Radiology

US-guided Percutaneous Microwave Coagulation of Small Breast Cancers: A Clinical Study[1]

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Purpose: To determine the feasibility of percutaneous microwave coagulation (PMC) for the treatment of small solitary breast cancers.

Materials and Methods: With approval of the institutional ethics committee and written informed consent, 41 patients with core-needle-biopsy–proved breast cancers 3.0 cm or less in diameter accessed by using ultrasonography (US) were recruited. US-guided PMC was performed with general anesthesia, followed immediately by mastectomy. Histochemical staining with α-nicotinamide adenine dinucleotide, reduced (NADH)–diaphorase was used to determine cell viability and the extent of PMC lesions.

Results: The mean tumor volume was 5.26 cm^3 ± 3.80 (standard deviation), with a range from 0.09 to 14.14 cm^3. PMC was successfully performed in all cases, with complete tumor ablation as assessed by using US. The mean time to reach complete ablation was 4.48 minutes, ranging from 3 to 10 minutes. With microscopic examination, 37 of 41 cases (90%; 95% confidence interval [CI]: 76.9%, 97.3%) showed complete tumor coagulation, as observed by using α-NADH–diaphorase staining. Of 38 cases diagnosed with invasive ductal carcinoma, 36 cases (95%; 95% CI: 82.3%, 99.4%) showed complete tumor coagulation. Slight thermal injuries to the skin and pectoralis major muscle, which proved reversible, were found in three cases.

Conclusion: US-guided PMC of small solitary breast cancers is feasible. Nevertheless, larger-scale clinical trials are still needed to validate PMC for adoption into a standard clinical practice.

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Breast cancer is a common malignant disease worldwide, and its incidence has been increasing, especially in developing countries (1). Because of implementation of screening techniques (2), more patients with small (≤3 cm) breast carcinomas have been diagnosed with the disease. Because, for small breast carcinomas, the survival difference between mastectomy and breast-conserving surgery with combined radiation therapy is not obvious, the latter approach has been accepted as a standard of care by both patients and physicians (3). However, about 20% of patients are not satisfied with the cosmetic outcomes after such breast-conserving therapies (4–7). Thus, for patients with small breast cancers, there is a growing trend to apply minimally invasive tumor therapies (8–13), including radiofrequency (RF) ablation, high-intensity focused ultrasound (HIFU), cryotherapy, and laser therapy.

Percutaneous microwave coagulation (PMC) is a promising minimally invasive local therapy that destroys tumors in situ by means of thermal coagulation or protein denaturation. Up to now, PMC has been mainly used in the treatment of hepatic tumors and myomas in the uterus, and it was recognized as an effective therapy for these two types of tumors (14–20). To our knowledge, ultrasonography (US)-guided PMC in the treatment of breast cancer has not been reported. Compared with other minimally invasive technologies, including RF ablation and cryotherapy, PMC shows improved convection profile, larger ablation volumes, and shorter ablation times (19–22). Compared with other noninvasive techniques, including HIFU and focused microwave thermotherapy, PMC heats focal lesions with a higher temperature and shorter ablation times rather than the wider separated regions in HIFU and focused microwave thermotherapy. In addition, microwave energy can preferentially heat and damage high-water-content breast carcinomas, compared with the heating that occurs in lower-water-content normal breast tissue (23–28). PMC may be simple to perform but have higher potential for complete destruction of focal lesions (21,22,29), especially for breast cancer. Focused microwave thermotherapy (26,27), another microwave-based therapy, uses totally different instrumental designs and temperature modes compared with PMC. The energy of focused microwave thermotherapy reaches widely separated regions within the breast. Therefore, the microscopic carcinoma cells in the breast can be destroyed, which is similar to full-breast radiation therapy; however, PMC heats focal lesions with a higher temperature.

The purpose of this nonrandomized clinical study was to determine the feasibility of US-guided PMC for the local treatment of solitary breast cancer 3 cm or less in greatest diameter.

Advances in Knowledge

- US-guided percutaneous microwave coagulation (PMC) was feasible for small invasive breast cancers, with a high complete coagulation rate (95%, 36 of 38).
- Because of a low complete coagulation rate (33%, one of three), patients with ductal carcinoma in situ may be unsuitable for PMC treatment.

Implications for Patient Care

- Patient selection, evaluation of extent of breast cancers, and position of the antenna are major concerns for complete microwave coagulation of breast cancers.
- Although US-guided PMC of small breast cancers is feasible, larger-scale clinical trials are still needed to validate PMC for adoption into a standard clinical practice.

Materials and Methods

Patient Enrollment

Between February 1, 2010, and August 30, 2011, patients diagnosed with breast cancer in our hospital (The First Affiliated Hospital, Nanjing Medical University, Nanjing, China) were recruited in this prospective nonrandomized study, with the approval of the institutional ethics committee and written, informed consent.

