suspicious mass on imaging despite the benign histology on core needle biopsy.

The first outcome consisted of the accurate excision of the non-palpable lesion. The second outcomes were the ease of the procedure for the radiologist and for the surgeon, and the length of time of the localization procedure and the surgery.

Variables that were recorded included the Breast Imaging Reporting and Data System (BIRADS) of the breast mass according to the American College of Radiology (ACR) [8], the time of the localization procedure, the time of the operation from the incision to tumor excision, the ease of the procedure as graded by the radiologist and the surgeon, the weight of the excised specimens, the size and histology of the lesions and the accurate excision of the pertinent mass (by considering the histologic report and the follow-up US).

Eligible women were interviewed by the Breast Clinic Nurse at the time of entry in the study, and the study form including demographic data of each patient was filled. Also, the weight and height of all participants was measured recorded. Then, based on a random number table, eligible women were accidentally assigned to either Group 1 (the LOCSI Group), or to Group 2 (the GWI Group). In the latter group, GWI was performed by a breast-dedicated, board-certified radiologist under US guidance; the exact location of the tip of the wire regarding the tumor boundaries was reported to the surgeon. The location of the lesion was also marked on the skin in the supine position, arms abducted in 90 degrees to mimic the position on the operating table. Then, the lesion was excised under general anesthesia by the breast surgeon via excision of the breast tissue around the wire in a conical shape, apex up. In Group 1, the location of the lesion was marked as a shadow representing the shape and site of the tumor on the skin (skin inking) in the same position as patients in Group 2 by the same radiologist, and the local coordinates (LOC) of the last border of the lesion relative to the breast skin (depth) and the nipple were reported. Then the surgeon followed the instructions and excised that part of breast tissue, where the lesion was palpable at this stage, or

where the still non-palpable lump was expected to be. In both groups, the fascia of the pectoralis major muscle under the lesion was excised as the deep margin.

During the localization procedure in the Radiology ward, a trained radiology technician recorded the time; and then questioned the radiologist about how she rated the ease of that procedure on a 4-point scale including "very easy", "easy", "hard", and "very hard".

During the operation, a trained nurse recorded the time of the procedure. Because the technique of breast parenchyma and wound closure was very different in various patients and even included flap transfer for cosmetic results in some patients, the considered time only included the time from the first incision to the excision of the lesion in all patients. Then the ease of the excision was scored by the surgeon based on the same 4-point scale.

After excision, the specimens were processed according to standard protocols, and were then assessed histologically by a dedicated pathologist, who recorded the weights of the excised specimens, the histologic type of the lesion, and its size.

A breast US was performed 4 to 6 months later by the same radiologist to assess the disappearance of the mass.

Results

The COVID-19 conditions imposed a substantial limitation [9] on the project, because only benign masses had been considered in the inclusion criteria (in order to avoid the risk of not finding the lesion in malignant cases). During the pandemic, the indications and the number of operations for benign breast lesions was significantly reduced, and most cases of elective excision of non-malignant lumps were deferred. Therefore, we could only include 29 patients in the study. Of these, 18 were in Group 1, and 11 in Group 2. In all participants, the tumor was non-palpable, either due to its small diameter, or its deep location in a large breast.

The mean age of the patients was 37.52 ± 8.92 years, and the mean body mass index (BMI) was 24.96 ± 3.71 kg/m^2. These variables were not statistically different in the two groups, including 38.67 ± 9.25 and 35.64 ± 8.42 years (P = 0.384), and 24.93 ± 4.25 and 25.01 ± 2.81 kg/m^2 (P = 0.958) for the age and BMI in groups 1 and 2, respectively. The characteristics of the procedures and the lesions are demonstrated in Table 1. In all cases, the mass was not detected in the follow-up breast US. Considering the histologic results, all the lesions were correctly excised.

Table 1 Characteristics of procedures and lesions

Variables		LCSD Group	GWI Group	P value
Ultrasound BIRADS	2.00	2 (18.2%)	0 (0%)	0.169 [a]
	3.00	7 (63.6%)	3 (42.9%)	
	4.00	2 (18.2%)	4 (57.1%)	
Mean localization time [b] (minutes)		7.17 ± 3.62	7.10 ± 1.87	0.949 [b]
Mean excision time [b] (minutes)		10.56 ± 4.72	15.10 ± 9.14	0.088 [b]
Mean surgical specimen weight (milligrams)		15.24 ± 10.43	37.60 ± 19.24	0.001 [b]
Mean surgical specimen size [b] (cm^3)		34.89 ± 19.51	45.78 ± 26.72	0.223 [b]
Mean mass largest diameter [b] (cm)		1.19 ± 0.78	1.58 ± 0.65	0.230 [b]
Histology of resected lesion (number)	Fibroadenoma	7	2	-----
	Complex fibroadenoma	3	3	
	Fibroadenomatoid mastopathy	2	1	
	Intraductal papilloma	3	2	
	Papilloma with atypia	0	1	
	Sclerosing adenosis	1	0	
	Adenosis tumor	1	0	
	Benign phyllodes	0	1	
	Apocrine hydrocystoma [d]	0	1	
	Sarcoidosis [e]	1	0	
Procedure ease, radiologist's view	Very easy	10 (55.6%)	3 (27.3%)	0.342 [a]
	Easy	2 (11.1%)	4 (36.4%)	
	Hard	3 (16.7%)	2 (18.2%)	
	Very hard	3 (16.7%)	2 (18.2%)	
Procedure ease, surgeon's view	Very easy	11 (61.1%)	4 (36.4%)	0.157 [a]
	Easy	3 (16.7%)	6 (54.5%)	
	Hard	2 (11.1%)	1 (9.1%)	
	Very hard	2 (11.1%)	0 (0%)	

[a] Chi-Square Tests; [b] T-test; [c] Mean ± Standard Deviation; [d] In a large accessory breast; [e] In the axillary tail of a large breast; BIRADS, Breast Imaging-Reporting and Data System; GWI, guide wire insertion; LCSD, local coordinates and skin delineation

Neither the patient, nor the radiologist, surgeon and pathologist were blind to the grouping, because the type of the localization could not be hidden.

