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Review

Advancements in microwave ablation for tumor treatment and future directions

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SUMMARY

Microwave ablation (MWA) is a minimally invasive treatment that uses thermal energy to target and destroy tumors. Compared to other ablation methods, such as radiofrequency ablation (RFA), MWA operates at higher frequencies, allowing for faster ablation and larger treatment areas. In addition to its direct tumor-destroying effects, MWA has been shown to activate immune responses, contributing to long-term antitumor effects. MWA can also be combined with surgery, chemotherapy, and immunotherapy to enhance treatment outcomes. This review examines the current research on MWA's technical innovations, clinical applications, and its potential in improving cancer treatment efficacy.

INTRODUCTION

Microwave ablation (MWA) has emerged as a pivotal technique in the management of various solid tumors, offering a minimally invasive option that effectively induces tumor necrosis through localized heating. Since its inception, MWA has gained significant attention due to its ability to deliver precise, controlled energy that leads to efficient tumor destruction with minimal damage to surrounding tissues.[1–6] Unlike other thermal ablation techniques such as radiofrequency ablation (RFA) and cryoablation, MWA typically operates at frequencies ranging from 915 MHz to 2.45 GHz, with the most commonly used frequency being 2.45 GHz. This higher frequency enables faster heating and larger ablation zones, which are particularly advantageous in treating larger or multiple tumors.[7–9] Table 1 compares various parameters of the three ablation methods, and Figure 1 shows how they work.[4] The growing interest in MWA is driven by the increasing prevalence of cancers that are amenable to localized treatment, such as liver, lung, and kidney tumors. Traditional surgical resection remains the gold standard for many solid tumors; however, surgery is not always feasible, especially in patients with comorbidities or in cases where tumors are inoperable due to location or size. In these scenarios, MWA offers an alternative that is not only less invasive but also associated with shorter recovery times and fewer complications.[10–13]

Recent advancements in MWA technology, including the development of more sophisticated equipment and the refinement of ablation parameters, have further expanded its clinical applications.[14,15] Additionally, the integration of MWA with imaging modalities such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) has enhanced the precision of tumor targeting, thus improving therapeutic outcomes.[16,17] The enduring antitumor immune response triggered by MWA also plays a crucial role in its therapeutic function.[18,19] Additionally, MWA can be combined with various treatments, such as surgery, chemotherapy, and immunotherapy, to manage advanced cancer cases. Studies have shown that such combination therapies can effectively overcome the limitations of traditional single-modality treatments, including drug resistance and systemic toxicity.[20–22] As a result, MWA is increasingly being adopted in clinical practice and is considered a viable option for both curative and palliative treatment of various tumors.

Despite these advancements, the application of MWA is not without challenges. Issues such as variability in treatment response, the potential for incomplete ablation, and the occurrence of complications like thermal injury to adjacent structures require ongoing research and clinical evaluation. Moreover, there is a need for standardized protocols to optimize treatment parameters and improve patient selection criteria to maximize the benefits of MWA.

In this review, we aim to provide a comprehensive overview of the current state of MWA in tumor treatment. We will discuss the underlying principles of the technology, its clinical applications across different tumor types, and the outcomes associated with its use. Furthermore, we will explore the role of MWA in combination with other therapies and address the challenges and future directions in this rapidly evolving field. To ensure a comprehensive and relevant literature review, we conducted a systematic search in the PubMed database using the keywords "microwave ablation," "thermal ablation," "tumor treatment," "image-guided ablation," and "combination therapy." We included peer-reviewed original research articles and clinical studies published in English, focusing on the technical advancements, clinical applications, and immunological effects of MWA

Table 1. Comparison of parameters of different ablation methods

Treatment mode	Action time	Scope of action	Complete inactivation rate
MWA	~4.5 min	~2.5 cm (1.0–4.0 cm)	95%
RFA	10–15 min	<2.0 cm (0.6–3.0 cm)	90%
cryoablation	10–12 min	<1.5 cm (0.5–2.0 cm)	78%

in tumor treatment. Articles such as conference abstracts and studies lacking detailed data on MWA efficacy were excluded. By synthesizing the latest research and clinical findings, this review seeks to highlight the potential of MWA as an integral component of multimodal cancer therapy and to identify areas where further investigation is needed.

OVERVIEW OF MWA TECHNOLOGY

MWA is a therapeutic technique that induces irreversible tumor cell necrosis through localized heating generated by high-frequency electromagnetic waves. The fundamental principle of MWA lies in the absorption and conversion of electromagnetic energy into heat as the waves propagate through tissues, governed by the tissue's dielectric properties such as electrical conductivity and permittivity. This heating effect rapidly elevates local tissue temperatures to between 60°C and 100°C, leading to the swift destruction of tumor cell structures and functions.[23–30]

Compared to RFA, MWA offers several technical advantages. First, MWA operates at higher frequencies, typically ranging from 915 MHz to 2.45 GHz, allowing faster heat generation and the formation of larger ablation zones.[31–33] This feature is particularly beneficial when treating larger or multifocal tumors. Additionally, due to the higher penetration power of microwaves, MWA can efficiently transmit energy in tissues with high water content, minimizing energy loss in fatty tissues, which is critical for the treatment of deeply located tumors.[24,34]

MWA devices primarily consist of three core components. The first is the microwave generator, which provides microwave energy at specific frequencies (typically ranging from 915 MHz to 2.45 GHz) and amplifies the signal using a radiofrequency (RF) power amplifier. The second is the antenna system, whose design directly affects the efficiency of microwave energy transmission and the morphology of the ablation zone. The third is the cooling system, which reduces probe temperature through water- or gas-based cooling, preventing tissue carbonization and minimizing thermal damage to surrounding healthy tissues. For instance, water-cooling systems maintain probe stability by circulating chilled water, while gas-cooling systems (e.g., using carbon dioxide) are suitable for tissue regions sensitive to liquid cooling.[35–38] Different treatment sites (e.g., liver, lung, and breast) require specific antenna types, with designs tailored to tumor location, size, tissue characteristics, and microwave energy distribution requirements.[39] The monopolar antenna is simple in structure and cost-effective, concentrating thermal energy through an external electrode, making it suitable for rapid ablation of small superficial tumors (e.g., breast cancer), although the ablation zone may be irregular in shape.[38,40] The bipolar antenna utilizes dual electrodes to alternately emit microwaves, ensuring more uniform energy distribution, and is suitable for larger tumors or deeper tissues (e.g., renal tumors).[41,42] The antenna array, composed of multiple emitters working in synergy, covers a larger area and reduces cold spots, making it ideal for deep-seated tumors (e.g., liver or lung cancer).[43,44] Triaxial and choked antennas are also commonly used; triaxial antennas create spherical ablation zones through multidirectional radiation, improving uniformity for large tumors, while choked antennas minimize backward heating, reducing damage to adjacent critical organs.[39,45,46] Slot antennas optimize energy focusing through their slot structure, enhancing ablation precision, and are suitable for tumors with complex morphologies.[46,47] The shape of the antenna must also adapt to the anatomical characteristics of the tumor. Straight antennas are used for smaller tumors,

