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REVIEW

US-guided ablation of tumors – where is it used and how did we get there

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Abstract

Ablation under ultrasound (US) guidance for the treatment of various tumors in liver, thyroid, prostate, kidney, uterine and many other organs evolved extensively in the past decades. Major ablative techniques, including radiofrequency ablation, microwave ablation, high intensity focused ultrasound, cryoablation, percutaneous ethanol injection, laser ablation and irreversible electroporation, have all been widely applied and ablation is recommended by several guidelines as first-line or alternative therapy e.g. hepatocellular carcinoma in early stage, T1a stage renal cell carcinoma and thyroid nodules. In the current article, we reviewed 2508 articles on tumor ablation under US guidance and present the status of US-guided tumor ablation globally.

Highlights

- Radiofrequency is the most used technique for ablation in solid tumors.
- Asia accounted more than a half in ultrasound-guided tumor ablation.
- Thyroid nodules have developed rapidly since 2010.

Keywords Ablation · Ultrasound · Tumor

Introduction

During the past three decades, modern medicine has moved toward precision medicine and minimal-invasive therapy for treatment of various tumors. Although surgery remains the standard treatment, many patients are not candidates for surgery due to poor status of health, insufficient sparing of organs or cosmetic considerations [1–4] and consequently percutaneous ablation became an option.

The concept of percutaneous ablation implies localized and in situ treatment of cancer. This form of therapy has often been referred to as interstitial tissue destruction and its use as a treatment of malignant tumors is ancient. Surprisingly, the first known reference dates back to approximately 2000 B.C. where in ancient Egypt the use of cauterization for treatment of localized breast cancer, by means of a heated poker, was described [5]. The advent of interventional ultrasound (US) brought about a revival of this ancient concept of interstitial tissue destruction when prof Hans Henrik Holm and coworkers in 1981 published their work on US-guided

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brachytherapy, a novel technique for precise percutaneous placement of radioactive seeds in abdominal mass-forming cancers [6].

Following the initial reports of brachytherapy, the 1980s quickly saw other methods of tissue destruction being utilized [7, 8]. A novel principle for tumor treatment had been introduced and this sparked the beginning of a truly remarkable line of cancer therapy known today as ablation and utilized for treatment of a diverse range of neoplasia in different organs such as prostate, uterus, liver, kidney, lung, thorax, thyroid, parathyroid and the brain [9–27], and performed by means of different physical methods such as heat, cold (cryoablation, CA), radioactivity, high voltage electric current, high intensity focused ultrasound (HIFU) or chemical agents such as percutaneous ethanol injection (PEI). Several of these techniques today present themselves as established treatments for multiple neoplastic diseases and among these thermal ablation of liver tumors by means of heating through laser ablation (LA), radiofrequency ablation (RFA) or microwave ablation (MWA), likely is the most widely used worldwide. Throughout the 1990s and first two decades of twenty-first century, percutaneous ablation for both malignant and benign conditions guided by different imaging modalities, but most frequently ultrasound, has grown tremendously and today holds an established position in many oncological protocols with RFA and MWA as the leading ablation modalities [9–17]. Among the various percutaneous ablation imaging guidance modalities, US-guidance is the most widely used imaging-guided modality due to its numerous advantages. One of its key benefits is its real-time monitoring capability, which allows for precise and accurate guidance during medical procedures. In comparison to computed tomography (CT) and magnetic resonance imaging (MRI), ultrasound has the added advantage of providing real-time, dynamic observations, making it an ideal option for surgical planning, real-time monitoring during ablation procedures, and post-operative evaluation of ablation effectiveness. Another significant advantage of ultrasound is its non-radiation nature, making it a safe option for patients. Additionally, ultrasound boasts high soft tissue resolution, which allows for clear images of internal structures. Lastly, compared to other imaging modalities, ultrasound is relatively low in cost, making it a more accessible option for patients and healthcare providers alike. Numerous dedicated professionals [14–27] took part in the early pioneering work of US-guided ablative techniques. The development of the concept along with the principles we are guided by today should be attributed to this group and their worldwide movement with accompanying network, rather than trying to point out one single person as the originator. Therefore, this study aims to review tumor ablation under US guidance to present the status of this field.

Literature search and selection

We searched the PubMed, Embase and Cochrane database. The beginning date of published articles for searching was not set, and the deadline was set in November 2021. The research strategy which included Mesh word and free word is as followed: (((ablation therapy) or (ablation) or (radiofrequency) or (radiofrequency therapy)) or ((laser) or (laser*)) or ((microwaves) or (microwave*) or (MWA)) or ((cryoablation*) or (cryosurgery*) or (cryosurgery)) or ((high-intensity focused ultrasound) or (HIFU)) or (ultrasound therapy) or ((irreversible electroporation) or (IRE))) and ((neoplasm) or (neoplas*) or (tumor*) or (cancer*) or (malignancy*) and (ultrasound guidance) or (ultrasonography guided) or (US-guided))). After searching the database, 139,606 articles were retrieved. 108,231 articles removed because of duplication. The inclusion criteria are as followed: 1) ablation was performed by US-guided; 2) studies of human beings; 3) clinical study for safety and efficacy about different ablative technique; 4) malignant and benign tumor. The exclusion criteria are as followed: 1) review, meta-analysis, consensus, case report, conference abstracts, editorial comments, guidelines, letters, responses; 2) studies for the ability of imaging to evaluate technique success or studies for reporting complications; 3) studies not associated with ablation. If the study included both US-guidance or other modalities of guidance, only US-guidance was counted when possible. If the research included other therapy such as surgery or radiotherapy, only data regarding ablation were included. The publications which match all inclusion criteria are included, and publications which match any of exclusion criteria are excluded. Finally, a total of 2508 articles were included, the process of searching and screening is shown in Fig. 1.

Development of ablation techniques worldwide

A total of 58 countries had published articles in the field of US-guided ablation for tumor treatment. The continent which has published most articles is Asia (55.14%, 1383/2508), followed by Europe (29.90%, 750/2508), North America (12.84%, 322/2508), Africa (0.88%, 22/2508), South America (0.68%, 17/2508), and Oceania (0.56%, 14/2508). And the following review of ablation is mainly focused on Asia, Europe and North America due to these three continents accounting for more than 97% of the total. The top five countries publishing ablation for the treatment of tumors is China (33.97%, 852/2508), followed by Japan (11.00%, 276/2508), Italy (10.96%, 275/2508), United States (10.25%, 257/2508) and South Korea (8.21%, 206/2508). The distribution of geography for articles is shown in Fig. 2.

