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van de Voort, Elles M F; Struik, Gerson M; Birnie, Erwin; Moelker, Adriaan; Verhoef, Cornelis; Klem, Taco M A L

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Review Article

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Thermal Ablation as an Alternative for Surgical Resection of Small (≤ 2 cm) Breast Cancers: A Meta-Analysis

Elles M.F. van de Voort,[1] Gerson M. Struik,[1,2] Erwin Birnie,[3,4] Adriaan Moelker,[5] Cornelis Verhoef,[6] Taco M.A.L. Klem[1]

Abstract

Women with early-stage breast cancer have an excellent prognosis with current therapy, but could presumably be treated less invasively, without the need for surgery. The primary goal of this meta-analysis was to examine whether thermal ablation is an effective method to treat early-stage breast cancer. Studies reporting on complete ablation rate after thermal ablation as a treatment of small breast cancers (≤ 2 cm) were included. Methodologic quality of included studies was assessed using MINORS criteria. Complete ablation rates are given as proportions, and meta-regression and subgroup analyses were performed. The overall complete ablation rate in 1266 patients was 86% and was highest after radiofrequency ablation (RFA) (92%). Local recurrence rates varied from 0% to 3%, with a median follow-up of 15 to 61 months. Overall, complication rates were low (5%-18% across techniques) and were highest after high-intensity focused ultrasound ablation and lowest after cryoablation. Cosmetic outcome was good to excellent in at least 85% of patients but was reported infrequently and long-term results of cosmetic outcome after thermal ablation and radiotherapy are still lacking. Thermal ablation techniques treating early-stage breast cancer (≤ 2 cm) are safe and effective based on complete ablation rate and short-term local recurrence rates. Especially, RFA, microwave ablation, and cryoablation are promising techniques as an alternative to surgical resection without jeopardizing current treatment effectiveness or safety. Owing to great heterogeneity in the included studies, a formal recommendation on the best technique is not possible. These findings warrant the design of large randomized controlled trials comparing thermal ablation and breast-conserving surgery in the treatment of T1 breast cancer.

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Introduction

Breast cancer is the most frequently diagnosed malignancy worldwide among women.[1-3] Improvements in screening and imaging have led to the detection of smaller and earlier stage breast cancers.[4] Almost half of all tumors are smaller than 2 cm at time of diagnosis.[5,6] With current therapy, these women have an excellent prognosis with a 5-year survival rate of 98% to 99%.[4] However, current treatment protocols may have also led to overtreatment, as these early-stage tumors could presumably be treated less invasively without the need for surgery.[4,6]

Over the years, the golden standard of treatment of breast cancer has evolved from mastectomy to lumpectomy to reduce morbidity and increase quality of life without jeopardizing treatment effectiveness.[7-9] As an alternative to surgical resection, thermal ablation using extreme hyperthermia or hypothermia destroys viable cells within a designated target volume. The most studied thermal ablation techniques as a treatment of breast cancer are cryoablation, microwave ablation (MWA), radiofrequency ablation (RFA), laser ablation, and high-intensity focused ultrasound (HIFU). These devices can ablate an area up to 3 cm with a single probe. Because a margin of 0.5 to 1.0 cm should be included in the ablation volume, thermal ablation appears a particularly suitable candidate treatment of early-stage breast cancer, with tumors up to 2 cm.[10-12]

Previous reviews and meta-analyses on thermal ablation as a treatment of breast cancer show large variations in complete ablation

[1]Department of Surgery, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands
[2]Department of Surgery, Reinier de Graaf Gasthuis, Delft, the Netherlands
[3]Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands
[4]Department of Statistics and Education, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands
[5]Department of Interventional Radiology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands
[6]Department of Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands

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Address for Correspondence: Elles M.F. van de Voort, MD, Franciscus Gasthuis and Vlietland, Department of Surgery, Kleiweg 500, 3045 PM Rotterdam, Zuid-Holland, the Netherlands.
E-mail contact: e.voort@franciscus.nl

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rates.[8,9,13] However, included studies were heterogeneous with various tumor sizes, and complete ablation was not always the objective of the study. Over time, devices improved, operators became more experienced, and patient selection changed. To examine whether thermal ablation is an effective method to treat small breast cancers (≤ 2 cm), all available clinical trials that assessed the complete ablation after thermal ablation of these tumors were reviewed. Additionally, the variables accounting for heterogeneity between studies will be explored. The results of this study should serve as a guidance for future clinical trials comparing thermal ablation techniques to breast-conserving surgery with regard to efficacy.

Methods

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[14]

Search Strategy

A PROSPERO search was performed, and no studies on thermal ablation for patients with breast cancer were found. For this review, all studies that reported on thermal ablation as a primary treatment of breast cancer were included in this meta-analysis. Embase, Medline (OvidSP), Web of Science, Scopus, Cinahl, Cochrane, PubMed publisher, and Google Scholar were searched using the following keywords and their analogues: thermal ablation, cryoablation, radiofrequency ablation, microwave ablation, breast cancer, treatment. The search was performed in June 2019 and updated in May 2020. An expert medical librarian was consulted to develop the search strategy.

Inclusion Criteria

Studies were included if (1) an English version was available; (2) it concerned a clinical study in humans with breast cancer; (3) the treatment success was reported as complete ablation on imaging and/or histology; (4) at least 10 patients with tumors ≤ 2 cm on pretreatment imaging were treated per ablation method; and (5) thermal ablation with either MWA, RFA, cryoablation, HIFU, or laser ablation was performed. Studies that also included tumors > 2 cm could only be included in this review if separate results were presented for (at least 10) tumors ≤ 2 cm. Only these results from tumors ≤ 2 cm were included in this meta-analysis. References of reviews were used to identify potential additional articles for inclusion. Conference abstracts were included to include the most recent results of thermal ablation. All abstracts and full articles were checked for duplicate data and if this was the case only the most recent publication was included in this review.

Exclusion Criteria

Preclinical studies and reviews were excluded, as were studies that used an ablative technique after surgical excision.

Data Extraction

All variables were extracted using a data extraction sheet. One author (EV) extracted the following data: ablation method; complete ablation rate for tumors ≤ 2 cm on pretreatment imaging; and if available, study characteristics; inclusion criteria; patient, tumor, and procedure characteristics; methods of evaluation; and imaging performed before, during, and after treatment.

Quality Assessment of Included Studies

All studies were assessed for methodological quality using MINORS criteria (methodological index for nonrandomized studies). This is a standardized and validated instrument in which noncomparative studies are scored on 8 items, and comparative studies on 12 items.[15] These items included a clear aim, inclusion of consecutive patients, prospective data collection, appropriate endpoints and unbiased assessment of these endpoints, follow-up period, loss to follow-up, study size calculation, adequate control group, contemporary groups, baseline equivalence, and adequate statistical analyses (Appendix A). Each item was scored as not reported (0), reported but inadequately (1), or adequately reported (2). Maximum score is 16 for noncomparative studies and 24 for comparative studies.

Study selection, data extraction, and quality assessment was performed by the first author (EV) and reviewed by a second author (GS). Disagreements were resolved by discussion. When no consensus could be reached, a third author was consulted (TK).

Statistical Analysis

All extracted data were tabulated and presented as means (SD) or median (range), and proportions. Proportions of complete ablation were pooled for all included studies and for each technique separately and were presented with the Wilson 95% binominal proportion confidence intervals (CIs).[16] Heterogeneity was tested using the Cochrane Q-test and I^2 statistics. When the assumption of homogeneity was rejected ($P < .05$), the random effect model (meta regression) was used. When the assumption of homogeneity was not rejected ($P > .05$), a fixed effect model was used. It should be mentioned that by doing so, there is a chance of unseen homogeneity that could unduly reduce the standard of error of the effect size.