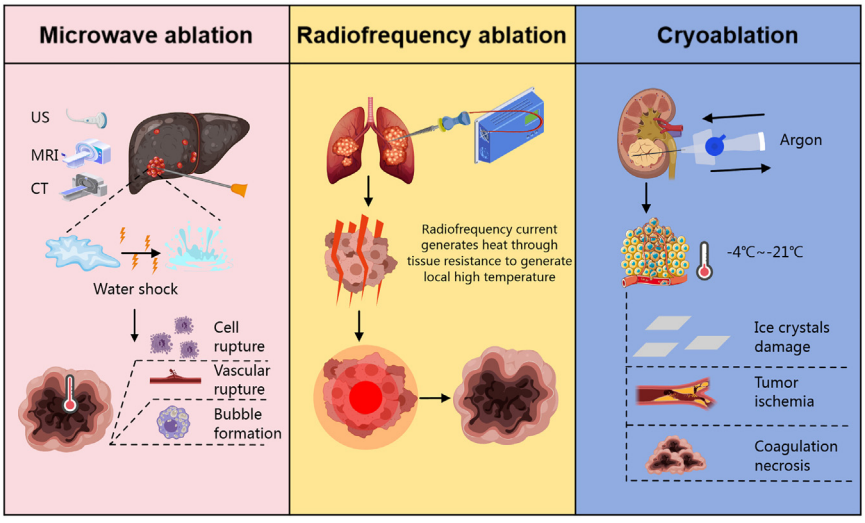

Figure 1. Overview of how MWA, RFA, and cryoablation work

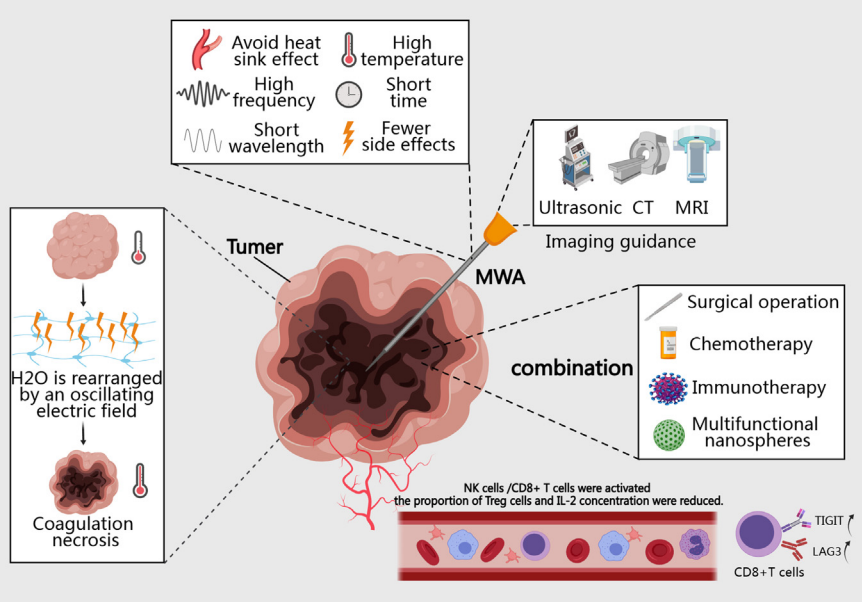

Figure 2. Overview of microwave ablation technology

Through various imaging methods, ablation probes that can emit microwave electromagnetic fields are guided into tumor tissues. Under the action of electromagnetic fields, polar molecules (mainly H_2O) in the tissues are forced to continuously rearrange with the oscillating electric field, thereby increasing their kinetic energy, rapidly raising the tissue temperature in a short time, and causing coagulative necrosis of the target tissues. In addition, MWA can also exert antitumor effects by eliciting an immune response or when combined with other treatment options.

particularly superficial ones such as skin or breast cancer.[25,48] Curved antennas are designed for complex tumor morphologies, such as lung cancer, to better conform to irregular tumor contours.[49,50] Spherical antennas are suitable for deep-seated tumors requiring larger treatment zones, such as those in the liver or kidneys.[51] Microwave frequency (ranging from 915 MHz to 2.45 GHz) and the power-time combination are critical parameters influencing ablation efficacy. The choice of frequency affects the distribution range and efficiency of thermal effects, depending on the treatment site and tumor size. The 915 MHz frequency offers greater penetration depth (3–4 cm), making it suitable for deep or large-volume tumors (e.g., liver and kidney), and is typically used with higher power (80–100 W) and longer durations (10–15 min) to expand the ablation zone.[52–55] The 2.45 GHz frequency allows faster energy absorption, making it ideal for superficial or small tumors (e.g., breast or lung cancer), and is often used with moderate power (40–60 W) and shorter durations (5–10 min) for precise ablation.[52–54,56] Tissue water content is another important factor; high-water-content tissues (e.g., liver parenchyma) exhibit higher dielectric loss and microwave absorption efficiency compared to low-water-content tissues (e.g., fat or bone), necessitating dynamic power adjustments based on target tissue characteristics.[57,58] The synergistic optimization of power and time is also crucial, as clinical practice requires balancing these parameters to avoid excessive power causing carbonization (which impedes energy conduction) or prolonged durations leading to complications. For example, in liver tumor ablation, 100 W power combined with 10 min can create an ablation zone of 3–4 cm in diameter, while extending to 15 min may expand it to 5 cm, though with increased risk of bile duct or vascular injury.[59,60] Commonly used devices include the Valleylab FT10 (2.45 GHz, monopolar/bipolar antennas), suitable for tumors in the liver, lung, and kidney,[61] and the Amica system (915 MHz, antenna array), designed for deep-seated and large tumors.[62] The anatomical features of each treatment site and tumor morphology dictate the choice of specific antenna types and frequencies. For liver tumors, which are often deep and large, the 915 MHz frequency combined with an antenna array is typically used.[55] For lung tissue, which is soft and may harbor irregularly shaped tumors, curved or array antennas with a 2.45 GHz frequency are commonly selected.[49,50] Breast tumors, being generally superficial, are suitable for rapid ablation using a 2.45 GHz frequency and monopolar antenna.[56] For kidney tumors, which may be deep and surrounded by abundant vasculature, the 915 MHz frequency with a bipolar antenna is often preferred.[63]

Another important development in MWA technology is its integration with image-guided systems. The use of ultrasound, CT, and MRI to guide MWA allows clinicians to monitor and assess the ablation zone in real time, thereby improving the precision and safety of the treatment.[17,64–66] These real-time imaging systems not only aid in optimizing antenna placement and energy output but also enable the early identification and management of potential complications during the procedure.

Beyond its fundamental principles, MWA also exerts antitumor effects by stimulating immune responses and by being combined with other treatment modalities (Figure 2).[18,67–74]

CLINICAL APPLICATIONS OF MWA IN TUMOR TREATMENT

MWA has been applied to treat liver cancer, lung cancer, breast cancer, thyroid cancer, kidney cancer, colorectal cancer, and metastases to the liver and lungs. Numerous studies have confirmed its safety and effectiveness. MWA has shown a more favorable prognosis in certain cases compared to other treatments (Table 2). We will next discuss the application of MWA in treating different types of cancer.

