

## Medical Policy



### Title: Microwave Tumor Ablation

Related Policies:	<ul style="list-style-type: none"> <li>▪ <i>Cryosurgical Ablation of Primary or Metastatic Liver Tumors</i></li> <li>▪ <i>Radiofrequency Ablation of Primary or Metastatic Liver Tumors</i></li> <li>▪ <i>Cryoablation of Tumors Located in the Kidney, Lung, Breast, Pancreas, or Bone</i></li> <li>▪ <i>Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors</i></li> <li>▪ <i>Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies</i></li> <li>▪ <i>Radioembolization for Primary and Metastatic Tumors of the Liver</i></li> </ul>
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#### Professional / Institutional

Original Effective Date: October 1, 2016

Latest Review Date: November 17, 2023

Current Effective Date: January 13, 2021

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Populations	Interventions	Comparators	Outcomes
Individuals: • With an unresectable primary or metastatic hepatic tumor	Interventions of interest are: • Microwave ablation	Comparators of interest are: • Radiofrequency ablation • Transcatheter arterial chemoembolization	Relevant outcomes include: • Overall survival • Disease-specific survival • Symptoms • Quality of life

Populations	Interventions	Comparators	Outcomes
			<ul style="list-style-type: none"> <li>Treatment-related mortality</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With an unresectable primary or metastatic lung tumor</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Microwave ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> <li>Cryoablation</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Disease-specific survival</li> <li>Symptoms</li> <li>Quality of life</li> <li>Treatment-related mortality</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With an unresectable primary or metastatic renal tumor</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Microwave ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> <li>Cryoablation</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Disease-specific survival</li> <li>Symptoms</li> <li>Quality of life</li> <li>Treatment-related mortality</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With an unresectable primary or metastatic solid tumor other than liver, lung, or renal</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Microwave ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Standard of Care</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Disease-specific survival</li> <li>Symptoms</li> <li>Quality of life</li> <li>Treatment-related mortality</li> <li>Treatment-related morbidity</li> </ul>

## DESCRIPTION

Microwave ablation (MWA) is a technique to destroy tumors and soft tissue using microwave energy to create thermal coagulation and localized tissue necrosis. Microwave ablation is used to treat tumors not amenable to resection and to treat patients ineligible for surgery due to age, comorbidities, or poor general health. Microwave ablation may be performed as an open procedure, laparoscopically, percutaneously, or thoracoscopically under image guidance (e.g., ultrasound, computed tomography, magnetic resonance imaging) with sedation, or local or general anesthesia. This technique is also referred to as microwave coagulation therapy.

## OBJECTIVE

The objective of this evidence review is to determine whether the use of microwave ablation improves the net health outcome in individuals with unresectable primary or metastatic solid tumors.

## BACKGROUND

### Microwave Ablation

Microwave ablation (MWA) uses microwave energy to induce an ultra-high-speed, 915 MHz or 2 450 MHz (2.45 GHz), alternating electric field, which causes water molecule rotation and creates heat. This results in thermal coagulation and localized tissue necrosis. In MWA, a single microwave antenna or multiple antennas connected to a generator are inserted directly into the tumor or tissue to be ablated; energy from the antennas generates friction and heat. The local heat coagulates the tissue adjacent to the probe, resulting in a small, 2 to 3 cm elliptical area of tissue ablation. In tumors greater than 2 cm in diameter, 2 to 3 antennas may be used simultaneously to increase the targeted area of MWA and shorten the operative time. Multiple antennas may also be used simultaneously to ablate multiple tumors. Tissue ablation occurs quickly, within 1 minute after a pulse of energy, and multiple pulses may be delivered within a treatment session, depending on tumor size. The cells killed by MWA are typically not removed but are gradually replaced by fibrosis and scar tissue. If there is a local recurrence, it occurs at the margins. Treatment may be repeated as needed. Microwave ablation may be used for the following purposes: (1) to control local tumor growth and prevent recurrence; (2) to palliate symptoms; and (3) to prolong survival.

Microwave ablation is similar to radiofrequency (RFA) and cryosurgical ablation. However, MWA has potential advantages over RFA and cryosurgical ablation. In MWA, the heating process is active, which produces higher temperatures than the passive heating of RFA and should allow for more complete thermal ablation in less time. The higher temperatures reached with MWA ( $>100^{\circ}\text{C}$ ) can overcome the "heat sink" effect in which tissue cooling occurs from nearby blood flow in large vessels, potentially resulting in incomplete tumor ablation. Microwave ablation does not rely on the conduction of electricity for heating and, therefore, does not flow electrical current through patients and does not require grounding pads, because there is no risk of skin burns. Additionally, MWA does not produce electric noise, which allows ultrasound guidance during the procedure without interference, unlike RFA. Finally, MWA can take 20% to 30% less time than RFA, because multiple antennas can be used simultaneously for multiple ablations. There is no comparable RFA system with the capacity to drive multiple electrically dependent electrodes.

### Adverse Events

Complications from MWA may include pain and fever. Other complications associated with MWA include those caused by heat damage to normal tissue adjacent to the tumor (e.g., intestinal damage during MWA of the kidney or liver), structural damage along the probe track (e.g., pneumothorax as a consequence of procedures on the lung), liver enzyme elevation, liver abscess, ascites, pleural effusion, diaphragm injury, or secondary tumors if cells seed during probe removal. Microwave ablation should be avoided in pregnant women because potential risks to the patient and/or fetus have not been established, and in patients with implanted electronic devices (e.g., implantable pacemakers) that may be adversely affected by microwave power output.

## Applications

Microwave ablation was first used percutaneously in 1986 as an adjunct to liver biopsy. Since then, MWA has been used to ablate tumors and tissue to treat many conditions including hepatocellular carcinoma, breast cancer, colorectal cancer metastatic to the liver, renal cell carcinoma, renal hamartoma, adrenal malignant carcinoma, non-small-cell lung cancer, intrahepatic primary cholangiocarcinoma, secondary splenomegaly and hypersplenism, abdominal tumors, and other tumors not amenable to resection. Well-established local or systemic treatment alternatives are available for each of these malignancies. The potential advantages of MWA for these cancers include improved local control and other advantages common to any minimally invasive procedure (e.g., preserving normal organ tissue, decreasing morbidity, shortening length of hospitalization). Microwave ablation also has been investigated as a treatment for unresectable hepatic tumors, as both primary and palliative treatment, and as a bridge to a liver transplant. In the latter setting, MWA is being assessed to determine whether it can reduce the incidence of tumor progression while awaiting transplantation and thus maintain a patient's candidacy while awaiting a liver transplant.

## REGULATORY STATUS

Multiple MWA devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. These devices are indicated for soft tissue ablation, including partial or complete ablation of nonresectable liver tumors. Some devices are specifically cleared for use in open surgical ablation, percutaneous ablation, or laparoscopic procedures. Table 1 is a summary of selected MWA devices cleared by the FDA.

The FDA used determinations of substantial equivalence to existing radiofrequency and MWA devices to clear these devices. FDA product code: NEY.

This evidence review does not address MWA for the treatment of splenomegaly or ulcers, for cardiac applications, or as a surgical coagulation tool.

**Table 1. Selected Microwave Ablation Devices Cleared by FDA**

Device	Indication	Manufacturer	Date Cleared	510(k) No.
MedWaves Microwave Coagulation/Ablation System	General surgery use in open procedures for the coagulation and ablation of soft tissues	MedWaves Incorporated	12/2007	K070356
Acculis Accu2i pMTA Microwave Tissue Ablation Applicator Acculis Accu2i pMTA Applicator and SulisV <sup>pMTA</sup> Generator	Intraoperative coagulation of soft tissue Software addition	Microsoulis Holdings, Ltd	8/2010 11/2012	K094021 K122762
MicroThermX Microwave Ablation System	Coagulation (ablation) of soft tissue; may be used in open surgical as well as percutaneous ablation procedures	BSD Medical Corporation	8/2010	K100786

<b>Device</b>	<b>Indication</b>	<b>Manufacturer</b>	<b>Date Cleared</b>	<b>510(k) No.</b>
Emprint™ Ablation System	Percutaneous, laparoscopic, and intraoperative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumors			
Emprint™ Ablation System	Same with design modification of device antenna for percutaneous use	Medtronic	4/2014	K133821
Emprint™ SX Ablation Platform with Thermosphere™ Technology	3-D navigation feature assists in the placement of antenna using real-time image guidance during intraoperative and laparoscopic ablation procedures		12/2016	K163105
Emprint™ Ablation Platform with Thermosphere™ Technology and Emprint™ SX Ablation Platform with Thermosphere™ Technology	Antenna modification and update to instructions for use		9/2017	K171358
			2/2020	K193232
Certus 140 2.45 GHz Ablation System and Accessories	Ablation (coagulation) of soft tissue			
Certus 140™ 2.45 GHz Ablation System and Accessories	Ablation (coagulation) of soft tissue in percutaneous, open surgical and in conjunction with laparoscopic surgical settings	Johnson & Johnson	10/2010	K100744
CertuSurg <sup>GT</sup> Surgical Tool	Surgical coagulation (including Planar Coagulation) in open surgical settings		01/2012	K113237
Certus 140™ 2.45 GHz Ablation System and Accessories	Same indication with probe redesign		7/2013	K130399
Certus 140 2.45GHz Ablation System	Ablation (coagulation) of soft tissue in percutaneous, open surgical and in conjunction with laparoscopic surgical settings, including the partial or complete ablation of non-resectable liver tumors		5/2016	K160936
			10/2018	K173756
NEUWAVE Flex Microwave Ablation System (FLEX)	Ablation (coagulation) of soft tissue; design evolution of Certus 140 2.45GHz Ablation System (K160936)	Johnson & Johnson	3/2017	K163118
Solero Microwave Tissue Ablation (MTA) System and Accessories	Ablation of soft tissue during open procedures	Angiodynamics, Inc.	5/2017	K162449
Microwave Ablation System	Coagulation (ablation) of soft tissue	Surgnova Healthcare Technologies (Zhejiang) Co., Ltd	7/2019	K183153
NEUWAVE Microwave Ablation System and Accessories	Ablation (coagulation) of soft tissue in percutaneous, open surgical and in conjunction with laparoscopic surgical	Johnson & Johnson	11/2020	K200081

Device	Indication	Manufacturer	Date Cleared	510(k) No.
	settings, including the partial or complete ablation of non-resectable liver tumors; not intended for use in cardiac procedures			

FDA: U.S. Food and Drug Administration.