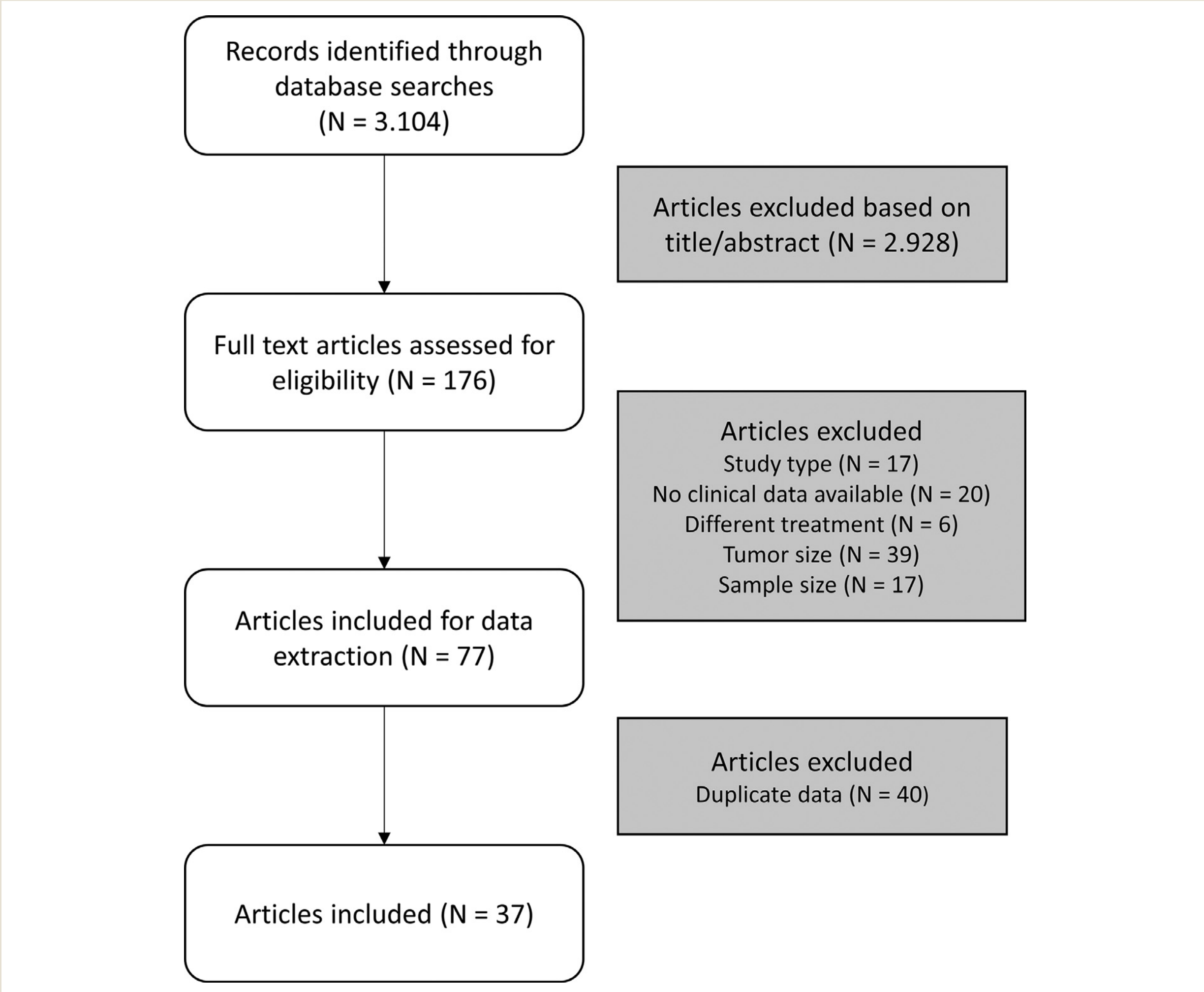
The possibility of publication bias was assessed both visually with a funnel plot and formally with Egger's test. Meta-regression was performed for all techniques bundled and per individual technique. The following covariates were used for meta-regression and subgroup analyses: technique, device, year of publication, type of article, timing of resection, method of resection, inclusion/exclusion of an extensive intraductal component (EIC), magnetic resonance imaging (MRI) before the procedure, and type of staining at histologic evaluation of the specimen (full classification in Appendix B). For subgroup analyses, studies in which no information was available for the concerning variable were excluded. All statistical analyses were performed using Comprehensive Meta-Analysis (CMA) software (version 3.3.070).

Results

Literature Search

A total of 3104 records were identified through the database search (Appendix C). After screening of titles and abstracts, 176 publications were checked for eligibility and eventually 37 studies were included (Figure 1). Most studies were excluded because of the

Figure 1 Selection of included studies.



absence of specific data on complete ablation of tumors ≤ 2 cm. No additional articles were found by checking references of reviews and included articles.

Quality of Included Studies

Quality of the studies ranged from 7 out of 16 to a 15 out of 16 score for noncomparative studies (N = 37), and from 16 out of 24 to 24 out of 24 score for comparative studies (N = 3) (Table 1A-E). In none of the studies the patient or physician was blinded, and in only 3 studies the pathology review was done by central review or by at least 2 independent pathologists.[17-19] A sample size calculation or estimation was given in only 5 studies[11,20-24] (Appendix D).

Study Characteristics

An overview of the characteristics of included studies per technique can be found in Table 1A-E. Patient age ranged from 35 to 92 years and the mean or median age was older than 45 years in all studies except 1.[25] One study reported on percutaneous MWA, 2 on HIFU, 5 on laser ablation, 8 on cryoablation, and 22 on RFA. Cryoablation, laser ablation, and HIFU were almost exclusively performed under local anesthetics, whereas RFA and MWA were mainly performed under general anesthesia (17 of 23 studies) (Table 1). Tumor type was reported in 32 studies; of 1067 tumors, 943 were of the invasive ductal carcinoma type (88%), 42 lobular (4%), 39 ductal carcinoma in situ (DCIS) (4%), and 43 were other types (4%). Magnetic resonance guidance was always used for HIFU ablation,[26-28] and in 1 cryoablation study.[29] All other procedures were performed under ultrasound (US) guidance, with the exception of 2 laser ablation studies (Table 1A-E).[17,30]

Complete Ablation Rates

Complete ablation was achieved in 1093 of 1266 patients (86%, binominal exact 95% CI, 84%-88%). A substantial heterogeneity was found with $I^2 = 68\%$ for the overall complete ablation rate ($P < .001$). The random effect model showed a pooled complete ablation rate of 84% (95% CI, 79%-88%; Appendix E;

Table 1 (A) Characteristics of Included Studies on Radiofrequency Ablation as a Treatment of Breast Cancer