Liver cancer

Hepatocellular carcinoma (HCC) has become the sixth most common cancer worldwide and the third leading cause of cancer-related deaths as of 2020.[1] Previous studies have demonstrated the safety and efficacy of MWA in treating HCC and liver

Table 2. Clinical applications of microwave ablation in tumor treatment

Cancer type	Application	Advantages	Side effects
Liver cancer	isolated tumor, 3–5 cm in size.	increased OS and local tumor PFS, low complication rate, less intraoperative blood loss, short operation time and hospital stay.	pleural effusion, right upper abdominal pain, malignant transformation of residual injury site.
Lung cancer	small recurrent focus; tumor less than 4 cm; bone metastasis.	satisfactory OS, DFS; the incidence of pneumothorax was low.	pneumothorax, pleural effusion, and intercostal neuralgia.
Breast cancer	small solitary tumor; spinal metastasis; breast-conserving surgery.	better short-term efficacy and higher aesthetic satisfaction.	common complications of ablation.
Thyroid cancer	primary, single-focus, low-risk tumor.	short operation time; reduced blood loss; cost-effective.	bleeding, earache, toothache, postoperative hoarseness.
Colorectal cancer	liver/lung metastases.	LTP increases; postoperative recovery days are less; fewer major complications; the long-term prognosis is good.	pneumothorax, hemorrhage.
Renal cancer	cT1 stage.	less kidney damage.	bleeding, urological symptoms, death
Prostate cancer	low to intermediate-risk tumors.	subjective symptoms and quality of life were significantly improved.	temporary urinary symptoms and anterior rectal fistula.

metastases from other cancer types.[75–79] In a study conducted by Yu et al., the prognosis of 5,326 HCC patients treated with MWA was analyzed. Over a 12-year follow-up period, patients with Barcelona Clinic Liver Cancer (BCLC) stage 0-B HCC exhibited an upward trend in survival following MWA, with significant survival benefits also observed in patients experiencing early recurrence.[2] Furthermore, in patients with metastatic liver tumors, MWA resulted in satisfactory overall survival (OS) and local progression-free survival (PFS).[79]

Numerous studies have compared MWA with surgical resection, RFA, and other treatment modalities for liver cancer. For patients with BCLC stage 0, liver resection (LRE) and MWA showed comparable OS, recurrence-free survival (RFS), and postoperative complication rates.[80] For single HCC lesions measuring $\leq$ 3 cm, the efficacy of RFA was similar to that of MWA, with comparable 5-year OS rates of 81.8% vs. 77.1% ($p = 0.170$), and better 5-year RFS with MWA (34.6% vs. 24.0%, $p = 0.042$).[81–83] For solitary HCC lesions between 3 and 5 cm, particularly in patients unsuitable for laparoscopic liver resection (LLR), MWA may serve as an alternative to LLR.[84,85] Additionally, for primary intrahepatic cholangiocarcinoma within the Milan criteria, MWA could be a feasible option if an adequate margin can be achieved.[86] However, it is worth noting that the rate of local tumor recurrence was significantly higher in MWA patients compared to those who underwent LRE.[87]

Although the safety of MWA for treating liver tumors has been well established, previous reports have highlighted some side effects associated with MWA in liver cancer treatment, including minor pleural effusion, right upper abdominal pain, tissue damage, and pro-inflammatory effects.[88,89] Jones et al. demonstrated that hepatic thermal ablation could potentially promote metastasis at the site of injury in colon cancer patients.[90] Furthermore, studies have shown that the malignant transformation of residual hepatocytes post-thermal ablation is a key factor in the progression of HCC. This mechanism involves sublethal heat stress-induced O-GlcNAcylation, which stabilizes hypoxia inducible factor-1 (HIF-1α) and modulates the Warburg effect in HCC cells, thereby promoting tumor progression after thermal ablation. Inhibition of O-GlcNAcylation may present a potential target for controlling postoperative recurrence and metastasis in HCC.[91]

Lung cancer

Ablation therapy for lung tumors has been employed for over 20 years; however, due to respiratory motion, the ablation of lung tumors is more challenging than that of other solid tumors. MWA is a safe and effective treatment option for patients with small focal recurrence of non-small cell lung cancer (NSCLC) following radical surgery.[92,93] Additionally, MWA is a reliable method for treating malignant lung tumors smaller than 4 cm.[94] Notably, MWA has demonstrated significant efficacy in alleviating pain associated with bone metastasis from lung cancer.[95] The apparent diffusion coefficient post-ablation of lung tumors can serve as an early predictor of treatment outcomes following MWA.[96]

Given the continuous motion of the lungs, selecting an appropriate treatment strategy is crucial for patient safety. Surgical resection remains the optimal choice for stage I. NSCLC; however, for patients unable to tolerate surgery, ablation offers promising outcomes in terms of disease-free survival (DFS), disease-specific survival, and OS.[97] There is no significant difference in the reduction rate of ablation area volume between MWA and cryoablation, but, when the ablation area involves the pleura, the risk of persistent air leakage is lower with cryoablation compared to MWA. Temporary enlargement of thoracic lymph nodes has been observed following MWA but not after cryoablation.[98,99] Quantitative analysis demonstrated a significantly lower incidence of pneumothorax with MWA (20/81, 24.7%) compared to RFA (32/79, 40.5%) ($p = 0.049$).[100] The effectiveness of MWA devices also varies. High-frequency spatial energy control MWA technology achieves a more spherical ablation zone and a larger ablation margin compared to traditional low-frequency MWA technology.[101]

The primary complications of MWA include pneumothorax, pleural effusion, and intercostal neuralgia.[102] It is noteworthy that severe intraoperative pain may reduce the efficacy of the procedure.[103]

Colorectal cancer

MWA is not typically used for primary colorectal cancer but plays a critical role in managing colorectal liver and lung metastases. Metastatic progression is the leading cause of mortality in colorectal cancer, with a 5-year survival rate of only 15%, and the liver and lungs are the most common sites of metastasis.[104,105]

Thermal ablation has been shown to be an effective and safe treatment for small (0–3 cm) colorectal liver metastases (CRLMs).[106–109] Nieuwenhuize et al. established criteria for CRLM treatment, with hepatectomy remaining the gold standard. Thermal ablation is suitable for unresectable or deeply resectable CRLM, and local treatment should be considered for patients with an eastern cooperative oncology group score $\leq$2, American Society of Anesthesiologists Physical Status Classification System score $\leq$3, and Charlson Comorbidity Index $\leq$8.[5]

MWA and open surgery for colorectal liver and lung metastases show no significant differences in OS or DFS. However, MWA offers faster recovery and fewer major complications, though it may increase the risk of local tumor progression (LTP).[78,110–112] For CRLM patients with RAS mutations (RAS) mutations, expanding the ablation margin is necessary to reduce LTP incidence.[113]

In lung metastases, MWA outcomes are mainly determined by the size of the metastasis and its proximity to the pleura, with prognosis influenced by the number of metastases and the location of the primary tumor. Metastasis size, ablation time, and energy do not significantly affect prognosis.[79,114] However, some studies suggest that the location of the primary colorectal cancer does not impact survival after MWA in patients with lung metastases.[115]

Renal cancer

Current evidence demonstrates that MWA is a safe and effective treatment for early-stage renal cancer.[116–119] Ultrasound-guided percutaneous MWA shows promise for treating cT1b renal tumors in high-risk areas.[120] For low-invasive early-stage renal cell carcinoma, percutaneous MWA and laparoscopic partial nephrectomy offer comparable outcomes and complication rates, but MWA results in less bodily damage.[121] However, for T1b renal cancer, the local recurrence rate after thermal ablation is significantly higher than that of robot-assisted partial nephrectomy.[122] For tumors measuring 3.1–4 cm, tumor-specific mortality after thermal ablation is twice that of cryoablation, although both methods are equally effective for tumors $\leq$3 cm.[6]

Complications of percutaneous MWA for renal cancer include bleeding and urologic-related issues, with reports of MWA-related fatalities.[123] Studies indicate that intravenous administration of iodine contrast agents immediately after thermal ablation of T1a renal cancer does not affect glomerular filtration rate.[124] Notably, patients with Radius, Exophytic/endophytic, Nearness to collecting system, Anterior/posterior, Location (RENAL) and modified-RENAL scores above 6.5 are at higher risk of disease progression following MWA treatment.[125]

