Percutaneous Image-Guided Ablation of Breast Tumors: An Overview

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Abstract

Keywords

- ▶ percutaneous ablation
- ▶ breast cancer
- ▶ fibroadenoma
- ▶ immunomodulation
- ▶ interventional radiology

Percutaneous non-surgical image-guided ablation is emerging as an adjunct or alternative to surgery in the management of benign and malignant breast tumors. This review covers the current state of the literature regarding percutaneous image-guided ablation modalities, clinical factors regarding patient selection, and future directions for research.

Objectives: Upon completion of this article, the reader will be able to explain the current status of image-guided percutaneous ablation of breast tumors, including clinical factors surrounding patient selection, technical aspects of ablation procedures, treatment outcomes, and future directions for research.

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One of the most promising areas of current interventional research is the development and validation of image-guided ablation as a non-surgical minimally-invasive therapy for breast tumors, including newly diagnosed, non-metastatic

breast cancer. This is part of the global paradigm shift toward minimally-invasive, cosmetically-appealing, and cost-effective therapies.

In many ways, the breast is the perfect organ for ablation. Covered only by skin with no intervening structures, the breast tissue can be compressed asymmetrically to achieve strategic skin-to-lesion geometries, and imaged effectively with ultrasound. The main factors driving ablation for breast tumors are^{1,2}:

1. Increasing detection of breast tumors, owing to improved and widespread mammographic screening;
2. Increasing survival of breast cancer patients, with a renewed focus on cosmetic and functional outcomes;
3. Decreasing size of early breast cancer on presentation, owing to screening and neoadjuvant chemotherapy;
4. Desire to avoid scars from treatment for fibroadenoma, the most common breast tumor.

Breast cancer is managed based on tumor stage (TNM), histology, and biologic receptor status (► **Table 1**).³ Outpatient oncoplastic breast surgery has improved in speed and cosmetic outcomes and provides surgical pathologic margins. Ablation is less invasive but relies on imaging to determine

Table 1 Treatment of breast cancer by Stage; NCCN guidelines with summaries by Bitton et al⁶ and cross-referencing of relevant available literature

Pathology and Stage	Current Management	Relevant Studies Regarding Future Role of Ablation	
Pure DCIS Tis, N0, M0	Mastectomy or BCS + HT		
Invasive IDC or ILC <5 mm T1a, N0, M0	Mastectomy or BCS		
Invasive IDC or ILC >5 mm T1b–T2, N0–1, M0	Mastectomy or BCS + HT + Directed Therapy if Her2Neu positive <i>Consider neoadjuvant therapy for large T2 tumors.</i>	Izzo, 2001 (RFA) ⁵¹ Burak, 2003 (RFA) ¹¹ Fornage, 2004 (RFA) ⁵² Earashi, 2007 (RFA) ⁵³ Marcy, 2007 (RFA) ⁵⁴ Imoto, 2009 (RFA) ⁵⁶ Medina-Franco, 2008 (RFA) ⁵⁵ Manenti, 2009 (RFA) ⁵⁷ Kinoshita, 2011 (RFA) ¹³ Noguchi, 2012 (RFA) ¹² Palussière, 2012 (RFA) ⁵⁸ Yoshinaga, 2012 (RFA) ⁵⁹ Kreb, 2013 (RFA) ⁵	Pfleiderer, 2002 (Cryo) ⁶³ Sabel, 2004 (Cryo) ⁴ Roubidoux, 2004 (Cryo) ⁶⁵ Pfleiderer, 2005 (Cryo) ⁶⁶ Niu, 2007 (Cryo) ⁶⁸ Pusztaszeri, 2007 (Cryo) ⁶⁷ Manenti, 2011 (Cryo) ⁶⁹
Invasive IDC or ILC >5 mm T3, N0–1, M0	Mastectomy or Neoadjuvant chemotherapy + BCS <i>Consider adjuvant systemic chemotherapy Consider chest wall irradiation</i>	Jeffrey, 1999 (RFA) ¹⁴	Morin, 2004 (Cryo) ⁶⁴
Metastatic IDC or ILC Any T, N2, M1	Chemotherapy <i>Consider surgery for local control Consider radiation for local control.</i>	Leylek 2013 (Ethanol/RFA) ⁸⁸	

