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ONCOLOGY

Ultrasound-guided percutaneous microwave ablation for 755 benign breast lesions: a prospective multicenter study

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Abstract

Objectives To evaluate the clinical efficacy of microwave ablation (MWA) of benign breast lesions (BBLs) and compare the learning curves of international radiologists (IRs) and surgeons.

Methods In total, 440 patients with 755 clinicopathologically confirmed BBLs from 5 centers were prospectively enrolled from February 2014 to July 2018. Technical success, complications, volume reduction ratio (VRR), palpability, and cosmetic satisfaction after ablation were analyzed. In addition, the ablation time (AT) and energy (AE) with the number of procedures were analyzed for learning curve evaluation.

Results The mean maximum diameter was 1.7 ± 0.6 cm. The complete ablation rate reached 100%, including 45.8% lesions adjacent to the skin, pectoralis, or areola. After a median follow-up of 13.7 months, the 12-month VRR of all lesions was 97.9%, and that for 1.0- to 2.0-cm and ≥ 2.0-cm lesions was 98.6% and 96.9%, respectively. A total of 55.9% of BBLs became nonpalpable (palpable in 85.7% of cases before MWA) by both the clinician and patient. The cosmetic and minimally invasive satisfaction rates were good or excellent in 98.4% and 94.5% of patients, respectively. The median AT/cm^3 and AE/cm^3 decreased as experience increased. The AE/cm^3 of the IR with 5 years of experience was lower than that of the IR with 1 year of experience and the surgeons, while the AT/cm^3 of surgeons was comparable with that of the IR with 5 years of experience at relatively mature phase.

Conclusions Ultrasound-guided percutaneous MWA is a valuable technique for the treatment of BBLs.

Trial registration: ClinicalTrials.gov (NCT02860104)

Key Points

- *Ultrasound-guided percutaneous microwave ablation has the potential to become a valuable technique for the treatment of benign breast lesions.*
- *A skilled interventional radiologist shows a rapid improvement in mastering the technique.*

Keywords Ultrasonography · Prospective study · Learning curve · Breast neoplasms · Ablation techniques

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Abbreviations

AE	Ablation energy
AP	Ablation power
AT	Ablation time
BBL	Benign breast lesion
BI-RADS	Breast Imaging Recording and Data System
CEMRI	Contrast-enhanced magnetic resonance imaging
CEUS	Contrast-enhanced US
IR	Interventional radiologist
LC	Learning curve
MWA	Microwave ablation
US	Ultrasound
VRR	Volume reduction ratio

Introduction

Benign breast diseases such as mammary adenosis and fibroadenoma exhibit a wide spectrum of histological changes and are common among women worldwide. Such diseases usually present as multiple palpable lesions or masses [1–4]. Breast-related symptoms including nipple discharge, mastalgia, and gradual growth are the most common symptoms reported by women to obstetrician-gynecologists and surgeons [4]. Benign breast disease is also an important risk factor for a later breast cancer. A 15-year follow-up of 9087 women with benign breast lesions (BBLs) showed that 7.8% of women with benign breast diseases developed breast cancer [5]. Although definitive surgical excision is preferred by both clinicians and patients for symptomatic BBLs to alleviate anxiety regarding the potential for growth or malignancy as well as physical discomfort, surgical excision can be associated with complications such as breast volume loss, nipple distortion or displacement, and poor cosmetic outcomes such as scar formation and breast asymmetry [6]. Therefore, minimally invasive techniques have been considered as potential alternatives for the treatment of BBLs by both interventional radiologists (IRs) and surgeons and have demonstrated better cosmetic outcomes. Such techniques include vacuum-assisted percutaneous biopsy and percutaneous thermal ablation with radiofrequency, microwave, high-intensity focused ultrasound (US), laser therapy, or cryotherapy [6–8].

Although the vacuum-assisted biopsy system has been widely developed to remove BBLs, complete removal is challenged by the needle gauge and the number and size of the target lesions [9]. Advantages of ablation over the vacuum-assisted biopsy system include simultaneous treatment of multiple tumors, a shorter treatment time, and no tumor size limitation. Among these percutaneous ablation techniques, microwave ablation (MWA) has higher thermal efficiency because of the larger coagulation volume, more homogeneous shape of the coagulation zones, and higher intratumor temperatures than with radiofrequency ablation, which is the most popular ablation technique [10, 11]. In contrast to its previous clinical application in organs such as the liver, thyroid, and kidney, MWA for BBLs is a relatively new minimally invasive treatment application. Limited studies have explored the therapeutic efficacy, tumor volume reduction, and cosmetic satisfaction of MWA for BBLs [12–15]. Additionally, most were based on small sample sizes and personal and center-specific experiences of IRs.

Therefore, we conducted a prospective multicenter study to investigate the clinical outcomes, feasibility, and efficacy of US-guided minimally invasive percutaneous treatment of BBLs and compare the learning curves of IRs and surgeons.