Thyroid cancer

MWA is well established in the treatment of thyroid cancer. MWA offers several advantages, including shorter operation times, reduced bleeding, and lower costs.[126] It is a viable option for treating T1aN0M0 single-focal low-risk papillary thyroid carcinoma (PTC), but its application for PTC larger than 1 cm and multifocal micro-papillary thyroid carcinoma (PTMC) remains controversial.[127] Supervised MWA is considered safe and effective for low-risk multifocal PTMC (fewer than 3 foci).[128,129]

In early low-risk PTMC treatment, MWA is comparable to surgical resection in terms of disease progression and major complications.[130–134] Notably, Chorti et al. conducted a systematic review and Bayesian network meta-analysis comparing RFA, laser ablation, MWA, high-intensity focused ultrasound, and conventional surgery for benign thyroid nodules. Quantitative analysis demonstrated that MWA was associated with significantly lower risks of vocal cord complications (relative risk [RR] 0.25, 95% confidence interval [CI]: 0.09–0.60), transient laryngeal nerve injuries (RR 0.16, 95% CI: 0.02–0.73), and hypothyroidism (RR 0.00, 95% CI: 0.00–0.03) compared to conventional surgery.[135]

The main complications of MWA for benign and malignant thyroid nodules include bleeding, earache, toothache, postoperative hoarseness, and intracystic hemorrhage.[136–138] Older patients, those with larger calcifications, and larger PTMCs are less likely to achieve complete ablation zone loss; however, complete loss of the ablation zone is not associated with recurrence.[139]

Breast cancer

The treatment of breast cancer using MWA has recently become a prominent area of research. Previous studies have established the safety and efficacy of ultrasound-guided percutaneous MWA for benign breast lesions.[140,141] Zhou et al. have suggested that ultrasound-guided percutaneous microwave coagulation therapy is a feasible option for treating small, isolated breast cancer.[4] Furthermore, MWA has proven to be a safe and efficient method for treating painful spinal metastases.[142] Pan et al. have shown that, in cases of T1/T2 breast cancer, the preoperative application of MWA can accurately direct breast-conserving surgery without impacting sentinel lymph node biopsy.[143] A comparison between MWA and nipple-sparing mastectomy revealed that MWA provides similar short-term efficacy while achieving higher aesthetic satisfaction.[144]

Prostate cancer

MWA is also under investigation as a treatment for prostate cancer. Targeted perineal MWA is safe, feasible, and well-tolerated in patients with moderate to low-risk prostate cancer.[145] Most patients report significant improvements in subjective symptoms and quality of life following MWA. Complications observed post-treatment include temporary urinary symptoms and anterior rectal fistula, with a 55% reduction in Prostate-Specific Antigen (PSA) levels at 6 months post-surgery.[65,146]

Table 3. Various image-guided MWAs

	Advantage	Shortcoming
US	easy to operate, real-time ablation monitoring.	operator dependent, image clarity is average, penetration ability is limited
CT	intraoperative monitoring, better evaluation of the minimum ablation boundary, improved ablation rate, soft tissue and bone visualization, deep tissue visualization.	radiation, contrast agent
MRI	low overall complication rate, high soft tissue resolution, real-time evaluation of ablation.	high price and time cost

Ablation range assessment

Although the safety and efficacy of thermal ablation for various solid tumors have been well established, these conclusions are primarily based on complete ablation. Studies indicate that only ablation with a margin of 5 cm or more achieves optimal local control of colorectal cancer liver metastases, while incomplete ablation may promote tumor progression.[147,148] Therefore, accurate assessment of the ablation range and ensuring complete ablation are crucial. Currently, the primary imaging modalities for guiding and evaluating MWA include ultrasound, MRI, and CT, each with distinct advantages (Table 3). Ultrasound is widely used for real-time guidance in MWA of soft tissue masses due to its ability to visualize and predict coagulative necrosis. CT is preferred for guiding MWA in patients with bone metastases.[64,65] MRI-guided MWA offers greater precision.[149]

Contrast-enhanced ultrasound provides clear imaging for MWA combined with hydrodissection in thyroid cancer[133] (Figure 3A). Intraoperative enhanced CT can more accurately identify the minimum ablation boundary. If intraoperative images show incomplete ablation, adjustments to the ablation needle position can be made for supplemental ablation, significantly improving the success rate[150] (Figure 3B). MRI-guided MWA demonstrates superior accuracy in positioning, guiding ablation, and achieving complete ablation (Figure 3C), with a significantly lower total complication rate compared to CT-guided MWA, and shows notable advantages in median PFS and OS.[149]

MWA for lung tumors presents unique challenges due to respiratory movement. Research has found that the average dielectric properties of lung tumor tissues are twice those of non-tumor lung specimens, while the properties of dense fibrotic tissues are similar to those of tumor tissues. Significant differences in dielectric properties between the expiratory and inspiratory phases and the proximity of tumors to bronchial vascular bundles also contribute to the risk of local progression post-MWA. Adjusting MWA parameters to destroy cancer cells without damaging surrounding tissues is essential to reduce the risk of local progression in these lesions and warrants further exploration.[151–153] Models for more accurate prediction of ablation range are also under development.[46,154–158]

During MWA treatment, real-time temperature monitoring of the ablation area is crucial for ensuring both therapeutic effectiveness and safety.[159] Currently, temperature monitoring methods can be broadly categorized into imaging techniques and invasive temperature monitoring techniques. Imaging

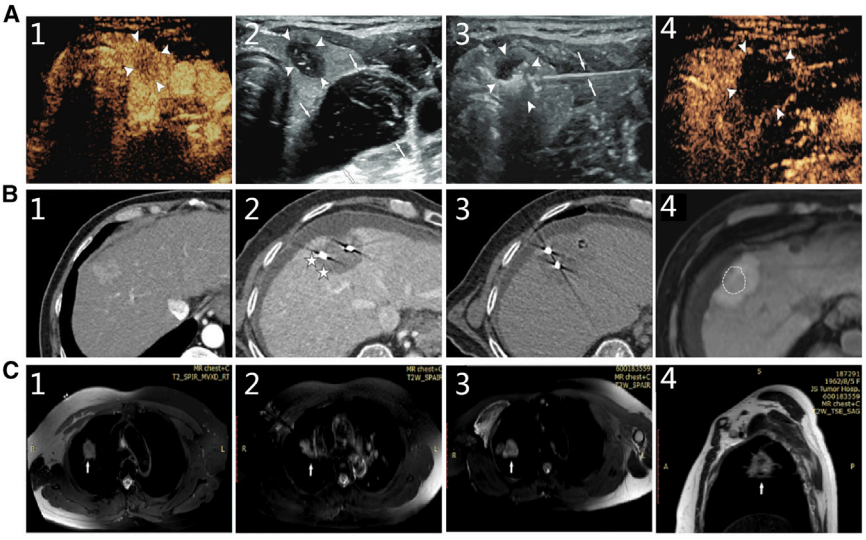

Figure 3. Image guidance and evaluation during MWA

(A) Ultrasound-guided MWA in the treatment of papillary thyroid carcinoma. (1) Preoperative contrast-enhanced (CE) ultrasound images showing a low-enhancement pattern of the tumor (arrow); (2) ultrasound images of the carotid artery and vagus nerve (arrow) surrounding the tumor were protected by hydrodissection technique (arrow); (3) hyperechoic pattern of the tumor during ablation (arrow); (4) The CE US image after ablation showed no enhancement of the tumor (arrow).[133]

(B) (1) Preoperative arterial CT axial flow imaging showed vascular liver cancer in section VIII of the liver; (2) the ablation margin on the right (star) side of the tumor was assessed as inadequate on intraoperative CT images after the expected ablation was completed. (3) Immediate supplementary ablation is performed by repositioning the MWA probe to cover areas with insufficient margins; (4) MRI assessed that the tumor (dashed line) was completely ablated.[150]