Study	CA Determination Method	Tumor Size Included in Study	N Tumors ≤ 2 cm Included in Meta-Analysis/ N Total Enrolled in Study		CA	Single/ Multiarray	Mean Age (range) in Years	Mean Tumor Size (range) in mm	% LRR	Anesthesia	MINORS Score
Burak et al. 2003[25]	Delayed surgery after 1-3 weeks	< 2 cm	10/10		90%	Multi	36 (37-67)	15 (8-22)	NA	Local	11
Fornage et al. 2004[40]	Direct surgery	≤ 2 cm	19/21	Two patients with initial T2 tumors received NAC before RFA and are excluded from this review	100%	Multi	56 (38-80)	12 (6-20)	NA	General	11
Khatri et al. 2007[23]	Direct surgery	≤ 1.5 cm	15/17	One patient withdrew consent, in another patient the tumor could not be visualized with US	87%	Single	63 (39-83)	13 (8-15)	0%, 25 mo (NR)	General	13
Oura et al. 2007[45]	No resection cytology after 3-4 weeks, MRI after 1-3 months	≤ 2 cm	52/52		100%	Single	55 (37-83)	13 (5-20)	0%, 15 mo (6-30)	General	10
Medina-Franco et al. 2008[43]	Direct surgery	< 4 cm	14/25	Only patients with tumors ≤ 2 cm pretreatment were included in this review	93%	Single	55 (42-89) [c]	21 (9-38) [b,c]	NA	General	11
Oura et al. 2009[46] [a]	No resection cytology + MRI after 3-4 weeks	< 2 cm	100/100		100%	Multi (5) and single (95)	NR	15 (5-20)	0%, 31 mo (16-54) [b]	NR	8
Hung et al. 2009[42]	Direct surgery	< 2 cm	20/20		90%	Multi (10) and single (10)	59 (NR)	14 (NR)	NA	General	19 [d]
Imoto et al. 2009[31] [a]	Direct surgery	≤ 2 cm	30/30		87%	NR	NR (38-76)	17 (9-24)	NA	General	10
Motoyoshi et al. 2010[39]	All	< 2 cm	33/34		100%	Multi				General	11
	Direct surgery		17/17		100%		55 (33-78) [b]	15 (5-21)	6%, 49 mo (38-65) [b]		
	Delayed VAE after 30-202 days		16/17	VAE was not performed in 1 patient	100%		45 (22-59) [b]	12 (5-20)	0%, 23 mo (3-36) [b]		
Onishi et al. 2010[41] [a]	Histologic evaluation, timing unknown	≤ 2 cm	20/20		80%	NR	NR	15 (NR)			8
Wiksell et al. 2010[18]	Direct surgery	< 1.6 cm	31/33	Two patients excluded prior to treatment because of tumor location and poor US visualization	84%	Single	64 (46-83)	12 (7-18)	NA	General	14

(*continued on next page*)

Table 1 (*continued*)

Study	CA Determination Method	Tumor Size Included in Study	N Tumors $\leq$ 2 cm Included in Meta-Analysis/ N Total Enrolled in Study		CA	Single/ Multiarray	Mean Age (range) in Years	Mean Tumor Size (range) in mm	% LRR	Anesthesia	MINORS Score
Ohtani et al. 2011[35]	All		41/41		88%	Single	59 (38-92) [b]	13 (5-18) [b]	NA		10
	Direct surgery		9/9		NR					General	
	Delayed surgery after 1-2 months		32/32		NR					Local	
Kinoshita et al. 2011[33]	Direct surgery	$\leq$ 3 cm	29/50	Only patients with tumors $\leq$ 2 cm pretreatment were included in this review	86%	Single	61 (36-82) [b,c]	17 (5-30) [b,c]	NA	General	11
Yamamoto et al. 2011[34]	Delayed VAB after 3-4 weeks	$\leq$ 2 cm	26/30	First 3 patients no NADH results available, in 1 patient no tumor tissue was found in VAB	92%	Single	56 (38-78) [c]	13 (5-19) [c]	0%, 17 mo (2-41) [b]	General	10
Manenti et al. 2013[37]	Delayed surgery after 30-45 days	$\leq$ 2 cm	40/40	N = 80 total included; N = 40 RFA, N = 40 cryoablation	93%	Single	73 (64-82) [c]	NR	0%, 18 mo (NR)	General	15 [d]
Yoshinaga et al. 2013[44]	All	$\leq$ 2 cm	12/14	NADH staining available for only 12 patients	100%	Single	67 (45-82) [b]	12 (6-20) [b]		General	9
	Direct resection		5/6		100%				NA		
	No resection US, MRI, and CNB direct, at 3 and 6 months		7/8		100%				0%, 39 mo (NR) [b]		
Schassburger et al. 2014[36]	Delayed surgery after 3 weeks	$\leq$ 2 cm	18/18		89%	Single	67 (46-84) [b]	11 (5-20) [b]	NA	Local	11
Waaijer et al. 2014[24]	Direct surgery	< 2 cm	15/15		67%	Bipolar	63 (50-76) [b]	13 (5-20) [b]	NA	General	12
Chappuis et al. 2016[38] [a]	Surgery, timing unknown	$\leq$ 2 cm	15/15		80%	NR	NR	NR	NA	NR	8
Kinoshita et al. 2017[47] [a]	No resection VAB and imaging after 3 months	$\leq$ 1 cm	57/57		91%	Single	NR	NR	0%, 61 mo (15-85) [b]	General	9
Imoto et al. 2017[22] [a]	No resection CNB/VAB after 1 month	$\leq$ 2 cm	34/34		97%	Single	NR	13 (NR)	3%, NR	NR	12
García-Tejedor et al. 2018[21]	Direct surgery	$\leq$ 2 cm	20/20		100%	Single	64 (48-86)	13 (NR) [b]	0%, 25 mo (1-83) [b]	General	24 [d]

(*continued on next page*)

Table 1 (*continued*)

B											
Study [a]	**Resection**	**Tumor size included in study**	**N tumors ≤ 2 cm included in meta-analysis/ N total enrolled in study**		**CA**	**Single/ multi array**	**Mean age (range) in years**	**Mean tumor size (range) in mm**		**Anesthesia**	**MINORS score**
Zhou et al. 2012[19]	Direct surgery	≤ 3 cm	23/31	Only patients with tumors ≤ 2 cm pretreatment were included in this review	87%	Single	56 (38-78) [c]	20 (1-23) [c]		General	13
C											
Study	**Resection**	**Tumor size included in study**	**N tumors ≤ 2 cm included in meta-analysis/ N total enrolled in study**		**CA**	**Method**	**Mean age (range) in years**	**Mean tumor size (range) in mm**	**LRR**	**Anesthesia**	**MINORS score**
Sabel et al. 2004[50]	Delayed surgery after 7-30 days	≤ 2 cm	27/29	In 2 cases the cryoprobe could not accurately be placed and no results are given for these patients	85%	Argon gas	53 (34-77) [b]	12 (5-20)	NA	Local	11
Pfleiderer et al. 2005[53]	Delayed surgery after 11 ± 9.2 days	≤ 2 cm	29/30	Procedure was stopped after 5 min because of leakage in the handpiece	83%	Argon gas	62 (46-80) [b,c]	12 (5-15) [c]	NA	Local	10
Pusztaszeri et al. 2007[29]	Delayed surgery after 4-5 weeks	≤ 2 cm	11/11		18%	Argon gas	63 (52-78)	14 (0-20)	NA	Local	11
Manenti et al. 2013[37]	Delayed surgery after 30-45 days	≤ 2 cm	40/40	N = 80 total included; N = 40 RFA, N = 40 cryoablation	95%	Argon gas	73 (64-82) [c]	NR	0%, 18 mo (NR)	Local	15 [d]
Gajda et al. 2014[51]	Delayed surgery after 1-45 days	NR	41/51	Two cases were excluded becaude the procedure waspremature terminated because of gas leakage. Only patients with tumors ≤ 2 cm pretreatment were included in this review	71%	NR	61 (38-81) [c]	15 (5-37) [c]	NA	Local	10
Poplack et al. 2015[49]	Delayed surgery after 4-6 weeks	< 1.5 cm	20/20		85%	Argon gas (15) or liquid nitrogen (5)	61 (36-91) [b]	11 (7-15) [b]	NA	Local	14
Simmons et al. 2016[11]	Delayed surgery after < 28 days	≤ 2 cm	87/87		76%	Liquid nitrogen	61 (42-81)	1.2 (0.5-1.9)	NA	NR	15
Fine et al. 2018[20] [a]	No resection imaging after 6 and 12 months	≤ 1.5 cm	140/143	Three screening failures	100%	Liquid nitrogen	75 (58-94)	9 (0-17)	1.3%, NR (0-36 mo)	Local	12