**POLICY**

- A. Microwave ablation of primary or metastatic hepatic tumors may be considered **medically necessary** under the following conditions:
  - 1. The tumor is unresectable due to location of lesion[s] and/or comorbid conditions
  - 2. A single tumor of ≤5 cm or up to 3 nodules <3 cm each
- B. Microwave ablation of primary or metastatic lung tumors may be considered **medically necessary** under the following conditions:
  - 1. The tumor is unresectable due to location of lesion and/or comorbid conditions
  - 2. A single tumor of ≤3 cm
- C. Microwave ablation of more than a single primary or metastatic tumor in the lung is considered **experimental / investigational**.
- D. Microwave ablation of primary or metastatic tumors other than liver or lung is considered **experimental / investigational**.

**Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**RATIONALE**

The evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through August 25, 2023.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

## **UNRESECTABLE PRIMARY OR METASTATIC SOLID ORGAN TUMORS**

### **Clinical Context and Therapy Purpose**

The purpose of microwave ablation (MWA) in individuals who have unresectable primary or metastatic solid organ tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

#### ***Populations***

The relevant population of interest is those with unresectable primary or metastatic hepatic, lung, renal, and solid tumors other than hepatic, lung, or renal. In patients with disseminated disease or in cases where age or comorbidity precludes a surgical approach, volume reduction, symptom relief, and palliation may be appropriate. In select patients with small tumors, ablation techniques may provide a minimally invasive alternative to surgery.

#### ***Interventions***

The therapy being considered is MWA.

#### ***Comparators***

The following therapies are currently being used to manage unresectable primary or metastatic hepatic, lung, or renal tumors: radiofrequency ablation (RFA).

Transcatheter arterial chemoembolization (TACE) may be used in the management of unresectable primary or metastatic hepatic tumors. Cryoablation may be used in the management of unresectable primary or metastatic renal and lung tumors.

The following therapies are currently being used to manage other unresectable primary or metastatic solid tumors: standard of care, which may include systemic therapy, radiotherapy, and/or select local ablation therapies.

#### ***Outcomes***

The general outcomes of interest are overall survival (OS), disease-specific survival, symptoms, QOL, and treatment-related mortality and morbidity.

Treatment-related morbidities may vary by tumor type. For example, treatment for lung cancer may lead to pneumothorax. Follow-up for treatment-related morbidity is months post procedure. Follow-up to monitor for OS and recurrence rates may be measured in years of follow-up.

## Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs and systematic reviews of these studies;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

## UNRESECTABLE PRIMARY OR METASTATIC HEPATIC TUMORS

### REVIEW OF EVIDENCE

#### Systematic Reviews

Several systematic reviews have evaluated MWA for patients with liver tumors.<sup>1,2,3,4,5</sup> The 4 most recent, published in 2016,<sup>1</sup> 2019,<sup>4</sup> 2020,<sup>5</sup> and 2022<sup>6</sup> are summarized in Tables 2 through 4. Two of these reviews compared MWA to RFA,<sup>6,1</sup> 1 compared MWA to resection,<sup>4</sup> and 1 compared MWA to a variety of therapies, including RFA and resection.<sup>5</sup>

**Table 2. Microwave Ablation for Hepatic Tumors: Comparison of Trials/Studies Included in SR & MA**

Study	Chinnaratha et al (2016) <sup>1</sup>	Glassberg et al (2019) <sup>4</sup>	Cui et al 2020 <sup>5</sup>	Dou et al (2022) <sup>6</sup>
Seki et al (1999) <sup>7</sup>			●	
Shibata et al (2002) <sup>8</sup>	●		●	●
Xu et al (2004) <sup>9</sup>	●			●
Lu et al (2005) <sup>10</sup>	●		●	●
Tanaka et al (2006) <sup>11</sup>		●		
Wang et al (2008) <sup>12</sup>		●		
Ohmoto et al (2009) <sup>13</sup>	●		●	●
Yin et al (2009) <sup>14</sup>	●			●
Kuang et al (2011) <sup>15</sup>	●			●
Imura et al (2012) <sup>16</sup>		●		
Qian et al (2012) <sup>17</sup>	●			●
Chinnaratha et al (2013) <sup>18</sup>	●			
Ding et al (2013) <sup>19</sup>	●		●	●
Stattner et al (2013) <sup>20</sup>		●		

<b>Study</b>	<b>Chinnaratha et al (2016)<sup>1</sup>,</b>	<b>Glassberg et al (2019)<sup>4</sup>,</b>	<b>Cui et al 2020<sup>5</sup>,</b>	<b>Dou et al (2022)<sup>6</sup>,</b>
Takami et al (2013) <sup>21</sup> ,		●		
Zhang et al (2013) <sup>22</sup> ,	●		●	●
Abdelaziz et al (2014) <sup>23</sup> ,			●	●
Shi et al (2014) <sup>24</sup> ,		●	●	
Tan et al (2014) <sup>25</sup> ,		●		
Zhang et al (2014) <sup>26</sup> ,			●	
Abdelaziz et al (2015) <sup>27</sup> ,			●	
Vogl et al (2015) <sup>28</sup> ,			●	●
Xu et al (2015) <sup>29</sup> ,		●		
Potretzke et al (2016) <sup>30</sup> ,			●	●
Zhang et al (2016) <sup>31</sup> ,		●	●	
Li et al (2017) <sup>32</sup> ,		●		
Philips et al (2017) <sup>33</sup> ,		●		
Ryu et al (2017) <sup>34</sup> ,		●		
Song et al (2017) <sup>35</sup> ,		●		
Xu et al (2017) <sup>36</sup> ,			●	●
Yu et al (2017) <sup>37</sup> ,			●	●
Zhang et al (2017) <sup>38</sup> ,		●		
Chen et al (2018) <sup>39</sup> ,		●		
Chong et al (2018) <sup>40</sup> ,		●		
Chinnaratha et al (2015) <sup>41</sup> ,				●
Cillo et al (2014) <sup>42</sup> ,				●
Correa et al (2014) <sup>43</sup> ,				●
Di Vece et al (2014) <sup>44</sup> ,				●
Hompes et al (2010) <sup>45</sup> ,				●
Kamal et al (2019) <sup>46</sup> ,				●
Lee et al (2017) <sup>47</sup> ,				●
Liu et al (2013) <sup>48</sup> ,				●
Liu et al (2018) <sup>49</sup> ,				●

<b>Study</b>	<b>Chinnaratha et al (2016)<sup>1</sup>,</b>	<b>Glassberg et al (2019)<sup>4</sup>,</b>	<b>Cui et al 2020<sup>5</sup>,</b>	<b>Dou et al (2022)<sup>6</sup>,</b>
Sakaguchi et al (2009) <sup>50</sup> ,				●
Santambrogio et al (2017) <sup>51</sup> ,				●
Sever et al (2018) <sup>52</sup> ,				●
Shady et al (2017) <sup>53</sup> ,				●
Simo et al (2011) <sup>54</sup> ,				●
Sparchez et al (2019) <sup>55</sup> ,				●
Tian et al (2014) <sup>56</sup> ,				●
van Tilborg et al (2016) <sup>57</sup> ,				●
Vietti et al (2018) <sup>58</sup> ,				●
Yang et al (2017) <sup>59</sup> ,				●

MA: meta-analysis; SR: systematic review.