DCIS, ductal carcinoma in situ; IDC, invasive ductal cancer; ILC, invasive lobular cancer; IDC, infiltrating ductal carcinoma; ILC, infiltrating lobular carcinoma; BCS, breast conserving surgery; lumpectomy with tumor-free resection margin and radiation therapy; HT, hormone therapy; ER, estrogen receptor; PR, progesterone receptor; Her2Neu directed therapy includes cytotoxic therapy and trastuzumab; RFA, radiofrequency ablation; Cryo, cryoablation.

effectiveness; in determining reliable follow-up methodology, robust research is needed before imaging can replace the microscope. Three main investigational themes are currently underway, including³: cosmetic outcomes with ablation versus lumpectomy for malignancy <5 cm; survival outcomes with ablation for local recurrence in patients who are not candidates for surgery; clinical outcomes following ablation of fibroadenoma.

Pre-Ablation Evaluation and Patient Selection

Considerations for patient selection include:

Imaging findings of the primary cancer. Multifocal tumors with subtle non-calcified⁴ components and indistinct margins on pre-ablation imaging pose challenges for successful ablation. This can be seen with multifocal invasive lobular carcinoma, DCIS, and mucinous colloid carcinoma.³ Cases of non-calcified DCIS causing failure of radiofrequency ablation (RFA)⁵ might prompt MRI guidance.

Size and location of the lesion. Smaller lesions are more readily ablated. If the lesion is close to skin, nipple, chest wall, or breast implant, then hydrodissection with lidocaine or

nonionic 5% dextrose (saline and other ionic solutions conduct electrical current during RFA) should be planned, as well as topical thermal countermeasures, to prevent non-target tissue injury. Temperature probes can be placed near vital structures for real-time monitoring during the ablation.

Co-morbidities. Ablation may have the greatest role in elderly patients (>70 years old), in whom 92% of breast cancers are stage I or II; up to 50% of these patients have co-morbidities affecting treatment decisions.^{6,7} Instead of surgery with general anesthesia, most patients can undergo ablation with sedation (or sometimes even with only local anesthetic, for example with cryoablation) in the outpatient setting. Pacemakers require attention if MRI-guidance is considered.

Pathology. Once a tumor has been ablated, tumor markers cannot be reliably assessed.⁸ Therefore, complete prognostic and histologic evaluation including estrogen and progesterone receptors, HER-2/neu, and markers of proliferation, apoptosis, differentiation, and cell regulation, should be performed by biopsy prior to ablation.^{3,8} Cryoablation is more effective for invasive cancer than ductal carcinoma in situ (DCIS).⁸

Stabilization. If treatment will involve multiple applicators, breast stabilization should be planned, although lesions

still may be displaced from the needle despite this.³ If MRI guidance is used, the operator must be aware that breast compression affects gadolinium kinetics.⁹

Background breast composition. It is reasonable to expect that the fibrous: fatty tissue ratio of the breast will have an effect on thermal ablation, and it is anticipated that fat necrosis in the vicinity of an ablation cavity may make interpretation of post-ablation follow-up imaging difficult.³

Percutaneous Radiofrequency Ablation (RFA) for Breast Cancer and Fibroadenoma

With a reputation for predictable ablation volume and quicker ablation time than cryoablation, radiofrequency ablation (RFA) works by heating water molecules and causing coagulation. Cancer cells contain more water than normal cells, and the neoplastic vasculature is fragile (more susceptible to heat-induced thrombosis).¹ The treatment goal for RFA is to ablate the whole lesion plus a 1 cm tissue rim to between 50–100°C for 9 minutes.¹⁰ Therefore, the target should be at least 1 cm away from skin, nipple, chest wall, or breast implant. The ablation can be observed with real-time ultrasound as echogenic microbubbles are formed.

