Medical Policy

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Title: Microwave Tumor Ablation

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Populations	Interventions	Comparators	Outcomes
Individuals: • With an unresectable primary or metastatic solid tumor (eg, breast, hepatic [primary or metastatic], pulmonary, renal)	Interventions of interest are: • Microwave ablation	Comparators of interest are: • Radiofrequency ablation • Transcatheter arterial chemoembolization • Cryoablation	Relevant outcomes include: • Overall survival • Disease-specific survival • Symptoms • Quality of life • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

Microwave ablation (MWA) is a technique to destroy tumors and soft tissue using microwave energy to create thermal coagulation and localized tissue necrosis. MWA is used to treat tumors not amenable to resection or to treat patients ineligible for surgery due to age, comorbidities, or poor general health. MWA may be performed as an open procedure, laparoscopically, percutaneously, or thoracoscopically under image guidance (eg, 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 use of microwave ablation improves the net health outcome in individuals with unresectable primary or metastatic solid tumors (eg, breast, primary and metastatic hepatic, pulmonary, or renal 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 (5x3 cm) 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 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 local recurrence, it occurs at the margins. Treatment may be repeated as needed. MWA 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 duration.

MWA 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°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. MWA 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 less time than RFA, because multiple antennas can be used simultaneously.

Adverse Events

Complications from MWA are usually mild and may include pain and fever. Other complications associated with MWA include those caused by heat damage to normal

tissue adjacent to the tumor (eg, intestinal damage during MWA of the kidney or liver), structural damage along the probe track (eg, 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. MWA 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 (eg, implantable pacemakers) that may be adversely affected by microwave power output.

Applications

MWA 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 (eg, preserving normal organ tissue, decreasing morbidity, shortening length of hospitalization). MWA also has been investigated as a treatment for unresectable hepatic tumors, as both primary and palliative treatment, and as a bridge to 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

Several devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for microwave ablation (MWA). Covidien's (now Medtronic's) Evident™ Microwave Ablation System was cleared for marketing through the 510(k) process for soft tissue ablation, including partial or complete ablation of nonresectable liver tumors. The following devices have 510(k) clearance for MWA of (unspecified) soft tissue:

- BSD Medical's (now Perseon) MicroThermX® Microwave Ablation System (MTX-180)
- Valleylab's (subsidiary of Covidien) VivaWave® Microwave Ablation System
- Vivant's (now Valleylab in 2005) Tri-Loop™ Microwave Ablation Probe
- MicroSurgeon's Microwave Soft Tissue Ablation System
- Microsulis Medical's (now AngioDynamics) Acculis® Accu2i
- NeuWave Medical's Certus® 140

FDA determined that these devices were substantially equivalent to existing radiofrequency and MWA devices. FDA product code: NEY.

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

POLICY

Microwave ablation of primary and metastatic tumors is considered **experimental / investigational**.

RATIONALE

The evidence review has been updated with searches of the MEDLINE database. The most recent literature update was performed through July 9, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, 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 one 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. RCTs 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

Unresectable Primary or Metastatic Solid Tumor

Clinical Context and Therapy Purpose

The purpose of microwave ablation (MWA) in patients who have unresectable primary or metastatic solid tumors (eg, breast, primary and metastatic hepatic, pulmonary, or renal tumors) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of MWA improve the net health outcome in individuals with unresectable primary or metastatic solid tumors?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant populations of interest are those with unresectable primary or metastatic solid tumors such breast, primary or metastatic hepatic, pulmonary, or renal cancer.

Interventions
The therapy being considered is MWA.

Comparators
The following therapies are currently being used to make decisions about managing unresectable primary or metastatic solid tumors: radiofrequency ablation (RFA), transcatheter arterial chemoembolization (TACE), and cryoablation.

Outcomes
The general outcomes of interest are overall survival, tumor recurrence rates, complete ablation, and pain. Treatment-related morbidities may vary by tumor type. For example, treatment for lung cancer may lead to pneumothorax.