Materials and methods

Design and overview

This multicenter, prospective study was performed from February 2014 to July 2018. Patients with BBLs who provided informed consent to participate in this study were enrolled from five Chinese hospitals in different regions. MWA was performed by two IRs (GZ.H. and J.Y., with 1 and 5 years of experience in ablation, respectively) and three surgeons (BH. C., H.L., and XP.W, all with > 10 years of experience in mastectomy and 2 months of training in MWA of breast lesions). The learning curves (LCs) of two IRs with 1 and 5 years of experience in ablation and one surgeon with > 10 years of experience in mastectomy for US-guided MWA of BBLs were evaluated to determine whether the LC can be reduced as experience increases. This multicenter study was approved by the institutional ethics committee of each center and was registered at ClinicalTrials.gov (NCT02860104). Written informed consent was received from all patients.

Patient enrollment

The inclusion criteria were as follows: (1) confirmation of benign lesions via breast biopsy; (2) lesion size of ≥ 1.0 cm; (3) the patients with tumor-related symptoms including pain, nipple discharge, and discomfort, or evident psychological pressure due to the risk of developing breast cancer; (4) patient refusal to accept other treatments as a result of the patient's physical condition or cosmetic considerations; (5) US Breast Imaging Recording and Data System (BI-RADS) score of 4 but with biopsy-proven benign results; and (6) a Karnofsky Performance Status of > 70%. The exclusion criteria are summarized in Appendix 1.1 in the Supplementary Material.

US techniques and measurements

For assessment of the size, number, and location of lesions, conventional US and contrast-enhanced US (CEUS) with the

contrast agent of Sonovue (Bracco Company) were performed in all patients using a GE LOGIQ E9 scanner (GE Medical Systems) with a 6.0–15.0-MHz matrix linear array multifrequency transducer. For patients with a maximum lesion diameter of ≥2.0 cm, or with more than three lesions, both contrast-enhanced magnetic resonance imaging (CEMRI) using a 3.0-T system (Signa Echo-Speed, GE Medical Systems) with the contrast agent of gadopentetate dimeglumine (Magnevist; Bayer Schering Pharma) and CEUS were performed. The maximum diameters of lesions in three axes were measured at CEUS, and their volumes were calculated as follows [16]:

$$\text{Volume} = \pi/6 \times \text{length} \times \text{width} \times \text{height}$$

The volume reduction ratio (VRR) was calculated as follows:

$$\text{VRR} = (\text{initial volume} - \text{final volume}) \times 100\%/\text{initial volume}$$

US-guided MWA

All newly diagnosed BBLs at each center were discussed at weekly multidisciplinary meetings to determine the optimal treatment strategy after a definitive diagnosis. After the meeting, the patients decided whether to undergo MWA.

All MWA procedures at each center were performed according to the same protocol. Details of the ablation technique for BBLs used at different centers have been described previously [13, 14]. Briefly, all patients were treated with a MWA system (KY-2000; Canyon Medical) at a frequency of 2450 MHz. The microwave unit was capable of producing a maximum power of 100 W. The active tip lengths of microwave transmission were 3 and 5 mm. All treatments were performed under local anesthesia with a 1:1 mixture of 2% lidocaine and 1% ropivacaine. For all BBLs, only one antenna was accurately placed along the long axis of the BBL for ablation via conventional US guidance. For < 2.0-cm lesions, a 20-W power output and 3-mm active tip antenna were applied. For ≥2.0-cm lesions, a 30-W power output and 5-mm active tip antenna were applied. The pull-back technique was necessary for all lesions. If the lesion was adjacent to a high-risk position such as the skin, pectoralis, or areola (distance of < 2 mm), the hydro-dissection technique was necessary to protect the adjacent tissue.

Follow-up and imaging analysis

All patients underwent CEUS at 1 month after MWA for assessment of the therapeutic effect. For patients with a maximum lesion diameter of ≥2.0 cm, or with more than three lesions, both CEMRI and CEUS were performed. Irregular peripheral nodular enhancement, which suggested the presence of a residual unablated lesion, was noted at CEUS/CEMRI. Further ablation was then considered if the patient still met the criteria for MWA. The BBLs were evaluated using conventional US at 3 and 6 months after MWA and then every 6 months to evaluate the long-term efficacy. Follow-up was terminated at the time of complete lesion absorption or the last visit. Complications, ablation variables, technique success, VRR, palpability after ablation, and cosmetic satisfaction were recorded during the post-MWA follow-up.

Technical success was defined as ablation of the target lesion according to the protocol and complete coagulation necrosis at 1 month after MWA [17]. Complications were categorized as major or minor [17] and were reported using the Society of Interventional Radiology Classification standard table so that they can be categorized consistently according to severity [18]. The patients evaluated the cosmetic outcome as excellent, good, acceptable, or poor using a self-reported questionnaire at median 13.7-month follow-up after MWA.

Learning curves

We preliminarily evaluated the LC of MWA as an emerging technology for BBLs. We investigated whether the ablation time (AT) and ablation energy (AE) per unit volume decreased with experience, and we compared the AT/cm^3 and AE/cm^3 in different periods. AE (in joules) was calculated on the basis of AT (in seconds) and ablation power (AP, in watts) as follows: AE = AT × AP. The first 150 cases at each center were used to draw the LC curve. All 150 procedures were performed by the same doctors. Initially, we divided these 150 lesions at each center into 3 groups of 50 procedures per group. We then analyzed the first 50 and last 50 MWA procedures to observe the difference in AT/cm^3 and AE/cm^3 between the initial phase and the relatively mature phase. Because the ablation and surgical experiences of the three surgeons were similar, we averaged their results.