**Table 3. Microwave Ablation for Hepatic Tumors: SR and MA Characteristics**

<b>Study</b>	<b>Dates</b>	<b>Trials</b>	<b>Participants</b>	<b>Comparison</b>	<b>N (Range)</b>	<b>Design</b>	<b>Duration</b>
Chinnaratha et al (2016) <sup>1</sup> ,	1980-2014	10	Adults with either very early stage, early-stage (single tumor or up to 3 nodules with each measuring ≤3 cm), or multifocal/large HCC outside Milan criteria	MWA vs. RFA	1066 (42 to 198)	1 RCT, 9 observational (1 prospective, 8 retrospective)	5 to 45 months
Glassberg et al (2019) <sup>4</sup> ,	2006-2018	16	Adult patients with confirmed HCC or liver cancer	MWA vs. Resection	965 MWA; 755 resections (22 to 424)	1 RCT, 15 observational (2 prospective, 13 retrospective)	15 months to 5 years
Cui et al (2020) <sup>5</sup> ,	1994-2017	15	Adults with HCC without extrahepatic malignant manifestations, vascular invasions, or	MWA vs. RFA MWA vs. Resection	2458 (53 to 460)	4 RCT, 11 nonrandomized clinical trials	15 to 53 months

Study	Dates	Trials	Participants	Comparison	N (Range)	Design	Duration
			contraindications for MWA				
Dou et al (2022) <sup>6</sup>	2002-2018	33	Adult patients with confirmed HCC or liver cancer	MWA vs. RFA	4589 (19 to 562)	7 RCT, 26 observational (2 prospective, 24 retrospective)	5 to 62 months

HCC: hepatocellular carcinoma; MA: meta-analysis; MWA: microwave ablation; RCT: randomized controlled trial; RFA: radiofrequency ablation; SR: systematic review.

**Table 4. Microwave Ablation for Hepatic Tumors: SR and MA Results**

Study	Local Tumor Recurrence/Progression	Overall Survival	Disease-free Survival	Adverse events
Chinnaratha et al (2016) <sup>1</sup>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>		<i>MWA vs. RFA</i>
Total N	1298	538	NR	<i>Major Complications</i> 1043
Pooled odds ratio (95% CI), p value	1.01 (0.67 to 1.50); p=.98	1 year: 1.18 (0.46 to 3.03), p=.73  3 year: 0.76 (0.44 to 1.32), p=.33	NR	0.63 (0.29 to 1.38), p=.25
I <sup>2</sup> , p value	I <sup>2</sup> =23%, p=.23	1 year: I <sup>2</sup> =32%, p=.2  3 year: I <sup>2</sup> =53%, p=.09	NR	I <sup>2</sup> =0%, p=.8
Glassberg et al (2019) <sup>4</sup>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>
Risk ratio (95% CI), p value	2.49 (1.19 to 5.22), p=.016	1 year: 1.01 (0.99 to 1.03), p=.409  3 year: 0.94 (0.88 to 0.99), p=.03  5 year: 0.88 (0.80 to 0.97), p=.01	1 year: 0.95 (0.90 to 1.01), p=.085  3 years: 0.78 (0.65 to 0.94), p=.009  5 years: 0.83 (0.58 to 1.17), p=.284	<i>Overall complications</i> 0.31 (0.19 to 0.51), p<.001  <i>Major complications</i> 0.24 (0.10 to 0.61), p=.002
Cui et al (2020)	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>
Pooled odds ratio (95% CI), p value	<i>Local tumor progression at 1 year</i> 1.28 (0.52 to 3.18) p=.59	3 year: 0.94 (0.66 to 1.34), p=.74	NR	<i>Major complications</i> 1.04 (0.56 to 1.93) p=.90

<b>Study</b>	<b>Local Tumor Recurrence/Progression</b>	<b>Overall Survival</b>	<b>Disease-free Survival</b>	<b>Adverse events</b>
	<i>Progression-free survival at 3 years</i> 1.05 (0.77 to 1.43), p=.74	5 year: 0.83 (0.58 to 1.18), p=.29		
I <sup>2</sup> , p value	<i>Local tumor progression at 1 year</i> I <sup>2</sup> =8%, p=.34 <i>Progression-free survival at 3 years</i> I <sup>2</sup> =35%, p=.19	3 year: I <sup>2</sup> =40%, p=.12 5 year: I <sup>2</sup> =23%, p=.27	NR	<i>Major complications</i> I <sup>2</sup> =0%, p=.47
Cui et al (2020) <sup>5</sup>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>	<i>MWA vs. resection</i>
Pooled odds ratio (95% CI), p value	NR	3 year: 0.89 (0.59 to 1.35), p=.59	NR	NR
I <sup>2</sup> , p value	NR	3 year: I <sup>2</sup> =0%, p=.91	NR	NR
Dou et al 2022 <sup>6</sup>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>
Pooled odds ratio (95% CI), p value	0.78 (0.64 to 0.96); p=.02	RCTs 1 year: 1.86 (0.91 to 3.80), p=.09 3 year: 1.16 (0.77 to 1.74), p=.49 5 year: 0.79 (0.51 to 1.21), p=.27 Cohort Studies 1 year: 0.97 (0.69 to 1.36), p=.85 3 year: 0.92 (0.75 to 1.13), p=.64 5 year: 1.12 (0.93 to 1.36), p=.22	RCTs 1 year: 1.04 (0.48 to 2.24), p=.92 3 year: 3.00 (0.91 to 9.87), p=.07 Cohort Studies 1 year: 1.20 (0.96 to 1.51), p=.11 3 year: 1.15 (0.93 to 1.41), p=.20 5 year: 0.84 (0.67 to 1.05), p=.13	NR
I <sup>2</sup> , p value	5 RCTs (I <sup>2</sup> =32%); 28 cohort studies (I <sup>2</sup> =39%)	5 RCTs, 1 year (I <sup>2</sup> =52%); 28 cohort studies, 3 year (I <sup>2</sup> =64%)	No significant heterogeneity found	NR

CI: confidence interval; MA: meta-analysis; MWA: microwave ablation; N: sample size; NR: not reported; RFA: radiofrequency ablation; SR: systematic review.

Chinnaratha et al (2016) published a systematic review of RCTs and observational studies that compared the effectiveness and safety of RFA with MWA in patients who had primary hepatocellular carcinoma (HCC).<sup>1</sup> PubMed, EMBASE, and Cochrane Central databases were searched between 1980 and 2014 for human studies comparing the 2 technologies. The primary outcome was the risk of local tumor progression; secondary outcomes were complete ablation, OS, and major adverse events. Odds ratios were combined across studies using a random-effects model. Ten studies (1 RCT<sup>8</sup>, 1 prospective cohort, 8 retrospective) were included. One study was conducted in Australia and the others in China or Japan. Using the modified Newcastle-Ottawa quality assessment scale, the reviewers rated 5 of 10 studies high quality. The overall local tumor progression rate was 14% (176/1298). There was no difference in local tumor progression rates between RFA and MWA (odds ratio [OR], 1.01; 95% confidence interval [CI], 0.67 to 1.50; p=.98). The complete ablation rate, 1- and 3- year OS, and major adverse events were similar between the 2 modalities (p>.05 for all). Subgroup analysis showed local tumor progression rates were lower with MWA for treatment of larger tumors (OR, 1.88; 95% CI, 1.10 to 3.23; p=.02). No significant publication bias was detected nor was interstudy heterogeneity ( $I^2<50\%$ , p>.1) observed for any measured outcomes. The reviewers concluded that both MWA and RFA are effective and safe.

Glassberg et al (2019) conducted a systematic review of MWA compared to resection in patients with HCC or metastatic liver cancer. One RCT (Xu et al [2015]<sup>29</sup>) was included; the other studies (n=15) were observational (2 prospective, 13 retrospective). Patients who received MWA had a significantly higher risk of local tumor progression compared to those who received resection (relative risk [RR], 3.04; p<.001). At 1 year, OS did not differ between MWA and resection but 3- and 5-year OS was significantly higher in patients who had received resection. Overall and major complications were lower with MWA compared to resection. Additionally, operative time, intraoperative blood loss, and hospital length of stay were significantly lower with MWA. Some studies included patients that were nonresectable in the MWA treatment arm, but due to limited reporting and patient preference affecting which treatment was performed, the reviewers were not able to calculate the number of patients who were nonresectable or to conduct subgroup analyses by resectable versus unresectable tumors. Microwave ablation was typically selected for patients with smaller and/or deeper tumors, more comorbidities, and a preference for a less invasive procedure. The reviewers concluded that MWA can be an effective and safe alternative to hepatic resection in patients or tumors that are not amenable to resection, but more studies are needed to determine the target population that would benefit most from MWA.

Cui et al (2020) conducted a systematic review and meta-analysis of MWA compared to various treatment modalities. The analysis included 4 RCTs, with 3 comparing MWA to RFA<sup>37,8,23</sup>, and 1 comparing MWA to TACE.<sup>27</sup> The remaining 11 studies were nonrandomized trials comparing MWA to RFA (n=8 studies), resection (n=2 studies), or ethanol ablation (n=1 study). Meta-analyses were not performed for MWA versus TACE or ethanol ablation, because these comparisons were only examined in 1 study each. Meta-analyses of studies comparing MWA to RFA found no difference in 3-year OS, 5-year OS, local tumor progression at 1 year, progression-free survival at 3 years, or major complications. A meta-analysis of 2 nonrandomized studies comparing MWA to resection found no difference in 3-year OS between treatments; however, this comparison is limited by the small number of studies and lack of RCTs included. The reviewers concluded that MWA showed similar safety and efficacy compared with RFA, but higher quality clinical studies are needed to validate the superiority of MWA.

Dou et al (2022) conducted a systematic review and meta-analysis that compared the safety and efficacy of MWA compared to RFA in patients with HCC.<sup>6</sup> The analysis included 28 cohort studies and 5 RCTs. Overall, there was no significant difference in disease-free survival, OS, or major complications between the 2 groups. In the cohort studies, MWA had a lower local tumor progression rate than RFA (OR, 0.78; 95% CI, 0.64 to 0.96; p=.02). The reviewers concluded that there were various differences in the included studies (e.g., equipment used, operator experience) and that more high-quality RCTs are needed to draw a definitive conclusion on the pros versus cons of MWA and RFA in this patient population.