Timing
Follow-up for treatment-related morbidity is months postprocedure. Follow-up to monitor for overall survival and recurrence rates may be measured in years of follow-up.

Setting
Typically, MWA is performed under conscious sedation in an outpatient setting.

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;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer 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.

Breast Cancer
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.[1] The studies identified by reviewers were mostly feasibility and pilot studies conducted in research settings.

Prospective Studies
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, 0.09-14.14 cm).[2] Complete tumor ablation was found by microscopic evaluation in 37 (90%) of the 41 tumors ablated (95% confidence interval [CI], 76.9% to 97.3%). Reversible thermal injuries to the skin and pectoralis major muscle occurred in 3 patients.

Hepatocellular Carcinoma
Systematic Reviews
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 HCC.[3] MEDLINE, 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 (LTP); secondary outcomes were complete ablation, overall survival (OS), and major adverse events. Odds ratios were combined across studies using a random-effects model. Ten studies (2 prospective, 8 retrospective) were included. The overall LTP rate was 14% (176/1298). There was no difference in LTP rates between RFA and MWA (odds ratio, 1.01; 95% CI, 0.67 to 1.50; p=0.9). The complete ablation rate, 1- and 3- year OS, and major adverse events were similar between the 2 modalities (p>0.05 for all). Subgroup analysis showed LTP rates were lower with MWA for treatment of larger tumors (odds ratio, 1.88; 95% CI, 1.10 to 3.23; p=0.02). No significant publication bias was detected nor was interstudy heterogeneity (I^2<50%, p>0.1) observed for any measured outcomes.

Bertot et al (2011) conducted a systematic review of ablation techniques for primary and secondary liver tumors.[4] Reviewers selected 2 studies using MWA (total N=1185 patients). Pooled analysis was performed using a random-effects model because of significant study heterogeneity. The pooled mortality rate for MWA was 0.23% (95% CI, 0.0% to 0.58%). The pooled rate of major complications following MWA was 4.6%.

Ong et al (2009) conducted a systematic review of studies on MWA for primary and secondary liver tumors.[5] Results pooled from 25 clinical studies suggested MWA is an effective and safe technique for liver tumor ablation and has low complication rates and OS rates comparable to hepatic resection. However, rates of local recurrence after MWA were higher than hepatic resection. In most studies, mean HCC recurrence rates were approximately 10% but were as high as 50% in some studies. OS rates for HCC were as high as 92% at 3 years and 72% at 5 years, comparable to OS rates for RFA and percutaneous ethanol injections. Pain and fever were the most frequently reported complications, which increased with more tumors, larger tumors, and number of microwave antennas used.

Randomized Controlled Trials

Taniai et al (2006) reported on 30 patients with multiple HCC tumors who underwent reduction hepatectomy with postoperative TACE.[6] Before surgery, patients were randomized to no intraoperative adjuvant therapy (n=15) or intraoperative adjuvant therapy with MWA (n=10) or RFA (n=5) of satellite lesions. No significant differences were identified between the no intraoperative adjuvant therapy and intraoperative adjuvant therapy groups, including sex, age, nodule size (maximum tumor size, 4.3 cm vs 3.8 cm, respectively), Child-Pugh cirrhosis class, and number of nodules. Cumulative survival rates at 3 and 5 years did not differ significantly between the no intraoperative adjuvant therapy group (35.0% and 0%, respectively) and the intraoperative adjuvant therapy group (35.7% and 7.7%, respectively). The α-fetoprotein level, number of tumors, maximum tumor size, and clinical stage, but not intraoperative adjuvant therapy, were identified as independent prognostic survival factors.