Success of ablation is currently determined in two ways: Imaging and histopathologic analysis. Imaging analysis has focused on MRI evidence of non-enhancement encompassing the area of ablation.¹¹ Until six months post-RFA,¹² the histopathologic analysis must go beyond a routine H&E stain, since cells at the periphery of an ablation zone can be activated for apoptosis but still appear morphologically “normal” on an H&E slide.⁸ Therefore, in addition to H&E, a “viability stain” is performed, most frequently NADHD (nicotinamide adenine dinucleotide-diaphorase).¹³

Ever since the first feasibility study in 1999 showing technical success in four of five breast tumors treated with RFA,¹⁴ most of the literature on breast cancer ablation has focused on RFA. Currently, RFA is considered by many to be the most promising ablation modality for breast cancer.¹² ▶Table 2 highlights existing and forthcoming research on RFA for breast cancer.

In contrast to cancer ablation, the RFA literature for fibroadenoma is extremely limited.³ Teh et al reported treatment in two patients in 2010¹⁵; both patients had complete clinical and technical success assessed at 6 month followup.

Percutaneous Cryoablation for Carcinoma, Fibroadenoma, and Immunomodulation

Cryoablation is the original ablative modality,¹ and was the first modality used for breast cancer. The first-ever attempt at ablative therapy for resectable breast tumors was by Rand et al^{1,16} who demonstrated a 70% reduction in local tumor recurrence after neoadjuvant cryoablation and surgical resection in a mouse model in 1985.

Since then, cryoprobe technology has entered its third generation (from original nitrogen cooled applicators to smaller thermoelectric applicators and finally thinner gas

refrigerated applicators).¹⁷ Due to the analgesic effect of cold temperatures, the procedure is virtually painless to the awake patient, and can be performed safely in the office with no sutures and little to no scarring.^{18,19}

With percutaneous cryoablation, a cryoprobe is rapidly cooled to subzero Celsius temperatures to create an iceball. Pure water forms ice crystals that shear the cytoskeleton; the remaining solutes concentrate and cause osmotic shifts. The combination causes microcirculatory disruption and necrosis of the target tissue (▶Fig. 1A, 1B, 1C).

For cryoablation of breast cancer, studies from Germany, China, and the United States have shown high clinical success rate for cryoablation of tumors 1.5 cm or less in diameter.²⁰ ▶Table 3 highlights existing and forthcoming research on cryoablation for breast cancer.

The implications of fibroadenoma to the interventional breast specialist are significant. Almost 1 in 10 women will be diagnosed with a fibroadenoma in their lifetime, and ~500,000 women undergo fibroadenoma excision each year.^{18,21} Fibroadenomas usually present clinically when they are between 1–3 cm in diameter and can be multiple and bilateral.²² Treatment options include serial observation, excision by core biopsy, ablation, and surgery. Complete excision by large (8 gauge) core biopsies has a clinical success rate of only 80% and can result in hematoma when fibroadenomas are larger than 2 cm.^{23,24} Cryoablation can be performed in the office¹⁹ with only local anesthesia, whereas surgery is more expensive and may have poor cosmetic outcome.²³ Reimbursement for this procedure by third-party payers has varied from none to substantial.¹

In 2002, the Food and Drug Administration (FDA) approved cryoablation for treatment of fibroadenoma based on results of a single-arm, nonrandomized safety and efficacy study of 30 patients with 37 core biopsy- and ultrasound-confirmed fibroadenomas up to 4 cm in diameter.²⁵ Littrup et al²⁶ performed cryoablation in 42 patients with biopsy-proven fibroadenoma, demonstrating 73% size reduction on average. ▶Table 4 highlights existing and forthcoming research on cryoablation for fibroadenoma.

One of the most fascinating areas of research in cryoablation is that of cryo-immunology and immunomodulation. Early reports of abscopal effect in cryosurgery patients with stage IV breast cancer by Suzuki²⁷ and LePivert²⁸ have sparked an entire field of immunomodulation research. In the abscopal effect, the ablation of a single lesion triggers regression of distant metastases. It is thought that this results from the host immune system receiving antigens from the ablation bed, and acquiring immunity against the cancer. In essence, the ablation creates a pool of presentable antigens as an in situ personalized cancer vaccine. Based on work by Matzinger,²⁹ this process is thought to be dependent on necrosis, which is disordered, and releases immunostimulatory intracellular contents that lead to dendritic cell maturation and macrophage activation.^{30,31} Specific to cryoablation, Sabel further showed in a murine model that a rapid freeze cycle ablation (more necrotic) was immunostimulatory, while a slow freeze cycle ablation (more apoptotic) was