(*continued on next page*)

Table 1 (*continued*)

D

Study	Resection	Tumor size included in study	N tumors ≤ 2 cm included in meta-analysis/ N total enrolled in study		CA	Device	Mean age (range) in years	Mean tumor size (range) in mm	Anesthesia	MINORS score
Furusawa et al. 2006[27]	Delayed surgery after 5-23 days	< 3.5 cm	24/30	Only patients with tumors ≤ 2 cm pretreatment were included in this review	63%	ExAblate 2000	67 (41-79) [c]	13 (5-25) [c]	Local	12
Cavallo et al. 2015[28]	Delayed surgery after < 14 days	< 2 cm	10/10		60%	ExAblate 2100	NR	12 (NR)	Local	9

E

Study	Resection	Tumor size included in study	N tumors ≤ 2 cm included in meta-analysis/ N total enrolled in study		CA	Device	Mean age (range) in years	Mean tumor size (range) in mm	LRR	Anesthesia	MINORS score
Dowlatshahi et al. 2002[30]	Delayed surgery after 1-8 weeks	< 1.5 cm	54/54		70%	Diomed	60 (42-80) [b]	13 (5-23)	NR	Local	8
Haraldsdóttir et al. 2008[54]	Delayed surgery after 4-23 days	< 3 cm	20/24	Only patients with tumors ≤ 2 cm pretreatment were included in this review	15%	Diomed-25	61 (39-84) [c]	12 (5-18) [b,c]	NR	Local	9
Esser et al. 2009[56]	Direct surgery	≤ 2 cm	14/14		50%	Microdom LITT	55 (35-85) [b]	15 (9-20) [b]	NR	General	11
Schwartzberg et al. 2018[17]	Delayed surgery after < 28 days	≤ 2 cm	61/61		84%	Novilase	64 (42-77)	11 (4-19)	3%, 43 mo (34-65)	Local	12
Nori et al. 2018[55]	No resection	≤ 2 cm	12/12		100%	EchoLaser	79 (75-92)	13 (7-20)	0%, 26 mo (6-51 mo)	Local	9

CA = complete ablation rate; CNB = core needle biopsy; LITT = laser-induced thermal therapy; LRR = local recurrence rate; MINORS = methodological index for non-randomized studies; MRI = magnetic resonance imaging; NAC = XXXX neoadjuvant chemotherapy; NADH = nicotinamide adenine dinucleotide; NA = not available; NR = not reported; RFA = radiofrequency ablation; US = ultrasound; VAB = vacuum-assisted biopsy; VAE: vacuum-assisted excision.

[a] Conference abstract.

[b] Not mean but median (range) is given.

[c] Age/tumor size is given for all enrolled patients.

[d] Comparative study (maximum score of 24).

Table 2 Subgroup Analyses with all Included Studies

		No. of Studies	CA	95% CI	Q-value	Significance
Technique	Cryoablation	8	80.3%	66%-89%		
	HIFU	3	61.8%	45%-76%		
	Laser ablation	5	64.0%	36%-85%		
	MWA	1	87.0%	67%-96%		
	RFA	24	89.1%	86%-92%		
					22.15	$P < .001$
Year of publication	Before 2009	11	75.4%	58%-87%		
	Between 2009 and 2016	22	85.3%	80%-90%		
	From 2016 and later	8	90.1%	81%-95%		
					3.72	$P = .155$
Type of article	Full text	34	82.1%	76%-87%		
	Conference abstract	6	94.0%	84%-98%		
					4.16	$P = .041$
Timing of resection	Direct	13	85.0%	77%-91%		
	Delayed < 2 weeks	8	67.1%	53%-79%		
	Delayed > 2 weeks	10	86.4%	76%-93%		
	No resection	6	97.6%	92%-99%		
	Unknown	3	83.8%	74%-91%		
					19.27	$P = .001$
Method of resection	Surgery	31	79.8%	74%-85%		
	Biopsy and/or imaging	9	96.2%	92%-98%		
					18.76	$P < .001$
EIC as exclusion criteria	No	5	72.8%	63%-81%		
	Yes	21	86.6%	82%-90%		
	Unknown	14	86.4%	70%-94%		
					8.61	$P = .014$
MRI before procedure	No	8	80.6%	61%-92%		
	Yes	23	86.8%	81%-91%		
	Unknown	9	81.1%	69%-89%		
					1.47	$P = .4379$
Method of histology	NADH	19	88.4%	84%-92%		
	Other	15	71.5%	62%-79%		
	No histology performed	6	97.6%	92%-99%		
					24.21	$P < .001$

CA = complete ablation; CI = confidence interval; EIC = extensive intraductal component; HIFU = high-intensity focused ultrasound; MRI = magnetic resonance imaging; MWA = microwave ablation; NADH = nicotinamide adenine dinucleotide; RFA = radiofrequency ablation.

Figure 1). Egger's test suggested a risk for publication bias ($P < .001$; Appendix E; Figure 2). When all conference abstracts were excluded, complete ablation rate was 82.1% (95% CI, 76%-87%). Six subgroup analyses showed significant differences in complete ablation rates (Table 2). The highest complete ablation rates were seen after RFA, in conference abstracts, when no resection was performed, when tumors with an EIC were excluded, and when only biopsy and/or imaging was used for the evaluation of complete ablation. When histologic evaluation was done, complete ablation was higher in those studies using nicotinamide adenine dinucleotide (NADH) staining compared with other types of staining. Heterogeneity could be decreased to moderate ($I^2 = 47.52\%$, $P = .002$) when the variables technique, method of resection, EIC as an exclusion criterion, and the method of histological evaluation were included in a meta-regression. None of the covariates had a significant effect by themselves in this meta-regression (Appendix F).

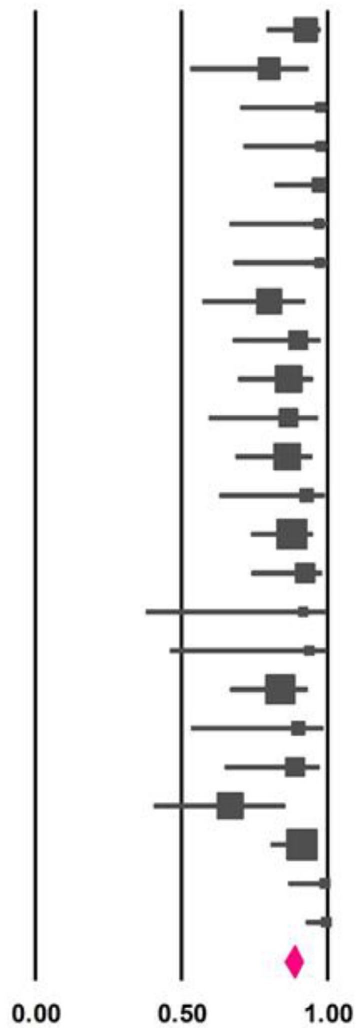
Subgroup analyses per technique did not show statistically significant differences for the year of publication and type of device, except in laser ablation, which will be reported in detail in the following sections.