The eligibility criteria included the following: *(a)* a single tumor without intraductal spread out of the mass, confirmed by using both mammography and US, with a distance of at least 1 cm to the skin and chest wall with the patients supine; *(b)* breast cancer proved by using core-needle biopsy; *(c)* breast cancer 3.0 cm or less in greatest diameter confirmed by using US; and *(d)* Karnofsky performance status greater than 70% (27). The exclusion criteria included the following: *(a)* patients with an extensive intraductal component in invasive cancer; *(b)* patients who were pregnant or breast-feeding; *(c)* patients with evidence of coagulopathy, chronic liver diseases, or renal failure; and *(d)* patients who wanted to undergo breast-conserving surgery. Prior to PMC, hormone receptor and human epidermal growth factor receptor 2 status were determined by using immunohistochemical analysis of tissue from a core-needle biopsy specimen.

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Abbreviations:
CI = confidence interval
DCIS = ductal carcinoma in situ
HIFU = high-intensity focused ultrasound
IDC = invasive ductal carcinoma
NADH = nicotinamide adenine dinucleotide, reduced
PMC = percutaneous microwave coagulation
RF = radiofrequency

Author contributions:
Guarantor of integrity of entire study, S.W.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, W.Z., Y.N., S.W.; clinical studies, W.Z., X.Z., X.L., Q.D., Ling Chen, Y. Zhang, Y.X., Lin Chen, Y. Zhao, S.W.; statistical analysis, W.Z., X.Z., Y.N., Y.X., S.W.; and manuscript editing, W.Z., Q.D., Y.N., Y. Zhang

Potential conflicts of interest are listed at the end of this article.

Instrumentation

The microwave delivery system consists of a microwave generator, a flexible coaxial cable, and an internally water-cooled-shaft antenna. The microwave irradiation frequency is 2450 MHz. Output powers can be modulated from 10 to 100 W, and 40 W was selected in this study according to the previous PMC studies (13,16,30) and our own experience.

As shown in Figure E1 (online), the cooled-shaft antenna (2 mm in diameter) used for PMC therapy consists of a 10-cm-long cable connection portion, and a 15-cm-long shaft. The projection to microwave generator and both entrance and exit of cooling water are located in the connection port. The irradiating segment of 2 mm in length is 1 cm away from the shaft tip. The cooling system consists of two lumens in the shaft for circulating the cooling water to the tip of the shaft from a 500-mL bottle, driven by a peristaltic pump.

US-guided PMC

Preoperative US evaluation and interventional breast US were performed by one radiologist with 10 years of experience in breast US. All PMC procedures were performed in the operating room by surgeons (X.Z. and X.L., with more than 15 years of experience in breast surgery). After induction of general anesthesia, the patient was positioned supine on the operating table. US was used to identify the lesion and measure it in three dimensions (Fig E2 [online]). An image in the maximum transverse axis, which was vertical of the longest axis, was acquired. The plane including the above two axes (the longest axis of the tumor and the maximum transverse axis vertical of the longest axis, respectively) was recognized as the maximum plane, and the two axes were considered as the long axis and short axis, respectively.

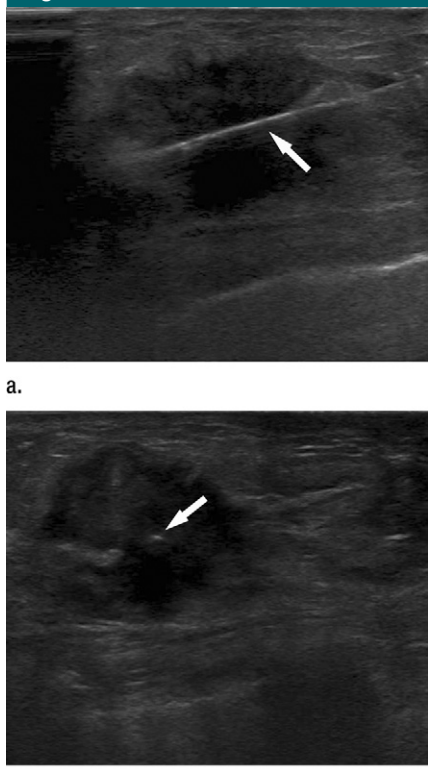
After a small skin incision was made, the antenna was placed into the tumor, with US guidance, along the longest axis. Because the estimated coagulation zone was elliptically shaped (Fig E3 [online]), the tumor should be covered by the estimated coagulation zone properly. Two-dimensional examination of the antenna position was critical (Fig 1). The needle antenna was connected to the microwave generator through a flexible coaxial cable, and the two cooling-water tubes were connected. After testing the cold-water (4°C) cycling system, the PMC procedure was started for 3–10 minutes to cover the entire tumor. During the procedure, the antenna should not be moved, and continual US monitoring was performed to evaluate the effect of tissue coagulation. The echogenicity of the tumor was assessed with US during the PMC procedure and 5 minutes after the procedure. The echogenicity of the deep portion of the tumor may be influenced by the superficial echogenicity, so US monitoring of the superficial portion may be more accurate. When the tumor disappeared completely with US, the PMC therapy was stopped. A special antenna with temperature sensor (Nanjing Yigao Microwave Electric Institute, Nanjing, China) was used to measure the temperature 5 mm from the site of irradiation once a minute for the first three cases.