Table 2 RFA for breast carcinoma

	Year	No. of patients	No. of tumors treated	Tumor Characteristics	Technical Success (Complete Ablation)	Reported Major Clinical Complications or Failures
Jeffrey ¹⁴	1999	5	5	4–7 cm	80%	None
Izzo ⁵¹	2001	26	26	0.7–3.0 cm	96%	Skin burns
Burak ¹¹	2003	10	10	0.8–1.6 cm	89%	None
Fornage ⁵²	2004	20	21	≤ 2 cm	100%	1/20 pt. with imaging-occult tumor found 4 cm away from ablation
Earashi ⁵³	2007	24	24	0.5–2.4 cm	100%	None
Marcy ⁵⁴	2007	4	5	1.8–2.2 cm	100%	1/4 pt. with local recurrence at 4 months
Medina-Franco ⁵⁵	2008	25	25	0.9–3.8 cm	76%	None
Imoto ⁵⁶	2009	30	30	0.9–2.4 cm	92%	Skin and muscle burns
Manenti ⁵⁷	2009	34	34	< 2 cm	97%	None
Kinoshita ¹³	2011	49	49	0.5–3.0 cm	61%	Skin and muscle burns
Palussière ⁵⁸	2012	21	21	≤ 3 cm	95%	Skin burns
Noguchi ¹²	2012	18	19	0.5–2.0 cm	100%	“Persistent lump” in 50%
Kreb ⁵	2013	20	20	0.4–1.5 cm	85%	n/a; ex vivo study
Yoshinaga ⁵⁹	2013	14	14	0.6–2.0 cm	100%	None
UC Davis NCT00388115 ⁶⁰	Ongoing Clinical Trial	Pilot study of RFA followed by surgery for breast cancers ≤ 2 cm				
Institut Bergonie NCT00210223 ⁶¹	Completed Clinical Trial	Pilot study of RFA-only for breast cancers ≤ 2 cm				

RFA, Radiofrequency ablation.

actually immunosuppressive.³² If the specifics of immunomodulation can be unlocked, the implications for interventional oncology will be significant.

Percutaneous Microwave Ablation for Breast Carcinoma

Microwave ablation (MWA) heats tissue more efficiently than RFA,³³ and specifically heats water molecules, which are more abundant in cancer cells compared with normal cells. The most promising MWA study³⁴ was reported by Zhou et al who used a 2.5 GHz device under general anesthesia and found complete thermal damage to lesions in 37/41 cases (90%) using NADHD staining. ▶ **Table 5** highlights existing and forthcoming research on MWA in breast cancer.

Percutaneous Interstitial Laser Ablation for Breast Carcinoma and Fibroadenoma

Interstitial Laser Ablation (ILA) uses a portable diode laser to generate heat in tissues. The photothermal effect can be

followed by MR thermometry or by internal and accessory temperature monitors placed into the tissue. The volume of literature on ILA for breast tumors is relatively small. The largest study to date was in 2002, an ablate-and-resect study of 54 patients with tumors <2.3 cm in whom 16/51 patients had treatment failure with tumor found in the ablation volume.³⁵ The ABLATE registry (American Breast Laser Ablation Therapy Evaluation, NCT00807924)³⁶ is underway and will examine the safety and efficacy of ILA for benign breast conditions, mainly fibroadenoma.