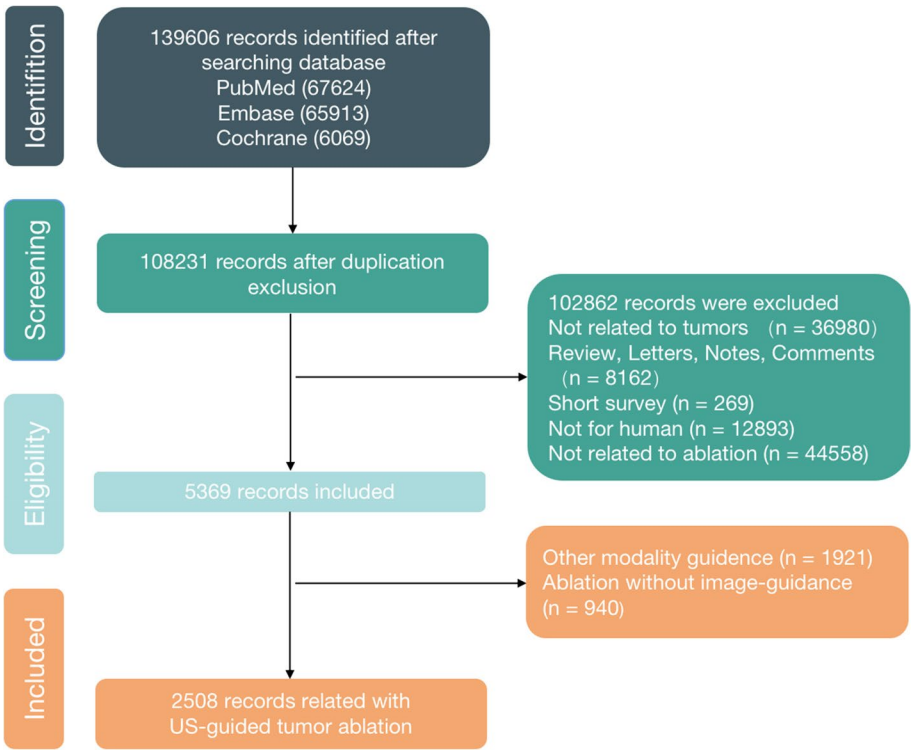

Fig. 1 Flow diagram outlining the article selection process

Although there are 7 major ablation modalities, RFA had the most publications among the ablation techniques all over the world accounting for 54.55% (1368/2508), followed by MWA (14.07%, 353/2508), HIFU (13.16%, 330/2508), CA (7.46%, 187/2508), PEI (6.26%, 157/2508), LA (2.39%, 60/2508) and IRE (2.11%, 23/2508). In different regions, the second most published technique is different. MWA is listed number 2 in Asia (19.45%, 269/1383) and HIFU (16.80%, 126/750) in Europe, with CA (22.98%, 74/322) number 2 in North America. All seven major techniques

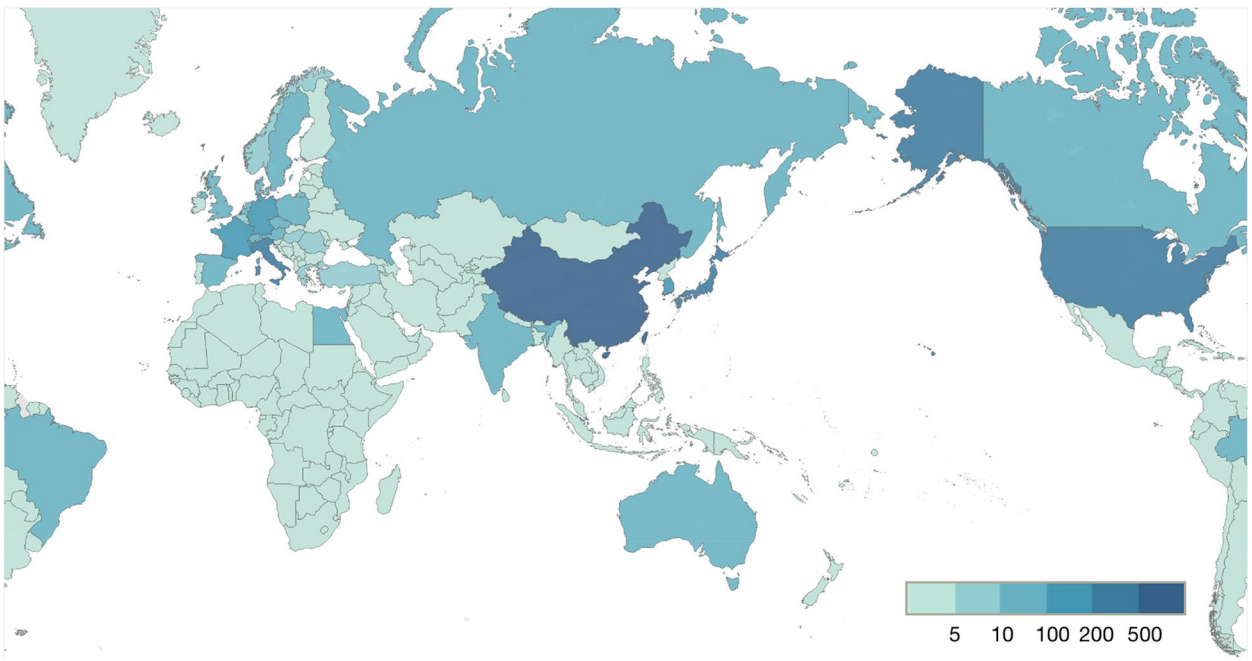

Fig. 2 Geographical distribution of published articles

are applied in Asia, Europe, and North America. Figure 3A shows the distribution of different ablation techniques in various regions. Figure 3B shows the dynamic variations over time of different ablative techniques, demonstrating a dramatically increasing use, especially thermal ablation techniques rapidly raising in numbers since the turn of the millennium. Studies published after 1999 account for 96.09% (2410/2508) of all included publications, and specifically for MWA and HIFU, articles published after 2010 represent 78.47% (277/353) and 79.09% (261/330) of their respective total.

Figure 4A shows the distribution in different tumors treated by ablation under US-guidance. Liver tumor (55.38%, 1389/2508) accounts for the most in US-guided ablation for tumors, followed by thyroid (12.24%, 307/2508), prostate (9.25%, 32/2508), kidney (7.26%, 182/2508), uterine (4.82%, 121/2508), pancreas (3.71%, 93/2508), breast (3.51%, 88/2508), other superficial organs (1.63%,41/2508) such as parathyroid and metastasis lymph nodules, and other organs (2.19%, 55/2508) such as peripheral lung cancer, bone tumor, etc. In Asia, the application of ablation of liver cancer accounted for 65.58% (907/1383), which is higher than Europe (45.60%,342/750) and North America (35.09%, 113/322). Thyroid nodules ranked second in Asia (11.79%, 163/1383). However, prostate cancer is the second most commonly treated by ablation in Europe (17.33%,130/750). In North America, renal tumors and prostate cancers are the second most commonly treated with ablation (18.32%,59/322) under US-guidance. Figure 4B shows the dynamic variations of the number of published articles of various tumors treated by US-guided ablation. In recent years, the application of ablation in thyroid nodules seems rapidly developing, where 74.18% (227/306) of articles were published after 2010.