After PMC treatment, the antenna was removed. The prescheduled mastectomy and axillary lymph node dissection were performed immediately. Patients were monitored during the PMC treatment, the following surgery, and the 2 days after surgery for any complications that might be induced by the interventions. The complications were assessed by the same breast surgeons.

Pathologic Evaluation

After surgery, the breast specimen was sliced sequentially into 5-mm sections involving the treated tumor and adjacent tissue. Half of the sections were fixed in formalin, embedded in paraffin, sectioned into 4-μm slices, and stained with hematoxylin-eosin. The other half of the sections were snap-frozen in liquid nitrogen. Cryosections of 8 μm thick were made for cell viability staining with α-nicotinamide adenine dinucleotide, reduced (NADH)–diaphorase. The frozen unfixed sections were mounted on glass slides and covered with 150 μL of incubation media for 20 minutes at room temperature. This incubation medium was prepared as described previously (9). After incubation, viable cells show an intense blue cytoplasmic pigment, which is absent in nonviable cells. A section of normal muscle was used as a positive control, and a section of muscle that had been heated to 100°C was used as a negative control. Macroscopically, a clear and sharp margin of the coagulation zone was not seen in all cases, so the maximum extent of the coagulation zone could not be measured. Therefore, the area of α-NADH–diaphorase staining negative

Figure 1



a.

b.

Figure 1: Intraoperative US in 51-year-old woman demonstrates the successful placement of the antenna before PMC. **(a)** Longitudinal sonogram shows centrally placed antenna (arrow) in the tumor. However, it is not possible to see the irradiating segment. **(b)** Coronal sonogram confirms the central placement of the antenna (arrow) within the tumor. The longitudinal and coronal two-dimensional sonographic examinations suggested that the antenna was located in the center of the tumor.

reaction was measured microscopically as the minimum extent of the coagulation zone. The size of tumors and the size of α-NADH–diaphorase staining negative reaction area were evaluated and recorded under the microscope by two pathologists (Y. Zhang and Y.X., with more than 10 years of experience in breast pathologic examination) independently. The antenna position in the pathologic specimen was also assessed. Disagreements were resolved with consensus opinion.

Data and Statistical Analysis

Numerical data were reported as the mean ± standard deviation. A clear and sharp margin of the coagulation zone was not seen in all cases, so the area of α-NADH–diaphorase staining negative reaction was defined as the minimum extent of the coagulation zone. The volume of coagulation was defined as the calculated volume, V, of an ellipsoid obtained by using the long axis (r_1) and short axis (r_2) ($V = 4\pi[r_1/2][r_2/2]^2/3$) (16). The volume of the tumor was calculated by using the three-dimensional axis (a, b, c) with the equation $V = 4\pi(a/2)(b/2)(c/2)/3$. The paired t test was performed to test the difference between the greatest diameter of the tumor at pathologic examination and US, and it was used to test the difference between the minimum coagulation volume and the mean tumor volume. The rate and 95% confidence interval (CI) were used to assess the effectiveness of the PMC treatment. The binomial exact test was applied to calculate the 95% CI. All statistical analyses were performed by using software (Stata version 11.0; StataCorp, College Station, Tex), and a significant difference was concluded for $P < .05$.

Results

Baseline Characteristics

Of the 43 patients enrolled in this study, one patient was excluded because one cooling water tube in the antenna leaked; another patient was excluded because the margin of the tumor at US was not clear. The vague margin at US might have been caused by prior core-needle biopsy. In the remaining 41 patients, the tumor was successfully identified and treated, and the clinical data of these patients are shown in the Table. The mean age was 55.5 years ± 11.4 (standard deviation), with a range of 38–78 years, and the mean longest tumor size assessed by using US was 2.0 cm ± 0.5, with a range of 1.0–3.0 cm. The tumor was found in the left breast in 19 patients and in the right breast in the other 22 patients. Of these 41 patients, 25 (61%) were estrogen receptor positive, 19 (46%) were progesterone receptor positive, and nine (22%) were human epidermal growth factor receptor 2 (HER2) positive.

Therapeutic Response

During the PMC procedure, there was a gradual and diffuse increase in the echogenicity of the tumor from the irradiating segment to the whole tumor (Fig 2). At the end of PMC, the tumor completely disappeared at US. The mean duration to reach complete ablation at US was 4.48 minutes ± 2.03, with a range from 3 to 10 minutes. However, after PMC, the echogenicity of the treated tumor decreased gradually and returned to the level prior to treatment in about 5 minutes. In two cases of invasive ductal carcinoma (IDC), the antenna was not placed very satisfactorily at the time of pathologic assessment, and, therefore, the tumor was untargeted by using PMC in the procedure. The temperature near the irradiating segment increased from 63.1°C (PMC for 1 minute) to 91.0°C (PMC for 3 minutes) in the first case, from 62.3°C (PMC for 1 minute) to 91.3°C (PMC for 3 minutes) in the second case, and from 64.8°C (PMC for 1 minute) to 90.4°C (PMC for 3 minutes) in the third case.