Shibata et al (2002) reported on 72 consecutive patients with 94 small HCC nodules randomized by sealed envelope to MWA or RFA performed by a single surgeon.[7] No significant differences were identified between treatment group characteristics (eg, sex, age, nodule size, Child-Pugh class, number of nodules). In the RFA group, complete ablation was seen in 46 (96%) of 48 nodules (mean size, 2.3 cm; range, 1.0-3.7 cm) and 41 (89%) of 46 nodules (mean size, 2.2 cm; range, 0.9-3.4 cm) treated with MWA (p=0.26). Treatment outcomes did not differ significantly between groups in rates of untreated disease during the 6- to 27-month follow-up (8/46 nodules for MWA vs 4/48 nodules for RFA), or major complication rates (4 vs 1, respectively). Major complications included 1 case of segmental hepatic infarction in the RFA group compared with 1 case of each of the following in the MWA group: liver abscess, cholangitis with intrahepatic bile duct dilatation, subcutaneous abscess with skin burn, and subcapsular hematoma. Life-

threatening complications were not reported. The number of treatment sessions required per nodule in the RFA group (1.1) was significantly lower than in the percutaneous MWA group (2.4; p<0.001).

Comparative Studies

The available studies are nonrandomized comparisons, except a retrospective study.

Abdelaziz et al (2015) reported on a prospective study that evaluated the efficacy and safety of MWA and TACE for large tumors (5-7 cm) and assessed their effects on LTP and survival.[8] Sixty-four patients with large lesions were divided into 2 groups treated by MWA or by TACE. Both groups were comparable in demographic and ultrasonographic tumor features. MWA completely ablated 75% of cases in fewer sessions than TACE, with a lower incidence of tumor recurrence (p=0.02), development of de novo lesions (p=0.03), and occurrence of posttreatment ascites (p=0.003). MWA also had higher OS rates (p=0.04) than TACE. Mean OS in the MWA group was 22 months and 14 months in the TACE group. Actuarial probabilities of survival at 12 and 18 months were 78% and 68%, respectively, in the MWA group and 52% and 29%, respectively, in the TACE group.

Vogl et al (2015) conducted a retrospective comparative study that enrolled 53 patients with 68 liver lesions due to HCC.[9] MWA was performed in 36 patients and RFA in 32 patients. There were no differences between groups for complete response immediately following treatment or for progression-free survival at 12 months or OS at 3 years.

Ding et al (2013) retrospectively compared 113 patients treated with MWA for 131 HCC tumors and 85 patients treated with RFA for 98 HCC tumors.[10] Rates of complete ablation, local recurrence, disease-free survival (DFS), and cumulative survival (at 1, 2, 3, and 4 years), and major complications did not differ significantly between groups.

In another study, Ding et al (2013) retrospectively compared complications for 556 patients treated with MWA for 1090 liver tumors (491 HCC, 18 cholangiocarcinoma, 47 liver metastases) and 323 patients treated with RFA for 562 liver tumors (279 HCC, 6 cholangiocarcinoma, 38 liver metastases).[11] Rates of death (2/556 MWA, 1/323 RFA patients), as well as major and minor complications, did not differ significantly between groups.

Takami et al (2013) reported on 719 patients treated with MWA for HCC (mean tumor size, 2.7 cm) at a single institution.[12] OS rates were 97.7% at 1 year, 62.1% at 5 years, and 34.1% at 10 years. For 390 patients with 3 or fewer tumors measuring 3 cm or less, OS rates were 97.9% at 1 year, 70.0% at 5 years, and 43.0% at 10 years. When MWA results were compared with 34 patients treated at the same institution with hepatic resection, OS, DFS, and local recurrence rates did not differ significantly.

In a single-center report on needle track seeding, Yu et al (2012) followed 1462 patients treated with MWA for 2530 liver tumors over a 14-year period.[13] Twelve seeding nodules with a mean size of 2.3 cm (range, 1.3-3.9 cm) were found in 11 patients within 6 to 37 months (median, 10 months) after receiving MWA.

Case Series

Zhou et al (2011) prospectively evaluated MWA in 215 patients with HCC tumors of 6. cm or less in size (median size, 2.9 cm) in a single-center, phase 2 study.[14] Technical effectiveness was reported in all patients. OS rates at 1, 2, 3, 4, and 5 years were 94%, 82.9%, 66%, 54.1%, and 44.4%, respectively, and median OS time was 40 months (range, 4-106 months). Complications related to the procedure included 3 cases of pleural effusion and a case of bile duct injury.