The application of ablation in various organs

Liver

Liver cancer remains a significant health challenge and is the 4th leading cause of cancer-related death globally [9, 28]. Hepatocellular carcinoma (HCC) is the most common type of liver cancer and hepatitis B virus accounts for approximately 50% of these worldwide and 69% in eastern Asia [29]. Excluding primary liver cancer, liver metastasis ablation also accounted for part of liver cancer ablation, especially for patients with colorectal cancer liver metastasis in which only 10%-15% patients can be candidates of resection [30]. Overall, of 1389 articles, 67.60% (939/1389) are concerned with primary liver tumor ablation and 18.14% (252/1389) are about liver metastasis ablation. Asia accounts for 65.30% (907/1389) in liver cancer ablation, followed by Europe (24.62%, 342/1389) and North America (8.14%, 113/1389). The top five countries that used ablation for the treatment of liver cancer are China (37.72%, 524/1389), Japan (16.41%, 228/1389), Italy (9.65%, 134/1389), South Korea (9.64%, 134/1389) and

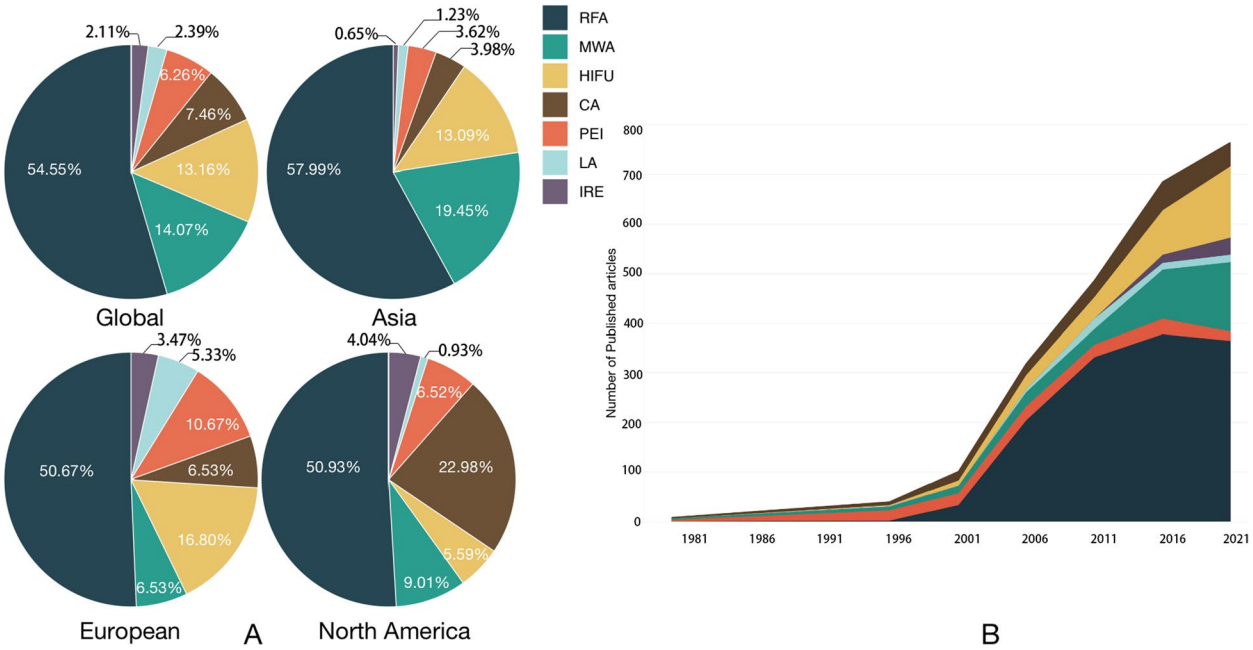

Fig. 3 **A**: The distribution of different ablative techniques according to geography; **B**: Overall trend of different ablative techniques

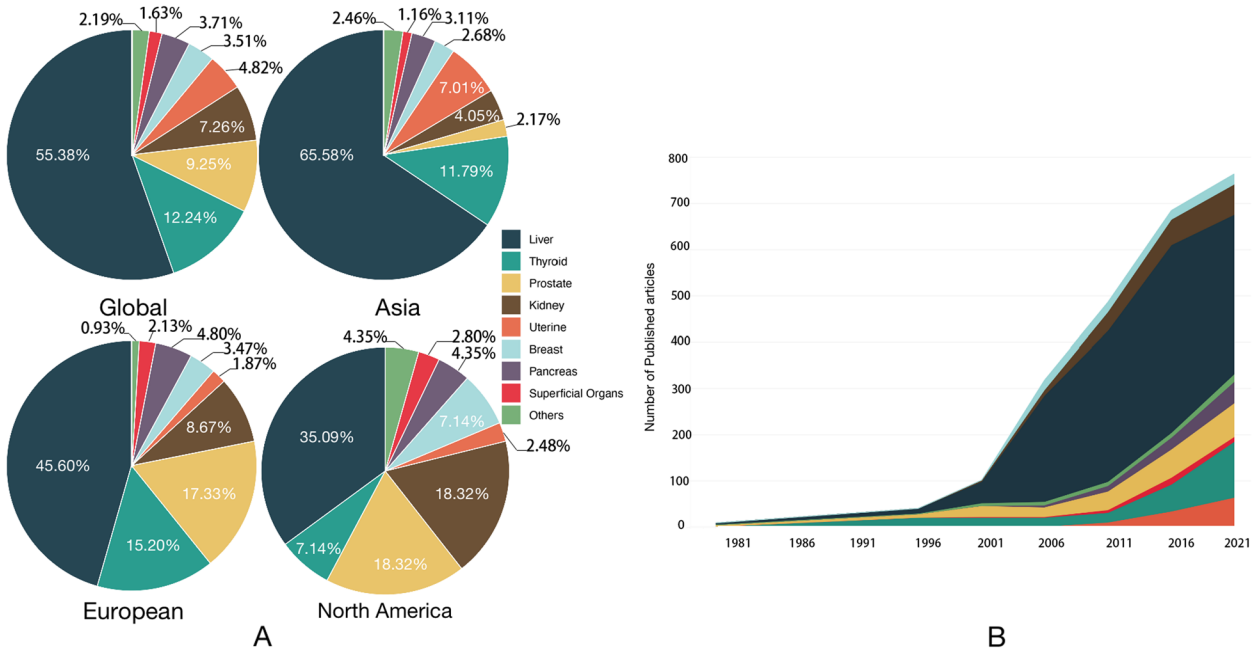

Fig. 4 **A**: The distribution of different tumors according to geography; **B**: Overall trend of tumors with ablation therapy

United States (6.55%, 91/1389). The most common ablative technique is RFA (73.87%, 1026/1389), followed by MWA (15.05%, 209/1389), CA (3.60%, 50/1389), HIFU (2.74%, 38/1389), PEI (2.23%, 31/1389), LA (1.51%, 21/1389) and IRE (1.01%, 14/1389). Commonly used ablation techniques can be seen in Table S 1.