Pathologic Outcomes

Histopathologically, all 41 patients were diagnosed with ductal carcinomas; 38 (93%) patients were diagnosed with IDCs and three (7%) were diagnosed with ductal carcinoma in situ (DCIS) by using core-needle biopsy, and 25 patients (61%) were node negative. However, a small area of invasive component was found in three DCIS cases in mastectomy specimens; in one IDC case (core-needle biopsy), DCIS component was found in a mastectomy specimen with a small area (Table). With core-needle biopsy, the stage of these three DCIS cases was underestimated. No additional tumors were found in the mastectomy specimen at pathologic examination. In gross specimens, the PMC-treated area appeared as a firm whitish zone surrounded by adipose or breast tissue (Fig 3). The coagulated area was easily identified in all lesions; however, the margin between the coagulated and viable breast tissue was not clear in 23 cases. The hyperemic area was clearly visible around the coagulated area in 18 cases (Fig 3). There was no charring observed in any case.

Hematoxylin-eosin staining of the coagulated lesions revealed a spectrum of changes, including pyknotic nuclei, spindling, cell heteropolarity, and cell shrinkage (Fig 4). However, the structure of the ablated tumor tissues was still intact, and no tumor disintegration was observed as a consequence of sudden tissue thermal coagulation. Although the tumors were completely ablated, the shape of tumor cells was still clear and appeared almost unchanged (Fig 4), which were defined as "ghost" phenomena. Similar ghost phenomena were observed in other studies (9,31,32). The mean greatest diameter of the tumor was 2.52 cm ± 0.80 (range, 1.0–4.0 cm). The mean greatest diameter at pathologic examination was larger than that assessed by using US (2.0 cm ± 0.5) ($P < .001$).

α-NADH–diaphorase staining revealed a negative reaction in 37 of 41 cases (90%; 95% CI: 76.9%, 97.3%), confirming complete thermal damage to the lesions (Fig 5). However, in the other four cases, staining revealed a partly positive reaction, indicating incomplete thermal injury. Of three DCIS cases, in only one (33%; 95% CI: 0.8%, 90.6%) was complete ablation achieved. In 38 IDC cases, complete ablation was achieved in only 36 (95%; 95% CI: 82.3%, 99.4%). In the other two cases

