Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

Policy Number: 7.01.95  Last Review: 3/2017

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for radiofrequency ablation of miscellaneous solid tumors excluding liver tumors when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Radiofrequency ablation may be considered medically necessary to palliate pain in patients with osteolytic bone metastases who have failed or are poor candidates for standard treatments such as radiation or opioids.

Radiofrequency ablation may be considered medically necessary to treat osteoid osteomas that cannot be managed successfully with medical treatment.

Radiofrequency ablation may be considered medically necessary to treat localized renal cell carcinoma that is no more than 4 cm in size when either of the following criteria are met:
- In order to preserve kidney function in patients with significantly impaired renal function (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate [GFR] of less than 60 mL/min per m²) when the standard surgical approach (i.e., resection of renal tissue) is likely to substantially worsen existing kidney function; or
- Patient is not considered a surgical candidate.

Radiofrequency ablation may be considered medically necessary to treat an isolated peripheral non-small cell lung cancer lesion that is no more than 3 cm in size when the following criteria are met:
- Surgical resection or radiation treatment with curative intent is considered appropriate based on stage of disease, however, medical co-morbidity renders the individual unfit for those interventions; AND
• Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.

Radiofrequency ablation may be considered **medically necessary** to treat malignant non-pulmonary tumor(s) metastatic to the lung that are no more than 3 cm in size when the following criteria are met:
• In order to preserve lung function when surgical resection or radiation treatment is likely to substantially worsen pulmonary status OR the patient is not considered a surgical candidate; AND
• There is no evidence of extrapulmonary metastases; AND the tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.

(See the Considerations section for additional criteria)

**When Policy Topic is not covered**
Radiofrequency ablation is considered **investigational** as a technique for ablation of:
• breast tumors;
• lung cancer not meeting the criteria above;
• renal cell cancer not meeting the criteria above;
• osteoid osteomas that can be managed with medical treatment;
• painful bony metastases as initial treatment; and
• all other tumors outside the liver including, but not limited to, the head and neck, thyroid, adrenal gland, ovary, and pelvic/abdominal metastases of unspecified origin.

**Considerations**
The following are additional criteria that have been developed by clinical judgment/consensus and existing guidelines for the use of RFA in metastatic tumors to the lung and include:
• No more than 3 tumors per lung should be ablated;
• Tumors should be amenable to complete ablation; AND
• Twelve months should elapse before a repeat ablation is considered.

**Description of Procedure or Service**

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<td>Comparators of interest are: • Medical management • Radiotherapy</td>
<td>Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Medication use • Treatment-related morbidity</td>
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In radiofrequency ablation (RFA), a probe is inserted into the center of a tumor and the non-insulated electrodes, which are shaped like prongs, are projected into the tumor; a heat is then generated locally by a high-frequency, alternating current that flows from the electrodes. The local heat treats the tissue adjacent to the probe, resulting in a 3 cm to 5.5 cm sphere of dead tissue. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edge and, in some cases, may be retreated. Radiofrequency ablation may be performed percutaneously, laparoscopically, or as an open procedure.

Osteolytic Bone Metastases
For individuals who have painful osteolytic bone metastases who have failed or are poor candidates for standard treatments who receive RFA, the evidence includes
case series. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. Case series have shown clinically significant pain relief and reduction in opioid use following treatment of osteolytic pain metastases. The population is comprised of patients with limited or no treatment options, for whom short-term pain relief is an appropriate clinical outcome. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Osteoid Osteomas**

For individuals who have painful osteoid osteomas who receive RFA, the evidence includes numerous observational studies and a systematic review of these studies. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. In a systematic review of thermal ablation techniques, clinical success (pain-free) was achieved in 94% to 98% of patients. Most patients (89%-96%) remained pain-free when assessed at longer term follow-up. Although no randomized trials of RFA for osteoid osteomas have been performed, the uncontrolled studies have demonstrated RFA can provide adequate symptomatic relief with minimal complications, for whom short-term symptom relief and avoidance of invasive procedures are appropriate clinical outcomes. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Localized Renal Cell Carcinoma**

For individuals who have localized renal cell carcinoma that is no more than 4 cm in size who receive RFA, the evidence includes 1 randomized controlled trial (RCT), a large number of observational studies, and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. A recent meta-analysis that included only an RCT and cohort studies found that RFA was as effective as nephrectomy for small renal tumors, with a reduction in complications. Another recent meta-analysis, which included case series of stage 1 (≤7 cm across) renal tumors, found that the rate of local progression was greater with RFA than with nephrectomy. The differing results in these meta-analyses may be due to differences in tumor size in selected studies as well as potential selection bias when evaluating case series. Although inconsistent, the evidence does suggest that for small renal tumors, RFA may result in a similar rate of disease progression with a lower complication rate than nephrectomy. However, comparative trials are needed to determine with greater certainty the effects of these treatments in the same patient population. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Inoperable Primary Pulmonary Tumors and Nonpulmonary Metastases**