In another prospective study by Zhou et al (2009), MWA was performed on 124 patients with 144 HCC lesions and 28 patients with 35 hepatic metastases.[15] Included in the 152 subjects were 59 patients with 61 lesions (mean size, 2.7 cm) located less than 0.5 cm from the gastrointestinal tract and 93 patients with 126 lesions (mean size, 2.4 cm) located more than 0.5 cm from the gastrointestinal tract. No procedural complications were noted, though tumor seeding occurred in 3 patients. Complete ablation was achieved in 47 (88.7%) of 53 lesions in the group with tumors near the GI tract and 116 (92.1%) of the other 126 lesions, as confirmed by imaging during the 3- to 32-month follow-up. LTP occurred in 16 tumors by 9 months. Separate treatment outcomes for HCC tumors and hepatic metastasis were not provided.

Lu et al (2005) reported on a retrospective comparison of 102 patients with HCC treated with MWA (49 patients with 98 nodules; mean size, 2.5 cm) or RFA (53 patients with 72 nodules; mean size, 2.6 cm).[16] Patient follow-up was about 25 months in both groups. Complete ablation did not differ significantly between groups (95% [93/98] tumors in the MWA group vs 93% [67/72] tumors in the RFA group). However, complete ablation rates improved for smaller tumors of less than 3 cm in size to 98.6% (73/74) in the MWA group and 98% (50/51) in the RFA group. In tumors larger than 3 cm, complete ablation rates declined to 83.3% (20/24) in the MWA group and 81% (17/21) in the RFA group. There were also no significant differences between groups in rates of local tumor recurrence (11.8% for MWA vs 20.9% for RFA), major complications (8.2% vs 5.7%, respectively), or DFS at 1, 2, and 3 years (45.9%, 26.9%, and 26.9% vs 37.2%, 20.7%, and 15.5%, respectively).

Hepatic Metastases From Primary Cancers From Other Sites

Systematic Reviews

A Health Technology Assessment by Loveman et al (2014)[17] and a Cochrane review by Bala et al (2013)[18] reported on ablation for liver metastasis. Reviewers found insufficient evidence to determine any benefits of MWA for liver metastasis over surgical resection.

In Bertot's 2011 systematic review (previously described), only 1 RCT was identified comparing MWA for hepatic metastases with the criterion standard of surgical resection.[4]

Pathak et al (2011) conducted a systematic review of ablation techniques for colorectal liver metastases, which included 13 studies on MWA (total N=406 patients) with a minimum of 1-year follow-up.[19] 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%.

In the systematic review by Ong (2009), previously described, local recurrence rates for liver metastases after MWA treatment averaged 15% but varied between 0% and 50% in the 7 studies that addressed liver metastases.[5]

Randomized Controlled Trials

Shibata et al (2000) reported on 30 patients with hepatic metastases from colorectal cancer randomized without stratification to MWA after laparotomy (n=14) or to hepatectomy (n=16).[20] Of the original 40 patients, 10 patients were excluded because researchers discovered intraoperatively that they did not meet study criteria (they had extensive metastasis or ≥10 tumors). The 2 treatment groups did not differ significantly in age (mean age, 61 years in both groups), number of tumors (mean, 4.1 vs 3.0, respectively), or tumor size (mean, 2.7 cm vs 3.4 cm, respectively). No significant differences were observed in survival (27 months for MWA vs 25 months for hepatectomy) or mean DFS (11.3 months for MWA vs 13.3 months for hepatectomy).

Complications in the MWA group included 1 hepatic abscess and 1 bile duct fistula. In the hepatectomy group, complications were 1 intestinal obstruction, 1 bile duct fistula, and wound infection.

Nonrandomized Trials

Liu et al (2013) reported on liver metastases for 35 patients treated with MWA (62 tumors) and 54 patients treated with RFA (70 tumors).[21] Ablation was complete in 89% (117/132) of tumors and did not differ significantly between tumor types: 86% (56/65) for metastatic colorectal cancer and 91% (61/67) for other metastatic diseases. Tumors 3.0 cm or smaller were completely ablated significantly more often than tumors larger than 3.0 cm (94% vs 67%, p=0.001).