Data of Patients Treated with PMC

		Pathologic Examination					Minimum Coagulation		
Patient No./Age (y)	Tumor Size on US Scan (cm)	Core-Needle Biopsy Results	Tumor Size (cm)	Tumor Volume (cm^3)	ER/PR/ HER2	Treatment Time (min)	Size (cm)	Volume (cm^3)	Complete Ablation
1/40	2.3 × 1.4	IDC	2.5 × 2.0 × 1.5	3.93	−/+/−	10	2.5 × 2.0	5.24	Yes
2/38	2.6 × 0.8	IDC	4.0 × 2.5 × 2.0	10.47	−/−/+	10	4.0 × 2.5	13.09	Yes
3/51	2.3 × 1.5	IDC	3.5 × 3.0 × 2.5	13.74	−/+/+	10	3.5 × 3.0	16.49	Yes
4/50	1.8 × 1.6	IDC	2.5 × 2.0 × 2.0	5.24	−/−/−	9	2.5 × 2.0	5.24	Yes
5/53	1.0 × 0.9	DCIS, Mic*	3.0 × 2.5 × 2.0	7.85	−/−/+	4	3.0 × 2.5	9.82	Yes
6/53	2.2 × 1.2	IDC	1.5 × 1.3 × 1.0	1.02	+/−/+	4	2.5 × 1.5	2.95	Yes
7/58	1.9 × 1.1	IDC	3.0 × 1.5 × 1.0	2.36	+/+/−	3	3.0 × 1.5	3.53	Yes
8/69	1.4 × 1.1	IDC	2.0 × 1.5 × 1.5	2.36	−/−/+	3	2.0 × 1.5	2.36	Yes
9/57	2.0 × 1.8	IDC	3.0 × 2.0 × 2.0	6.28	−/−/−	3	3.0 × 2.0	6.28	Yes
10/57	2.0 × 1.7	IDC	3.0 × 3.0 × 3.0	14.14	+/+/−	4	3.0 × 3.0	14.14	Yes
11/58	2.5 × 1.6	IDC	3.0 × 2.5 × 2.0	7.85	−/−/+	3	3.0 × 2.5	9.82	Yes
12/44	1.8 × 1.4	IDC	2.0 × 1.5 × 1.3	2.04	+/+/−	3	2.0 × 1.5	2.36	Yes
13/72	1.5 × 1.5	IDC	2.0 × 2.0 × 1.0	2.09	+/+/−	3	2.0 × 2.0	4.19	Yes
14/47	2.3 × 2.0	IDC	3.0 × 2.5 × 2.5	9.82	+/+/−	3	3.5 × 2.5	9.82	Yes
15/44	2.5 × 1.9	IDC	2.5 × 2.0 × 2.0	5.24	−/−/−	4	2.5 × 2.0	5.24	Yes
16/58	2.7 × 2.3	DCIS, Mic*	3.0 × 3.0 × 2.0	9.42	−/−/+	3.5	3.0 × 3.0	14.14	No
17/46	1.5 × 1.2	IDC	3.0 × 3.0 × 2.0	9.42	+/−/−	4	3.0 × 3.0	14.14	Yes
18/76	1.9 × 1.8	IDC	2.0 × 2.0 × 1.5	3.14	+/−/−	5	2.0 × 2.0	4.19	No†
19/38	1.6 × 1.5	IDC	2.5 × 2.5 × 2.0	6.55	−/−/−	6	2.5 × 2.5	8.18	Yes
20/77	2.0 × 1.1	IDC	2.5 × 2.5 × 2.0	6.55	+/+/−	7	2.5 × 2.5	8.18	Yes
21/76	2.5 × 0.7	IDC, DCIS*	2.0 × 1.5 × 1.0	1.57	−/−/−	4.5	2.5 × 1.5	2.36	Yes
22/71	1.2 × 1.1	DCIS, IDC*	3.0 × 2.5 × 2.5	9.82	+/+/−	3.5	2.0 × 1.2	1.51	No
23/49	1.9 × 1.7	IDC	3.5 × 2.5 × 2.5	9.82	−/−/−	6	4.0 × 2.5	13.09	Yes
24/43	2.4 × 1.6	IDC	3.0 × 2.0 × 1.5	4.71	+/+/−	6	3.0 × 2.0	6.28	Yes
25/48	2.5 × 1.9	IDC	2.5 × 1.8 × 1.0	2.36	+/+/−	5	3.0 × 2.0	6.28	Yes
26/54	1.9 × 1.5	IDC	2.0 × 2.0 × 1.5	3.14	+/+/−	4	3.0 × 2.0	6.28	Yes
27/59	1.5 × 1.4	IDC	4.0 × 2.0 × 1.5	6.28	+/+/−	4	4.0 × 2.0	8.38	Yes
28/48	2.3 × 1.5	IDC	3.5 × 3.0 × 2.0	11.00	−/−/−	5	3.5 × 3.0	16.49	Yes
29/49	1.8 × 1.6	IDC	2.0 × 1.7 × 1.5	2.67	+/−/−	5	3.0 × 2.0	6.28	Yes
30/59	1.1 × 1.0	IDC	1.0 × 0.5 × 0.5	0.13	−/−/+	3	2.0 × 1.5	2.36	Yes
31/61	2.5 × 1.7	IDC	2.0 × 1.5 × 1.0	1.57	+/−/−	4	3.0 × 2.0	6.28	Yes
32/73	1.1 × 1.1	IDC	1.0 × 0.6 × 0.3	0.09	+/+/−	3	1.5 × 1.0	0.79	Yes
33/56	1.7 × 0.9	IDC	1.2 × 0.8 × 0.6	0.30	+/−/−	3	2.0 × 1.5	2.36	Yes
34/57	1.3 × 1.0	IDC	1.0 × 0.8 × 0.8	0.34	−/−/+	3	1.0 × 1.0	0.52	Yes
35/54	2.8 × 1.2	IDC	1.5 × 1.5 × 1.5	1.77	+/+/−	3	3.0 × 2.0	6.28	Yes
36/78	2.2 × 1.6	IDC	2.3 × 2.0 × 2.0	4.82	+/−/−	4	3.0 × 2.0	6.28	Yes
37/41	2.0 × 1.5	IDC	2.0 × 2.0 × 1.6	3.35	+/+/−	3	3.0 × 2.0	6.28	Yes

(continues)

(continued)

Data of Patients Treated with PMC

Patient No./Age (y)	Tumor Size on US Scan (cm)	Pathologic Examination			ER/PR/ HER2	Treatment Time (min)	Minimum Coagulation		Complete Ablation
		Core-Needle Biopsy Results	Tumor Size (cm)	Tumor Volume (cm^3)			Size (cm)	Volume (cm^3)	
38/48	1.7 × 1.1	IDC	2.5 × 2.0 × 1.5	3.93	+/+/−	3	2.0 × 2.0	4.19	No†
39/49	2.5 × 1.4	IDC	4.0 × 2.2 × 2.0	9.22	+/+/−	3	4.0 × 2.2	10.14	Yes
40/70	2.3 × 2.0	IDC	3.0 × 2.0 × 2.0	6.28	+/2/2	4	3.0 × 2.0	6.28	Yes
41/48	3.0 × 1.2	IDC	3.0 × 2.0 × 1.0	3.14	+/+/−	3	3.0 × 2.0	6.28	Yes