Radiofrequency Ablation

Complete Ablation. Complete ablation was achieved in 602 out of 651 patients (92%, binominal exact 95% CI, 90%-94%). Q-

Figure 2A Meta-analysis of complete ablation rate per study, radiofrequency ablation.

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Manenti 2013	0.925	0.792	0.976	4.185	0.000
	Chappuis 2016	0.800	0.530	0.934	2.148	0.032
	Fornage 2004	0.975	0.702	0.998	2.558	0.011
	Garcia 2018	0.976	0.713	0.999	2.594	0.009
	Imoto 2017	0.971	0.819	0.996	3.445	0.001
	Motoyoshi 2010	0.971	0.664	0.998	2.436	0.015
	Motoyoshi 2010	0.972	0.678	0.998	2.479	0.013
	Onishi 2010	0.800	0.572	0.923	2.480	0.013
	Hung 2009	0.900	0.676	0.975	2.948	0.003
	Imoto 2009	0.867	0.694	0.949	3.485	0.000
	Khatri 2007	0.867	0.595	0.966	2.464	0.014
	Kinoshita 2011	0.862	0.685	0.947	3.403	0.001
	Medina-Franco 2008	0.929	0.630	0.990	2.472	0.013
	Ohtani 2011	0.878	0.739	0.948	4.136	0.000
	Yamamoto 2011	0.923	0.739	0.981	3.376	0.001
	Yoshinaga 2013	0.917	0.378	0.995	1.623	0.105
	Yoshinaga 2013	0.938	0.461	0.996	1.854	0.064
	Wiksell 2010	0.839	0.666	0.931	3.376	0.001
	Burak 2003	0.900	0.533	0.986	2.084	0.037
	Schassburger 2014	0.889	0.648	0.972	2.773	0.006
	Waaijer 2014	0.667	0.406	0.854	1.266	0.206
	Kinoshita 2017	0.912	0.806	0.963	5.001	0.000
	Oura 2007	0.991	0.866	0.999	3.275	0.001
	Oura 2009	0.995	0.926	1.000	3.741	0.000
Fixed		0.886	0.854	0.913	13.875	0.000



test showed minimal heterogeneity ($I^2 = 14.6\%$, $P = .259$) thus a fixed model was used to determine pooled proportion, resulting in 88.6% (95% CI, 85%–91%; Figure 2A). Table 1A shows that the lowest complete ablation rate was 67%,[24] whereas all other studies present complete ablation rates of ≥ 80%. In this outlier study a novel bipolar RFA device was used, whereas all other studies used unipolar devices.[24]

Explanation for Incomplete Ablation. In 24 out of 49 incompletely ablated tumors,[18,23-25,36,40,54] an explanation was given. Eleven tumors were mistargeted, in 8 tumors DCIS was still present adjacent to the ablation zone, the device malfunctioned in 3 procedures, and tumor size was underestimated in 2 tumors.

Complications. Nineteen studies reported on complications, which occurred in 49 out of 523 patients (pooled rate 9.4%, binominal exact 95% CI, 7%-12%). The most severe complication was a case of chronic granulomatous mastitis.[41] Avoidable complications were skin burns surrounding the grounding pads because of incorrect placement,[41] and a pneumothorax owing to probe misplacement.[24]

Imaging Techniques. Using MRI as a diagnostic tool did not result in a higher complete ablation rate (96.8%, 95% CI, 81%-91%) than not using MRI (81%, 95% CI, 62%-92%; $Q = 0.68$; $P = .409$). MRI was used as a tool to predict complete ablation in 5 studies. In 2 studies, MRI showed no residual enhancement, whereas residual lesions were found at histologic evaluation.[41,44] In 1 study, residual enhancement was correctly correlated to residual invasive carcinoma, but small areas of DCIS were missed on MRI in 4 patients.[39] In the last 2 studies, residual enhancement on MRI was only seen in patients with residual lesions at histologic evaluation.[25,42] In 1 of these articles, MRI was performed at 1 and 4 weeks after ablation.[42] After 1 week, suspicious residual enhancement was seen in 9 patients, but it appeared less suspicious at 4 weeks in 4 of these patients, suggesting reactive granulation tissue around the ablated area.

Method for Determining Complete Ablation and Timing of Resection. Subgroup analysis showed lower complete ablation rates when immediate resection was performed (86.2%, 95% CI, 80%-91%), compared with delayed resection (92.8%, 95% CI, 87%-96%), or no resection (96.8%, 95% CI, 87%-99%; Q = 6.1; P = .048). When only imaging and/or biopsy was performed, higher complete ablation rates were reported (95.0%, 95% CI, 90%-98%) than when histologic evaluation was performed (86.4%, 95% CI, 82%-90%). When histologic evaluation was performed, a higher complete ablation rate was found in studies using NADH staining (89.2%, 95% CI, 85%-92%)[22,23,31,33,35-43,45] than in studies using other staining techniques (81.3%, 95% CI, 69%-89%; Q= 16.49; P = .001).[18,24,25,44] A local recurrence, as reported in studies without subsequent resection, occurred in 1 out of 243 patients (0.41%, 95% CI, 0%-0.02%) after a median follow-up of 15 to 61 months (Table 1A).

Other Subgroup Analyses. Excluding patients with an EIC appeared to lead to higher complete ablation rates, but the effect was not significant (excluded: 85.8%, 95% CI, 81%-90%[18,32] vs. included: 76.0%, 95% CI 62%-86%, Q = 3.219; P = .073).[23-25,33-36,39-44] However, 7 studies did not report on this.[21,22,31,37,38,45,46]

Cosmetic Outcome. Eight studies reported on cosmetic outcome after RFA,[21,32,33,41-43,46,55] 6 of which categorized this as poor, fair, good, or excellent. In 181 of 212 patients (85%, binominal exact 95% CI, 80%-90%) the cosmetic outcome was excellent; for the remainder of the patients, the cosmetic outcome was fair (Table 3). The methods used to evaluate cosmetic outcome were sparsely described, and 3 studies did not describe this at all.[41,46,55] Two studies used a 4-point scaling system reported by either the patient,[33] the clinician,[42] or both.[21] In another study,[32] independent clinicians not involved in the study scored cosmetic outcome on a scale of 1 to 10, which was then categorized into 4 categories. In the last study, patients were interviewed, and cosmetic outcome was then graded into 4 categories.[43] None of the studies compared cosmetic outcome after RFA with cosmetic outcome after lumpectomy. In 1 study, cosmetic outcome after cryoablation was compared with cosmetic outcome after RFA, but no significant difference between the 2 techniques was found[42] (Table 3).

Microwave Ablation

Only 1 study[19] reporting on the use of MWA was included.

Complete Ablation. A complete ablation was reached in 20 out of 23 patients (87%, binominal exact 95% CI, 68%-95%). Pooled proportion using a fixed model was 87% with a 95% CI of 66.5%-95.7% (Table 1B; Figure 2B).

Explanation for Incomplete Ablation. In 2 cases, incomplete ablation was caused by poor positioning of the probe. In 1 of these lesions and a third lesion, size was underestimated on pretreatment imaging.

Complications. One epidermal skin burn and 2 slight thermal injuries to the pectoralis major muscle were found after MWA in the resected specimen (13%, 95% CI, 4.5%-32.1%). No other severe adverse events occurred.