Statistical analysis

All statistical analyses were performed using SPSS (version 19.0) and GraphPad Prism (version 5.0) software. Descriptive statistics are summarized as mean ± standard deviation or median, and categorical variables are summarized as number (percentage). Comparisons between groups were performed with Student's t test or the Mann–Whitney U test for quantitative variables and with the χ^2 test or Fisher's test for qualitative variables. According to the normality results, the tumor volume and VRR before MWA and at 3, 6, and 12 months after MWA were compared by the Mann–Whitney U test. All

statistical tests were two-sided, and differences with a p value of < 0.05 were considered statistically significant.

Data availability

We declare that all data supporting the findings of this study are included in the paper and supplementary materials. Restrictions apply to the availability of the medical data, which were used under the current study's license and are therefore not publicly available. Partial data may be available from the authors upon reasonable request and with permission of all centers of this study.

Results

Baseline characteristics

In this study, 116 patients with 394 lesions were excluded because of missing follow-up data (81 patients chose telephone follow-up and 15 patients refused both telephone and US follow-up) and lesion size < 1.0 cm. Finally, 440 patients with a median age of 29 years (range, 18–65 years) and a total of 755 BBLs were analyzed (Fig. 1). The median lesion size

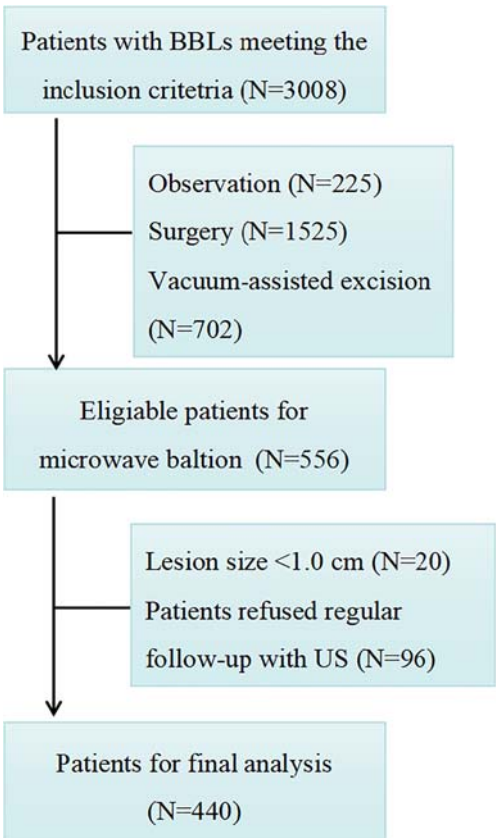

Fig. 1 Flow chart of patient enrollment in this prospective multicenter study. In total, 440 of 3008 patients were enrolled in the study. BBLs, benign breast lesions; MWA, microwave ablation

was 1.7 ± 0.6 cm (range, 1.0–6.1 cm). Among them, 75.1% (567/755) of the lesions was 1.0 to 2.0 cm in size and 34.8% (153/440) of patients had multiple lesions. In total, 305 patients with lesions of < 2.0 cm were enrolled because of obvious psychological pressure ($n = 279$), gradual growth ($n = 24$), and pain likely associated with the BBLs ($n = 2$).

All patients' diagnoses were confirmed by using core breast biopsy. The median follow-up period for the 440 patients after percutaneous MWA was 13.7 months (range, 3.1–35.9 months). The patient's descriptive statistics are summarized in Table 1.

Technique success and volume reduction

The technical effectiveness rate was 100% (755/755) through CEUS/CEMRI; one representative case is shown in Fig. 2. The median AT was 150 s (range, 13–1968 s), and the median AP was 30 W (range, 20–30 W). A total of 323 (42.8%) treatments underwent the hydro-dissection technique to protect adjacent tissues (Table 2). Most patients had a smooth recovery after ablation. The median lesion volume was 0.691 (0.084–24.421) mL before ablation. The median lesion volume was 0.282 (0.000–15.496), 0.132 (0.000–6.404), and 0.009 (0.000–3.266) mL at 3, 6, and 12 months after ablation, respectively. The overall median VRR was 58.7% (− 70.9 to 100%), 78.8% (range, − 18.8 to 100%), and 97.9% (16.7–100%) at the 3-, 6-, and 12-month follow-up, respectively (Fig. 3; Table 3). The lesion volume significantly decreased and the VRR significantly increased, and the changes in both variables remained statistically significant across different follow-up time points (both $p < 0.001$).

Stratified analysis

To evaluate the efficacy of MWA, stratification analysis was performed considering the patient age, lesion size, and lesion position. Patients were stratified into three age subgroups (18–30, 30–45, and 45–65 years), two lesion size subgroups (1.0–2.0, and ≥ 2.0 cm), and two lesion position subgroups (safe and high-risk). The high-risk position was defined as adjacent to a position such as the skin, pectoralis, or areola (distance of < 2 mm). The indexes compared in the stratified analysis were the post-ablation VRR and mass volume.