Numerous studies have proven ablation to be effective and safe for HCC and many studies have established the value of ablation techniques for very early stage HCC (solitary lesion ≤ 2 cm). Table 1 summarizes publications reporting sample size of more than 100 for HCC in very early stage treated by ablation, which indicated ablation to be an effective method as compared to surgery resection (SR). Most studies reported that for HCC < 2 cm, ablation could achieve a similar outcome compared with SR. As for HCC in early stage (Single or ≤ 3 nodules ≤ 3 cm), ablative techniques also achieved an accepted outcome (Table 1). For HCC within the Milan criteria (solitary lesion ≤ 5 cm, or 2-3 HCC, each ≤ 3.0 cm in diameter) treated by ablation, there are also many reports establishing that ablation is effective and safe, and could achieve similar outcome to SR, (Table 2).

In recent years, several randomized controlled trials have been published reporting results with different stages of HCC in which robust evidence was provided for ablation as a curative or alternative therapy in liver cancer and in addition, comparison of the efficacy with different ablative techniques were reported (Table 3). An open-label randomized clinical trial by Xia et al. [54] compare the outcome of repeat RFA and SR in 240 patients under the Milan criteria, there was no significant difference in overall survival (OS) ($P = 0.17$). And Fang et al. [55] compared the outcome of single HCC ≤ 3 cm undergoing RFA and SR, and there was also no difference in OS ($P = 0.207$) and disease-free survival ($P = 0.443$). Additionally, several randomized controlled trials compared the outcome of HCC treated by different techniques. Yu et al. [56] compared the outcome of RFA and MWA for the treatment of early stage HCC and the results showed that there was no difference in OS but MWA required fewer ablation sessions and application punctures. These results are similar to previous studies which found that there is no difference in technique success, complications and survival [57], but lower LTP (local tumor progression) rate in MWA group compared to RFA group [58], although MWA is less susceptible than RFA to heat-sink effects when lesions were closed to major vessels [59]. Due to the efficacy of ablation and the lack of liver donors and the candidates who are unsuitable for resection, ablation was accepted as first-line therapy for very early-stage HCC or as an alternative therapy for early-stage HCC (solitary tumor and the diameter up to 3 cm, or 2 -3 tumors ≤ 3 cm) and is recommended by several guidelines to potentially achieve similar outcomes compared to SR [60–67]. Additionally, ablation combined with thanscatheter artierial chemoembolzation (TACE) could achieve better performance for intermediate stage HCC than TACE alone, (Table 4). Other ablative techniques such as CA, HIFU and LA were also used as effective methods for the treatment of HCC [68–70]. The application of IRE in liver is limited compared with other techniques. In 2005, Davalos et al. [71] used IRE for the treatment of liver ablation ex vivo. And in 2012, IRE was used in hepatic

Table 1 Summary of solitary HCC < 2 or 3 cm treated by ablation with sample size > 100

Study	No. of Patients	Region	Ablation Technique	Endpoint	1 yr	2 yr	3 yr	4 yr	5 yr	*P* value
Solitary HCC < 2 cm										
Pompili et al. 2011 [31]	218	Italy	PEI	OS	97.80%	-	86.30%	-	73.00%	-
Peng et al. 2012 [32]	71 vs 74	China	RFA vs SR	OS	98.5% vs 90.5%	-	87.7% vs 70.9%	-	71.9% vs 62.1%	0.048
Kono et al. 2014 [33]	234	Japan	RFA	LTP	2.00%	3.00%	3.00%	-	-	-
Xu et al. 2017 [34]	301 vs 159	China	MWA vs RFA	OS	99.3% vs 98.7%	-	90.4% vs 90.4%	-	78.3% vs 73.3%	0.331
Huang et al. 2018 [35]	620 vs 213	China	RFA vs SR	OS	90% vs 89%	-	64% vs 75%	-	47% vs 62%	0.113
Takayasu et al. 2018 [36]	491 vs 176	Japan	RFA vs SR	OS	-	-	92% vs 91%	-	77% vs 71%	0.814
Chu et al. 2019 [37]	761 vs 661	Korea	RFA vs SR	OS	98.8% vs 99%	-	89.9% vs 94.8%	-	80% vs 89.5%	< 0.001
Solitary HCC < 3 cm										
Ikeda et al. 2007 [38]	117	Japan	MWA	LTP	-	-	4.30%	-	-	-
Okuwaki et al. 2009 [39]	115	Japan	RFA	IDR	11.80%	-	53.90%	-	75.80%	-
Nishikawa et al. 2011 [40]	231	Japan	RFA	OS	100.00%	-	81.40%	-	74.60%	-
Francica et al. 2013 [41]	363	Italy	RFA	OS	-	-	80.00%	-	64.00%	-
Brunello et al. 2013 [42]	209	Italy	RFA	OS	-	-	65.20%	-	44.30%	-
Kwon et al. 2019 [43]	189	Korea	CA	LTP	-	-	-	16.90%	-	-
Lee et al. 2021 [44]	140	Korea	RFA	LTP	0.70%	1.60%	-	-	-	-

LTP Local tumor progression, *OS* Overall survival, *IDR* Intrahepatic distant recurrence, *RFA* Radiofrequency ablation, *MWA* Microwave ablation, *CA* cryoablation, *PEI* percutaneous ethanol injection, *SR* Surgery

Table 2 Summary of studies in HCC ablation with Milan criteria

Study	No. of Patients	Region	Ablation Technique	Endpoint	1 yr	2 yr	3 yr	5 yr	*P* value
Pacella et al. 2006 [45]	148	Italy	LA	OS	89.00%	75.00%	52.00%	27.00%	-
Choi et al. 2007 [46]	570	Korea	RFA	OS	95.20%	82.90%	69.50%	58.00%	-
Takahashi et al. 2007 [47]	171	Japan	RFA	OS	98.80%	-	91.10%	76.80%	-
Wang et al. 2008 [48]	122 vs 109	China	MWA vs SR	DFS	72.8% vs 68.5%	-	54.0% vs 60%	33.0% vs 25.6%	> 0.05
Peng et al. 2013 [49]	89 vs 91	China	RFA vs SR	OS	93.2% vs 88.8%	-	71.1% vs 62.8%	55.2% vs 51.9%	0.305
Kim et al. 2013 [50]	1305	Korea	RFA	OS	95.50%		77.90%	59.70%	-
Ei et al. 2015 [51]	55 vs 64	Japan	CA vs RFA/MWA	DFS	-	80% vs 68%	-	-	0.2
Tan et al. 2017 [52]	516	China	RFA	OS	99.42%	-	83.97%	68.42%	-
Liu et al. 2018 [53]	126 vs 436	China	RFA vs MWA	OS	-	-	-	78.5% vs 80.1%	0.19