Note.—The mean age for all 41 patients was 55.5 years ± 11.4, the mean tumor size at US was 2.0 × 1.4 cm, the mean tumor size at pathologic examination was 2.52 × 1.99 × 1.62 cm, the mean tumor volume at pathologic examination was 5.26 ± 3.80 cm^3, the mean treatment time was 4.48 minutes ± 2.03, the mean minimum coagulation size was 2.77 × 2.06 cm, and the mean minimum coagulation volume was 6.94 cm^3 ± 4.27. ER = estrogen receptor, HER2 = human epidermal growth factor receptor 2, Mic = microinvasive, − = negative, + = positive, PR = progesterone receptor.

* The labeled pathologic finding was found in the mastectomy specimen.

† Poor position of the antenna at pathologic examination.

with unsuccessful ablation, failure occurred as a result of poor position of the antenna. Furthermore, there were six cases with the greatest diameter larger than 3.0 cm at final pathologic examination in these 38 patients, and in all of them, complete ablation was achieved (Table).

The mean diameter of the long axis in the coagulation zone was 2.77 cm ± 0.68 (range, 1.0–4.0 cm), and the mean diameter of the short axis was 2.06 cm ± 0.53 (range, 1.0–3.0 cm). The mean minimum coagulation volume (6.94 cm^3 ± 4.27) was larger than the mean tumor volume (5.26 cm^3 ± 3.80) ($P < .001$).

Adverse Events

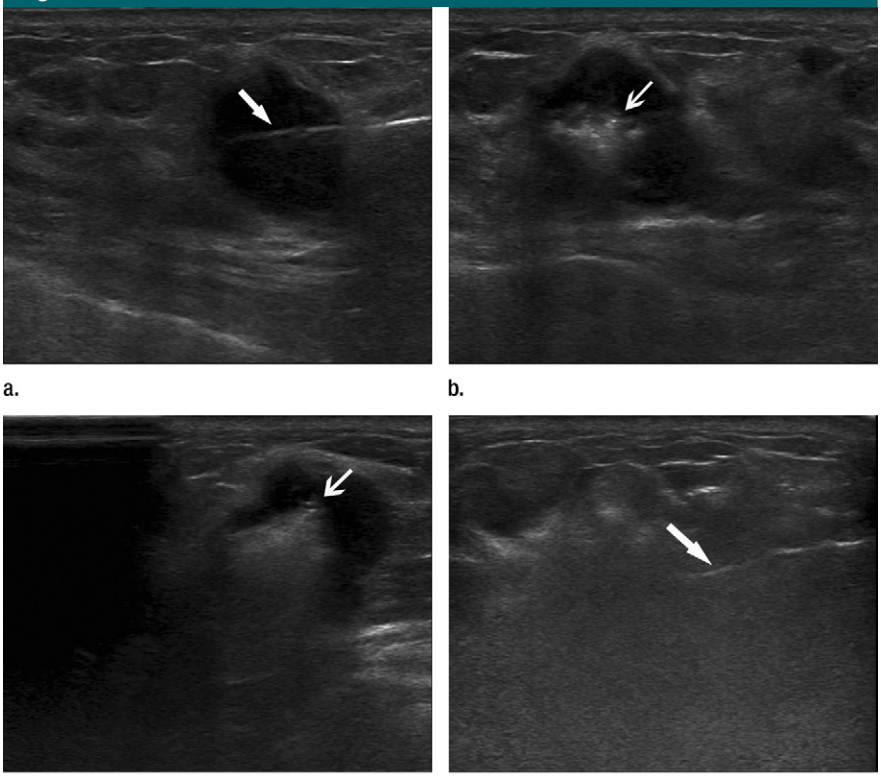
Minor complications were encountered with PMC. In these 41 patients, an epidermal burn measuring 1.5 cm in greatest dimension in the skin overlying a treated tumor in the mastectomy specimen was observed in one patient, and slight thermal injury to the pectoralis major muscle measuring 2.0 cm in greatest dimension was observed in another two patients. No necrosis of the skin flaps, infection, or other adverse effects were noted in all 41 patients during and after the procedure.

Discussion

We report successful experience of PMC in the ablation of small breast cancers. In 38 patients with invasive breast cancer, complete tumor coagulation was achieved with minor complications in 36 cases. Our results suggest that this procedure is feasible. However, there are still potential clinical problems to be settled for PMC to be considered as a standard treatment.