(C) MRI-guided MWA for the treatment of right upper lobe lung adenocarcinoma. (1) Guided by magnetic resonance imaging (MRI), skin markers were applied to locate the needle insertion site; (2) guided by magnetic resonance T1WI, 16G ablation antenna was inserted into the center of tumor lesion; (3 and 4) following two 8-min ablation cycles, tissue ablation areas were obtained, which can be clearly seen in axial (3) and sagittal (4) phase images with large areas of ground glass covering the entire tumor.[149] The US, MRI, and CT images were adapted and reprinted under terms of the CC-BY license from Cao et al.,[133] Shen et al.,[149] and Joo et al.[150], respectively. Copyright, 2021, Radiological Society of North America Inc. Copyright, 2022, Springer Verlag. Copyright, 2022, Frontiers Media S.A.

techniques, such as MRI, CT, and ultrasound, offer non-invasive temperature monitoring methods, but their clinical application still has certain limitations. In contrast, invasive temperature monitoring techniques, such as thermocouples, thermistors, and optical fiber sensors, offer unique advantages in terms of high accuracy and real-time monitoring during ablation procedures. Among imaging temperature monitoring technologies, MRI temperature imaging, which is currently the clinical gold standard, utilizes proton resonance frequency shift technology to provide high-resolution temperature distribution maps. However, MRI requires specialized imaging sequences, and its thermal sensitivity is tissue type dependent. Moreover, the high cost of MRI equipment, motion artifacts, and compatibility limitations with MR-compatible devices hinder its widespread clinical application.[160] CT can monitor temperature changes via ionizing radiation, but its thermal sensitivity also depends on tissue characteristics, and it requires multiple or continuous scans, increasing the risk of radiation exposure to patients. Additionally, CT has relatively low temporal resolution, and the reproducibility of quantitative measurements has not been fully validated, limiting its clinical application.[161] Ultrasound, with its advantage of real-time imaging, typically has a temperature monitoring range limited to below 50°C, and its thermal sensitivity is influenced by the tissue's acoustic properties, often resulting in measurement artifacts.[162] Although imaging technologies offer non-invasive temperature monitoring methods, their real-time control and accuracy in ablation treatments remain insufficient. Therefore, invasive temperature monitoring techniques play an irreplaceable role in clinical settings.

Thermocouples and thermistors are currently the most commonly used invasive temperature sensors in clinical practice. For example, the StarBurst XL RFA system and Neuwave Medical Certus 140 MWA probes are equipped with multiple thermocouples to monitor temperature in real-time during the ablation process, while minimizing invasiveness.[159] Optical fiber sensors, an emerging technology, demonstrate significant advantages in ablation treatments. Compared to traditional thermocouples and thermistors, optical fiber sensors have a spatial resolution of less than 0.1 mm and are unaffected by electromagnetic interference, making them suitable for high-energy treatment environments like MWA. Furthermore, optical fiber sensors are chemically inert, electrically neutral, and biocompatible, avoiding immune responses and ensuring patient safety. At the same time, optical fiber sensors are cost-effective, lightweight, and flexible, making them easy to integrate into existing ablation devices.[159] These characteristics enable optical fiber sensors to monitor temperature distribution in the ablation area in real time and with high precision, providing important technical support for ablation treatments. Despite their invasive nature, which may increase operational complexity, the high accuracy and real-time monitoring capabilities of optical fiber sensors make them promising for future clinical applications. With technological advancements, the combination of optical fiber sensors with imaging technologies may become a new direction for evaluating ablation areas. For example, integrating optical fiber sensors with MRI or ultrasound imaging can achieve both high-precision temperature monitoring and real-time spatial information, further enhancing the safety and effectiveness of ablation treatments. Additionally, the introduction of artificial intelligence (AI) technology holds promise for optimizing the analysis and prediction of temperature data, providing support for personalized treatment plans.

COMBINATION THERAPIES INVOLVING MWA

Due to the limitations of traditional ablation techniques, it is challenging to ensure complete ablation when treating large or multifocal tumors. Residual tumor tissue is a major risk of recurrence after treatment and may even accelerate tumor growth. Therefore, improving the thermal efficiency of MWA or using MWA-related combination therapy to fight against tumors is one of the current research hotspots.

MWA combined with chemotherapy

In patients with advanced NSCLC, MWA combined with chemotherapy has demonstrated a significant improvement in survival outcomes compared to chemotherapy alone. A prospective study involving 293 patients reported that the median PFS was 10.3 months (95% CI 8.0–13.0) in the MWA plus chemotherapy group, compared to 4.9 months (95% CI 4.2–5.7) in the chemotherapy-alone group (HR = 0.44, $p < 0.0001$). Moreover, the median OS was not reached in the MWA group, whereas it was 12.6 months (95% CI 10.6–14.6) in the chemotherapy group (HR = 0.38, $p < 0.0001$). These findings suggest that MWA, in combination with chemotherapy, offers a superior survival benefit for patients with advanced NSCLC.[20] When MWA is used in conjunction with doxorubicin, it enhances cell death through Reactive Oxygen Species (ROS)-induced apoptosis and DNA damage.[71] Encapsulating doxorubicin (DOX) and MW sensitizer (1-butyl-3-methylimidazolium-l-lactate, BML) into fucoidan conjugated liposomal nanoparticles (Targeted (P-selectin) Binding Particles [TBP]@DOX), followed by MWA treatment, achieves targeted accumulation and significant release of doxorubicin *in situ* for HCC and lung metastases, substantially improving efficacy without reported adverse metabolic events.[163] Factors influencing tumor progression after MWA combined with chemotherapy include weight loss, histology, clinical Tumor, Node, Metastasis (TNM) stage, clinical N type, tumor location, and tumor size.[164]

Microwave ablation combined with surgery

Compared to resection alone for liver metastases, combining surgery with ablation has been shown to improve perioperative outcomes without compromising long-term survival. A study analyzing 2,123 operative cases of hepatic colorectal metastases reported that patients undergoing combined ablation and resection (A/R) had significantly lower blood loss (300 mL vs. 500 mL, $p < 0.01$) and a shorter hospital stay (7 days vs. 9 days, $p < 0.01$) compared to those who underwent bilateral resection (BR). Moreover, the 5-year OS rate was comparable between the two groups (A/R: 56% vs. BR: 49%, $p = 0.16$), indicating that ablation combined with surgery is a viable approach that enhances perioperative recovery while maintaining long-term oncologic outcomes.[21] Some studies suggest that surgery plus intraoperative MWA provides comparable outcomes to surgery alone in colorectal cancer liver metastases. A

case-matched study reported no significant difference in RFS (p = 0.685) and OS (p = 0.151) between the two groups, with recurrence rates of 60% vs. 65% (p = 0.774), indicating that the choice of approach may depend on metastasis location and size.[165] Wu et al. demonstrated that ultrasound-guided percutaneous MWA combined with synchronous transcatheter arterial chemoembolization (TACE) is a safe and effective treatment for CRLM.[73] MWA combined with minimally invasive open decompression offers an alternative to open surgery for treating thoracic metastases from breast cancer, maintaining function and improving prognosis.[72] In retroperitoneal tumors, MWA combined with hydrodissection achieved a LTP rate of 3.4%, a median treatment-free interval of 18 months, and an overall complication rate of 15.8%, with only one major complication, demonstrating effective local control and prolonged systemic therapy-free periods.[77] Ultrasound-guided MWA combined with feeding artery ablation significantly reduced the regrowth rate (7.2% vs. 22.6%), improved ablation efficiency (lower Ablation Energy Required Per Milliliter (AERPM) of 956.3 ± 38.5 J/mL vs. 1,025.9 ± 121.5 J/mL), and decreased the complication rate (2.9% vs. 13.2%) when treating large benign thyroid nodules, offering insights for improving malignant tumor ablation and minimizing bleeding risks.[166]