DFS Disease free survival, *OS* Overall survival, *RFA* Radiofrequency ablation, *MWA* Microwave ablation, *CA* cryoablation, *PEI* percutaneous ethanol injection, *LA* Laser ablation, *SR* Surgery

tumors in human by Kingham et al. [72]. IRE was always applied for the lesions in the high-risk locations such as adjacent to main bile duct [73] where the non-thermal nature of IRE ablation could avoid critical structure damage.

US-Guided ablation of liver metastases is an application of great interest and has been utilized extensively, especially in treatment of metastasizing colorectal cancer where surgical resection of liver metastases is a potential cure but may not always be technically possible. With colorectal cancer being the third leading cause of cancer related death in western societies, this issue has for many years attracted huge interest, and the potential to perform ablation of non-resectable colorectal metastases was among the first applications to be explored with the advent of this new approach. One of the first principles to attract major interest was heating of tissue by laser light delivered interstitially through fibers placed under ultrasonic guidance. Various developments and testing took place in the late 1980s and early 1990s leading to the first small clinical series when Nolsøe et al. and Amin et al. used Nd-YAG laser to ablate colorectal liver metastases [16, 17] in 1993 leading to the current, widely accepted, technique of US-guided percutaneous ablation of malignant liver tumors including treatment of non-resectable colorectal liver metastases with various ablation modalities [14–17]. While today laser ablation is limitedly used, Lorentzen et al. used MWA to treat liver metastasis in 39 patients with 125 lesions under contrast enhanced ultrasound guidance, and proved this ablation technique to be safe and efficient [88]. Solbiati et al. [89] also reported a long-term follow-up of small liver metastasis treated by RFA and the 1, 3, 5, 7, 10-year OS was 98.0%, 69.3%, 47.8%, 25.0% and 18.0%, respectively, which were equivalent to surgery. And in 2015, a position paper was issued by an international panel of ablation experts to provide recommendations for colorectal liver metastasis [30].

Thyroid

As the advancement of ultrasonic technology, the detection rate of papillary thyroid carcinoma is on the rise, however, its mortality rate remains stable [90, 91]. In recent years, many researchers are investigating ablation as an alternative therapy to partial or total thyroidectomy. Current guideline recommends US-guided ablation for recurrent thyroid tumors when resection is not suitable [92]. In terms of thyroid nodule ablation, Asia accounts for the most US-guided procedures (53.09%, 163/307), followed by Europe (37.13%, 114/307) and North America (7.49%, 12/307). The top five countries using US-guided ablation for the treatment of thyroid nodules are China (32.25%, 99/307), Italy (23.13%, 71/307), South Korea (14.66%, 45/307), United States (5.21%, 16/307) and Germany (4.89%, 15/307). RFA is the most used technique in thyroid nodules (37.13%, 114/307), followed by PEI (35.51%, 109/307) and MWA (14.33%, 44/307). For benign thyroid nodules, ablative therapy could reduce the volumes of nodules and meet the aesthetic needs of patients. US-guided ablation for thyroid nodules can be traced back to 1990 when Livraghi et al. [93] applied PEI to treat autonomous thyroid nodules, which proved that PEI was a low-risk and easy to

Table 3 Summaries of Randomized Controlled Trials in ablation for HCC

Study	No. of Patients	Region	Ablation Technique	Endpoint	1 yr	2 yr	3 yr	5 yr	*P* value	Inclusion Criteria
Lencioni et al. 2003 [74]	52 vs 50	Italy	RFA vs PEI	OS	100% vs 96%	98% vs 88%	-	-	0.14	Milan Criteria
Brunello et al. 2008 [75]	70 vs 69	Italy	RFA vs PEI	CR	95.7% vs 65.6%	-	-	-	< 0.001	less than 3 lesions ≤ 3 cm
Huang et al. 2010 [76]	115 vs 115	China	RFA vs SR	OS	87.0% vs 98.3%	76.5% vs 96.5%	69.6% vs 92.2%	54.8% vs 75.7%	0.001	Milan Criteria
Peng et al. 2012 [77]	70 vs 69	China	RFA vs RFA + TACE	OS	82% vs 94%	-	47% vs 69%	36% vs 46%	0.037	Milan Criteria
Fang et al. 2013 [78]	60 vs 60	China	RFA vs SR	OS	97.5% vs 93.7%	91.2% vs 86.2%	82.5% vs 77.5%	-	0.207	Solitary ≤ 3 cm
Abdelaziz et al. 2014 [79]	45 vs 66	Egypt	RFA vs MWA	OS	67.6% vs 96.4%	47.4% vs 62%	-	-	0.49	less than 3 lesions ≤ 5 cm
Yu et al. 2017 [80]	203 vs 200	China	RFA vs MWA	OS	95.9% vs 96.4%	-	81.4% vs 81.9%	72.7% vs 67.3%	0.91	Milan Criteria
Vietti Violi et al. 2018 [81]	76 vs 76	Switzerland	RFA vs MWA	OS	-	84% vs 86%	-	-	0.87	less than 3 lesions ≤ 4 cm
Xia et al. 2019 [82]	120 vs120	China	RFA vs SR	OS	87.5% vs 92.5%	-	52.5% vs 65.8%	38.5% vs 43.6%	0.17	Milan Criteria

CR complete response, *OS* Overall survival, *IDR* = Intrahepatic distant recurrence, *RFA* Radiofrequency ablation, *MWA* Microwave ablation, *CA* cryoablation, *PEI* percutaneous ethanol injection, *LA* Laser ablation, *HIFU* High-intensity Focused Ultrasound, *SR* Surgery

Table 4 Summary of studies of HCC in Intermediate stage treated by ablation combined with TACE