### **Randomized Controlled Trials**

Five RCTs have compared MWA to RFA in patients with primary hepatic tumors<sup>58,8,37,23,60</sup>, and 1 RCT has compared MWA to resection;<sup>29</sup> the majority of these trials were included in the systematic reviews and meta-analyses described above and are not discussed in further detail here. Tables 5 and 6 summarize the characteristics and results of trials comparing MWA to RFA that have not been included in systematic reviews or meta-analyses. Tables 9 and 10 summarize the relevance, design, and conduct limitations of these trials.

An RCT by Vietti Violi et al (2018) compared the effectiveness of RFA and MWA in treating inoperable HCC in 152 patients with up to 3 lesions of 4 cm or smaller.<sup>58</sup> At 2 years, 6% (6/98) of lesions treated with MWA had local tumor progression versus 12% (12/104) of lesions treated with RFA (RR, 1.62; 95% CI , 0.66 to 3.94; p=.27). Few complications and no treatment-related deaths were reported for either group. Overall survival at 2 years was not significantly different between the groups. Because some patients did not receive the allocated treatment or were lost to follow-up, the analyses were per-protocol rather than intention-to-treat. In addition, the investigators had planned to assess the effects of the treatments on larger lesions, but only a few patients had lesions of nearly 4 cm, making a detailed analysis impossible. A 5-year follow-up is planned for this study. Chong et al (2020) conducted a RCT comparing MWA to RFA in 93 patients with HCC (up to 3 lesions of 5 cm or smaller).<sup>60</sup> Mean tumor size was 3.1 cm in the MWA group and 2.8 cm in the RFA group. The primary outcome of this study was the rate of complete ablation at 1 month, which did not differ significantly for MWA (95.7%) versus RFA (97.8%; p>.99). Rates of OS up to 5 years and rates of disease-free survival up to 3 years were similar between groups. However, the sample size calculations were based on rates of complete ablation at 1 month, so the study may not have been adequately powered to detect differences in OS or disease-free survival.

**Table 5. MWA versus RFA in Patients with Hepatic Tumors: Summary of Key RCT Characteristics**

<b>Study; Trial</b>	<b>Countries</b>	<b>Sites</b>	<b>Dates</b>	<b>Participants</b>	<b>Interventions</b>	
					MWA	RFA
Chong et al (2020) <sup>60</sup>	China	1	2011-2017	Patients age 18 or older, unresectable HCC or resectable HCC but patient opts for ablation, HCC lesion measuring 5 cm or smaller with up to 3 nodules, Child-Pugh score A or B, absence of extrahepatic metastases, absence of radiologic evidence of major vascular or bile duct invasion	47	46

<b>Study; Trial</b>	<b>Countries</b>	<b>Sites</b>	<b>Dates</b>	<b>Participants</b>	<b>Interventions</b>	
Vietti Violi et al (2018) <sup>58</sup> ,	France, Switzerland	4	2011-2015	Patients age 18 years or older, HCC lesion measuring 4 cm or smaller with up to 3 nodules, chronic liver disease (hepatitis) or cirrhosis with Child-Pugh score A or B, and adequate pre-ablation imaging within 4 weeks before starting the intervention	76	76

HCC: hepatocellular carcinoma; MWA: microwave ablation; RCT: randomized controlled trial; RFA: radiofrequency ablation.

**Table 6. MWA versus RFA in Patients with Hepatic Tumors: Summary of Key RCT Results**

<b>Study</b>	<b>Local Tumor Progression</b>	<b>Overall Survival</b>	<b>Disease-free Survival</b>	<b>Complications</b>
	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>	<i>MWA vs. RFA</i>
Chong et al (2020) <sup>60</sup> ,				
Percentage, p value	NR	1 year: 97.9% vs. 93.5% 3 year: 67.1% vs. 72.7% 5 year: 42.8% vs. 56.7% p=.899	1 year: 51.5% vs. 58.7% 3 year: 24.1% vs. 22.7% p=.912	<i>Postoperative complications</i> 2.1% vs. 2.2%, p>.999
Vietti Violi et al (2018) <sup>58</sup> ,				
Percentage, p value	2 year: 6% vs. 12%, p=.27	2 year: 86% vs. 84%, p=.87	NR	<i>Grade 4 complications</i> 2% vs. 0% <i>Grade 3 complications</i> 0% vs. 3%
Relative risk (95% CI)	2 year: 1.62 (0.66 to 3.94)	NR	NR	NR

CI: confidence interval; MWA: microwave ablation; NR: not reported; RCT: randomized controlled trial; RFA: radiofrequency ablation.

Zaitoun et al (2021) compared the safety and efficacy of combination therapy with TACE and MWA (n=89) compared to TACE (n=84) or MWA (n=92) only in patients with solitary HCC lesions measuring between 3 to 5 cm.<sup>61</sup> TACE was performed first, followed by MWA after 15 days. Mean tumor size was 3.6 cm, 3.9 cm, and 3.7 cm in the TACE, MWA, and combination groups, respectively (p=.053). Complete response at 1 month was achieved by 86.5% of patients who received combination therapy compared with 54.8% of patients treated with TACE and 56.5% of patients treated with MWA. Patients treated with combination therapy had a significantly lower recurrence rate at 12 months (p=.0001) and a significantly higher OS rate at 3 years (69.6%; p=.02). Post-procedural minor adverse events (e.g., nausea, vomiting, abdominal pain, and low-

grade fever) were reported in 24.7%, 47.6%, and 38% of patients in the combined, TACE, and MWA groups, respectively. Severe hepatic dysfunction was observed in 1 patient in the combined group and 3 patients in the TACE group. Tumor seeding was reported in 2 patients in the MWA group. A decrease in alpha-fetoprotein (AFP) concentration was observed in 75%, 63%, and 48% of patients who underwent combined therapy, MWA, or TACE, respectively. Study characteristics and results are summarized in Tables 7 and 8. Study relevance, design, and conduct limitations are summarized in Tables 9 and 10.

**Table 7. MWA versus TACE in Patients with Hepatic Tumors: Summary of Key RCT Characteristics**

<b>Study; Trial</b>	<b>Countries</b>	<b>Sites</b>	<b>Dates</b>	<b>Participants</b>	<b>Interventions</b>		
					MWA	TACE	MWA + TACE
Zaitoun et al (2021) <sup>61</sup>	Egypt	1	2017-2020	Patients with solitary HCC lesion >3 to <5 cm; absence of extrahepatic metastases; absence of a history of encephalopathy or refractory ascites; Child-Pugh score A or B; absence of severe coagulation disorders; lack of portal vein thrombosis; absence of renal impairment; no prior local ablation therapy of HCC	89 of 95 with follow-up	84 of 90 with follow-up	89 of 93 with follow-up

HCC: hepatocellular carcinoma; MWA: microwave ablation; RCT: randomized controlled trial; TACE: transarterial chemoembolization.

**Table 8. MWA versus TACE in Patients with Hepatic Tumors: Summary of Key RCT Results**

<b>Study; Trial</b>	<b>Treatment Response, n (%)<sup>a</sup></b>	<b>Recurrence Rate, n (%)</b>	<b>Overall Survival, n (%)<sup>b</sup>; median duration</b>	<b>Mean Progression-Free Survival</b>	<b>Adverse Events, n (%)</b>
Zaitoun et al (2021) <sup>61</sup>	1 month	12 months	3 years		
MWA	CR: 52 (56.5) PR: 25 (27.2) SD: 6 (6.5) PD: 9 (9.8)	47 (51.1)	50 (54.3); 21 months	16.7 months	Nausea, vomiting: 7 (7.6) Abdominal pain: 20 (21.7) Low-grade fever: 8 (8.7) Tumor seeding: 2 (2.2)

<b>Study; Trial</b>	<b>Treatment Response, n (%)<sup>a</sup></b>	<b>Recurrence Rate, n (%)</b>	<b>Overall Survival, n (%) ; median duration</b>	<b>Mean Progression-Free Survival</b>	<b>Adverse Events, n (%)</b>
TACE	CR: 46 (54.8) PR: 27 (32.1) SD: 5 (6) PD: 6 (7.1)	51 (60.7)	46 (54.8); 19 months	15.4 months	Nausea, vomiting: 5 (6) Abdominal pain: 24 (28.6) Low-grade fever: 11 (13.1) Severe hepatic dysfunction: 3 (3.6)
MWA + TACE	CR: 77 (86.5) PR: 3 (3.3) SD: 5 (5.6) PD: 4 (4.55)	20 (22.47)	62 (69.6); 24 months	22.3 months	Nausea, vomiting: 4 (4.5) Abdominal pain: 15 (16.9) Low-grade fever: 3 (3.4) Severe hepatic dysfunction: 1 (1.1)
p value	.0002	.0001	.02	<.001	

CR: complete response; MWA: microwave ablation; PD: progressive disease; PR: partial response; RCT: randomized controlled trial; SD: stable disease; TACE: transarterial chemoembolization.

<sup>a</sup> Treatment response based on mRECIST criteria.

