Microwave Tumor Ablation

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Cryosurgery Ablation of Miscellaneous Solid Tumors other than Liver or Prostate Tumors or Breast Fibroadenomas is addressed separately in medical policy 00023.

Note: Radioembolization for Primary and Metastatic Tumors of the Liver is addressed separately in medical policy 00110.

Note: Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors is addressed separately in medical policy 00175.

Note: Radiofrequency Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00182.

Note: Cryosurgical Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00220.

Note: Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies is addressed separately in medical policy 00227.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers microwave ablation (MWA) of primary and metastatic tumors to be **investigational.***

Background/Overview

MICROWAVE ABLATION

MWA is a technique that 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 (5×3 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 extend 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 (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. 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 (e.g., 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 (HCC), breast cancer, colorectal cancer metastatic to the liver, renal cell carcinoma, renal hamartoma, adrenal malignant carcinoma, non-small-cell lung cancer (NSCLC), 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). 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 liver transplant.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Several devices have been cleared for marketing by the U.S. FDA through the 510(k) process for MWA. Covidien's (now Medtronic's) Evident™‡ Microwave Ablation System was cleared for marketing through the

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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 (acquired by Valleylab in 2005) Tri-Loop™‡ Microwave Ablation Probe;
- MicroSurgeon's Microwave Soft Tissue Ablation System;
- Microsulis Medical's (now part of AngioDynamics) Acculis®‡ Accu2i; and
- 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.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

Assessment of efficacy for therapeutic intervention involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition. The findings of the literature review are summarized next with select studies.

BREAST CANCER
A 2010 systematic review of ablation techniques by Zhao et al for breast cancer found that only 0% to 8% of breast cancer tumors were completely ablated with MWA. The studies identified by reviewers were mostly feasibility and pilot studies conducted in research settings.

In 2012, Zhou et al 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). 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 with primary HCC. 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 (ORs) 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 (OR=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 (OR=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. Reviewers selected 2 studies (see Case Series section) 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%.

In 2009, Ong et al conducted a systematic review of studies on MWA for primary and secondary liver tumors. 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.

Comparative Studies

No RCTs comparing MWA with RFA were identified. The available studies are nonrandomized comparisons, and all except 1 study is retrospective.

Abdelaziz et al (2015) reported on a prospective study that evaluated the efficacy and safety of MWA and transarterial chemoembolization (TACE) for large tumors (5-7 cm) and assessed their effects on LTP and survival. 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 published a retrospective comparative study in 2015. It enrolled 53 patients with 68 liver lesions due to HCC. MWA was performed in 36 patients and RFA in 32 patients. There were no differences between groups on complete response immediately following treatment or for progression-free survival at 12 months or OS at 3 years. In 2013, Ding et al retrospectively compared 113 patients treated with MWA for 131 HCC tumors and 85 patients treated with RFA for 98 HCC tumors. 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 2013 study by Ding et al, complications were retrospectively compared between 556 patients treated with MWA for 1090 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). Rates of death (2/556 MWA, 1/323 RFA patients), as well as major and minor complications, did not differ significantly between groups.

In 2013, Takami et al reported on 719 patients treated with MWA for HCC (mean tumor size, 2.7 cm) at a single institution. 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 2012 report on needle track seeding, Yu et al followed 1462 patients treated with MWA for 2530 liver tumors over a 14-year period. 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.

In 2011, Simo et al retrospectively compared MWA (13 patients with 15 HCC tumors) with RFA (22 patients with 27 HCC tumors) performed by a single surgeon. No significant differences were identified between treatment group characteristics, except for sex (54% vs 86% male, respectively). Average tumor size was 2.31 cm in the MWA group and 2.53 cm in the RFA group. Average tumor ablation volumes did not differ significantly for MWA (28.99 cm) and RFA (23.43 cm). In the MWA group, at a mean 7-month follow-up, the DFS rate was 54%, with 2 patients having received liver transplants, 31% having disease progression and 15% deceased. Mean follow-up in the RFA group was 19 months. This group experienced 50% OS: 4% of patients had liver transplants, 9% had disease progression, and 36% died. Operative times were shorter in the MWA group (112 minutes vs 149 minutes).

Case Series
In 2011, Zhou et al prospectively evaluated MWA in 215 patients with HCC tumors of 6. cm or less (median size, 2.9 cm) in a single-center, phase 2 study. 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 1 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. 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 (GI) tract and 93 patients with 126 lesions (mean size, 2.4 cm) located more than 0.5 cm from the GI tract. For lesions less than 0.5 cm from the GI tract, margin temperatures were monitored during ablation and, to prevent thermal injury, ethanol injections were placed into marginal tumor tissue in 33 lesions that protruded or were in contact with the GI 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.

In 2009, Liang et al retrospectively reviewed complications experienced with MWA for the treatment of 1928 malignant liver tumors in 1136 patients at a single institution. Each patient received an average of 1.8 treatment sessions (total treatment sessions, 3697). Thirty (2.6%) patients experienced major complications, which included 5 cases of liver abscess and empyema, 2 bile duct injuries, 2 colon perforations, 5 tumor seedings, 12 pleural effusions requiring thoracentesis, 1 hemorrhage requiring arterial embolization, and 3 skin burns requiring. Two deaths occurred within 14 days of MWA in patients with Child-Pugh class B uncompensated cirrhosis. One patient (age 78 years) had multiorgan failure and another (age 83 years) had respiratory and cardiac failure. Minor more frequent complications included fever (83.4%), pain (80.1%), asymptomatic pleural effusion (10.4%), and thickening of the gallbladder wall (2.8%), and arterioportal shunt (0.3%), small stricture of the bile duct (0.4%), and skin burn requiring no treatment (1.6. A significantly higher rate of major complications and more ablation sessions were experienced when a non-cooled-shaft antenna was used during the period of 1994 to 2005 (n=583) than with newer technology; cooled-shaft antennas were used beginning in 2005 (n=583).