High-Intensity Focused Ultrasound for Breast Carcinoma and Fibroadenoma

High-Intensity Focused Ultrasound (HIFU) is a relatively new non-invasive ablation modality. Using either magnetic resonance imaging (MRI) guidance (“MRgFUS”) or ultrasound (US) guidance, HIFU delivers ultrasound energy upon a very small focus causing heat and coagulative necrosis. Many HIFU investigators believe that MRgFUS may ultimately replace lumpectomy.³⁷

Figure 1 T1-weighted fat suppression prone MR images of the right breast in sagittal plane through the center of target lesion. (A) Immediately pre-ablation contrast-enhanced MRI. At the 10:00 axis posterior third of the right breast there is a 2.3 × 1.6 cm lobulated enhancing mass (arrow). Biopsy of this mass was performed (14 Gauge × 7 cores) and a clip deployed at the biopsy site, per the particular research protocol prior to ablation. (B) During-ablation. Two Galil IceSeed applicators (Galil Medical, Inc., Arden Hills, MN) were placed via lateral approach in the axial plane. Freeze (10 minute) – Thaw (8 minute) – Freeze (8 minute) - Thaw (8 minute) cycles were performed at 60% and 40% power for the respective applicators according to the desired iceball geometry. Warmed sterile saline was injected near needle entry for skin protection. The iceball (arrow) covers the lesion completely but the margin is suboptimal as 100% therapeutic ablation was not mandatory for this particular research protocol. (C) The probes have been removed but the iceball (arrow) has not thawed completely. The patient was discharged home the same day after full recovery. The target lesion was surgically resected about one week later on schedule.

Table 3 Cryoablation for breast carcinoma

	Year	No. of patients	No. of tumors treated	Tumor Size	Complete Ablation	Reported Clinical Complications or Failures
Staren ⁶²	1997	1	2	0.5–0.8 cm	100%	None
Pfleiderer ⁶³	2002	15	16	0.9–2.0 cm	31% (5/16 tumors)	2/16 DCIS near ablation
Sabel ⁴	2004	29	27	0.6–2.0 cm	85% (23/27 tumors)	4/27 DCIS near/adjacent ablation 2/29 Applicator misplaced
Morin ⁶⁴	2004	25	25	1.2–6.0 cm	52%	None.
Roubidoux ⁶⁵	2004	9	9	0.8–1.8 cm	100% technical success 78% pathologic complete tumor necrosis	1/9 DCIS in ablation zone 1/9 Invasive Ca in ablation zone
Pfleiderer ⁶⁶	2005	30	29	0.5–1.5 cm	100% (29/29)	1/30 cryoprobe leak
Pusztaszeri ⁶⁷	2007	11	11	0.5–2.5 cm	90% (10/11) technical success 20% (2/10) pathologic complete tumor necrosis	1/11 applicator misplaced 2/11 residual DCIS 6/11 residual Ca +/- DCIS 5/11 Skin ulceration
Niu ⁶⁸	2007	27	27	0.8–2.5 cm	85%	None
Manenti ⁶⁹	2011	15	15	0.4–1.2 cm	93%	None
Memorial Sloan-Kettering Cancer Center NCT01502592 ⁷⁰	Ongoing Clinical Trial	Phase I non-randomized open label study of ipilimumab + MRI-guided cryoablation before total mastectomy in patients with early stage/resectable breast carcinoma. It is thought that ipilimumab can modulate T cell response to antigens presented during cryoablation, such that the patient develops immunity to their own cancer. Phase II study is planned.				
UCLA NCT00020852 ⁷¹	Completed Clinical Trial	Phase I study of neoadjuvant cryoablation before surgery for up to two lesions measuring 2 cm or less.				
M.D. Anderson Cancer Center NCT01388777 ⁷²	Ongoing Clinical Trial	Phase II study of neoadjuvant ultrasound-guided cryoablation before surgery.				

(Continued)

Table 3 (Continued)