Microwave ablation combined with immunotherapy

MWA can induce both local and systemic $CD8^+$ T cell responses, with a significant increase in plasma interferon (IFN)-γ levels when combined with programmed death-1 (PD1) or cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) inhibitors, indicating clinical potential.[167] In a case report, a patient with advanced squamous lung cancer resistant to immunotherapy showed long-lasting therapeutic effects following MWA treatment.[168] MWA combined with apatinib and camrelizumab in advanced HCC patients demonstrated strong clinical activity, with an objective response rate of 50%, disease control rate of 78.6%, and significant improvements in PFS (10.8 months) and OS (19.3 months), along with good tolerability and manageable adverse events.[169] Tremelimumab combined with tumor ablation has also been suggested as a potential strategy for advanced biliary tract cancer.[74] MWA in combination with AXL-Targeting Chimeric Antigen Receptor T Cells (AXL-CAR T cells) has shown enhanced antitumor effects, with MWA promoting the activation, invasion, persistence, and tumor suppression of AXL-CAR T cells in AXL-positive NSCLC patient-derived xenografts by remodeling the tumor microenvironment. This combination therapy also increased mitochondrial oxidative metabolism in tumor-infiltrating CAR T cells.[22] MWA combined with TACE and PD1 inhibitors provides a therapeutic option for tyrosine Kinase Inhibitor (TKI)-intolerant HCC patients, resulting in significantly improved PFS (10.0 vs. 4.7 months) and OS (17.0 vs. 8.5 months) compared to MWA-TACE alone.[170] The interaction between MWA and the immune microenvironment will be discussed in more detail later.

Application of nanomaterials in microwave ablation

Recent advances in nanotechnology have opened new avenues to address the critical limitations of MWA, including incomplete tumor eradication, off-target thermal damage, and post-ablation immunosuppressive microenvironment. Three synergistic strategies leveraging nanomaterials are systematically discussed in the following, supported by representative preclinical studies (summarized in Table 4).

Strategy 1 is enhancing microwave energy conversion efficiency (Figure 4A). Nanomaterials with high dielectric loss or ionic conductivity can amplify microwave energy absorption, enabling deeper penetration and larger ablation zones at reduced power inputs. Some examples are listed in the following. Cesium-based thermal accelerator (TA), a liquid-gel phase transition polymer,[14] demonstrated a 40% increase in temperature rise kinetics during MWA compared to controls in phantom models. Its radiopacity allows real-time CT-guided delivery to ablation margins, potentially targeting recurrence-prone zones. The injection of γ-Fe_2O_3 MNPs, a magnetic nanoparticles (MNPs), into HCC reduced required microwave power from 90 W to 35 W by generating localized eddy currents, achieving equivalent hyperthermia with minimized collateral damage.[15] Ca^{2+}-surplus alginate hydrogel can restricted heating zones while elevating extracellular Ca^{2+} levels. The combined Ca^{2+} overload and mild hyperthermia disrupted intracellular Ca^{2+} homeostasis, inducing immunogenic cell death in residual tumors.[172]

Strategy 2 is synergizing ablation with adjuvant therapies (Figure 4B). Nanoplatforms can convert MWA into multimodal therapies by integrating chemotherapeutic, dynamic, or anti-angiogenic agents. covalent organic framework cladding metal organic framework (MOF@COF) nanocapsules a covalent organic framework-clad Bi-Mn-porphyrin MOFs,[173] simultaneously acted as microwave sensitizers (generating heat and cytotoxic singlet oxygen) and apatinib carriers. This dual-action suppressed vascular Endothelial Growth Factor (VEGF)-driven angiogenesis and achieved 100% non-recurrence in colorectal cancer models. CuZr MOF is a microwave-activated Cu^{2+} ions in zirconium MOFs[174] enhanced Fenton-like reactions to produce ROS, synergizing thermal ablation with ferroptosis. The ROS surge also inhibited heat shock proteins (HSP70/HSP90), sensitizing tumors to hyperthermia. EF-DOX-Lips nanospheres a liposomes co-encapsulating ethyl formate and doxorubicin,[171] can downregulate EphA2 oncogenic pathways post-MWA, reducing residual tumor viability by 68% compared to ablation alone.

Strategy 3 is reprogramming the post-ablation immune landscape (Figure 4C). Nanomaterials can transform the immunosuppressive ‘‘"cold’’ tumor microenvironment into an immunogenic ‘‘hot’’ state. Post-MWA infiltration of mannose-coated iron oxide nanoparticles (man-IONPs) into peri-ablation zones[176] polarized pro-tumor M2 macrophages to antitumor M1 phenotypes, increasing $CD8^+$ T cell infiltration by 3.2-fold and suppressing recurrence in orthotopic HCC models. Mitochondria-targeted ZrO_2 nanoparticles (MZCNs), an internalize RGD/Triphenylphosphonium (iRGD/TPP) dual-targeted nanoparticles,[175] can accumulate in tumor mitochondria, amplifying microwave sensitivity to expand effective ablation areas (2.8× controls) while inducing mitochondrial apoptosis. Mannose-derived carbon dots (Man-CDs) can captured tumor antigens released during MWA and delivered them to dendritic cells, triggering systemic antitumor immunity.[177] Combined MWA/Man-CD treatment eradicated 85% of distant tumors in metastatic models.

Table 4. Combination therapies involving microwave ablation

	Types	Advantage	Reference
Surgery	combined with liver metastasis resection	improve perioperative prognosis without affecting long-term survival.	Karanicolas et al.[21]
	combined with minimally invasive open decompression for breast cancer with chest metastasis	maintain or improve functional outcomes.	Liu et al.[72]
	combined with hydrodissection for retroperitoneal tumors	high local control rate and few serious complications.	Rosebbo et al.[77]
	combined with simultaneous TACE treatment for CRLM	safe and effective	Wu et al.[73]
	combined with blood supply artery ablation to treat large solid benign thyroid nodules	low regeneration rate, high ablation efficiency, less bleeding; to provide reference for the ablation of malignant tumors.	Li et al.[166]
Chemotherapy	conventional chemotherapy drugs for lung cancer	longer PFS and OS were obtained than chemotherapy alone.	Wei et al.[20]
	DOX	cell death can be promoted by ROS-induced apoptosis and DNA damage.	Kong et al.[71]
	TBP@DOX	achieve specific accumulation and release and significantly improve the effect of DOX.	Xu et al.[163]
	EF-DOX-lips	inhibit tumor proliferation and angiogenesis, inhibit tumor growth and recurrence or metastasis.	Hou et al.[171]
Immunotherapy	AXL-CAR T	MWA enhanced the activation, invasion, persistence, and tumor inhibition properties of AXL-CAR T cells in patient-derived xenografts of AXL-positive NSCLC through TME remodeling.	Cao et al.[22]
	tremelimumab	potential treatment strategies for advanced biliary tract cancer.	Xie et al.[74]
	combined with PD1 or CTLA-4 blockers	induce local and systemic $CD8^+$ T cell response, significantly increase plasma IFN-γ concentration.	Zhu et al.[167]
	after immunotherapy resistance, combined with MWA.	achieve a durable abscopal effect.	Shao et al.[168]
Nanomaterials	TA based on cesium block copolymer compounds	the rate and amplitude of MWA temperature increase significantly.	Park et al.[14]
	MNPs	reduce MWA input power.	Minbashi et al.[15]
	Ca^{2+}-surplus alginate hydrogel	improve the heating efficiency of MWA and induce antitumor immunity.	Zhu et al.[172]
	MOF@COF	enhance microwave thermal sensitivity and antitumor angiogenesis.	Li et al.[173]
	CuZr MOF	by producing abundant ROS, the heat shock protein is inhibited and the destructive effect on tumor is enhanced.	Feng et al.[174]
	MZCNs (mitochondria-targeting zirconia (ZrO_2) complex nanoparticles	enhance the effect of MWA, effectively inhibit tumor recurrence and metastasis.	Chen et al.[175]
	man-IONPs	M2 macrophages were induced to polarize into an antitumor M1 phenotype, transforming the immunosuppressive microenvironment into an immunoactivated microenvironment.	Cui et al.[176]
	Man-CD	induce strong tumor-specific immune response and effectively inhibit primary and distant tumors.	Zhou et al.[177]