For individuals who have inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung who receive RFA, the evidence includes observational studies and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. A multicenter study found that, for tumors less than 3.5 cm, RFA can lead to a complete response in as many as 88% of patients for at least 1 year.
Two-year survival has been reported to range from 41% to 75% in case series, with 5-year survival rates of 20% to 27%. In general, the evidence shows RFA results in adequate survival and tumor control in patients who are not surgical candidates, with low morbidity rates. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Breast Tumors**
For individuals who have breast tumors who receive RFA, the evidence includes observational studies and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Evidence has reported varied and incomplete ablation rates with concerns about postablation tumor cell viability. Long-term improvements in health outcomes have not been demonstrated. Additionally, available studies do not allow comparisons with conventional breast-conserving procedures. Further studies, with long-term follow-up, are needed to determine whether RFA of the breast for small cancers can provide local control and survival rates comparable with conventional breast-conserving treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Benign Thyroid Tumors**
For individuals who have benign thyroid tumors who receive RFA, the evidence includes RCTs, case series, and systematic reviews of these studies. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. A systematic review that included 4 RCTs and 5 observational studies found significant reductions in nodule size and withdrawal from methimazole following treatment with RFA. Reports of complications have varied. The most frequent major complication from a large multicenter series of specialty centers was voice change. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Miscellaneous Solid Tumors**
For individuals who have miscellaneous tumors (eg, head and neck, thyroid cancer, pancreas) who receive RFA, the evidence includes a small number of case series and retrospective comparative studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. There is a limited evidence base for each tumor type. Reporting on outcomes or comparisons with other treatments is limited. These studies are insufficient to evaluate the effect of RFA. The evidence is insufficient to determine the impact of the technology on health outcomes.

**Clinical Input**
Clinical input supported RFA for localized renal cell carcinoma that is no more than 4 cm in size when preservation of kidney function is necessary and a standard surgical approach is likely to substantially worsen kidney function or when the patient is not considered a surgical candidate. Thus, absent other treatment options, RFA for small renal cell tumors may be considered medically necessary.
Radiofrequency Ablation (RFA) was initially developed to treat inoperable tumors of the liver (see evidence review 7.01.91). Recently, studies have reported on use of RFA to treat other tumors. For some of these, RFA is being investigated as an alternative to surgery for operable tumors. Well-established local or systemic treatment alternatives are available for each of these malignancies. The hypothesized advantages of RFA for these cancers include improved local control and those common to any minimally invasive procedure (eg, preserving normal organ tissue, decreasing morbidity, decreasing length of hospitalization).

Goals of RFA may include (1) controlling local tumor growth and preventing recurrence; (2) palliating symptoms; and (3) extending survival duration for patients with certain tumors. The effective volume of RFA depends on the frequency and duration of applied current, local tissue characteristics, and probe configuration (eg, single vs multiple tips). RFA can be performed as an open surgical procedure, laparoscopically or percutaneously, with ultrasound or computed tomography (CT) guidance.

Potential complications associated with RFA include those caused by heat damage to normal tissue adjacent to the tumor (eg, intestinal damage during RFA of kidney), structural damage along the probe track (eg, pneumothorax as a consequence of procedures on the lung), or secondary tumors, if cells seed during probe removal.

Osteolytic Bone Metastases
After lung and liver, bone is the third most common metastatic site and is relatively frequent among patients with primary malignancies of the breast, prostate, and lung. Bone metastases often cause osteolysis (bone breakdown), resulting in pain, fractures, decreased mobility, and reduced quality of life. External-beam radiotherapy often is the initial palliative therapy for osteolytic bone metastases. However, pain from bone metastases is refractory to radiotherapy in 20% to 30% of patients, while recurrent pain at previously irradiated sites may be ineligible for additional radiation due to risks of normal tissue damage. Other alternatives include hormonal therapy, radiopharmaceuticals (eg, strontium 89), and bisphosphonates. Less often, surgery or chemotherapy may be used for palliation, and intractable pain may require opioid medications. RFA has been investigated as an alternative for palliation of bone metastases.