Study	No. of Patients	Region	Ablation Technique	Endpoint	1 yr	3 yr	5 yr	*P* value
Zhang et al. 2018 [83]	50 vs 100	China	MWA + TACE vs TACE	OS	93.1% vs 77.5%	79% vs 42.1%	67.7% vs 21%	0.002
Hirooka et al. 2018 [84]	89 vs 141	Japan	RFA + TACE vs TACE	OS	100% vs 86.3%	78.6% 43.5%	62.3% vs 15.8%	< 0.001
Ren et al. 2019 [85]	128 vs 271	China	RFA + TACE vs TACE	OS	90.6% vs 64.5%	76.6% vs 15.1%	68% vs 10.8%	< 0.001
Yin et al. 2014 [86]	55 vs 156	China	RFA + TACE vs TACE	OS	89.8% vs 67.2%	61.1% vs 36.6%	37.4% vs 16.5%	0.01
Lin et al. 2020 [87]	57 vs 231	China	RFA + TACE vs TACE	OS	86% vs 69.5%	7.9% vs 37%	38.2% vs 15.2%	< 0.001

OS Overall survival, *TACE* Transarterial chemoembolization, *RFA* Radiofrequency ablation, *MWA* Microwave ablation

perform procedure for thyroid nodules. After that, Damian et al. [94] used RFA to treat recurrent thyroid malignancy in eight patients and the preliminary results were promising. Nowadays, PEI was used more frequently for cystic nodules because it is less effective in solid nodules compared with thermal ablation. Most studies reported that the volume reduction rate (VRR) could achieve 80% during the follow-up time. Table 5 summarizes the ablation in benign thyroid, which indicates that ablation for the treatment of benign is an effective method with a low complication rate.

For malignant thyroid nodules such as papillary thyroid microcarcinoma (PTMC) and papillary thyroid carcinoma (PTC), there is an increasing number of studies published to prove the efficacy and safety of ablation as an alternative therapy to thyroidectomy [11, 106–108]. A prospective multicenter study showed the efficacy of using RFA or MWA for the treatment of PTC in 847 patients, where 100% complete ablation was achieved with a recurrence rate of 1.1% and a complication rate of 3.4%, which indicated that thermal ablation is a safe and effective method for PTC [11]. Zhang et al. [109]compared RFA (94 patients) and SR (80 patients) for the treatment of low-risk 174 PTMC patients and indicated that RFA was not inferior to SR in oncological outcomes with a higher quality of life. Table 6 summarizes the

Table 5 Summary of studies in benign thyroid nodules ablation that sample size > 100

Benign nodules	Region	Ablation Technique	No. of Patients	Gender (F/M)	Mean Age	VRR% at last time	Follow up (months)	Technical success %	Major Complication
Jeong et al. 2008 [95]	Korea	RFA	236	211/25	40.9	84.11 ± 14.93%	6	-	1.30%
Dobnig et al. 2018 [96]	Austria	RFA	277	215/62	52 ± 12.9	82 ± 13%	12	84%	2.10%
Jung et al. 2018 [97]	Korea	RFA	345	302/43	46.0 ± 12.7	95.30%	60	97.80%	0.70%
Su et al. 2021 [98]	China	PEI	201	145/56	50.89 ± 12.65	90.20 ± 8.18%	12	97.60%	4.98%
Luo et al. 2021 [99]	China	MWA	171	132/39	47.0 ± 14.2	90.10%	36	97.80%	4.09%
Xia et al. 2021 [100]	China	MWA	214	183/31	45.84 ± 14.32	85.60%	12	-	-
Gao et al. 2021 [101]	China	MWA	267	214/53	50.1 ± 11.7	93.3 ± 1.8%	15	-	0.74%
Yue et al. 2013 [102]	China	MWA	222	164/58	50.7 ± 10.5,	72 ± 51%	6	82.30%	3.60%
Papini et al. 2014 [103]	Italy	LA	101	85/16	51.5 ± 13.7	57 ± 25%	36	67.30%	0.99%
Cheng et al. 2017 [104]	China	RFA vs MWA	1252	977 vs 275	47.9 vs 47.1	89.6 vs 82.5%	12	80.2% vs 76.4%	4.78% vs 6.63%
Hamou et al. 2019 [105]	France	RFA vs LA	166	133 vs 33	49.7 vs 54.8	75% vs 83.9%	18	-	8.1% vs 6.0%

VRR Volume reduction ratio, *RFA* Radiofrequency ablation, *SR* Surgery, *MWA* Microwave ablation; Major complications include voice change, Nodule rupture, nodule rupture with abscess, hypothyroidism and brachial plexus injure

Table 6 Summary of studies for ablation of malignant thyroid nodules

Benign nodules	Region	Ablation Technique	No. of Patients	No. of Lesions	Type of nodule	Gender (F/M)	Age	Disappeared rate	VRR%	Follow up (months)	Technical success %	Recurrence	Major Complication
Lim et al.2019 [113]	Korea	RFA	133	152	PTMC	114/19	46 ± 12	91.40%	100.00%	48	100.00%	0.00%	0.80%
Zhang et al.2019 [114]	China	RFA vs SR	94/80	174	PTMC	130vs44	45.4vs44.1	-	-	67	100.00%	1.1% vs 1.3%	0% vs 3.8%
Wang et al.2019 [115]	China	MWA/RFA/LA	107	107	PTMC	76/31	44.1 ± 13.1	-	97.90%	18	-	0.00%	1.87%
Yue et al.2020 [116]	China	MWA	119	119	PTMC	92/27	48.7	93.30%	99.4 ± 2.2%	101	100.00%	0.88%	6.70%
Chung et al.2020 [117]	Korea	RFA	119	172	PTC	86/33	50.7 ± 16.0	72.10%	81.2% ± 55.7%	128	95.00%	0.00%	21.40%
Wu et al.2020 [118]	China	RFA	198	204	PTMC	141/57	42.5 ± 9.5	100.00%	99.8 ± 1%	24	100.00%	0.00%	2.53%
Zhu et al.2021 [119]	China	RFA	102	102	PTMC	82/20	43	100.00%	100.00%	60	85.70%	1.90%	3.70%
Cao et al. 2021 [120]	China	MWA/RFA	645/202	847	PTC	660/187	46 ± 11	0.68	-	12	100%	1.10%	3.00%
Xiao et al.2021 [121]	China	RFA vs SR	91/91	182	PTC	140vs42	40.7vs40.2	-	99.0% ± 3.4%	50	100.00%	0.00%	0% vs 4.4%
Cao et al.2021 [122]	China	MWA/RFA	123/49	172	PTC	38/134	45.9 ± 12.6	61.60%	100.00%	48	100.00%	1.20%	4.60%
Cao et al.2021 [123]	China	MWA/RFA	542/183	725	PTMC	573/152	46 ± 11	71.00%	71.00%	60	-	0.80%	2.60%

Nodule rupture, nodule rupture with abscess, hypothyroidism and brachial plexus injure

VRR Volume reduction ratio, *PTC* Papillary thyroid carcinoma, *PTMC* papillary thyroid microcarcinoma, *RFA* Radiofrequency ablation, *SR* Surgery, *MWA* Microwave ablation; Recurrence include recurrence, metastatic cervical lymph nodes, or distal metastasis, Major complications include voice change

studies of ablative techniques for the treatment of malignant thyroid nodules. The most common complication during ablation is voice changes caused by injury of the laryngeal nerve [110], but hydrodissection techniques help avoid this complication effectively [111]. And in 2009, South Korea issued a guideline for RFA in thyroid [112]. Although the application of ablative therapy is promising in thyroid nodules, the current studies are mostly retrospective and short-term follow-up time and more prospective and long-term follow-up time studies are needed.