Taniai et al (2006) reported on 30 patients with multiple HCC tumors who underwent reduction hepatectomy with postoperative TACE. Before surgery, patients were randomized to no intraoperative adjuvant therapy (n=15) or intraoperative adjuvant therapy with either 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.

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).

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).

In 2002, Shibata et al reported on 72 consecutive patients with 94 small HCC nodules randomized by sealed envelope to MWA or RFA performed by a single surgeon. No significant differences were identified between treatment group characteristics (e.g., 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). However, treatment time per session was significantly shorter with MWA (33 minutes) than with RFA (53 minutes).

HEPATIC METASTASES FROM PRIMARY CANCERS FROM OTHER SITES

Systematic Reviews

A 2014 Health Technology Assessment and a 2013 Cochrane review 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.

In 2011, Pathak et al 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. 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 2009 systematic review by Ong (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.

Randomized and Nonrandomized Trials
In 2013, Liu et al reported on liver metastases for 35 patients treated with MWA (62 tumors) and 54 patients treated with RFA (70 tumors). 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).

In 2011, Lorentzen et al retrospectively reviewed 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 GI stromal tumor (n=1). 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 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 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). 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 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.

In 2000, Shibata et al reported on 30 patients with hepatic metastases from colorectal cancer randomized without stratification to MWA after laparotomy (n=14) or to hepatectomy (n=16). 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). However, intraoperative blood loss was significantly lower, and no blood transfusions were required in the MWA group (6 patients in the hepatectomy group required transfusions). 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.

LUNG CANCER
In 2015, Acksteiner and Steinke reported a retrospective study that evaluated the safety, effectiveness, and follow-up imaging of MWA in 10 patients (age range, ≥75 years) with early-stage NSCLC. Follow-up with computed tomography and fluorine 18 fluorodeoxyglucose-positron emission tomography (FDG-PET) extended for 30 months (median, 12 months). No periprocedural deaths or major complications were

reported. Seven patients were DFS. Three patients showed growth of the treated lesions, 1 patient died (age 90) due to unknown cause 18 months postsurgery. 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.

A 2015 observational study evaluated the clinical efficacy and utility of percutaneous MWA therapy for lung cancer without surgical treatment. 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. Average surgical time was 8 minutes (range, 5-12 minutes). Eight, 14, 4, and 3 patients achieved complete remission, partial remission, stable status, and progression, respectively, 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.

In 2012, Lu et al retrospectively reviewed 69 patients treated with MWA for inoperable lung cancer or metastatic pulmonary metastases. 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 NSCLC at 1, 2, and 3 years were 73%, 50%, and 27%, respectively. OS rates were 67% at 1, 45% at 2, and 25% at 3 years. Pneumothorax occurred in 25% of patients.

In 2013, Belfiore et al reported on a retrospective review of 56 patients treated with MWA for inoperable lung cancer or metastatic pulmonary metastases. DFS rates were 69% at 1 year, 54% at 2 years, and 49% at 3 years. Pneumothorax was reported in 18 (32%) patients.

In 2011, Vogl et al prospectively assessed 80 patients treated with MWA for inoperable pulmonary metastases. 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 2014 systematic review and meta-analysis, Katsanos et al compared thermal ablation (MWA and RFA) with surgical nephrectomy for small renal tumors (mean size, 2.5 cm). The analysis included 1 randomized study on MWA (described below) and 5 cohort studies on RFA (total N=587 patients). In the ablation group, complication rates and renal function declined 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 conducted a meta-analysis comparing MWA with cryoablation for small renal tumors in 2013. 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 than for cryoablation (17.86 months vs 30.22 months, respectively, p=0.07). While 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.

Clinical Studies
In 2012, Guan et al 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. 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). Longer follow-up is needed.

In 2012, Yu et al reported on a retrospective review of 46 patients treated with MWA for renal cell carcinoma. 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.

In 2011, Muto et al reported on complete tumor coagulation necrosis in 10 patients treated with MWA for clear cell renal carcinoma (median tumor size, 2.75 cm). Depending on tumor size, the microwave antennas were used 1 to 3 times and mean application time was 14.1 minutes. 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). In this study, evidence of disease progression was not found at a median follow-up of 20 months, including a patient with incomplete ablation followed for 31 months. Complications reported were mild (18.2%), and renal function did not significantly deteriorate.

In a 2011 study of 10 patients with solid-enhancing renal tumors (median size, 3.65 cm) who were treated with MWA, Castle et al reported tumor recurrence in 3 of 8 tumors at a mean follow-up of 17.9 months. Because tumor size was larger in this study, mean ablation time was 21 minutes. Additionally, 20% 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. 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 in 2014. Reviewers found limited evidence on the use of MWA for pancreatic cancer.

Case studies and retrospective reviews on MWA for adrenal carcinoma, metastatic bone tumors, intrahepatic primary cholangiocarcinoma, benign thyroid tumors, and other nononcologic conditions (i.e., bleeding peptic ulcers, esophageal varices, secondary hypersplenism) were identified.

SUMMARY OF EVIDENCE

For individuals who have an unresectable primary or metastatic tumor (e.g., 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 OS, 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 (e.g., ≤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 (e.g., 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 over other established techniques (e.g., surgical resection, RFA) are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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01/01/2018 Coding update
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07/11/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 07/2019

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Code Type	Code
CPT	19499, 32998, 47382. 50592, 76940, 77499 Code deleted eff 1/1/18: 0301T
HCPCS	No codes
ICD-10 Diagnosis	All related diagnosis codes

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A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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