Lorentzen et al (2011) retrospectively reviewed use of MWA in 39 patients with 125 liver metastases from the primary sites of colorectal cancer (n=31), breast cancer (n=6), carcinoid tumor (n=1), and gastrointestinal stromal tumor (n=1).[22] Complete ablation was achieved in 100% of tumors (median size, 1.5 cm) with 1 treatment session in 34 patients, in 2 sessions for 4 patients, and in 3 sessions for 1 patient. One case of a liver abscess, which resolved after percutaneous drainage, was the only major complication reported. Four minor complications were reported (1 incidence of ascites, 3 complaints of puncture site pain). At a median follow-up of 11 months, LTP was seen in 12 (10%) of 125 tumors in 10 (26%) of the 39 patients.

In a prospective, single-institution, phase 2 study, Martin et al (2010) reported on 100 patients treated with 270 open or MWA for HCC (n=17) and liver metastases from the primary sites of colorectal (n=50), carcinoid (n=11), and other cancers (n=22, including cholangiocarcinoma, metastatic breast, renal cell carcinoma, bladder, carcinoid, melanoma, and sarcoma).[23] Median tumor size was 3.0 cm. Thirty-eight patients received MWA, 53 patients had MWA plus concomitant hepatic resection, and 9 patients had MWA concomitant with other organ resection. Only 2 patients had incomplete ablations after the procedure. No bleeding complications were experienced, but 2 cases of hepatic abscess and 2 cases of hepatic insufficiency occurred. At a median follow-up of 36 months, 5 patients had incomplete ablations, and 2 (2%) patients had local tumor recurrence; 37 (37%) patients developed recurrence at nonablated sites.

Lung Cancer

Acksteiner and Steinke (2015) reported on a retrospective study that evaluated the safety, effectiveness, and follow-up imaging of MWA in 10 patients (age range, ≥75 years) with early-stage non-small-cell lung cancer.[24] Follow-up with computed tomography and fluorine 18 fluorodeoxyglucose-positron emission tomography extended for up to 30 months (median, 12 months). No periprocedural deaths or major complications were reported. Three patients showed growth of the treated lesions, 1 patient died (age 90) due to unknown causes. One patient still living presented with local progression and disseminated metastatic disease at 12 months. One patient showed increasing soft tissue mass at the ablation site 15 months posttreatment, but 3 consecutive core biopsies over 2 months failed to confirm tumor recurrence.

An observational study by Sun et al (2015) evaluated the clinical efficacy and utility of percutaneous MWA therapy for lung cancer without surgical treatment.[25] Thirty-nine lesions in 29 patients with peripheral lung cancer were treated by percutaneous MWA therapy under local anesthesia. Treatments were completed in 29 patients. Eight, 14, 4, and 3 patients, respectively, achieved complete remission, partial remission, stable status, and progression for an effectiveness rate of 76%. Complications included 5, 2, and 15 cases of pneumothorax, pleural effusion, and fever, respectively. No complications from needle track insertion were observed.

Mean progression-free survival was 15 months. One- and 2-year OS rates were 91% and 83%, respectively.

Belfiore et al (2013) retrospectively reviewed data on 56 patients treated with MWA for inoperable lung cancer or metastatic pulmonary metastases.[26] DFS rates were 69% at 1 year, 54% at 2 years, and 49% at 3 years. Pneumothorax was reported in 18 (32%) patients.

Lu et al (2012) retrospectively reviewed 69 patients treated with MWA for inoperable lung cancer or metastatic pulmonary metastases.[27] OS rates for patients with pulmonary metastases at 1, 2, and 3 years were 48%, 24%, and 14%, respectively. The recurrence-free survival rates for patients with non-small-cell lung cancer at 1, 2, and 3 years were 73%, 50%, and 27%, respectively. OS rates for all patients were 67% at 1, 45% at 2, and 25% at 3 years. Pneumothorax was reported in 25% of patients.