	Year	No. of patients	No. of tumors treated	Tumor Size	Complete Ablation	Reported Clinical Complications or Failures
Fukuma et al Ka-medea Medical Center, Japan ⁷³	Ongoing Clinical Trial	Phase I/II study since 2006 of ultrasound- or MRI-guided cryoablation + radiation + adjuvant chemotherapy in 38 patients with 1 cm or smaller tumors. Phase I/II study since 2012 of ultrasound-guided cryoablation-only (followed by immediate post-ablation biopsy). Presented at American Society of Breast Surgeons 2013 in Chicago, USA.				
UCLA/Morgan Cancer Center/M.D. Anderson Cancer Center NCT00723294 ⁷⁴	Ongoing Clinical Trial	Phase II study of cryoablation + resection for invasive ductal breast carcinoma less than or equal to 2.0 cm in greatest diameter. This study will determine effectiveness of ablation, as well as the negative predictive value of MRI for residual in situ and invasive disease. Blood samples will be collected before cryoablation, after cryoablation, and after surgery to analyze for development of anti-tumor immunity resulting from cryoablation. ⁴⁵				
Immunovative Therapies NCT02018419 ⁷⁵	Ongoing Clinical Trial	Phase I/II study of cryoablation + intralesional AlloStim™ (bioengineered allogeneic immune cells) into a <i>metastatic</i> breast cancer lesion. It is thought that AlloStim™ will allow the patient to develop immunity to their own cancer.				
Immunovative Therapies NCT01741038 ⁷⁶	Approved Clinical Trial, Not Yet Active	Phase II/III study of cryoablation + intralesional AlloStim™ into a <i>metastatic</i> breast cancer lesion.				

Regarding HIFU for breast carcinoma, three main studies have been reported. In 2003, Wu et al performed a randomized ablate-and-resect study, performing US guided HIFU on 24 patients with tumors 6 cm or less in maximum diameter. These authors reported a 100% technical success rate and demonstrated coagulative necrosis within the entire ablation volume. In 2005, the same group reported a 89% recurrence-free survival rate with favorable cosmetic results in 22 patients at median 54.8 months follow-up after US-guided HIFU with adjuvant chemoradiation and hormone therapy.^{38,39} In 2006, Furusawa et al performed MRgFUS on 30 patients with tumors <3.5 cm in their ablate-and-resect study; they reported a 93% technical success rate (28/30 patients).³⁷ The same group reported successful results in 2007 with MRgFUS in 21 patients, finding only 1 recurrence at median 14 month MRI follow-up (in a patient with mucinous carcinoma).⁴⁰ The results of ongoing NCT00008437 Phase II clinical trial using MRgFUS in an ablate-and-resect fashion for patients with Stage I, Stage II, or Stage IIIA breast cancer are pending.⁴¹

HIFU can be used to treat fibroadenoma as well. In 2001, Hynynen et al treated 11 fibroadenomas with MRgFUS and had technical success in 72% (8/11), defined as partial or complete non-enhancement on follow-up MRI.⁴² The ongoing clinical trial NCT01331954 is studying the use of HIFU in the treatment of fibroadenoma.⁴³

Irreversible Electroporation for Breast Carcinoma

Irreversible electroporation (IRE) is an ablation modality that uses pulsed-current to create permanent nanopores in

cell membranes, causing cells to die while preserving the extracellular matrix. IRE is a relatively new modality and has been used more extensively elsewhere in the body.⁴⁴ Neal et al have published two studies on IRE for breast cancer.^{45,46} Because of muscular excitation during IRE, paralytics are necessary,³³ as well as general anesthesia; in addition, electrocardiographic gating is necessary to prevent dysrhythmias.

Plasma Ablation for Breast Carcinoma (Experimental)

Cold atmospheric plasma (CAP) is an ionized gas at room temperature that contains a rich milieu of subatomic particles including electrons, excited molecules and charged particles, UV photons, and transient electric fields. Wang et al have demonstrated breast-cancer cell-specific plasma ablation in vitro.^{47,48} The ability to target cancer cells in situ with specificity has been separately shown as well.⁴⁹

Gold Nanoshell Microcapsule Thermotherapy for Breast Carcinoma (Experimental)

Gold nanoshelled microcapsules (GNS-MCs) serve the dual purpose of being an ultrasound contrast agent as well as a thermal ablation agent capable of optical absorption of photothermal energy from near-infrared laser source. Wang et al have shown 85% technical success (6/7 implanted breast cancers completely ablated) when using this technology in mice.⁵⁰