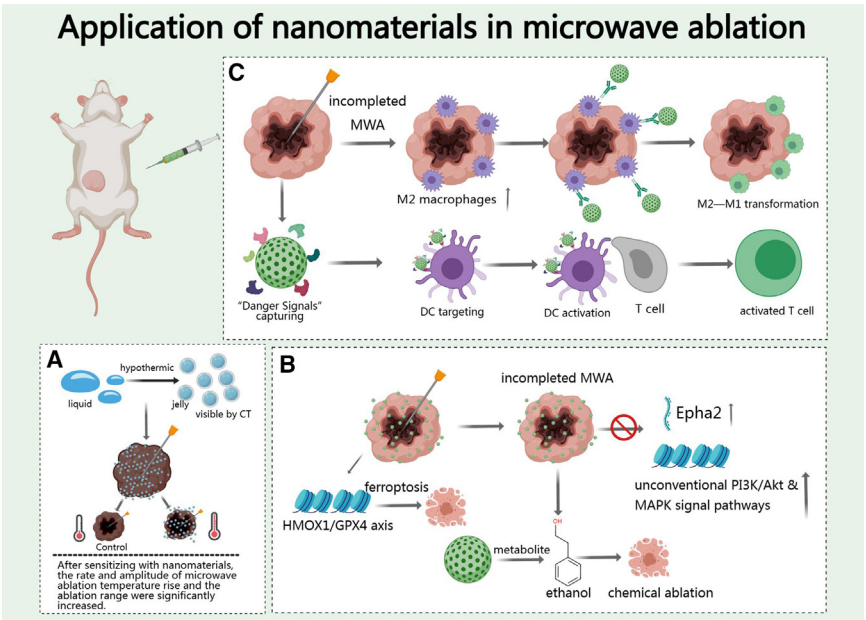

Figure 4. Application of nanomaterials in microwave ablation

(A) Multifunctional nanospheres, when enriched in the tumor area, enhance the heating efficiency of MWA, significantly improving the speed and amplitude of heating, and also expand the ablation range.

(B) Multifunctional nanospheres, when combined with MWA, can activate the body's antitumor immune response, yielding a better therapeutic effect.

(C) Multifunctional nanospheres used in conjunction with MWA can induce changes in specific gene pathways, enhancing antitumor efficacy.

While preclinical studies highlight the transformative potential of nanomaterial-enhanced MWA, clinical translation requires addressing key challenges: (1) standardizing nanoparticle delivery routes (e.g., intraoperative vs. image-guided injection), (2) balancing microwave absorption efficiency with long-term biocompatibility, and (3) developing multifunctional nanosystems with dual imaging/therapeutic capabilities for personalized treatment monitoring.

Antitumor immune response induced by MWA

MWA not only treats various malignant tumors through thermal effects but also activates the immune system, producing long-lasting antitumor effects. Studies have shown that 30% of HCC patients develop new or enhanced tumor-specific immune responses following thermal ablation.[178]

Zhou et al. conducted single-cell RNA sequencing of peripheral blood mononuclear cells from six breast cancer patients before and after MWA, revealing activation of $CD8^+$ T cells, enhanced co-stimulatory capacity of $CD4^+$ T cells, increased T cell clonality, and strengthened interactions between B cells and $CD4^+$ T cells. Notably, the expression of genes such as GZMB, GNLY, PRF1, KLRD1, SPON2, FCER1G, XCL2, and XCL1 significantly increased, indicating enhanced cytotoxicity and chemokine activity of peripheral natural killer (NK) cells post-MWA. This provides a comprehensive view of MWA-induced systemic immune responses.[18]

Similarly, another study observed an increase in $CD8^+$ T cells and a decrease in Regulatory T cells (Treg cells) and interleukin (IL)-2 levels in peripheral blood after MWA treatment for lung cancer.[67] Another study demonstrated that MWA significantly elevated Inducible T cell CO-Stimulator+ (ICOS+) activated $CD4^+$ T cells and serum IFN-γ levels, with the MWA-induced $CD4^+$ effector memory T cell response persisting after treatment.[68] Additionally, MWA not only inhibits the growth of primary tumors but also exerts systemic effects by enhancing antitumor immunity.[179] Yu et al. found that MWA at the primary site of metastatic breast cancer can prevent metastatic progression through the macrophage/IL-15/NK cell pathway, highlighting MWA's potential in treating stage IV breast cancer.[19]

After MWA, the expression of immune targets such as T cell immunoglobulin and ITIM domains (TIGIT) and lymphocyte Activation Gene 3 (LAG3) increased in untreated tumors. Combining MWA with blockade of these targets significantly enhanced the proliferation of $CD8^+$ tumor-infiltrating lymphocytes (TILs) and remodeled the tumor microenvironment.[69,70] Furthermore, combining MWA with anti-PD1/CTLA-4 or OK-432 amplifies systemic antitumor immunity.[180,181]

In conclusion, MWA can activate systemic antitumor immune responses and induce distant effects, inhibiting the growth of untreated tumors. Figure 5 illustrates the immune changes triggered by MWA.

FUTURE PERSPECTIVES

Although MWA technology has made significant strides in cancer treatment, its future development is still full of potential and challenges. With the continuous advancement of medical technology, MWA will continue to play a crucial role in oncology, particularly in the areas of technological innovation, personalized treatment, and multidisciplinary integration. Our future outlook and discussion are summarized in Table 5.

One of the key ways to further improve the efficacy and safety of MWA is through the optimization of equipment and technical parameters. Miniaturization, intelligent design, and multifunctionality of microwave antennas will enhance the precision of ablation while minimizing damage to surrounding healthy tissues. In addition, advancements in computational modeling and simulation technologies will allow for more accurate prediction and control of thermal field distribution during MWA, further enabling personalized treatment optimization. Exploring new ablation strategies, such as incorporating localized drug delivery systems into MWA, also holds promise for improving therapeutic outcomes and prolonging antitumor effects.