Vogl et al (2011) prospectively assessed 80 patients treated with MWA for inoperable pulmonary metastases.[28] Rates were 91% at 1 year and 75% at 2 years. Pneumothorax occurred in 11 (9%) of 130 MWA sessions, and pulmonary hemorrhage occurred in 8 (6%) of 130 sessions.

Primary Renal Tumors

Systematic Reviews

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).[29] The analysis included 1 randomized study on MWA[30] (described below) and 5 cohort studies on RFA (total N=587 patients). In the ablation group, complication rates and renal function declines were significantly more than in the nephrectomy group (p=0.04 and p=0.03, respectively). The local recurrence rate was 3.6% in both groups (relative risk, 0.92; 95% CI, 0.4 to 2.14; p=0.79) and DFS up to 5 years did not differ significantly between groups (hazard ratio, 1.04; 95% CI, 0.48 to 2.24; p=0.92).

Martin et al (2013) conducted a meta-analysis comparing MWA with cryoablation for small renal tumors.[31] The analysis included 7 MWA studies (n=164 patients) and 44 cryoablation studies (n=2989 patients). Selected studies were prospective or retrospective, nonrandomized, noncomparative studies. Mean follow-up duration was shorter for MWA (17.86 months) than for cryoablation (30.22 months; p=0.07). Mean tumor size was significantly larger in the MWA studies than in the cryoablation studies (2.58 cm vs 3.13 cm, respectively, p=0.04), LTP (4.07% vs 2.53%, respectively; p=0.46) and progression to metastatic disease (0.8% vs 0%, respectively; p=0.12) did not differ significantly.

Randomized Controlled Trials

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.[30] 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=0.019). MWA patients also had significantly less postoperative renal function declines (p<0.009) and estimated perioperative blood loss (p<0.001) 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=0.541).

Case Series

Yu et al (2012) reported on a retrospective review of 46 patients treated with MWA for renal cell carcinoma.[32] Complete ablation occurred in 98% (48/49) of tumors (mean tumor size, 3.0 cm). At a median follow-up of 20.1 months, all 46 patients were metastasis-free. OS rates were 100% at 1 and 2 years and 97.8% at 3 years.

Muto et al (2011) reported on complete tumor coagulation necrosis in 10 patients treated with MWA for clear cell renal carcinoma (median tumor size, 2.75 cm).[33] No complications were reported during or after the procedure. Bai et al (2010) reported complete laparoscopic MWA in 17 of 18 clear cell renal carcinoma tumors (mean tumor size, 2.8 cm).[34] In this study, evidence of disease progression was not found at a median follow-up of 20 months. Complications reported were mild (18.2%), and renal function did not significantly deteriorate.

In a study of 10 patients with solid-enhancing renal tumors (median size, 3.65 cm) who were treated with MWA, Castle et al (2011) reported tumor recurrence in 3 of 8 tumors at a mean follow-up of 17.9 months.[35] Twenty percent of patients experienced intraoperative complications while 40% experienced postoperative complications, including perinephric hematoma, splenic capsular tear, pleuritic chest pain, skin burn, fever, hematuria, genitofemoral neuralgia, and urinoma.

In another study, Guan et al (2010) reported on the safety of MWA for renal hamartoma.[36] In this case series, 15 of 16 patients had complete tumor ablation. Disease recurrence was not reported at a median follow-up of 16 months.

Other Tumors or Conditions

No RCTs on the use of MWA for other tumors or conditions have been identified. A systematic review of ablation therapies, including MWA, for locally advanced pancreatic cancer was published by Keane et al (2014).[37] Reviewers found limited evidence on the use of MWA for pancreatic cancer.

Case studies and retrospective reviews on the use of MWA for adrenal carcinoma,[38] metastatic bone tumors,[39] intrahepatic primary cholangiocarcinoma,[40] benign thyroid tumors,[41] and other nononcologic conditions (ie, bleeding peptic ulcers, esophageal varices, secondary hypersplenism) were identified.