**Table 9. Study Relevance Limitations**

<b>Study</b>	<b>Population<sup>a</sup></b>	<b>Intervention<sup>b</sup></b>	<b>Comparator<sup>c</sup></b>	<b>Outcomes<sup>d</sup></b>	<b>Follow-Up<sup>e</sup></b>
Zaitoun et al (2021) <sup>61</sup> ,	2. Unclear if patients presented with resectable disease			1. Primary outcome was rate of complete response at 1 month	
Chong et al (2020) <sup>60</sup> ,	3. Included some patients with resectable disease			1. Primary outcome was rate of complete ablation at 1 month	
Vietti Violi et al (2018) <sup>58</sup> ,					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.

Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 10. Study Design and Conduct Limitations**

Study	Allocation <sup>a</sup>	Blinding <sup>b</sup>	Selective Reporting <sup>c</sup>	Data Completeness <sup>d</sup>	Power <sup>e</sup>	Statistical <sup>f</sup>
Zaitoun et al (2021) <sup>61</sup> ,	3. Allocation concealment unclear	1-3. Blinding not described		6. Analysis not intention-to-treat		
Chong et al (2020) <sup>60</sup> ,						
Vietti Violi et al (2018) <sup>58</sup> ,		3. Physicians not blinded		6. Analysis not intention-to-treat		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.

<sup>b</sup> Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.

<sup>d</sup> Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

## HEPATIC METASTASES FROM PRIMARY CANCERS FROM OTHER SITES

### Systematic Reviews

A Health Technology Assessment by Loveman et al (2014)<sup>62</sup>, and a Cochrane review by Bala et al (2013)<sup>63</sup>, reported on ablation for liver metastasis. Reviewers found insufficient evidence to determine any benefits of MWA for liver metastasis over surgical resection.

Pathak et al (2011) conducted a systematic review of ablation techniques for colorectal liver metastases, which included 13 studies on MWA (N=406 ) with a minimum of 1-year follow-up.<sup>64</sup> Mean survival rates were 73%, 30%, and 16% and ranged from 40% to 91.4%, 0% to 57%, and 14% to 32% at the 1-, 3-, and 5-year follow-ups, respectively. Minor and major complication rates were considered acceptable and ranged from 6.7% to 90.5% and 0% to 19%, respectively. Local recurrence rates ranged from 2% to 14%.

Mimmo et al (2022) conducted a systematic review of MWA for colorectal liver metastases.<sup>65</sup> Twelve studies (N=741) were included, and 395 patients were treated with MWA versus conventional surgical procedure (n=346). The mean follow-up duration was 20.5 months. Pooled data analysis showed mean recurrence free rates for MWA at 1, 3, and 5 years were 65.1%, 44.6%, and 34.3%, respectively. Mean OS rates for MWA at 1, 3, and 5 years were 86.7%, 59.6%, and 44.8%, respectively. Mean local recurrence rates for MWA at 3, 6, and 12 months were 96.3%, 89.6%, and 83.7%, respectively.

### **Section Summary: Hepatic Tumors**

For individuals who have an unresectable primary or metastatic hepatic tumor who receive MWA, the evidence includes RCTs, comparative observational studies, and systematic reviews comparing MWA to RFA or TACE and to surgical resection. The body of evidence indicates that MWA is an effective option in patients for whom resection is not an option. Although studies had methodological limitations, they consistently showed that MWA and RFA had similar survival outcomes with up to 5 years of follow-up in patients with a single tumor <5 cm or up to 3 nodules <3 cm each. In a meta-analysis of observational studies, patients receiving MWA had higher local recurrence rates and lower survival than those who received resection but the patient populations were not limited to those who had unresectable tumors. Microwave ablation was associated with lower complications, intraoperative blood loss, and hospital length of stay. A single RCT showed that patients with solitary lesions >3 and <5 cm treated with combination MWA plus TACE achieved higher overall and progression-free survival compared to MWA or TACE only. However, it is unclear whether patients in this study were classified with unresectable disease.

## **UNRESECTABLE PRIMARY OR METASTATIC LUNG TUMORS**

### **REVIEW OF EVIDENCE**

#### **Systematic Reviews**

Three systematic reviews have compared MWA to RFA for lung cancer (Tables 11 to 13).<sup>66,67,68</sup>

Nelson et al (2019) included 12 retrospective observational studies of MWA in patients with primary or metastatic lung tumors.<sup>68</sup> The reviewers did not pool results due to clinical and methodological heterogeneity across the studies. The studies varied with regard to patient characteristics (tumor size, histology, number of treated nodules), outcome measures, and technical experience of surgeons performing the procedures. The primary outcome was local recurrence, and survival outcomes were not assessed. Overall, local recurrence rates ranged from 9% to 37% across the studies. Newer reports and those that targeted smaller tumors showed more favorable efficacy rates. Results in patients with multiple tumors were not reported separately. Four studies reported results by tumor size; the local recurrence rates for large tumors (>3 or 4 cm depending on the study) were 50%, 75%, 36%, and 26%. In the same 4 studies, for small tumors (<3 or 3.5 cm depending on the study), local recurrence rates were 19%, 18%, 18%, and 5%, respectively. The most frequent adverse event with MWA was a pneumothorax requiring a chest tube. The reviewers concluded that MWA may be a useful tool in selected patients who are not ideal surgical candidates.

In a meta-analysis of observational studies, Yuan et al (2019) found higher OS for patients who received RFA compared to those who received MWA.<sup>66</sup> However, these estimates were not

directly comparable because they came from different sets of studies, and the reviewers concluded that percutaneous RFA and MWA were both effective with a high safety profile. The studies used different patient eligibility criteria (e.g., tumor size, lesion number, age, follow-up). Subgroup analyses by tumor size or tumor number were not possible from the data reported.

Jiang et al (2018) conducted a network meta-analysis to determine the effectiveness of different ablation techniques in patients with lung tumors.<sup>67</sup> Tumor size, stage of the disease, and primary versus metastatic disease were not accounted for in the analysis. For MWA, weighted average OS rates were 82.5%, 54.6%, 35.7%, 29.6%, and 16.6% at 1, 2, 3, 4, and 5 years, respectively.

**Table 11. Comparison of Trials/Studies Included in SR & MA of MWA in Lung Cancer**

Study	Nelson et al (2019) <sup>68</sup> ,	Yuan et al (2019) <sup>a66</sup> ,	Jiang et al (2018) <sup>a67</sup> ,
He et al (2006) <sup>69</sup> ,			●
Wolf et al (2008) <sup>70</sup> ,	●		
Vogl et al (2011) <sup>71</sup> ,	●	●	
Lu et al (2012) <sup>72</sup> ,	●	●	
Carrafiello et al (2013) <sup>73</sup> ,		●	
Liu et al (2013) <sup>74</sup> ,			●
Vogl et al (2013) <sup>75</sup> ,	●	●	
Wei et al (2014) <sup>76</sup> ,	●		
Yang et al (2015) <sup>77</sup> ,		●	
Zheng et al (2014) <sup>78</sup> ,	●		
Acksteiner et al (2015) <sup>79</sup> ,			●
Wei et al (2015) <sup>80</sup> ,		●	
Egashira et al (2016) <sup>81</sup> ,	●		
Ko et al (2016) <sup>82</sup> ,	●	●	
Li et al (2016) <sup>83</sup> ,			●
Macchi et al (2017) <sup>84</sup> ,			●
Maxwell et al (2016) <sup>85</sup> ,			●

<b>Study</b>	<b>Nelson et al (2019)<sup>68</sup>,</b>	<b>Yuan et al (2019)<sup>a66</sup>,</b>	<b>Jiang et al (2018)<sup>a67</sup>,</b>
Vogl et al (2016) <sup>86</sup> ,	●	●	●
Zheng et al (2016) <sup>87</sup> ,	●	●	●
Healey et al (2017) <sup>88</sup> ,		●	
Nour-Eldin et al (2017) <sup>89</sup> ,		●	
Wei et al (2017) <sup>90</sup> ,		●	●
Yang et al (2017) <sup>91</sup> ,	●		
Zhong et al (2017) <sup>92</sup> ,	●		

MA: meta-analysis; MWA: microwave ablation; SR: systematic review.

<sup>a</sup>Studies of MWA only.

**Table 12. Characteristics of Systematic Reviews of MWA in Lung Cancer**

<b>Study</b>	<b>Dates</b>	<b>Trials</b>	<b>Participants</b>	<b>N (Range)</b>	<b>Designs</b>	<b>Duration</b>
Nelson et al (2019) <sup>68</sup> ,	Up to October 3, 2017	12	Primary or secondary lung malignancies	985 (15 to 184)	12 retrospective observational; excluded case series with <30 lesions	9 to 47 months
Yuan et al (2019) <sup>66</sup> ,	2010-2017	12	Primary or secondary lung malignancies	800 (15 to 183)	12 retrospective observational	Median 10 to 35 months (range, 3 to 75 months), NR in 3 studies
Jiang et al (2018) <sup>67</sup> ,	Up to December 31, 2017	9	Primary lung cancer or pulmonary metastases from other primary tumors	438 (5 to 183)	1 RCT, 8 retrospective observational; excluded studies that used other treatments combined with thermal ablation	Median 12 to 35 months (range, 3 to 108 months)

MWA: microwave ablation; N: sample size; NR: not reported; RCT: randomized controlled trial.