Discussion

We performed a study to assess whether excision of US-detected breast non-palpable breast masses was feasible by LOCSI, without using any specialized device, and compared it with a standard method. We showed that LOCSI was a practicable and appropriate technique.

There was no significant difference between the size of the masses in the two groups ($P = 0.230$). However, the weights of the resected specimens were significantly higher in those excised by wire localization ($P = 0.001$). This is because the surgeon had to resect breast tissue all around the wire, while in the LOCSI technique, the surgeon went directly over the designed area in the breas; and could resect less volume while finding the correct placement of the mass. Thus, LOCSI could prevent excessive tissue extraction.

Both procedures (GWI and LOCSI) were easy to perform for the radiologist in most of the cases, and the surgeon also reported to handle the surgery easily in both groups; but both clinicians identified the technique to be "very easy" in LOCSI cases more frequently than in GWI patients.

Interestingly, excision of the lesions took less time in the LOCSI technique, although the difference was not statistically significant.

Today, various techniques are being used for localization of non-palpable breast lesions, all of them can effectively assist in finding the lesion, and each has some benefits and some drawbacks [2]. GWI is the oldest technique and involves a low cost in comparison with others, although the wire and needle must be available and even this low price is not easy to cover in low-economy areas. This is an effective method and is relatively easy to perform. The main disadvantage of GWI is the necessity of organizing the schedules of the Radiology and Surgery wards, which might affect the insertion procedure due to the rush while the surgical team is waiting, and may cause a loss of time in the operating room [10,2]. Some complications have been reported for GWI, these include wire break up during patient transfer or during the operation, wire migration (both in-breast or to other body parts), unesthetic surgical results due to placement of the surgical incision on the insertion point of the guide wire [2], vasovagal episodes [11], and retained wire pieces [12]. Another technique is the injection of a radiotracer in the lesion, which is then detected by a handheld probe during the operation. The esthetic concern mentioned for GWI does not exist with this method, and the length of the localization procedure is shorter [13]. However, it is an expensive technique [14], requires availability of the tracer and the possibility to manage the radioactive waste, and the injection should take place on the same day as the surgery, or the day-before [15]. Radioactive seed localization consists of the insertion of a small titanium seed containing radioactive iodine into the lesion under image guidance. In the operative setting, a handheld detection probe is used to locate the seed [16]. As per de present guidelines, this can be performed up to one week before the operation [2], and this is a major advantage of this technique over GWI [10]. However, this method has also a few disadvantages. The probe is expensive, the seeds should be available, and the setting for handling radioactive material should be available. The emission of radioactivity limits its use in pregnant women and under MRI guidance [10], and the patient should avoid pregnant women; the placement of multiple seeds in multiple breast lesions also may disturb the intraoperative detection process [17]. Another type of localization seed is the magnetic seed, which has no time limitation after placement. The seed is detected by the surgeon via a magnetic detection probe. It has all the advantages of the radioactive seed in addition to the lack of radioactivity, but is limited by depth of the breast lesion, the interfering of iron-containing objects which limits the use of usual surgical tools and prevents its use in patients with metallic implants [18], and the high cost of the equipment. Radio-frequency reflector is another type of marker that is placed under image guidance, and is detected intra-operatively by a radiofrequency reader. The advantages are similar to the radioactive seed, and it does not include the drawbacks of radioactive activity. However, it needs costly equipment, and is not suitable for large breasts or deep breast lesions [19].

One study [20] has recently investigated a technique similar to ours; it included 155 cases and found that the technique was simple and useful for localization of breast masses. However, palpable masses were also included in the study, and the method was not compared with any other standard procedure. Also, they did not measure the time of the operation, and did not report the ease of the procedures as cited by the clinicians. In this regard, our study is the first to explore and compare the LOCSI technique with a standard method, and has shown favorable results.

Whereas all the existing methods of localization mentioned above are appropriate for non-palpable breast masses, they are all dependent on specialized equipment. The simplest is the guide wire, which by itself needs the wire and needle and has a few other disadvantages as well. The LOCSI technique we are proposing is simple, does not need any equipment except the US device, does not involve any extra cost, does not affect the postoperative esthetic result, has no time limit, has shown to be suitable for localization of non-palpable masses in

this study, and according to the physicians' scoring was very easily performed. Considering the problems with availability of specific devices and their prices in areas with limited resources, this technique can be very helpful in these places. Though, considering the accuracy of the localization and the simplicity of the technique, it might be more cost-effective than other localization methods in developed countries as well.

Our study had some limitations. First, we only included benign masses for the sake of patient safety, and thus we cannot report the status of margin excision. This has to be investigated in further studies. Second, we did not include very large breasts and pendulous breasts, and these features could be a limitation of the method also. Third, our sample size was small. We propose that similar studies with a larger sample size be performed while considering all breasts sizes and shapes, including cancerous non-palpable cases, and comparing the costs of this method with present localization techniques.

Conclusions

This study showed that LOCSI can be a suitable method for localization of US-guided non-palpable breast masses in areas with limited resources. We propose similar studies with a larger sample size, inclusion of malignant cases for margin assessment, and estimation of the cost-effectiveness of the technique.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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