Prostate

Prostate cancer is the second most diagnosed cancer in males worldwide [124]. For US-guided ablation in prostate cancer, Europe accounts for 56.03% (130/232), followed by North America (25.43%, 59/232) and Asia (12.93%, 30/232). The top five countries which used ablation in prostate cancers are the United States (19.40%, 45/232), France (14.66%, 34/232), Germany (13.79%, 32/232), England (8.19%, 19/232) and Japan (6.90%, 16/232). HIFU is the most commonly used technique in prostate cancer ablation (53.88%, 125/232), followed by CA (30.60%, 71/232) and IRE (8.19%, 19/232). In 1983, prof Hans Henrik Holm and co-workers introduced a never before seen technique when they published their work on US-Guided transperineal brachytheraphy of prostate cancer, a technique that gained widespread use and was accepted as equal to surgery treatment for localized prostate cancer [125–127]. In 1993, Onik et al. [128] used transrectal US-guided CA for prostate cancer and supplied real-time images for monitoring conditions of ablation which was the key innovation of CA. In 1995, Madersbacher et al. investigated the effect of HIFU in prostate cancer under transrectal US-guidance in 29 patients [129]. American Society Radiation Oncology (ASTRO) criteria and the Phoenix criteria were used to report biochemical recurrence-free survival (BCR-FS). A multicenter study reported the long-term results of 140 patients with prostate cancer undergoing transrectal HIFU, where the 5- and 7-year biochemical failure-free survival was 77% and 69%, respectively, which indicated that HIFU is effective for prostate cancer patients [130]. For CA, a prospective study investigated early-medium term outcome in CA for the treatment of prostate cancer in 80 patients, where the 3-year failure-free survival was 84.7% in the high-risk group and 93.3% in the intermediate-risk group [131]. And a retrospective long-term follow-up study reported 94 patients with prostate cancer underwent whole-gland CA, with the complication rate being 3%, and a 5-year recurrence free survival of 83% overall [132]. Garcia-Barreras et al. [133] compared robot-assisted radical prostatectomy (472 patients) with HIFU (188 patients) or CA (48 patients) in 708 patients with prostate cancer, which indicated that HIFU and CA could offer oncologic local control with fewer side effects although with a higher risk of salvage treatment. LA and IRE have also been used in prostate cancer, but the studies were limited and more robust evidence is needed on long-term follow-up to conclude the benefits (Table 7).

Kidney

Kidney cancer ranked as the 9th most common cancer in males and 14th in females, and renal cell carcinoma (RCC) accounts for 90% of kidney cancer [134, 135]. Although the rate of mortality has been stabilizing or decreasing for decades and the diameter of the tumor by detection decreasing

Table 7 Summary of ablation in prostate cancer with sample size > 100

Study	No. of Patients	Region	Ablation Technique	Ablation Type	Biochemical Failure Definition	Median Follow-up time	Endpoints	
Uchida et al. 2006 [154]	181	Japan	HIFU	Whole-gland	ASTRO	18 months	BCR-FS at 5 yr	78.00%
Poissonnier et al. 2007 [155]	227	France	HIFU	Whole-gland	-	20.5 months	PFS at 5 yr	66.00%
Komura et al. 2014 [156]	171	Japan	HIFU	-	Phoenix	43.0 months	BCR-FS at 5 yr	69.00%
Blana et al. 2018 [157]	140	Germany	HIFU	-	-	153.6 months	BCR-FS at 5 yr	77.00%
T. Shah et al. 2019 [158]	122	England	CA	Whole-gland	-	37.8 months	PFS at 3 yr	90.50%
Aminsharif et al. 2019 [159]	108	Iran	CA	Whole or focal gland	Phoenix	43.1 months	BCR-FS at 5 yr	48.30%
Wu et al. 2020 [160]	128	China	HIFU	Whole-gland	Phoenix	53.7 months	BCR-FS at 5 yr	64.80%

CA cryoablation, *HIFU* High-intensity Focused Ultrasound, *BCR-FS* biochemical recurrence-free survival, *ASTRO* American Society for Therapeutic Radiology and Oncology, *PFS* Progression Free Survival

in many countries, many cases present in older people for which organ preservation and good renal function are vital for their prognosis [135–137]. The application of ablation for renal tumors under US-guidance is less than cross-sectional imaging guidance [138, 139]. However, US-guided ablation has the advantages of no ionizing radiation and low cost compared with other guidance. Indeed, ablative techniques have been used in small renal tumors (diameter < 4 cm) for decades. Europe ranks first in renal tumor ablation (35.71%,65/182), followed by North America (32.42%, 59/182) and Asia (30.77%, 56/182). The top five countries in renal tumor ablation are the United States (28.02%, 51/182), China (21.98%, 40/182), Italy (11.54%, 21/182), France (7.69%, 14/182) and Japan (4.4%, 8/182). The most commonly used techniques are RFA (48.90%, 89/182), MWA (24.73%, 45/182) and CA (18.68%, 34/182). In 1995, Uchida et al. [140] reported the first experience of cryoablation for the treatment of renal tumors under US-guidance and achieve technique success. In 1997, Zlotta et al. [141] reported the initial experience of using US-guided RFA in renal tumors and associated safety. The application of MWA in the renal tumor is later than CA and RFA. In 2008, Liang et al. [142] reported on 12 patients with renal tumors less than 4 cm undergoing MWA and for the first time, showed that ablation in T1 stage renal tumor was effective and safe. Breen et al. [143] reported on 433 patients with 484 T1 stage renal tumors after CA, where the 3-, 5-year OS was 91.7% and 78.8%, respectively. Veltri et al. [144] reported on 137 patients with 203 renal tumors in T1a stage treated by RFA and found the 3-, 5-year OS was 84% and 75%, respectively. Hao [145] et al. used MWA to treat 162 patients with 171 RCC tumors, where the 1-, 3-, 5-year OS was 92.8%, 85.9%, and 82.1%, respectively. The comparison between ablative techniques is controversial [146–148] and prospective studies are needed to compare the efficacy of different ablative modalities. Yu et al. [149] compared MWA with laparoscopic partial nephrectomy (LPN) for T1a stage renal tumors and found MWA was a slightly inferior to LPN in OS ($P = 0.042$), but with no difference in LTP, distant metastasis, and cancer-specific survival. Table 8 summarizes the studies of different ablation methods for renal tumors in T1 stage. The ablative techniques are also recommended by several guidelines for the treatment of renal masses, especially for elderly people and small renal masses [150–153].