The pre-ablation and 3-, 6-, and 12-month post-ablation mass volumes and VRRs are shown in Fig. 4 and Table E1. The median VRR of 1.0- to 2.0-cm lesions at 3, 6, and 12 months after ablation was 58.8% (− 44.0 to 100.0%), 81.0% (− 18.8 to 100.0%), and 98.6% (16.7 to 100.0%), respectively. The median VRR of ≥ 2.0-cm lesions at each time point was 56.2% (− 66.7–100.0%), 76.5% (− 10.1–100.0%), and 96.9% (23.2–100.0%), respectively (Fig. 4; Table E1). Additionally, a significant decreasing trend in tumor volume was observed at 3, 6, and 12 months after ablation compared with before ablation (Fig. 4; Table E1). The Mann–Whitney U

Table 1 Baseline characters of patients

Variables	Values, *n* (%)
Age (year), median (range)	29 (18–65)
Maximum diameter	1.7 ± 0.6 cm
Number of lesions	
1.0–2.0 cm	567 (75.1%)
≥ 2.0 cm	188 (24.9%)
Number of patients	
Single	287 (65.2%)
Multiple	153 (34.8%)
Tumor location	
Left breast	371 (49.1%)
Adjacent to skin (≤ 2 mm)	96 (25.9%)
Adjacent to areola (≤ 2 mm)	60 (16.2%)
Adjacent to pectoralis (≤ 2 mm)	69 (18.6%)
Right breast	384 (50.9%)
Adjacent to skin (≤ 2 mm)	97 (25.2%)
Adjacent to areola (≤ 2 mm)	64 (16.7%)
Adjacent to pectoralis (≤ 2 mm)	71 (18.4%)
Histopathology	
Fibroadenoma	583 (77.2%)
Adenosis	109 (14.4%)
Fibroadenoma + adenosis	36 (4.8%)
Hyperplastic nodule	22 (2.9%)
Fibrous epithelioid tumor	5 (0.7%)
Reasons for ablation	
Psychological pressure	376 (85.5%)
BI-RADS 3	110 (25.0%)
BI-RADS 4	209 (47.5%)
Family history of breast cancer	57 (13.0%)
Gradually growth	46 (10.4%)
Pain	11 (2.5%)
Multiple lesions	7 (1.6%)
Mass appearance	
Palpable	647 (85.7%)
Impalpable	108 (14.3%)
Laboratory examination	
Hb (/L)	128.0 (75.0–159.0)
WBC ($\times 10^9$)	6.1 (3.3–13.6)
PLA ($\times 10^9$)	246.0 (96.0–503.0)
PT (s)	12.1 (8.1–16.4)
PTA (%)	97.0 (78.0–138.0)
INR	1.0 (0.70–1.5)
Follow-up, median (range)	13.7 (3.1–35.9)
3.0–6.0 month	44 (10.0%)
6.0–12.0 month	125 (28.4%)
> 12.0 month	271 (61.6%)

BI-RADS, Breast Imaging Recording and Data System; *Hb*, hemoglobin; *WBC*, white blood cell; *PT*, prothrombin time; *PTA*, prothrombin activity; *INR*, international normalized ratio

test for inter-group comparisons showed statistically significant differences in the VRR at 3, 6, and 12 months after ablation ($p < 0.001$) (Fig. 4).

Tumor volume was significantly different among the two groups at the 3-, 6-, and 12-month follow-ups ($p < 0.01$) (Table E1). Additionally, at the 6- and 12-month follow-ups, the VRR for ≥ 2.0-cm tumors was lower than that of 1.0- to 2.0-cm tumors ($p < 0.01$).

Similarly, a significant decreasing trend was observed in tumor volume at 3, 6, and 12 months after ablation compared with before ablation when stratified by tumor location (Fig. E1; Table E2) and patient age (Fig. E2; Table E3). See the supplementary materials for details.

Learning curve

For the LC of the IR with 5 years of experience, the AT/cm^3 and AE/cm^3 decreased as experience increased (Fig. 5). The median AT/cm^3 and AE/cm^3 decreased from 180.6 (20.1–1910.8) s and 3743.3 (402.3–57,324.8) J, respectively, at the first 50 cases to 128.3 (33.4–1427.2) s and 2610.1 (668.1–2258.5) J, respectively, at the last 50 cases (Table E4). The AT/cm^3 and AE/cm^3 were significantly different between the first 50 procedures (initial learning phase) and last 50 procedures (relatively mature phase, $p < 0.001$). In contrast, the LC of the IR with 1 year of experience rose after the first 50 procedures and then fell after 100 procedures, while the LC of the surgeon was almost flat.

The technical effectiveness rate of each group was all 100%. Although the lesions treated by the IR with 1 years of experience were smaller and safer than those treated by with 5 years of experience at relatively mature phase, the AT/cm^3 and AE/cm^3 of the IR with 5 years of experience were lower than those of the IR with 1 year of experience ($p < 0.001$) (Fig. 5; Table E5). Between the IR with 5 years of experience and surgeons, there was no significant difference in baseline at relatively mature phase. Figure 5 showed that the AE/cm^3 of the IR with 5 years of experience were lower than those of the surgeon ($p < 0.001$), while the AT/cm^3 was comparable between both ($p = 0.560$).