A high rate (95%, 36 of 38) of complete ablation was observed in IDC cases in our study, which was not lower than the rate of other minimally invasive therapies. A 90% rate for complete tumor ablation was observed in RF ablation (9,10), while cryotherapy showed 78% complete tumor ablation (29). Lower rates of complete ablation were reported in other therapies, including laser therapy (70%), HIFU

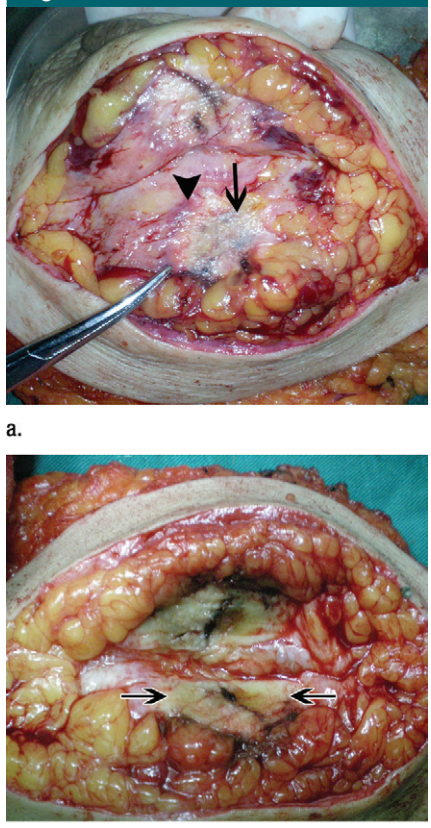
Figure 2



a. b. c. d.

Figure 2: Intraoperative longitudinal US images in 50-year-old woman during a PMC procedure for ablation of spheroid-shaped tumor. **(a)** Sonogram shows successful placement of the antenna (arrow). **(b)** Sonogram shows increased echogenicity of the tumor (arrow) near the irradiating segment of the antenna at the beginning of PMC session. **(c)** Sonogram shows the area with increased echogenicity covering approximately one-half of the tumor (arrow) in the middle of PMC session. **(d)** Sonogram shows the tumor obscured by an echogenic area, with the antenna (arrow) still clearly visible at the end of the PMC session. The sonograms show a gradual and diffuse increase in the echogenicity of the tumor from the irradiating segment to the whole tumor.

Figure 3



a. b.

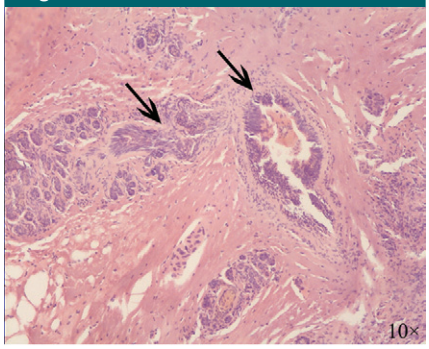
Figure 3: Macroscopic appearances of excised specimens after PMC therapy. **(a)** In 47-year-old woman, the coagulation area (arrow) can be easily identified, and the hyperemic area (arrowhead) is clearly visible around the coagulation area. **(b)** In 40-year-old woman, the coagulation area (arrows) is easily identifiable, but the margin between coagulated and viable breast tissues is less discernible.

(53.5%–100%), and focused microwave thermotherapy (10.5%) (26,27,33–35). Previous studies (20,22) and our study showed that PMC could increase the temperature quickly, and a shorter session might be needed for complete ablation. The average treatment time was 30 minutes in laser therapy of small breast cancers (33), and more than 1 hour was needed with HIFU (34–36). The treatment time was 10–15 minutes for complete RF ablation (9,10). In our study, the mean ablation time was only 4.5 minutes, which was also less than that for focused microwave thermotherapy (50–206 minutes) (26–28).

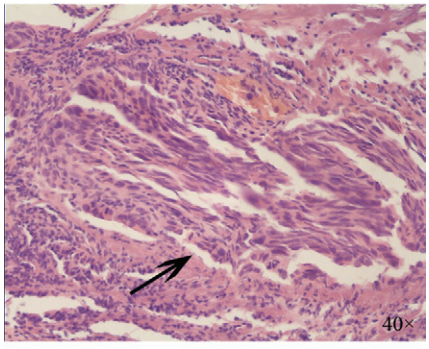
Researchers in previous studies suggested that PMC can cause a large coagulation volume (21). The mean greatest diameter of the tumor in our study was 2.5 cm, which was larger than that reported in the studies about other minimally invasive therapies (9,12,27,29,33,37,38), including RF ablation (mean, <2.0 cm; range, 0.6–3.0 cm), cryotherapy (mean, <1.5 cm; range, 0.5–2.0 cm), focused microwave thermotherapy (mean, 1.8 cm; range, 0.7–3.8 cm), and laser therapy (median, 1.3 cm; range, 0.5–2.3 cm). Our study results indicated that PMC may cause a large coagulation volume with shorter ablation time. Indeed, PMC is convenient, simple to perform, but more effective, and, hence, may be a more promising minimally invasive therapy.