Uterine

Uterine fibroids rank first for the incidence of uterine tumors, where the incidence is nearly 70% by the age of 50 [161] and 15–30% patients with uterine fibroids had symptoms such as abnormal bleeding, hypermenorrhea, anemia, recurrent pregnancy, etc. [162, 163]. The application of ablation for uterine fibroids is mainly in China (69.42%, 84/121) and HIFU is the most popular ablation technique (69.42%, 84/121), in which temperature at the focal location reaches 80 °C leading to cell death. In 2002, Chan et al. [164] reported that they designed and developed the US-guided HIFU device for uterine fibroids and applied the same in six patients, providing a promising non-surgical method for uterine fibroids. Subsequently, HIFU became popular as a non-invasive treatment method. Several studies reported that HIFU is effective in terms of symptom relief, improvement in Quality of Life (QoL) with less complication and hospitalizations [165–169]. Wang et al. [169] investigated the efficacy and safety of US-guided HIFU for submucosal fibroids in 76 patients, the average volume reduction was 46.7%, 68.2%, 78.9% and 90.1% at 3, 6, 12 and 24 months, without complications. A series of studies compared the QoL, recovery, complications and pregnancies between HIFU and myomectomy and indicated that HIFU is superior to surgery. Liu et al. [170] compared HIFU and myomectomy for recurrent uterine fibroids, which indicated that the time to re-intervention was longer in HIFU group with fewer adverse events. Chen et al. [171] evaluated 2411 women with symptomatic fibroids treated by HIFU (1353 patients), hysterectomy (472 patients) and myomectomy (586 patients) and the results showed that HIFU caused less morbidity than surgery with similar QoL in long-term follow-up and call for more randomized controlled trial studies of HIFU for the treatment of fibroids. For other techniques, RFA and MWA were also applied in uterine fibroids [172–175]. But the levels of evidence were still low with need more for more robust studies (Table 9).

Other organs

US-guided ablative techniques have also been applied in wide fields for the treatment of solid tumors such as peripheral lung cancer, bone tumors, breast cancer, adrenal adenomas, metastatic lymph nodes, etc. [192–195]. Yang et al. [196] used MWA for the treatment of benign breast lesions in 440 patients with 755 lesions, where the VRR was 97.9% at 12 months. Zhou et al. [197] used MWA in small breast cancers and 90.24% (37/41) appeared to have complete tumor coagulation. Additionally, endoscopic ultrasound-guided (EUS-guided) ablation has been applied to some cancers, especially for pancreatic cancers [198–200]. Song et al. [201] applied EUS-RFA to treat unresectable pancreatic cancer in 6 patients and proved ablation under EUS guidance is technical feasibility. Although the evidence of these fields is not strong and cases are limited, the future of the ablation technique is very promising.

Conclusion

In this review, we analyzed the status of US-guided ablative techniques in various tumors by counting numbers of articles in the field and reviewed the historical development.

Table 8 Summary of studies of ablation in T1 renal tumor with sample size > 100

Study	Region	Ablation Technique	No. of Patients	TNM stage	Median age (years)	mean follow Up duration	OS	CSS	LTP	*P* value
Duffey et al. 2012 [176]	USA	CA	116	T1	69.5 (25–95)	27.4	77% at 5-yr RFS	-	3.44%	-
Atwell et al. 2013 [177]	USA	RFA vs CA	222 vs 163	T1a	70 (28–91)	21.6	98.1% vs 90.6% at 5-yr OS	-	3.2% vs 2.8%	0.09
Wah et al.2014 [178]	England	RFA	165	T1	67.7 (21–88.6) *	58.3	75.8% at 5-yr OS	97.9% at 5-yr	2.50%	-
Veltri et al.2014 [179]	USA	RFA	137	T1a	65.0 (22–88)	39	75%at 5-yr OS	91% at 5-yr	2.20%	-
Thompson et al. 2014 [180]	USA	CA vs RFA	187 vs 180	T1	72 vs 72	60	88% vs 82% at 3-yr OS	-	4.17% vs 6.94%	0.021
Hao et al.2018 [181]	China	MWA	162	T1a	62.6 (21–86) *	45.5	82.1% at 5-yr OS	-	2.90%	-
Breen et al. 2018 [182]	England	CA	433	T1	69 (19–90)	31	78.8% at 5-yr OS	94.4% at 5-yr	1.39%	-
Maciolek et al.2019 [183]	USA	MWA	148	T1a	67 (62–74)	32	96% at 3-yr OS	100% at 3-yr	4.00%	-
Lim et al.2020 [184]	USA	CA	180	T1	70.1 (34.1–88.9)	28.3 ± 13.8	94.9% at 5-yr PFS	-	1.67%	-
Yu et al. 2020 [185]	China	MWA vs LPN	185 vs 185	T1a	63.2 vs 50.9 *	40.6	86.3% vs 91.9% at 5-yr OS	-	3.2% vs 0.5%	0.042

OS Overall survival, *CSS* Cancer Specific Survival, *PFS* Progression Free Survival, *RFS* Recurrence Free Survival, *LTP* Local tumor progression, *RFA* Radiofrequency ablation, *LPN* laparoscopic partial nephrectomy, *MWA* Microwave ablation, *CA* cryoablation

*mean age; *P* value is for OS

Table 9 Summary of studies in uterine fibroid ablation

Study	No. of Patients	Region	Ablation Technique	Median Follow-up time	Fibroid Volume Reduction	Symptom relief	Symptom recurrence	*P* value
Ren et al. 2009 [186]	119	China	HIFU	20 months	50.3% at 12 months	85.50%	-	-
Liu et al. 2016 [187]	311	China	MWA	12 months	86.7% at 12 months	-	-	-
Wang et al. 2012 [188]	76	China	HIFU	30 months	90.10%	89.50%	-	-
Li et al. 2020 [189]	381	China	HIFU	70 ± 9 months	81.90%	86.40%	-	-
Lee et al. 2019 [190]	928	Korea	HIFU	12 months	73.80%	-	-	
Liu et al. 2020 [191]	101 vs 87	China	HIFU vs myomectomy	44 months	-	-	21.1% vs 26.2%	> 0.05

HIFU high intensity focused ultrasound, *MWA* Microwave ablation

Ablation has developed rapidly in past decades and been applied in numerous solid tumors. RFA is the most commonly used modality in ablative techniques with the application of other ablative techniques such as MWA and HIFU also increasing rapidly. Ablation has been recommended by several international guidelines for liver, thyroid and renal tumors. More long-term studies and high-level evidence are needed for supporting these applications.

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Declarations

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