Cosmetic outcomes and complications

Among the whole cohort, 23.4% (103/440) and 15.5% (68/440) of patients experienced a slight sensation of pain [19] and swelling in the ablation site during the MWA procedure, respectively, whereas no one claimed the procedure to stop. After the procedure, 0.7% (3/440) of the patients sustained third-degree skin scalding that was treated with dressing for 1 month (Supplementary Fig. E3). Additionally, a total of 0.7% (3/440) and 1.6% (7/440) of patients experienced fat liquefaction and first-degree skin scalding, respectively, and all of which disappeared within the subsequent 1 week without other treatments

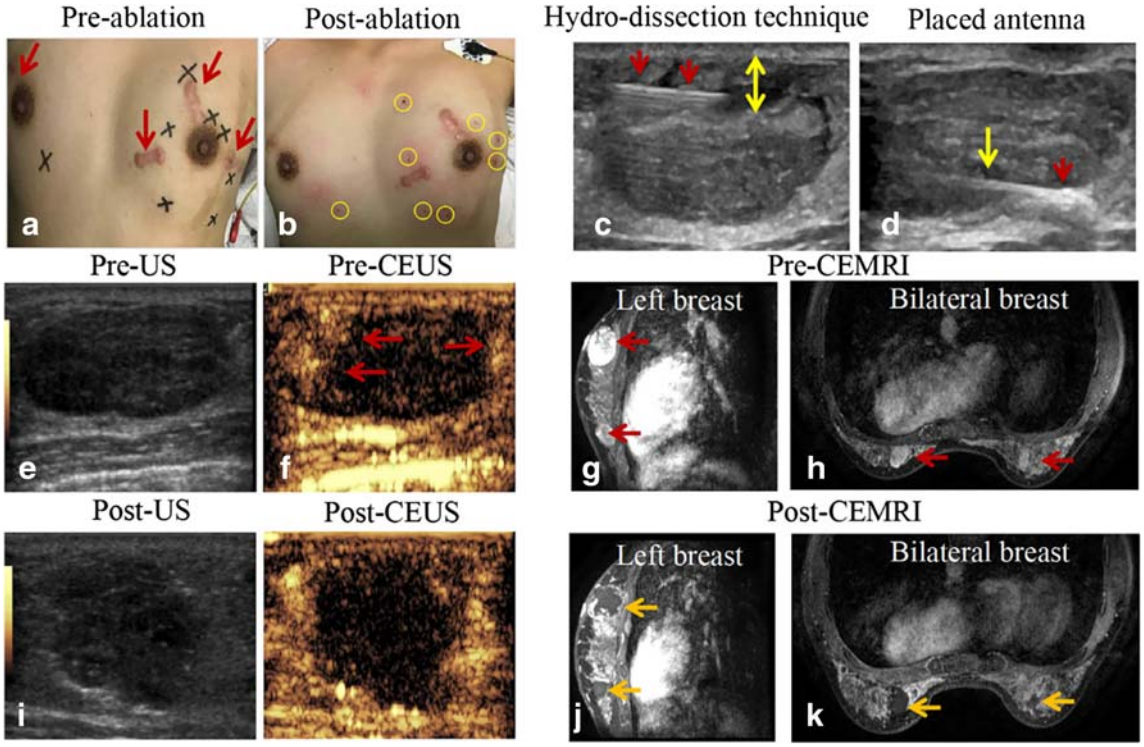

Fig. 2 Technical success of MWA in one representative case (a 20-year-old woman with eight fibroadenoma in bilateral breast). **a** Appearance of the skin before MWA. The red arrow is pointing to the scar from the surgery for fibroadenoma before 9 months. The black marker indicates the location of the breast lesions. **b** The yellow ring indicates the needle site after MWA. **c** The needle (red arrows) was inserted into the space between the lesion margin and the skin to infusion of saline, which increased the distance (yellow arrow) between the lesion and the skin. **d** US scan shows the antenna tip was placed in the deepest site of lesion increased echogenicity (red arrow) near the irradiating segment of the antenna (yellow arrow) at the beginning of MWA session. **e** US scan shows the hypoechoic lesion before MWA. **f** Contrast-enhanced US shows the lesion is hyper-enhancement (red arrow) at the margin of lesion in arterial phase. **g**, **h** Transverse contrast-enhanced MRI shows hyperintensity lesion in bilateral breast (arrow) before MWA in arterial phase. The lesion is adjacent to the skin and the size is 3.9 cm × 2.6 cm × 2.5 cm. **i** Contrast-enhanced US after MWA shows the lesion is non-enhancement in arterial phase. **j**, **k** Contrast-enhanced MRI imaging shows hypointensity treatment zone and the peripheral nodular enhancement in arterial phase. The volume of lesion decreased at third day after MWA and the size is 3.3 cm × 2.7 cm × 2.5 cm. MWA, microwave ablation; MRI, magnetic resonance imaging; US, ultrasound

(Table 2). The lesion palpability was evaluated by physical examinations. At the median 13.7-month follow-up, most of the ablated lesions had shrunk and become softened in texture, and the number of palpable lesions had significantly decreased (from 85.7% before MWA to 44.1% after MWA) (Table 2).