For widespread clinical introduction of PMC, several concerns should be considered. First, patient selection before PMC is very important. To obtain complete ablation and prevent adverse events, only a small single tumor with a distance of at least 1 cm to the skin and to the chest wall was selected for minimally invasive therapies (9,10,12,26,29,33,35,37). Furthermore, patients with an extensive intraductal component in invasive cancer should not be considered as suitable candidates for PMC. In this study, both US and mammography were used to exclude an extensive intraductal component and to select patients for PMC.

Figure 4



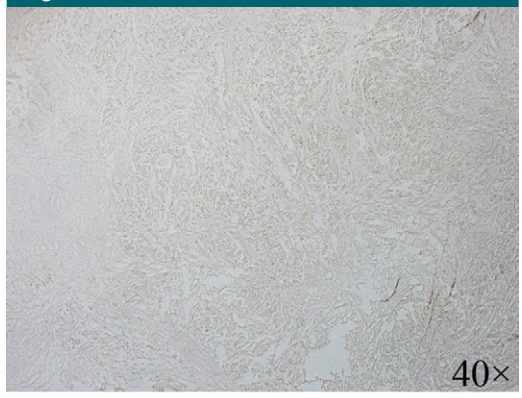
a.



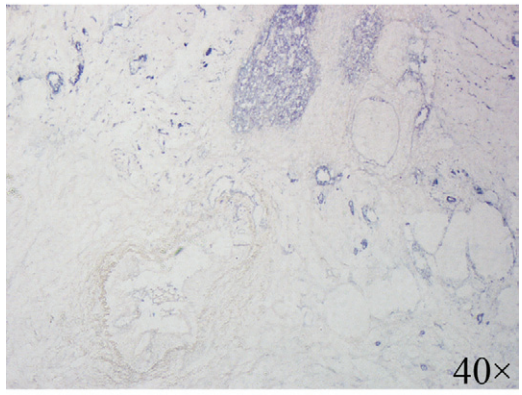
b.

Figure 4: Photomicrographs in 38-year-old woman from ablated tissue of IDC display pyknotic nuclei, cell heteropolarity, spindling, and cell shrinkage (arrows), with grossly intact structures in the two sections. **(a)** The structure of the ablated tissues (including the normal breast tissue and breast tumor) is intact and appears unchanged; however, the changes of breast cancer cells are not very clear (arrows); and **(b)** the structure of the ablated IDC tissue is intact with a spectrum of clear cell changes (arrow). (Hematoxylin-eosin stain.)

Figure 5



a.



b.

Figure 5: Photomicrographs from ablated tissue confirm effectiveness of PMC therapy. **(a)** Section of ablated IDC tissue shows a negative reaction to α-NADH-diaphorase stain or no viable tumor cells present after PMC therapy in 50-year-old woman. **(b)** Tissue section gained from the periphery of the tumor shows a sharp demarcation between the α-NADH-diaphorase–negative tissue (area at lower left) and the α-NADH-diaphorase–positive breast tissue (blue-stained area at upper right) in 76-year-old woman.

Magnetic resonance (MR) imaging may be useful in excluding an extensive intraductal component. However, both mammography and MR imaging may fail to depict a low-grade extensive intraductal component (10). Core-needle biopsies to assess the tissue surrounding the tumor for the presence of an extensive intraductal component may be helpful. In addition, three of 41 patients were diagnosed with DCIS by using core-needle biopsy. In two of these three cases, ablation was not complete, so patients with DCIS may be unsuitable for the PMC treatment.

Second, our results suggested that use of US may lead to underestimation of the microscopic extent of the tumor, which can cause incomplete ablation. The same results were reported in a previous study (39). MR imaging has proved useful in the evaluation of the extent of breast cancers preoperatively (39). Preferably, MR imaging should be applied before PMC to validate the extent and location of the tumor. Furthermore, MR imaging has also been applied to guide some minimally invasive therapies for breast cancers (11,40), which may be more sensitive and effective but at a price of higher costs and increased technical complexity. Third, the position of the antenna is another major concern to obtain complete ablation. Poor position will lead to an unsuccessful ablation. In our study, the PMC procedures were performed by surgeons experienced in breast surgery. However, there still were two IDC cases with poor position of the antenna, which led to unsuccessful ablation. Close attention should be paid to the examination of the antenna position after the antenna is placed into the tumor.

Our study had limitations. First, because we performed mastectomy and axillary lymph node dissection immediately after the PMC procedure, the

long-term effects of PMC were not assessed. Second, we used general anesthesia, and therefore patient tolerance of the procedure with local anesthesia was not assessed. Third, there is still room to improve US guidance and monitoring to better delineate the margin of ablation and to assure complete tumor destruction. Fourth, skin burns, which may influence the PMC procedure, were observed in one case in our study.

In the future, it will be important to further define the indications of PMC. The results in prospective studies in regard to the survival and cosmetic effect of PMC were not clear, so future clinical studies should be undertaken to investigate these areas of concern. In conclusion, US-guided PMC of small solitary breast cancers is feasible.

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