**Table 13. Results of Systematic Reviews of MWA in Lung Cancer**

<b>Study</b>	<b>Overall Survival</b>	<b>Progression-free Survival</b>	<b>Local Recurrence Rate</b>	<b>Adverse Events</b>
Nelson et al (2019) <sup>68</sup> ,				
Range of effect sizes	NR (primary analysis was local recurrence)	NR	9% to 37% 25% or greater (n=4 studies); less than 25% (n=7 studies); less than 15% (n=2 studies) 7 studies found a significantly higher likelihood of local recurrence with larger tumors (>3 cm)	<i>Pneumothorax</i> 1% to 15% <i>Skin burns</i> 1.5% to 6% <i>Periprocedural mortality</i> 1 patient (0.5%) from ventricular tachycardia
			<i>Local tumor progression-free</i>	
Yuan et al (2019) <sup>66</sup> ,				
Pooled estimate (95% CI)	1 year: 79.3% (73.7% to 85.0%) 2 year: 51.9% (46.2% to 57.5%) 3 year: 34.6% (26.8% to 42.5%)	1 year: 64.8% (37.1% to 92.4%) 2 year: 43.1% (1.5% to 84.7%) 3 year: 56.0% (41.1% to 70.9%)	1 year: 84.6% (72.9% to 96.3%) 2 year: 68.5% (51.8% to 85.1%) 3 year: 72.2% (64.5% to 79.9%) 4 year: 74.1% (67.0% to 81.2%) 5 year: 48.0% (23.8% to 72.2%)	<i>Pneumothorax</i> 33.9% (23.8% to 44.8%) <i>Pneumothorax needing intervention</i> 11.0% (4.5% to 19.7%) <i>Pleural effusion</i> 9.6% (1.5% to 22.4%) <i>Pleural effusion needing intervention</i> 0.3% (0% to 1.4%)
$I^2$ , p value	1 year: $I^2=37.7\%$ , p=.155 2 year: $I^2=0\%$ , p=.691 3 year: $I^2=7.6\%$ , p=.458	1 year: $I^2=88.4\%$ , p=.003 2 year: $I^2=94.3\%$ , p<.001 3 year: NA	1 year: $I^2=87.9\%$ , p<.001 2 year: $I^2=81.9\%$ , p=.019 3 year: $I^2=15.1\%$ , p=.278 4 year: NA 5 year: NA	NA
Jiang et al (2018) <sup>67</sup> ,				
Weighted average	1 year: 82.5% 2 year: 54.6% 3 year: 35.7% 4 year: 29.6% 5 year: 16.6%	NR	10.9%	<i>Major complications</i> 22.5%

CI: confidence interval; MWA: microwave ablation; N: sample size; NA: not applicable; NR: not reported.

### Randomized Controlled Trials

There is a single RCT of MWA compared to RFA for lung tumors, conducted by Macchi et al (2017), (Tables 14 and 15).<sup>84</sup> Patients were eligible for the study if they had a single tumor up to 5 cm, and up to 5 metastases up to 5 cm. However, at baseline, the mean tumor size was 2.21 cm (standard deviation [SD], 0.89) in the MWA group and 1.64 cm (SD, 0.80) in the RFA group. Mortality rates at 6 and 12 months did not differ between groups, and complications were significantly lower in the MWA group. Limitations of this study are summarized in Tables 16 and 17 and include its small sample size, lack of reporting on blinding, and relatively short follow-up period (12 months). Results were not reported by tumor size or the number of metastases.

**Table 14. Summary of Key RCT Characteristics: MWA versus RFA in Patients with Lung Tumors**

<b>Study; Trial</b>	<b>Countries</b>	<b>Sites</b>	<b>Dates</b>	<b>Participants</b>	<b>Interventions</b>	
					MWA	RFA
Macchi et al (2017) <sup>84</sup>	Italy	Multisite, NR	NR	Age 18 years or older; patient has tumors considered surgically inoperable, or patient did not respond to standard chemotherapy or radiotherapy, or patient refused surgery, or patient is affected by conditions with high morbidity rates that are contraindicative to surgery; maximum diameter of the primary lesion <5 cm; percutaneous accessibility of the lesion; for those with pulmonary metastases, number of metastases <5, each with maximum diameter of 5 cm	24	28

MWA: microwave ablation; NR: not reported; RCT: randomized controlled trial; RFA: radiofrequency ablation.

**Table 15. Summary of Key RCT Results: MWA versus RFA in Patients with Lung Tumors**

<b>Study</b>	<b>Local Tumor Recurrence</b>	<b>Survival time</b>	<b>Mortality at 6 months</b>	<b>Mortality at 12 months</b>	<b>Complications</b>
Macchi et al (2017) <sup>84</sup>					
MWA	NR	(graph only)	4/24 (16.7%)	4/20 (20.0%)	8/24 (33.3%)
RFA			3/28 (10.7%)	5/25 (20.0%)	16/28 (57.1%)
p value		.883	.35	<.0001	.05

MWA: microwave ablation; NR: not reported; RCT: randomized controlled trial; RFA: radiofrequency ablation.

**Table 16. Study Relevance Limitations**

<b>Study</b>	<b>Population<sup>a</sup></b>	<b>Intervention<sup>b</sup></b>	<b>Comparator<sup>c</sup></b>	<b>Outcomes<sup>d</sup></b>	<b>Follow-Up<sup>e</sup></b>
Macchi et al (2017) <sup>84</sup> ,	1. Did not report results by tumor size, histology, or number of tumors 5. Combined patients with primary and metastatic tumors in analyses			1. Local recurrence not reported	1. 12 months only

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

<sup>b</sup> Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5. Other.

<sup>c</sup> Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

<sup>d</sup> Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

<sup>e</sup> Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 17. Study Design and Conduct Limitations**

<b>Study</b>	<b>Allocation<sup>a</sup></b>	<b>Blinding<sup>b</sup></b>	<b>Selective Reporting<sup>c</sup></b>	<b>Data Completeness<sup>d</sup></b>	<b>Power<sup>e</sup></b>	<b>Statistical<sup>f</sup></b>
Macchi et al (2017) <sup>84</sup> ,		4. Not reported			1. Power calculation not reported	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.

<sup>b</sup> Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.

<sup>d</sup> Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.

<sup>f</sup> Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

## Section Summary: Lung Tumors

For individuals who have an unresectable primary or metastatic lung tumor who receive MWA, the evidence includes a single RCT, retrospective observational studies, and systematic reviews of these studies. The body of evidence indicates that MWA is an effective option in patients for whom resection is not an option. In the RCT, direct comparison of MWA and RFA in patients with primary or metastatic lung cancer (mean tumor size, 1.90 cm [ $\pm$  0.89] at baseline) found similar

mortality rates up to 12 months of follow-up. In the first of 3 systematic reviews that included 12 retrospective observational studies, local recurrence rates were similar for MWA and RFA at a range of 9 to 47 months of follow-up. In the second systematic review with a meta-analysis, there was lower OS with MWA compared to RFA, but studies were not directly comparable due to clinical and methodological heterogeneity. However, the authors concluded that percutaneous RFA and MWA were both effective with a high safety profile. In the third systematic review using a network meta-analysis, the weighted average OS rates for MWA were 82.5%, 54.6%, 35.7%, 29.6%, and 16.6% at 1, 2, 3, 4, and 5 years, respectively. Limitations of the body of evidence included a lack of controlled studies and heterogeneity across studies. The RCT did not report results by tumor size or the number of metastases. The observational studies included in the systematic reviews did not report sufficient information to assess the effectiveness or safety of MWA in subgroups based on the presence of multiple tumors or total tumor burden. Therefore, conclusions about the evidence sufficiency can only be made about patients with single tumors.

## UNRESECTABLE PRIMARY OR METASTATIC RENAL TUMORS

### REVIEW OF EVIDENCE

#### Systematic Reviews

Uhlig et al (2019) published a systematic review with meta-analyses to compare partial nephrectomy, RFA, cryoablation, and MWA and the effect on oncologic, perioperative, and functional outcomes in studies published from 2005 to 2017.<sup>93</sup> Microwave ablation was a treatment in 344 of 24,077 patients and represented in 6 of 47 studies. The review included the single RCT (Guan 2012<sup>94</sup>), which is the only study with results for all 3 outcomes of interest. No new data were included, but the review utilized a network meta-analyses technique. Microwave ablation when compared to partial nephrectomy, the comparator of interest, was reported to have a lower procedural complication rate but higher local recurrence and cancer-specific mortality rates.<sup>93</sup>

In a systematic review and meta-analysis, Katsanos et al (2014) compared thermal ablation (MWA and RFA) with surgical nephrectomy for small renal tumors (mean size, 2.5 cm).<sup>95</sup> The analysis included 1 randomized study on MWA<sup>94</sup> (described below) and 5 cohort studies on RFA (N=587 patients). In the ablation group, complication rates and renal function declines were significantly higher than in the nephrectomy group ( $p=.04$  and  $p=.03$ , respectively). The local recurrence rate was 3.6% in both groups ( RR, 0.92; 95% CI, 0.4 to 2.14;  $p=.79$ ) and disease-free survival up to 5 years did not differ significantly between groups (hazard ratio [HR], 1.04; 95% CI, 0.48 to 2.24;  $p=.92$ ).