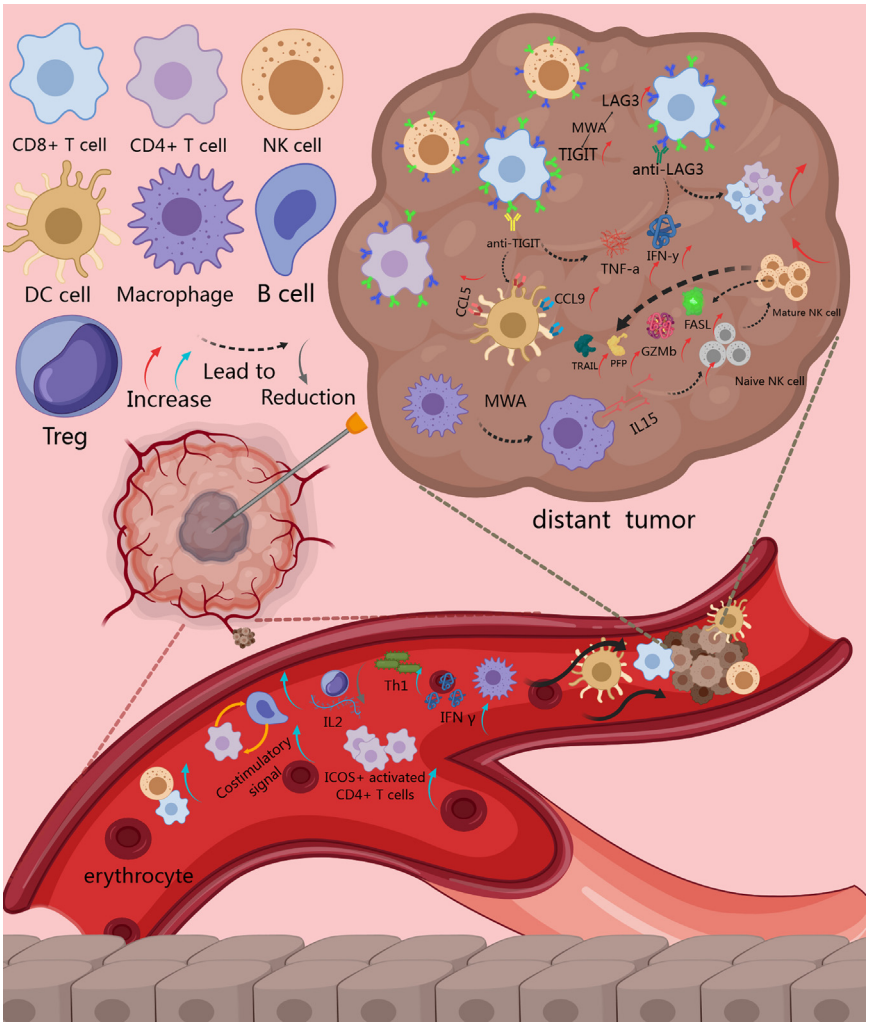

Figure 5. Antitumor immune response induced by MWA

After MWA treatment, there was an increase in the proportion of $CD8^+$ T cells in the peripheral blood, a decrease in the proportion of Treg cells and the concentration of IL-2,[67] an enhancement in the costimulatory properties of $CD4^+$ T cells, an amplification in T cell clonality, and an improved interaction between B cells and $CD4^+$ T cells.[18] Additionally, MWA induced ICOS+ activated $CD4^+$ T cells and a significant increase in serum interferon-gamma levels. It can also have abscopal effects on distant untreated tumors, resulting in upregulated expression of TIGIT and LAG3 in immune cells within those tumors. Combining MWA with TIGIT/LAG3 blockade can significantly enhance the expansion of $CD8^+$ TILs and reshape the tumor microenvironment.[69,70]

The changes in the immune microenvironment induced by MWA also represent a key research area. In recent years, immune checkpoint inhibitors, represented by PD1/PD-L1 monoclonal antibodies, have significantly improved the prognosis of patients with malignant tumors.[182,183] The immune microenvironment changes caused by thermal ablation are dual in nature, affecting both complete and incomplete ablation outcomes. Incomplete ablation may alter myeloid-derived suppressor cells, potentially promoting tumor progression.[148] Therefore, how to effectively combine MWA with immunotherapy to combat tumors is a subject worthy of further exploration.

Advancements in imaging-guided technologies will continue to drive the progress of MWA. Optimizing integrated systems of ultrasound, CT, MRI, and positron emission tomography (PET) multimodal imaging can further improve tumor targeting precision and real-time monitoring capabilities. These systems will not only assist in intraoperative localization but also support postoperative assessment and follow-up management, ultimately improving patient outcomes. The use of AI and machine learning to automate imaging analysis and provide intraoperative decision support will bring new breakthroughs in personalized treatment.

The combination of MWA with other treatment modalities, including surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy, is a future trend in MWA development. This multidisciplinary treatment strategy will help overcome tumor heterogeneity and improve overall therapeutic efficacy. Moreover, as research on tumor biomarkers progresses, MWA is expected to be incorporated into personalized medicine frameworks, where treatment plans tailored to patients' specific gene expression profiles and tumor microenvironment will become more precise and effective.

While MWA has been widely adopted worldwide, there is still a lack of standardized protocols and guidelines for its clinical application. Establishing unified guidelines and operational standards for MWA will be a critical step in promoting its broader use. This will help reduce variability in technique, ensure treatment reproducibility, and improve patient safety. Additionally, large-scale, multicenter randomized controlled trials will provide stronger evidence for the clinical application of MWA, further solidifying its role in cancer treatment.

Although MWA has demonstrated favorable short-term therapeutic outcomes, its long-term efficacy and safety remain to be fully validated. Therefore, accumulating and analyzing follow-up data to comprehensively evaluate the impact of MWA on patient survival, quality of life, and long-term complications are essential.

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Table 5. Summary of future perspectives and challenges in MWA technology

Research area	Innovations/strategies	Expected benefits	Challenges or considerations
Equipment & technical optimization	- miniaturization, intelligent design, and multifunctional microwave antennas - enhanced computational modeling/simulation for thermal field control - integration of localized drug delivery systems	- improved ablation precision - minimized damage to healthy tissues - personalized treatment optimization	- technical complexity - integration of multiple functions - balancing precision with safety
Imaging-guided technologies	- integration of multimodal imaging (ultrasound, CT, MRI, PET) - application of AI/ML for automated imaging analysis and intraoperative decision support	- enhanced tumor targeting and real-time monitoring - better intraoperative localization and postoperative assessment - advances in personalized treatment	- data integration and standardization - reliability of AI/ML algorithms - cost and accessibility of advanced imaging
Multidisciplinary integration & combination therapy	- combining MWA with surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy - incorporation into personalized medicine frameworks guided by tumor biomarkers	- overcoming tumor heterogeneity - improved overall therapeutic efficacy - tailored treatment plans	- coordination of multidisciplinary approaches - need for robust clinical validation
Immune microenvironment & immunotherapy	- investigating immune microenvironment changes induced by MWA - combining MWA with immune checkpoint inhibitors (e.g., PD1/PD-L1 antibodies)	- enhanced antitumor immune response - potential mitigation of tumor progression after incomplete ablation	- dual nature of immune responses - risk of promoting tumor progression with incomplete ablation
Standardization & clinical protocols	- development of unified guidelines and operational standards for MWA - execution of large-scale, multicenter randomized controlled trials	- reduced variability in clinical practice - improved reproducibility and patient safety - strengthened clinical evidence for MWA	- achieving consensus among clinicians - resource-intensive and time-consuming clinical trials
Long-term outcome evaluation	- accumulating and analyzing long-term follow-up data (patient survival, quality of life, long-term complications)	- comprehensive assessment of MWA's long-term efficacy and safety - better understanding of its impact on patient outcomes	- need for long-term studies and robust data collection - ensuring consistent follow-up protocols

AUTHOR CONTRIBUTIONS

X.L.: visualization and writing – review and editing. J.Z.: visualization and writing – review and editing. B.W.: conceptualization, visualization, writing – original draft, and writing – review and editing. Y.W.: visualization and writing – original draft. M.C.: conceptualization, visualization, writing – original draft, and writing – review and editing. W.L.: visualization and writing – review and editing. F.D.: visualization, writing – original draft, and writing – review and editing.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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