All patients completed the cosmetic outcome questionnaire at the median 13.7-month follow-up. Excellent, good, acceptable, and poor esthetic outcomes were recorded by 387 (88.0%), 46 (10.4%), 7 (1.6%), and 0 (0.0%) patients, respectively (Table 2). The acceptable esthetic outcomes were attributed to the scar of the needle hole for a thermal skin injury ($n = 3$) and scar diathesis ($n = 4$). With respect to the patients' satisfaction with minimally invasive ablation, 416 (94.5%) patients reported an excellent minimally invasive outcome, 20 (4.5%) reported acceptable satisfaction with continuously palpable lesions after ablation, and 4 (0.9%) reported that they would not be willing to undergo further MWA procedures because of the cost (about 2100 dollars) (Table 2).

Table 2 Microwave ablation procedure and clinical outcomes

Variable	Values, *n* (%)
Ablation time (s), median (range)	150 (13–1968)
Ablation power (W), median (range)	30 (20–30)
Hydro-dissection technique	
Yes	323 (42.8%)
No	432 (57.2%)
Complications	
Slight pain	103 (23.4%)
Fat liquefaction	3 (0.7%)
Swelling	68 (15.5%)
Skin scalding	10 (2.3%)
Degree I	7 (1.6%)
Degree III	3 (0.7%)
Palpability after ablation	
Yes	333 (44.1%)
No	422 (55.9%)
Satisfaction	
Esthetic	433 (98.4%)
Minimally invasive	416 (94.5%)

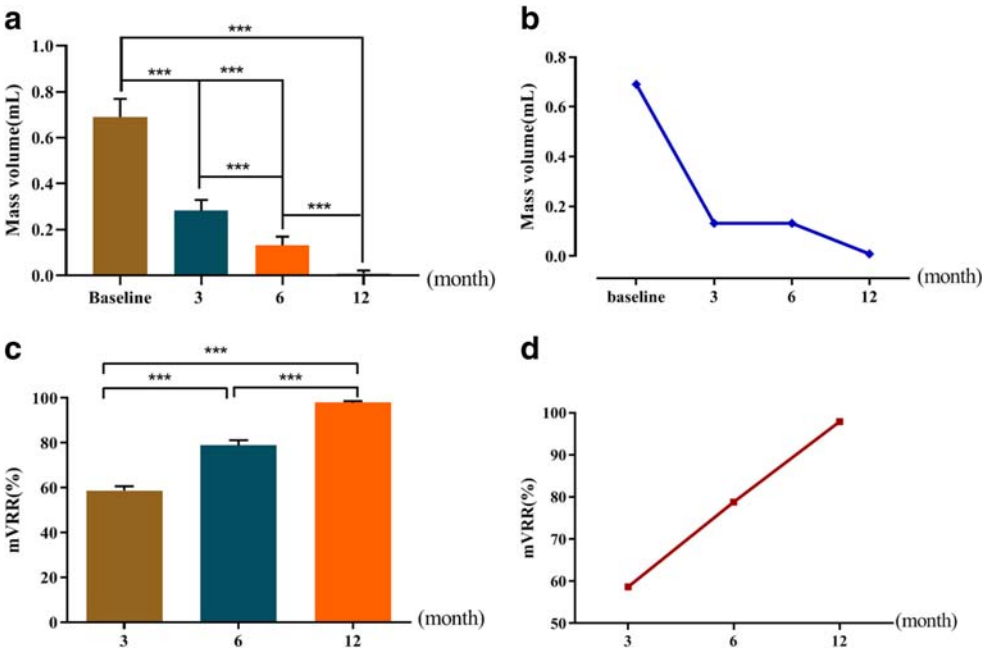

Fig. 3 BBL volume and VRR evaluation after ablation in different follow-up periods. **a** Volumes at baseline and at 3, 6, and 12 months. ***$p < 0.001$ by nonparametric test. **b** Median volume at baseline and at 3, 6, and 12 months. **c** VRRs at 3, 6, and 12 months. ***$p < 0.001$ by nonparametric test. **d** Median VRRs at 3, 6, and 12 months. BBL, benign breast lesion; VRR, volume reduction ratio

Discussion

We have herein presented our preliminary experience of MWA for management of BBLs in a prospective multicenter study. Analysis of 440 patients with BBLs who underwent 755 MWA procedures indicated that US-guided percutaneous MWA provides a technique success rate of 100% and a patient-reported post-ablation cosmetic satisfaction rate of up to 98.4%, which was consistent with those previous studies reported [12, 20]. At the median 13.7-month follow-up, 55.9% of BBLs were not palpable (palpable in 85.7% of the cases before MWA) by either the clinician or patient. At the median 13.7-month follow-up, the post-MWA lesion volume had significantly decreased and the median VRR had increased to 97.9%, which was higher than that on other thermal ablation techniques [7, 21, 22]. In total, 99.3% of the patients did not develop considerable complications after treatment by MWA. These results suggest that newer minimally invasive methods can be successfully used to manage patients with BBLs considering their extensive breast imaging, adequate degree of accuracy, and very few restrictions. Additionally, minimally invasive techniques have the potential advantage of an improved cosmetic outcome, which is consistent with the new treatment focus for breast disease given the nonmalignant nature of BBLs.