Other Subgroup Analyses. Because only 1 study reported on MWA, no subgroup analyses could be performed. Resection was performed immediately, and the ablation zone was assessed using NADH. Patients with DCIS were included, and no predictive value for MRI or cosmetic outcome was reported.

Cryoablation

Eight studies reported on complete ablation rate after cryoablation (Table 1C).[11,20,29,42,47-50,56] The complete ablation rates reported in full-text articles were significantly lower (76.9%, 95% CI, 64%-86%) than in the only conference abstract with 140 patients (99.6%, 95% CI, 95%-100%). Remarkably, the conference abstract was also the only study that assessed complete ablation rate based on follow-up imaging without performing subsequent resection.

Complete Ablation. Complete ablation was reported in 339 of 397 patients (85%, binominal exact 95% CI, 82%-89%). The Q-test of heterogeneity revealed a large variation between effect sizes of the studies (I^2 = 76.5%; P < .001). Pooled complete ablation rate was 80.3% (95% CI, 66%-89%) using a random effects model (Figure 2C). A remarkably low complete ablation rate (18%) was reported in 1 study.[29] Unique in this study was that cryoablation was performed under MRI guidance, whereas other studies used US guidance. Additionally, freezing cycles lasted only 5 minutes, instead of at least 6 minutes in other studies.[29] Therefore this study could be considered as not representative for the group.

Explanation for Incomplete Ablation. All but 1 study[29] mentioned explanations for incomplete ablation.[11,20,42,47-50] In 17 cases, multifocality was detected on histologic evaluation (of which 15 were in 1 study[11]). Other explanations were DCIS adjacent to the ablation zone in 10 cases, tumor mistargeting in 5, and tumor size was underestimated on pretreatment imaging in 4 tumors.

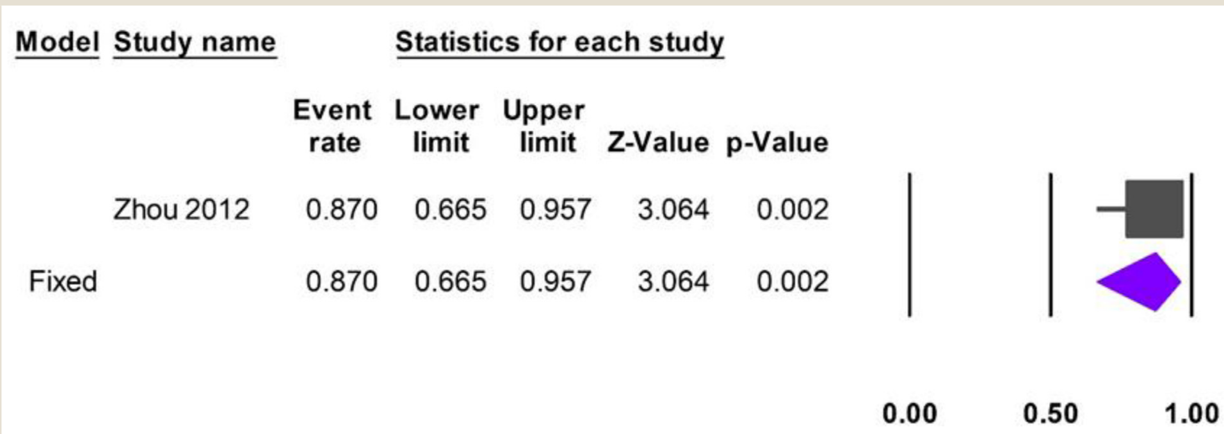
Complications. Only 2 studies reported complications associated with the low temperature of cryoablation. In these cases, the tumor was located within 2 cm of the skin surface.[20,29] Other reported complications included self-limiting ecchymosis, seroma, nodular thickening, and hematoma or swelling at the cryoablation site.[29,48,50,56] The most severe complication was an arterial bleed

Table 3 Cosmetic Results per Study

Study	Technique	Timing Resection	Timing Cosmetic Evaluation	Cosmetic Result				
				Excellent	Good	Fair	Poor	Other
Garcia et al. 2018[21]	RFA	Direct	15 days after RFA and BCS					85% good or very good
Kinoshita et al. 2017[47]	RFA	No resection	Not mentioned	54 (94%)				
Medina-Franco et al. 2008[43]	RFA	Direct	After RFA and BCS before radiotherapy	16 (80%)	4 (20%)			
Oura et al. 2007[45]	RFA	No resection	Not reported	43 (83%)	6 (12%)	3 (6%)		
Yamamoto et al. 2011[34]	RFA	Delayed	Not reported	29 (97%)				
Yoshinaga et al. 2013[44]	RFA	No resection	1 year after RFA	5 (63%)	1 (13%)	2 (25%)		
Manenti et al. 2013[37]	RFA	Delayed	4 weeks after RFA, before surgery	34 (85%)	3 (8%)	1 (3%)	2 (5%)	Poor result owing to skin necrosis in 1 patient and skin retraction in another
	Cryo	Delayed	4 weeks after Cryo, before surgery	40 (39%)	2 (5%)	1 (3%)		
Fine et al. 2018[20]	Cryo	No resection	During FU visit (exact timing unknown)					95% of patients and 98% of physicians were satisfied with the cosmetic results
Schwartzberg et al. 2018[17]	Laser	No resection	Not reported	39 (64%)	20 (33%)			

BCS = breast-conserving surgery; Cryo = cryoablation; FU = follow-up; RFA = radiofrequency ablation.

Figure 2B Meta-analysis of complete ablation rate per study, microwave ablation.



after removal of the cryoprobe, which stopped after 20 minutes of manual compression.[48] Overall, 14 complications in 283 patients were reported after cryoablation (5.0%, binominal exact 95% CI, 3.0%-8.1%).

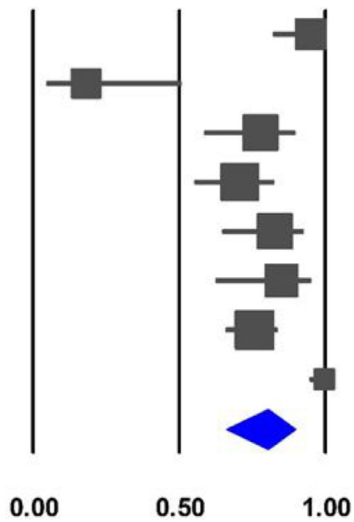
Imaging Techniques. MRI was used as a diagnostic tool in 4 studies,[11,29,42,50] in 2 studies no MRI was performed prior to cryoablation.[47,48] When MRI was used as a diagnostic tool, complete ablation rate did not increase (84.3%, 95% CI 66%-93%; Q = 0.01; P = .906). The predictive value of MRI for assessing complete ablation was 100% in 1 study in which an MRI was performed 1 and 4 weeks after cryoablation.[42] In the study by Simmons et al.[11] the negative predictive value of MRI was 81.2%, whereas in Poplack et al.[50] the residual disease seen in pathology was missed on MRI in all cases.

Method of Determining Complete Ablation and Timing of Resection. Immediate resection was not performed in any of the studies

Figure 2C Meta-analysis of complete ablation rate per study, cryoablation.