Martin et al (2013) conducted a meta-analysis comparing MWA with cryoablation for small renal tumors.<sup>96</sup> The analysis included 7 MWA studies (n=164 patients) and 44 cryoablation studies (n=2989 patients). Selected studies were prospective or retrospective, nonrandomized, and noncomparative. Mean follow-up duration was shorter for MWA (17.86 months) than for cryoablation (30.22 months;  $p=.07$ ). Mean tumor size was significantly larger in the MWA studies than in the cryoablation studies (2.58 cm vs. 3.13 cm, respectively,  $p=.04$ ). Local tumor progression (4.07% vs. 2.53%, respectively;  $p=.46$ ) and progression to metastatic disease (0.8% vs. 0%, respectively;  $p=.12$ ) did not differ significantly. In another meta-analysis comparing MWA with cryoablation, McClure et al (2023) identified 99 observational studies with 62 cryoablation arms and 41 MWA arms.<sup>97</sup> Local tumor recurrence at 1 year was lower with MWA

than cryoablation (OR, 0.33; 95% CI, 0.10 to 0.93; p=.04). No significant differences were found for OS or disease-free survival. The data is limited by the comparison of single-arm studies which were observational and primarily retrospective.

### **Randomized Controlled Trial**

Guan et al (2012) reported on a prospective randomized study that compared the use of MWA with partial nephrectomy (the criterion standard of nephron-sparing surgical resection) for solitary renal tumors less than 4 cm.<sup>94</sup> Forty-eight patients received MWA and 54 had partial nephrectomy. Patients in the MWA group (6 [23.5%]) had significantly fewer postoperative complications than in the partial nephrectomy group (18 [33.3%]; p=.019). Microwave ablation patients also had significantly less postoperative renal function declines (p<.009) and estimated perioperative blood loss (p<.001) than partial nephrectomy patients. At last follow-up, estimated glomerular filtration rate declines in both groups were similar (p=1.00). Disease-specific deaths did not occur, and overall local recurrence-free survival by Kaplan-Meier estimates at 3 years was 91.3% for MWA and 96.0% for partial nephrectomy (p=.541).

### **Case Series and Retrospective Reviews**

Note for reviewer: Removed older studies not included in recent meta-analyses.

Two recent retrospective reviews were not included in meta-analyses. Guo et al (2020) reported a retrospective review of 106 patients with 119 T1a renal cell carcinoma tumors treated with MWA.<sup>98</sup> Complete response was achieved in 95.3% of patients (mean tumor diameter, 2.4 cm; range, 1 to 4 cm). Local tumor progression was observed in 6 patients at a mean of 20 months post-procedure. Local progression-free survival rates were 100%, 92.8%, and 90.6% at 1, 2, and 3 years, respectively. Overall survival rates were 99%, 97.7%, and 94.6% at 1, 2, and 3 years, respectively. Complications were reported in 6 patients (5.7%) within 30 days of the procedure, but none of these required intervention. Aarts et al (2020) conducted another retrospective review of 100 patients with 108 T1 renal cell carcinomas treated with MWA.<sup>99</sup> The median tumor size in this study was 3.2 cm (interquartile range, 2.4 to 4 cm). Primary efficacy was achieved for 81% (88/108) of lesions overall, but primary efficacy rates were lower among patients with T1b tumors (52%) versus T1a tumors (89%; p<.001). Secondary efficacy was achieved for 97% (101/103). Over a median follow-up time of 19 months, local tumor recurrence was observed for 4 (4%) tumors.

### **Section Summary: Renal Tumors**

For individuals who have an unresectable primary or metastatic renal tumor who receive MWA, the evidence includes a single RCT that compared MWA to partial nephrectomy, systematic reviews, retrospective reviews, and case series. In the RCT, overall local recurrence-free survival at 3 years was 91.3% for MWA and 96.0% for partial nephrectomy (p=.54). However, there is a lack of controlled studies comparing MWA to other ablation techniques in patients with renal tumors.

## **UNRESECTABLE PRIMARY OR METASTATIC SOLID TUMORS OTHER THAN HEPATIC, LUNG, OR RENAL**

## **UNRESECTABLE PRIMARY OR METASTATIC BREAST TUMORS**

### **REVIEW OF EVIDENCE**

## Systematic Reviews

A systematic review by Zhao and Wu (2010) assessing ablation techniques for breast cancer found that only 0% to 8% of breast cancer tumors were completely ablated with MWA.<sup>100</sup> The studies identified by reviewers were mostly feasibility and pilot studies conducted in research settings.

## Case Series

Zhou et al (2012) reported on 41 patients treated with MWA directly followed by mastectomy for single breast tumors with a mean volume of 5.26 cm (range, 0.09 to 14.14 cm).<sup>101</sup> Complete tumor ablation was found by microscopic evaluation in 37 (90%) of the 41 tumors ablated (95% CI, 76.9% to 97.3%). Reversible thermal injuries to the skin and pectoralis major muscle occurred in 3 patients.

# OTHER UNRESECTABLE PRIMARY OR METASTATIC SOLID TUMORS

## REVIEW OF EVIDENCE

### Systematic Reviews

No RCTs on the use of MWA for other tumors or conditions were identified. A systematic review of ablation therapies, including MWA, for locally advanced pancreatic cancer was published by Keane et al (2014).<sup>102</sup> Reviewers found limited evidence on the use of MWA for pancreatic cancer. Cui et al (2019) conducted a non-comparative systematic review and meta-analysis of 5 retrospective studies and 2 prospective studies in patients with benign thyroid nodules or papillary thyroid microcarcinoma and found that MWA improved nodule volume and symptom scores in these patients.<sup>103</sup> Wu et al (2022) conducted a systematic review and meta-analysis comparing MWA versus conventional surgery for the treatment of papillary thyroid microcarcinoma.<sup>104</sup> There were 13 included studies which were all non-randomized. There was no differences between the 2 groups in recurrence rate or lymph node metastasis; however, the MWA group did have a shorter operation time, less intra-operative blood loss, shorter postoperative hospital stay, and few complications.

## Case Series

Case studies and retrospective reviews on the use of MWA for adrenal carcinoma,<sup>105</sup> metastatic bone tumors,<sup>106</sup> intrahepatic primary cholangiocarcinoma,<sup>107</sup> pancreatic neuroendocrine tumors,<sup>108</sup> and other nononcologic conditions (ie, bleeding peptic ulcers, esophageal varices, secondary hypersplenism) were identified.

## Subsection Summary: Other Solid Tumors

For individuals who have unresectable primary or metastatic solid tumors other than hepatic, lung, or renal. who receive MWA, the evidence includes systematic reviews and case series. No RCTs on the use of MWA for other tumors or conditions were identified.

## SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

**Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2016 Input**

In response to requests, input was received from 2 physician specialty societies and 1 academic medical center while this policy was under review in 2016. This number of responses was less than optimal. Input overall was mixed. There was some support for the medical necessity of microwave ablation (MWA) in each category, with some reviewers indicating that it was standard of care for certain tumors. However, there were no indications for which all 3 reviewers agreed that MWA should be medically necessary.

**2011 Input**

In response to requests, input was received from 2 physician specialty societies (3 reviews) and 4 academic medical centers (6 reviews) while this policy was in development. Eight reviewers considered MWA investigational to treat primary tumors such as hepatocellular carcinoma, benign and malignant renal tumors, lung tumors, adrenal tumors, or cholangiocarcinoma. The reviewers noted insufficient evidence and a need for further studies on MWA. However, 1 reviewer indicated MWA for primary tumors, including, but not limited to hepatocellular carcinoma, benign and malignant renal tumors, lung tumors, adrenal tumors, and cholangiocarcinoma, may be considered a treatment option, and another reviewer indicated that MWA for renal tumors may be considered a treatment option.

Four reviewers considered MWA investigational to treat liver metastases, and 2 reviewers indicated MWA for liver metastases may be considered a treatment option. One reviewer noted MWA may be appropriate for tumors not amenable to radiofrequency ablation or other local treatments. This reviewer also suggested MWA may be more appropriate for tumors located near large blood vessels.

**Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

**American College of Chest Physicians**

The American College of Chest Physicians (2013) evidence-based guidelines on the treatment of NSCLC noted that the role of ablative therapies in the treatment of high-risk patients with stage I NSCLC is evolving.<sup>109</sup> The guidelines deal mostly with radiofrequency ablation.

**American Urological Association**

The American Urological Association (2021) updated its guidelines on renal mass and localized renal cancer, which note that both RFA and cryoablation may be offered as options for patients who elect thermal ablation (Conditional Recommendation; Evidence Level: Grade C).<sup>110</sup> Thermal

ablation can be considered as an alternate approach in the management of T1a solid renal masses <3 cm. In these patients, a percutaneous technique is preferred (Moderate Recommendation; Evidence Level: Grade C). The guidelines do not specifically address MWA.

### National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guidelines on hepatocellular carcinoma (HCC) (v.1.2023) list MWA (along with radiofrequency ablation, cryoablation, and percutaneous alcohol injection) as a treatment option for HCC tumors in patients who are not candidates for potential curative treatments (e.g., resection and transplantation) and do not have large-volume extrahepatic disease.<sup>111</sup> Ablation should only be considered when tumors are accessible by percutaneous, laparoscopic, or open approaches. The guidelines indicate "Ablation alone may be curative in treating tumors less than or equal to 3 cm [...] Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, or with combination of an arterially directed therapy and ablation as long as tumor location is accessible for ablation."