Patients with BBLs, especially young women, generally desire to preserve their breast function and avoid surgical scars [6]. Accordingly, several minimally invasive imaging-guided treatments for BBLs have been explored in recent years to further reduce invasiveness [6], providing the chance to reduce functional and cosmetic drawbacks. Additionally, the incidence of major complications after ablation is lower than that reported in the standard surgical literature [9, 23]. In contrast to other ablation therapies, microwave energy is an attractive strategy because of the specificity of the tissue ablation, which can produce higher intratumoral heating, a larger ablation zone, shorter ablation time, and stable energy delivery [9–11]. Most studies on imaging-guided breast ablation have focused on the treatment of breast cancer [24–27]; however, only six studies before the present study have reported the results of MWA for BBLs [12–15, 20, 28].

Table 3 Changes in volume and VRR of the lesions after treatment

Group	Tumor volume (median, range, mL)	VRR (median, range, %)
Baseline	0.691 (0.084–24.421)	–
After 3 months	0.282 (0.000–15.496)**@@	58.7 (− 70.9–100.0)**@@
After 6 months	0.132 (0.000–6.404)**@@	78.8 (− 18.8–100.0)**@@
After 12 months	0.009 (0.000–3.266)**@@§§	97.9 (16.7–100.00)**@@§§

VRR, volume reduction ratio

**$p < 0.01$ for comparison between baseline before ablation and different follow-up time points after ablation

@@ $p < 0.01$ for comparison between 3 months after ablation and different follow-up time points after ablation

§§ $p < 0.01$ for comparison between 6 and 12 months after ablation

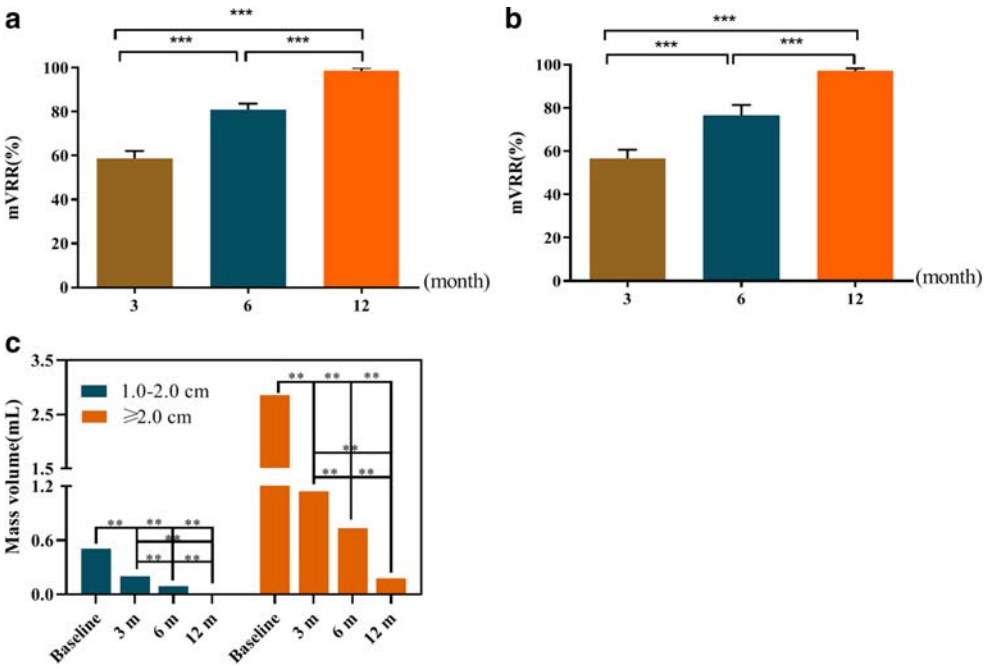

Fig. 4 Evaluation of lesion volume and VRRs stratified by lesion size at different follow-up months. **a** VRR of 1.0- to 2.0-cm lesions. **b** VRR of ≥ 2.0-cm lesions. **c** Trend of lesion volume at different follow-up months. Baseline indicates the time before the MWA procedure. ***$p <$ 0.001 by nonparametric test. MWA, microwave ablation; VRR, volume reduction ratio

Because of the superficial location of the breast and effective imaging with US, US-guided MWA is preferred for accurate guidance and effective surveillance. CEUS has the advantage of allowing for real-time assessment. If incomplete local treatment is observed, further ablation can be immediately performed during the procedure, overcoming the disadvantage of delayed MRI examination. Another important advantage of US-guided BBL ablation is that it can reduce the psychological impact on women and avoid unnecessary trauma caused by traditional surgical treatments. Finally, US-guided MWA is performed under local anesthesia, which avoided general anesthesia for hospitalized patients.

The current study is the largest prospective multicenter study to evaluate the efficacy of MWA therapy for BBLs and, importantly, is one of the only studies to compare the LCs of MWA between different specialties (IRs and