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Manenti 2013	0.950	0.821	0.987	4.059	0.000
	Pusztaszeri 2007	0.182	0.046	0.507	-1.924	0.054
	Sabel 2004	0.778	0.586	0.897	2.706	0.007
	Gajda 2014	0.707	0.552	0.826	2.571	0.010
	Pfleiderer 2005	0.828	0.647	0.926	3.191	0.001
	Poplack 2015	0.850	0.624	0.951	2.770	0.006
	Simmons 2016	0.759	0.658	0.837	4.571	0.000
	Fine 2018 US	0.996	0.946	1.000	3.980	0.000
Random		0.803	0.662	0.894	3.757	0.000

Statistics for each study



therefore the result of the subgroup analysis was the same for the timing and method of resection. Higher complete ablation rates were reported when no resection and thus only imaging and/or biopsy was performed (99.6%, 95% CI, 95%-100%)[20] than after delayed resection in which histologic evaluation was performed (76.9%, 95% CI, 64%-86%).[11,29,42,47-50] When no resection was performed, a local recurrence rate of 1.3% was reported within 12 months of follow-up on mammogram or MRI. One study[42] used NADH to determine complete ablation and showed a significantly higher complete ablation rate (95.0%, 95% CI, 82%-99%) than the other studies (73.5%, 95% CI, 61%-83%; Q = 5.99; $P = .014$).

Other Subgroup Analyses. Three studies that excluded tumors with an EIC reported slightly but not significantly higher complete ablation rates (85.6%, 95% CI, 69%-94%)[11,42,50] than 2 studies that included these patients (75.7%, 95% CI, 62%-86%; Q = 1.84; $P = .176$).[48,49] The authors of the latter 2 studies both argued that tumors with EIC are less suitable for cryoablation compared with invasive ductal carcinomas.[48,49]

Cosmetic Outcome. Two studies described the cosmetic outcome after cryoablation.[20,42] It was excellent in 37 out of 40 patients in 1 study,[42] and in the other study 95% of patients and 98% of physicians were satisfied with the cosmetic result (Table 3).[20]

High-intensity Focused Ultrasound Ablation

Complete Ablation. Results of HIFU were reported in 2 studies (Table 1D), and in 21 of 34 patients the tumor was completely ablated (61.8%, binominal exact 95% CI, 45%-76%).[26-28] The studies were highly homogeneous according to the Cochrane test ($I^2 = 0.00$; $P = .891$), and the fixed model showed a complete ablation rate of 61.8% (95% CI, 545%-76%; Figure 2D). No subgroup analyses were performed because only 2 studies were included.

Explanation for Incomplete Ablation. Incomplete ablation could be attributed to technical failure in 1 case, patient movement in 1 case, and to an incomplete treatment plan in another case. In 2 other tumors, viable cells in the center of the tumor surrounded by necrotic cells were found. It was postulated that in these cases morphologic aspects were preserved but functionality was eliminated. For the remaining 8 patients no explanation was given.

Complications. No adverse events occurred in 1 study, and 6 occurred in the other (pooled 17.7%, 95% CI, 8%-34%).[27,28] These 6 complications included pain (3), skin erythema (1), skin burn (1), and shoulder pain (1).

Imaging Techniques. One study[28] compared complete ablation rates on MRI to the histopathologic results. In 2 cases, a residual enhancing lesion was seen on MRI, which was confirmed at histologic evaluation. However, in 2 cases no residual enhancement was seen on MRI, but viable cells were found in the middle of the ablated area on histologic evaluation.

Other Subgroup Analyses. One study did not report on inclusion/exclusion of tumors with an EIC, or the method to determine complete ablation.[27] In the other study, hematoxylin and eosin staining was used, and tumors with an EIC were included.[28] In both studies, resection was planned within 25 days after ablation.

Figure 2D Meta-analysis of complete ablation rate per study, high-intensity focused ultrasound.

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Cavallo 2015	0.600	0.297	0.842	0.628	0.530
	Furusawa 2006	0.625	0.422	0.792	1.212	0.226
Fixed		0.618	0.447	0.763	1.358	0.175

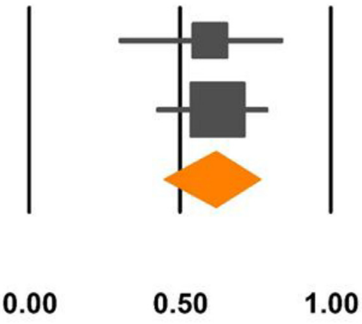
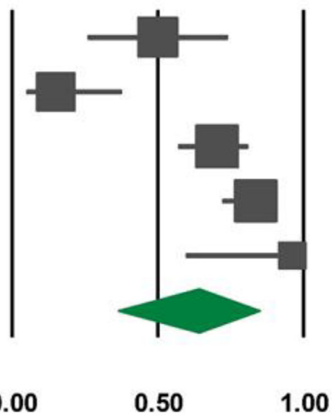


Figure 2E Meta-analysis of complete ablation rate per study, laser ablation.

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Esser 2009	0.500	0.260	0.740	0.000	1.000
	Haraldsdóttir 2008	0.150	0.049	0.376	-2.770	0.006
	Dowlatshahi 2002	0.704	0.570	0.810	2.902	0.004
	Schwartzberg 2018	0.836	0.721	0.909	4.711	0.000
	Nori 2018	0.962	0.597	0.998	2.232	0.026
Random		0.640	0.362	0.848	0.990	0.322



Cosmetic Outcome. None of the studies described the cosmetic result after HIFU ablation.

Laser Ablation

Complete Ablation. Complete ablation was reached in 111 out of 161 patients (68.9%, binominal exact 95% CI, 62%-79%), and varied from 15% to 100% among 5 studies (Table 1E; Figure 2E).[17,30,51-53] A large heterogeneity was found across studies (I^2 = 85.3%; P < .001), and a random effects model showed a pooled complete ablation rate of 64.0% (95% CI, 36%-85%). The study reporting the lowest complete ablation rate of 15% performed laser ablation with 1 to 4 probes,[51] whereas in all other studies only 1 probe was used in the center of the tumor.

Explanation for Incomplete Ablation. Explanations for incomplete ablation were specified in 3 studies,[17,30,52] and included suboptimal target visualization in 5, inadequate laser energy owing to learning phase in 4, device malfunctioning in 4, tumor mistargeting in 3, and underestimation of tumor size in 3 cases.

Complications. The most severe complication was a pneumothorax,[52] which occurred in a tumor close to the thoracic wall. Other reported complications were a palpable lump, skin or fat necrosis, hematoma, seroma, erythema, skin burns, or pain.[17,30,51-53] Overall, complications occurred in 20 out of 165 patients (12.1%, 95% CI 7.9%-18.0%).

Imaging Techniques. MRI had a higher negative predictive value than US and mammography, respectively 92%, 89%, and 75% in 1 study,[17] and was not reported in other studies.

Method of Determining Complete Ablation and Timing of Resection. A trend toward higher complete ablation rates was seen when no resection was performed[53] (96%, 95% CI, 60%-100%), compared with immediate[52] (50%, 95% CI, 26%-74%) and delayed resection (58.8%, 95% CI, 42%-86%).[17,30,51] However, subgroup analysis did not show a significant difference (Q = 4.38; $P = .112$) for this evaluation, nor for the comparison between histologic evaluation of the ablation zone (57.1%, 95% CI 29%-81%) and (96.2%, 95% CI 60%-100%; Q = 3.52; $P = .06$). Complete ablation rate assessment and follow-up were performed with US and mammography in the study without resection.[53] No local recurrences (0%, 95% CI, 0%-24%) were seen in 12 patients after 6 to 51 months (median 28.5 months) of follow-up with US and mammography.[53]

Other Subgroup Analyses. Newer studies reported higher complete ablation rates (85.9%, 95% CI, 70%-94%) than studies performed before 2009 (40.7%, 95% CI, 5%-90%) and between 2009 and 2016 (50.0%, 26%-74%; Q = 7.06, $P = .029$). Also, studies in which the Echolaser (96.2%, 95% CI, 60%-100%) or Novilase (83.6%, 95% CI, 72%-91%) were used to perform laser ablation showed higher complete ablation rates than studies in which Diomed (40.7%, 95% CI, 5%-90%) or Microdom LIT were used (50.0%, 95% CI, 26%-74%; Q = 9.99; $P = .019$). However, Diomed and Microdom lasers were used in older studies and EchoLaser and Novilase were used in newer studies, and thus these variables seemed to be interdependent. If patients with an EIC were excluded, the complete ablation rate was significantly higher (83.6%, 95% CI, 72%-91%) than when they were not excluded (63%, 95% CI, 43%-80%).