The guidelines on non-small cell lung cancer (NSCLC) (v.3.2023) state that image-guided thermal ablation therapies such as cryotherapy, microwave, or radiofrequency may be an option for select medically inoperable patients not receiving stereotactic ablative radiotherapy or definitive radiotherapy.<sup>112</sup> Image-guided thermal ablation therapy is considered an option for the management of NSCLC lesions <3 cm. Ablation for NSCLC lesions >3 cm has been associated with higher rates of local recurrence and complications.

Guidelines on small-cell lung cancer (v.3.2023) state, "stereotactic ablative radiotherapy is an option for certain patients with medically inoperable stage I to IIA small-cell lung cancer."<sup>113</sup>

The Network guidelines on neuroendocrine tumors (v.1.2023) state that cytoreductive surgery or ablative therapies (e.g., radiofrequency, cryotherapy, microwave) may be considered in patients with progressive hepatic-predominant metastatic disease to reduce tumor bulk and relieve symptoms of hormone hypersecretion (category 2B). Additionally, although prospective data for ablative therapy interventions are limited, the guideline notes that "percutaneous thermal ablation, often using microwave energy, can be considered for oligometastatic liver disease, generally up to 4 lesions each smaller than 3 cm."<sup>114</sup>

The guidelines on kidney cancer (v.1.2024) state that thermal ablation techniques (MWA, RFA and cryotherapy) may be an option for T1 renal lesions, particularly for masses <3 cm.<sup>115</sup>

The guidelines on breast cancer (v.4.2023) do not address thermal ablation techniques such as MWA.<sup>116</sup>

Thyroid cancer guidelines from NCCN (v.4.2023) recommend ablation techniques such as cryoablation or RFA as an option for metastatic disease in select patients.<sup>117</sup> There is not specific mention of MWA.

### National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2016) updated its guidance on MWA for treatment of metastases in the liver.<sup>118</sup> The revised guidance states:

- Current evidence on MWA for treating liver metastases raises no major safety concerns and the evidence on efficacy is adequate in terms of tumor ablation. Therefore this

procedure may be used provided that standard arrangements are in place for clinical governance, consent, and audit.

- Patient selection should be carried out by a hepatobiliary cancer multidisciplinary team.
- Further research would be useful for guiding the selection of patients for this procedure. This should document the site and type of the primary tumor being treated, the intention of treatment (palliative or curative), imaging techniques used to assess the efficacy of the procedure, long-term outcomes, and survival.

The Institute (2007) also published guidance on MWA for HCC.<sup>119</sup> This guidance indicated: "Current evidence on the safety and efficacy of MWA of hepatocellular carcinoma appears adequate to support the use of this procedure...." The guidance also stated there are no major concerns about the efficacy of MWA, but noted that limited, long-term survival data are available.

The Institute (2022 ) has published guidance on MWA for lung tumors as well.<sup>120</sup> This guidance indicated that, "Evidence on the safety of microwave ablation for treating primary lung cancer and metastases in the lung is adequate but shows it can cause infrequent serious complications. Evidence on its efficacy shows it reduces tumour size. But the evidence on improvement in survival, long-term outcomes and quality of life is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research." The guidance encourages further research.

### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

### **Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 18.

**Table 18. Summary of Key Trials**

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT04197960	A Prospective Multicenter Study to Compare the Therapeutic Outcomes of Microwave Ablation with Surgical Resection for Micropapillary Thyroid Carcinoma	973	Dec 2022
NCT04626986	Comparison of Ultrasound Guided Percutaneous Microwave Ablation With Breast Conserving Surgery for Breast Tumor	300	May 2023
NCT04081168	COLLISION XL: Unresectable Colorectal Liver Metastases (3-5cm): Stereotactic Body Radiotherapy vs. Microwave Ablation (COLLISION-XL)	68	Jan 2025
NCT03775980 <sup>a</sup>	CIRSE Emprint Microwave Ablation Registry (CIEMAR)	1000	Jul 2026
NCT04365751	To Compare the Efficacy of Microwave Ablation and Laparoscopic Hepatectomy for Hepatocellular Carcinoma	1134	Dec 2026
NCT04107766 <sup>a</sup>	NeuWave Observational Liver Ablation Registry (NOLA)	1500	Dec 2027

NCT: national clinical trial.

<sup>a</sup> Denotes industry-sponsored or cosponsored trial.

**CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.**

**Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.**

<b>CPT/HCPCS</b>	
32998	Ablation therapy for reduction or eradication of 1 or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, including imaging guidance when performed, unilateral; radiofrequency
47380	Ablation, open, of 1 or more liver tumor(s); radiofrequency
47382	Ablation, 1 or more liver tumor(s), percutaneous, radiofrequency
50592	Ablation, 1 or more renal tumor(s), percutaneous, unilateral, radiofrequency
76940	Ultrasound guidance for, and monitoring of, parenchymal tissue ablation
C9751	Bronchoscopy, rigid or flexible, transbronchial ablation of lesion(s) by microwave energy, including fluoroscopic guidance, when performed, with computed tomography acquisition(s) and 3-d rendering, computer-assisted, image-guided navigation, and endobronchial ultrasound (ebus) guided transtracheal and/or transbronchial sampling (e.g., aspiration[s]/biopsy[ies]) and all mediastinal and/or hilar lymph node stations or structures and therapeutic intervention(s)

<b>REVISIONS</b>	
10-01-2016	Policy published 09-01-2016. Policy effective 10-01-2016.
11-15-2017	<p>Description section updated</p> <p>Rationale section updated</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Revised CPT Code nomenclature: 32998</li> <li>▪ Added coding notations.</li> </ul> <p>References updated</p>
01-01-2018	<p>Policy published 01-01-2018. Professional effective date 01-01-2018. Institutional effective date 02-15-2018.</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Removed CPT Code: 0301T (Termed 12-31-2017)</li> <li>▪ Added CPT Code: 19499</li> </ul>
01-01-2019	<p>Description section updated</p> <p>Rationale section updated</p> <p>References updated</p>
05-18-2020	<p>Description section updated</p> <p>In Policy Section:</p>

<b>REVISIONS</b>	
	<p>Policy was revised from experimental / investigational to medically necessary for primary or metastatic hepatic and / or lung tumors.</p> <ul style="list-style-type: none"> <li>▪ The following language was added:</li> </ul> <p>"A. Microwave ablation of primary or metastatic hepatic tumors may be considered medically necessary under the following conditions:</p> <ol style="list-style-type: none"> <li>1. The tumor is unresectable due to location of lesion[s] and/or comorbid conditions</li> <li>2. A single tumor of ≤5 cm or up to 3 nodules &lt;3 cm each</li> </ol> <p>B. Microwave ablation of primary or metastatic lung tumors may be considered medically necessary under the following conditions:</p> <ol style="list-style-type: none"> <li>1. The tumor is unresectable due to location of lesion and/or comorbid conditions</li> <li>2. A single tumor of ≤3 cm</li> </ol> <p>C. Microwave ablation of more than a single primary or metastatic tumor in the lung is considered experimental / investigational.</p> <p>D. Microwave ablation of primary or metastatic tumors other than liver or lung is considered experimental / investigational."</p> <ul style="list-style-type: none"> <li>▪ The following E/I language was removed: "Microwave ablation of primary and metastatic tumors is considered experimental / investigational."</li> </ul>
Rationale section updated	
In Coding section:	
<ul style="list-style-type: none"> <li>▪ Added CPT Code: 47380</li> <li>▪ Removed CPT Codes: 19499, 50592, 76940</li> <li>▪ Added ICD-10 Codes: C22.0, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C34.11, C34.12, C34.2, C34.31, C34.32, C34.81, C34.82, C34.91, C34.92, C78.01, C78.02, C78.7, C7B.02</li> <li>▪ Removed E/I Statement: "Experimental / Investigational for all diagnoses related to this medical policy."</li> </ul>	
References updated	
01-13-2021	Updated Description section
	In Coding Section:
	<ul style="list-style-type: none"> <li>▪ Added CPT: 76940, C9751</li> </ul> <p>ICD10: D41.00, D41.01, D41.02, D41.10, D41.11, D41.12</p>
	Updated Rationale section
11-18-2021	Updated Reference sections
	Updated Descriptions Section
	Updated Rationale Section
11-22-2022	Updated References Section
	Updated Description Section
	Updated Rationale Section
	Updated Coding Section
	<ul style="list-style-type: none"> <li>▪ Added CPT code 50592</li> <li>▪ Removed Coding Bullets <ul style="list-style-type: none"> <li>○ There are no CPT codes specific to microwave ablation.</li> <li>○ According to an American Medical Association (AMA) publication (<i>Clinical Examples in Radiology</i>, 2012;8[3;]), "microwave is part of the radiofrequency spectrum, and simply uses a different part of the radiofrequency spectrum to develop heat energy to destroy abnormal tissue." Therefore, AMA recommends that microwave ablation be reported using CPT codes for radiofrequency ablation – 32998 (pulmonary), 47382 (liver), and 50592 (renal).</li> </ul> </li> </ul>

<b>REVISIONS</b>	
	<ul style="list-style-type: none"> <li>○ If there is no specific CPT code for ablation, the unlisted CPT code for the anatomic area should be reported, such as code 60699 for unlisted procedure, endocrine system (for adrenal or thyroid ablation), 19499 for the breast.</li> </ul>
11-17-2023	Updated References Section
	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> <li>▪ Removed ICD-10 Codes</li> </ul>
	Updated References Section

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