Summary of Evidence

For individuals who have an unresectable primary or metastatic tumor (eg, breast, hepatic [primary or metastatic], pulmonary, renal) who receive MWA, the evidence includes case series, observational studies, cohort studies, RCTs, and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, symptoms, quality of life, and treatment-related mortality and morbidity. Available studies have shown that MWA results in a wide range of complete tissue ablation (50%-100%) depending on tumor size, with complete ablation common and nearing 100% with smaller tumors (eg, ≤3 cm). Tumor recurrence rates at ablated sites are very low. However, tumor recurrence at nonablated sites is common and may correlate with disease state (eg, in hepatocellular carcinoma). Intraoperative and postoperative minor and major complications are low, especially when tumors are smaller and accessible. Patient selection criteria and rationale for using MWA instead of other established techniques (eg, surgical resection, radiofrequency ablation) are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 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

National Comprehensive Cancer Network

The National Comprehensive Cancer Network guidelines on hepatobiliary cancers (v.2.2018) list microwave ablation (MWA) (along with radiofrequency ablation, cryoablation, and percutaneous alcohol injection) as a treatment option for hepatocellular carcinoma (HCC) tumors in patients who are not candidates for potential curative treatments (eg, resection and transplantation) and do not have large-volume extrahepatic disease.[42] Ablation should only be considered when tumors are accessible by percutaneous, laparoscopic, or open approaches. The guidelines indicate "ablative therapies are most effective for [HCC] tumors less than 3 cm…". HCC tumors between 3 and 5 cm may also be treated with ablation to prolong survival when used in combination with arterial embolization. Additionally, the tumor location must be accessible to permit ablation of the tumor and tumor margins without ablating major vessels, bile ducts, the diaphragm, or other abdominal organs. However, only 2 randomized controlled trials were cited in the guidelines to support recommendations for MWA.

The Network guidelines on neuroendocrine tumors (v.2.2018) do not mention MWA.[43] Guidelines state that: "Cytoreductive surgery or ablative therapies such as radiofrequency ablation (RFA) or cryoablation may be considered if near-complete treatment of tumor burden can be achieved

(category 2B). For unresectable liver metastases, hepatic regional therapy (arterial embolization, chemoembolization, or radioembolization [category 2B]) is recommended."

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.[44] The revised guidance indicated that: "Current evidence on microwave ablation for treating liver metastases raises no major safety concerns and the evidence on efficacy is adequate in terms of tumor ablation."

The Institute (2007) also published guidance on MWA for HCC.[45] This guidance indicated: "Current evidence on the safety and efficacy of microwave ablation 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.

American College of Chest Physicians
The American College of Chest Physicians' 2013 evidence-based guidelines on the treatment of non-small-cell lung cancer noted that the role of ablative therapies in the treatment of high-risk patients with stage I non-small-cell lung cancer is evolving.[46] The guidelines deal mostly with radiofrequency ablation.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in August 2018 did not identify any ongoing or unpublished trials that would likely influence this review.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. 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.

CPT/HCPCS

19499	Unlisted procedure, breast
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
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

- There are no CPT codes specific to microwave ablation.
- According to an American Medical Association (AMA) publication (*Clinical Examples in Radiology*, 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).
- 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.

Diagnoses

Experimental / Investigational for all diagnoses related to this medical policy.

REVISIONS

10-01-2016	Policy published 09-01-2016. Policy effective 10-01-2016.
11-15-2017	Description section updated
	Rationale section updated
	In Coding section: ▪ Revised CPT Code nomenclature: 32998 ▪ Added coding notations.
	References updated
01-01-2018	Policy published 01-01-2018. Professional effective date 01-01-2018. Institutional effective date 02-15-2018.
	In Coding section: ▪ Removed CPT Code: 0301T (Termed 12-31-2017) ▪ Added CPT Code: 19499
01-01-2019	Description section updated
	Rationale section updated
	References updated

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