Cosmetic Outcome. One study reported on cosmetic outcome, which was rated as excellent in 64% of the 58 responding patients and as good in 33%.[17]

Discussion

In this systematic review and meta-analysis we evaluated the outcomes of 5 thermal ablation techniques in the treatment of small (≤ 2 cm) breast cancers. The overall high complete ablation rate of 86% in 1266 patients, the feasibility of treatment under local anesthesia, and low short-term complication rates suggest that thermal ablation could be a safe and effective alternative to surgical resection. Overall, included studies were noncomparative and often small-sized, with patient numbers ranging between 10 and 143 (median 24 patients). Therefore the results of this review should not lead to firm conclusions, but rather serve as a basis for larger phase 2 and 3 clinical trials.

The overall complete ablation rate after thermal ablation of tumors ≤ 2 cm was 86%, and the highest rates were reported with RFA (92%), MWA (87%), and cryoablation (85%). Complication rates varied from 5%-18% between techniques and were highest after HIFU ablation and lowest after cryoablation. Cosmetic outcome was good to excellent in at least 85% of patients, but cosmetic results were rarely reported. Long-term results of cosmetic outcome after thermal ablation and radiotherapy are still lacking. The biological subtype of tumors might have influenced treatment response and thus the estimates of complete ablation rates. However, these tumor characteristics were only sparsely reported, or could not be linked to complete ablation and could therefore not be included in this meta-analysis.

We found higher rates of complete ablation than previous meta-analyses on thermal ablation.[8,9] This may be explained by the inclusion of the most recent literature, and by including only small tumors (≤ 2 cm). Clinical success of a thermal ablation treatment is determined by the ability to create an adequate safety margin around the tumor. Given the predefined maximum ablation size of the techniques of only several centimeters, it would be logical to focus further research on the thermal ablation of smaller-sized tumors.

A strength of this meta-analysis is the specific inclusion of only patients with small tumors. As the number of tumors ≤ 2 cm is relatively limited, all studies that presented separate results for at least 10 tumors of ≤ 2 cm were also included. Although this might have led to a more heterogeneous sample, we considered completeness of data over a possible increase in homogeneity. By only including the results of tumors ≤ 2 cm, we aimed to provide a better estimate of the true treatment success in small tumors and identify factors that led to higher complete ablation rates. Subgroup analyses overall and per technique showed higher complete ablation rates when no resection was performed, and only imaging and/or biopsy was used to determine complete ablation. Higher complete ablation rates were also seen when tumors with an EIC were excluded and when NADH staining was used for the histologic evaluation. These variables seem to correlate because only biopsy and/or imaging was performed in studies without surgical resection, of which only a conference abstract of ongoing studies was available. Additionally, NADH staining was mainly used in RFA studies.

Using current guidelines, the overall complete ablation rate of 86% in this study may suggest that 14% of patients would have needed a re-intervention, which is comparable to re-excision rates after breast-conserving surgery (11%-28%).[57-61] However, an important challenge of thermal ablation will be the evaluation of complete ablation when no subsequent resection is performed. In our review, the evaluation of complete ablation using MRI showed ambiguous results. On the one hand, repeating postablation MRI may result in higher specificity and improved discrimination between reactive granulation tissue and residual disease.[42] On the other hand, DCIS or foci outside of the primary tumor could still be missed on postablation MRI.[11,39] The method for determining complete ablation should at least be sufficiently sensitive to maintain the current low local recurrence rates of patients with early-stage breast cancer. Previous and currently ongoing studies combine imaging with biopsies to detect residual disease.[20,22,32,34,46,53,55] Local recurrence rates in these studies are low (0%-3%), but longer follow-up of larger cohorts and eventually comparative studies are needed to corroborate these results.

Higher complete ablation rates were found in studies performing delayed resection or no resection at all than in studies performing immediate resection. Inevitably, when less material is available lower rates of residual disease will be found.[62-64] However, thermal ablation causes both immediate and delayed effects because the area of cell death will expand over time.[65,66] Delayed cell death occurs as a result of vascular thrombosis, resulting in progressive failure of the microcirculation and ultimately vascular stasis, tissue ischemia, or reperfusion injury.[67,68] Additionally, it is postulated that the immune system is activated by thermal ablation and will eradicate residual tumor cells over time.[68-72] It is therefore likely that because of these delayed effects, complete ablation rates increase when the interval between thermal ablation and evaluation of the specimen is prolonged.

In our study, exclusion of patients with tumors with an extensive DCIS component led to higher complete ablation rates overall and after laser ablation. A (nonsignificant) trend toward higher complete ablation rates was reported after RFA and cryoablation. Several studies suggest that tumors with an extensive DCIS component are not suitable for thermal ablation because of underestimation of tumor size on imaging.[18,19,23,25,33,40,41,43,44,48,49,52,73,74] Moreover, after breast-conserving surgery, the risk of positive margins and subsequent re-excisions is higher in patients with DCIS compared with patients with invasive breast cancer.[75] To minimize the risk of missing DCIS after thermal ablation, we recommend excluding patients with extensive DCIS components from thermal ablation treatment.

Based on the complete ablation rates reported in this review, RFA, MWA, and cryoablation are the most promising techniques. Of these, cryoablation has the lowest complication rate and the advantage of an analgesic effect.[42] A formal recommendation on the best technique is not possible because of large heterogeneity in the included studies. Additional important aspects such as cosmetic outcome, quality of life, and initiation of immune response are currently underreported in literature. We would therefore propose a prospective study comparing these 3 techniques using a uniform protocol. Based on this review, we recommend excluding tumors with an EIC, and include only patients with tumors that are visible on US. With current evidence, a treat and resect protocol would be most valuable as this will provide more data on differences in complete ablation and short-term complication rates between techniques, the concordance between MRI and histologic evaluation of complete ablation, and the potential of initiating an immune response per technique. The results of such a pilot study should aid in the design of a large phase III trial comparing lumpectomy plus radiotherapy to the most promising thermal ablation technique plus radiotherapy. Additionally, it should be investigated whether variables such as biological subtype of the tumor and breast density category influence treatment response.

Conclusion

This review demonstrates that thermal ablation techniques treating small-sized breast cancer are safe, using local anesthesia is feasible, and overall complete ablation rates are high. Especially, RFA, MWA, and cryoablation are promising techniques as an alternative to surgical resection without jeopardizing current treatment effectiveness or safety. Thermal ablation techniques can potentially reduce treatment burden and morbidity and improve cosmetic outcome in patients with early-stage breast cancer. These findings warrant the design of large randomized controlled trials comparing thermal ablation and breast-conserving surgery in the treatment of T1 breast cancer.

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Disclosure

The authors have stated that they have no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clbc.2021.03.004.

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