Table 4 Cryoablation for fibroadenoma

	Year	No. of patients	No. of Fibroadenomas treated	Fibroadenoma Characteristics	Complete Ablation	Reported Major Clinical Complications or Failures
Kaufman ¹⁸	2002	50	57	0.7–4.2 cm	100% Technical Success 92% Volume reduction (avg.)	None
Kaufman ⁷⁷	2004	63	(fibroadenoma) 66 (other benign) 12	0.8–4.2 cm	89% Technical Success (overall) 87.3% Volume reduction (fibroadenomas)	1/63 pt. with Abscess at 6 wks.
Kaufman ⁷⁷	2004	57	70	0.8–4.2 cm	Technical success 13% (61/70) Median 89% volumetric regression at 12 months	2/70 severe post-procedure pain
Edwards ⁷⁸ (FACT registry)	2004	Not reported	310	Mean 1.8 cm Range not reported	Technical Success not reported. Average volume regression by 97% at 12 months.	10/250 pts. with hematoma at 6 week follow-up
Caleffi ²² Group 1: Double HI Freeze Group 2: Tailored Freeze	2004	102	124	(Group 1) Mean 1.4 cm (Group 2) Mean 2.1 cm	Technical success not reported. Group 1: Volume reduction not evaluable (isoechoic ablation bed) Group 2: Volume reduction 91% median	1/82 Abscess 2/82 Severe Pain (Group 2)
Kaufman ¹⁹	2005	32	37	0.8–4.2 cm	87% Technical Success (due to protocol deviations, not specified) 99% Volume reduction	None
Littrup ²⁶	2005	29	42	Avg 4.2 +/– 4.7 cm ³	100% Technical Success 73% Volume reduction (avg.)	None
Nurko ⁷⁹ (FACT registry)	2005	Not reported	444	Mean 1.8 cm Range not reported	Technical success not reported. Complete regression by US in 71% at 12 month follow-up	22/87 pts. with residual pain at 1 year
Hahn ²³	2013	22	23	≤ 3 cm	91% Technical Success 80% Volume reduction (avg.)	1/22 pt. with severe pain

Table 5 Microwave ablation for breast carcinoma

	Year	No. of patients	No. of tumors treated	Tumor Characteristics	Technical Success (Complete Ablation)	Reported Clinical Complications or Failures
Gardner ⁸⁰	2002	10	10	1–8 cm	Not reported	None
Vargas ⁸¹	2004	25	25	0.7–2.8 cm	8% (2/24)	1/25 Ablation aborted due to pain
Dooley ⁸²	2010	34	34	0.8–7.8 cm	6% (2/34)	3/34 Skin burn 5/34 Intolerable pain 1/34 Abscess
Zhou ⁸³	2012	43	41	1–3 cm	90% (37/41)	1/43 Antenna leakage 1/43 US guidance not possible
Dooley/Keyserling NCT01204801 ⁸⁴	Ongoing Clinical Trial	Phase III study of neoadjuvant microwave ablation + neoadjuvant chemotherapy + surgery versus neoadjuvant chemotherapy + surgery. The study will measure if microwave ablation allows more patients to be converted from mastectomy to breast conservation surgery.				
Celsion, Multi-Institutional NCT00036998 ⁸⁵	Ongoing Clinical Trial	Phase II study of neoadjuvant microwave ablation + lumpectomy versus lumpectomy alone. Study will determine if there is an improvement in adequacy of surgical margins.				
Celsion, Multi-Institutional NCT00826085 ⁸⁶	Ongoing Clinical Trial	Phase I/II study of ThermoDox (Lyso-Thermosensitive Liposomal Doxorubicin) in patients with local-regional recurrent breast cancer. Patients will receive intravenous ThermoDox and undergo microwave thermotherapy to the tumor to lyse the liposomes and release doxorubicin specifically to the tumor. It is thought this will increase cytotoxic drug concentration in the tumor while sparing the remainder of the body.				
Celsion, Multi-Institutional NCT00036985 ⁸⁷	Ongoing Clinical Trial	Phase II study of neoadjuvant microwave ablation + neoadjuvant chemotherapy + surgery versus neoadjuvant chemotherapy + surgery. The study will measure if microwave ablation improves surgical margins and reduces resection and re-incision rates.				

Conclusion

Although surgery is considered the current standard of care for breast cancer, promising results from non-surgical image-guided therapies may provide a viable alternative first line treatment option in near future.

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