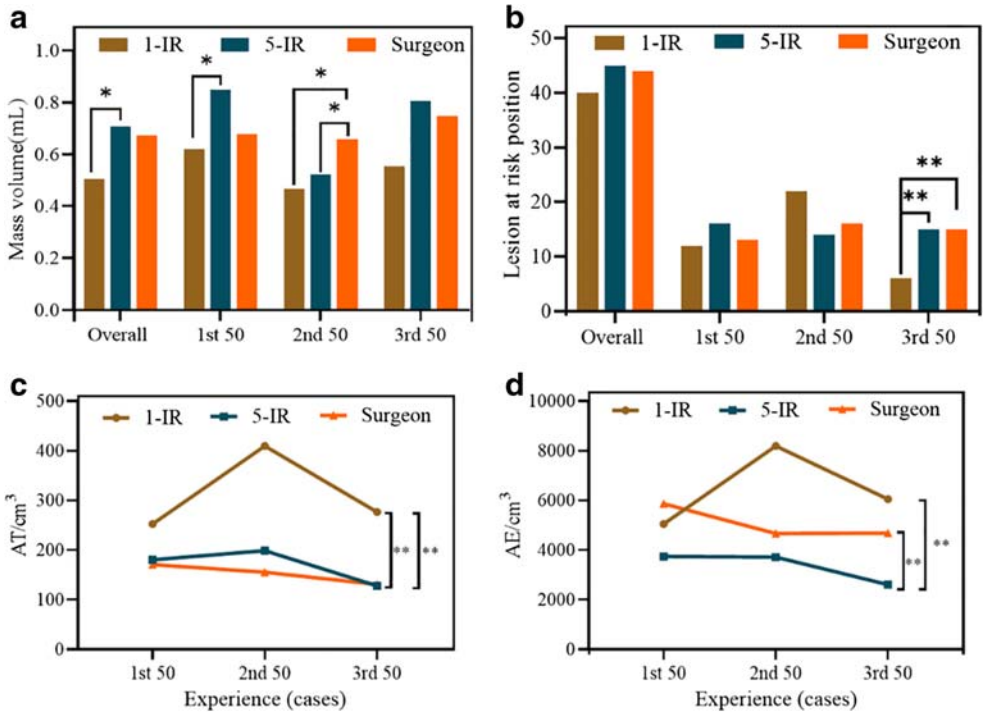

Fig. 5 Learning curves. **a** Lesion volume in the three groups. **b** The number of lesions at high-risk position in the three groups. **c** Trend of median ablation time per unit volume in the three groups (50 MWA procedures in each group). *$p < 0.05$, **$p < 0.01$ by nonparametric test. **d** Trend of median work done per unit volume in the three groups (50 MWA procedures in each group). 1-IR, interventional radiologist with 1 year of experience in ablation; 5-IR, interventional radiologist with 5 years of experience in ablation; MWA, microwave ablation; AT, ablation time; AE, ablation energy

surgeons). In total, 755 BBLs from 5 centers were analyzed, and the LCs of clinicians with different experience levels in ablation were compared. Additionally, a stratification analysis was performed considering the influence of lesion size and position. The results revealed a more significant decrease in tumor volume for smaller than larger lesions, while tumor volume's changes on that of larger lesion were also significant. And our results suggested that the lesions adjacent to the skin, pectoralis, or areola also obtained satisfactory clinical outcomes after percutaneous MWA.

In our study, 75.1% of lesions were < 2.0 cm in size. Considering the nonmalignant nature of BBLs, previous studies have suggested that most BBLs should undergo serial observation [2, 29, 30]. However, not all women are candidates for surveillance; the clinician should consider the patient's age, family history of breast cancer, gradual growth of lesions or presence of symptoms, and any data on proliferative changes in the breasts from previous biopsies [2, 3, 29–31]. Active local treatment is recommended in such cases [6, 7].

Although MWA for BLLs had satisfactory clinical outcomes in this study, it remains limited to a small number of highly experienced centers, and the feasibility of this procedure has not been reported. Thus, in our study, we preliminarily analyzed and compared the LCs of two IRs with 1 and 5 years of experience in ablation and one breast surgeon with > 10 years of experience. Comparison of the LCs showed that the IR with 5 years of experience acquired better outcomes than those of the surgeon and the IR with 1 year of experience. These findings indicate that the IR with richer experience had more comprehensive abilities in US imaging, thermal field management, and puncture technique. Therefore, the higher skill level of this IR shortened the AT and decreased the AE and complications. IRs have the potential to master the BBL ablation technique faster than surgeons. Certainly, MWA is an effective and safe procedure for the management of BBLs and is technically easy to master; even radiologists with limited experienced in tumor ablation can achieve rapid progression.

A limitation of this study is the relatively small number of patients with ≥ 2.0-cm BBLs. The main reason for this is that 77.2% (583/755) of BLLs were diagnosed as fibroadenomas in our study, while fibroadenomas are usually < 3 cm in diameter on clinical examination [30]. Another limitation is the relatively short median follow-up of 13.7 months. Therefore, a longer follow-up period is warranted to evaluate the long-term volume reduction rate for BBLs. In addition, an LC analysis in a large series of MWA procedures between doctors with different experience levels is needed. Finally, comparison between MWA and other ablation techniques is necessary to clarify the differences in efficacy.

In conclusion, our prospective, multicenter study shows that US-guided percutaneous MWA is a safe, effective, and feasible technique for minimally invasive treatment of BBLs with good cosmetic outcomes, even for patients with large and high-risk tumors. It can be mastered easily, and skilled IRs show a rapid improvement in mastering the technique. A further randomized controlled study is still needed to compare the treatment efficacy with those of other therapeutic options.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Ping Liang and Jie Yu.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported in Oncotarget and International Journal of Hyperthermia.

Methodology
- Prospective
- Observational
- Multicenter study

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