Osteoid Osteomas
Osteomas are the most common benign bone tumor, comprising 10% to 20% of benign and 2% to 3% of all bone tumors. They are typically seen in children and young adults, with most diagnosed in patients between 5 and 20 years of age. Osteomas are most common in the lower extremity (usually the long bones, mainly the femur) and less common in the spine. These tumors typically have a characteristic clinical presentation and radiologic appearance, with pain, usually continuous and worse at night, and usually relieved by aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs). The natural history of the osteoid osteoma varies based on location, and although they rarely exceed 1.5 cm in
diameter, may produce bone widening and deformation, limb length inequality, or angular deviations when near a growth plate. When located in the spine, these lesions may lead to painful scoliosis or torticollis. Sometimes, they heal spontaneously after 3 to 7 years.

Treatment options include medical management with NSAIDs, surgical excision (wide/en bloc excision or curetting), or the use of CT- or magnetic resonance imaging (MRI)-guided minimally invasive procedures including core drill excision, laser photocoagulation, or RFA. For many years, complete surgical excision was the classic treatment of osteomas, usually performed in patients with pain, despite medical management. However, a substantial incision may be necessary, with removal of a considerable amount of bone (especially in the neck of the femur). This increases the need for bone grafting plus internal fixation (which often necessitates a second procedure to remove the metal work). Other possible risks include avascular necrosis of the femoral head and postoperative pathologic fracture. In addition, surgical excision leads to a lengthier convalescence and postoperative immobilization. Anatomically inaccessible tumors may not be completely resectable and may recur. RFA of osteoid osteoma is done with a needle puncture, so no incision or sutures are needed, and patients may immediately walk on the treated extremity and return to daily activities when the anesthetic effect wears off. The risk of recurrence with RFA of an osteoma is 5% to 10%, and recurrent tumors can be retreated with RFA. In general, RFA is not performed in many spinal osteomas because of possible thermal-related nerve damage.

**Localized Renal Cell Carcinoma**

Radical nephrectomy remains the principal treatment of renal cell carcinoma; however, partial nephrectomy or nephron-sparing surgery has been shown to be as effective as radical nephrectomy, with comparable long-term recurrence-free survival rates, in a select group of patients. Alternative therapy such as RFA is of interest in patients with small renal tumors when preservation of renal function is necessary (eg, in patients with marginal renal function, a solitary kidney, bilateral tumors) and in patients with comorbidities that would render them unfit for surgery. Another consideration would be in patients at high risk of developing additional renal cancers (eg, von Hippel-Lindau disease).

**Primary Pulmonary Tumors and Nonpulmonary Metastases**

Surgery is the current treatment of choice in patients with stage 1 primary non-small-cell lung cancer (NSCLC; stage 1 includes 1a: T1N0M0 and 1b: T2N0M0). Approximately 20% of patients present with stage 1 disease, although this number is expected to increase as a result of screening programs, advances in imaging modalities, and widespread use of CT scans for other indications. Postsurgical recurrence rates of stage 1 NSCLC have been reported as between 20% and 30%, with most occurring at distant sites; locoregional recurrences occur in approximately 12%. Large differences in survival outcome are observed after surgery in stage 1 patients, with 5-year overall survival (OS) rates ranging from 77% for small T1 tumors to 35% for large T2 tumors. Untreated, stage 1 NSCLC has a 5-year OS rate of 6% to 14%.
Patients with early-stage NSCLC who are not surgical candidates may be candidates for radiotherapy with curative intent. In the 2 largest retrospective radiotherapy series, patients with inoperable disease treated with definitive radiotherapy achieved 5-year survival rates of 10% and 27%. In both studies, patients with T1N0 tumors had better 5-year survival rates of 60% and 32%, respectively.

Stereotactic body radiotherapy (SBRT) has gained more widespread use, because it is a high-precision mode of therapy that delivers very high doses of radiation. Two- to 3-year local control rates of stage 1 NSCLC with SBRT have ranged from 80% to 95%. SBRT has been investigated in patients unfit to undergo surgery, with survival rates similar to surgical outcomes.

RFA also is being investigated in patients with small primary lung cancers or lung metastases who are deemed medically inoperable.

**Thyroid Tumors**
Surgical resection is the primary treatment choice for medically unresponsive, symptomatic benign thyroid tumors and thyroid carcinomas. However, techniques for ablation of thyroid tumors (eg, RFA, microwave ablation) are being investigated.

**Miscellaneous Tumors**
RFA has been investigated for use in individuals with different lesions in different anatomic sites. They include, but are not limited to, breast and head and neck.

**Breast Tumors**
The treatment of small cancers of the breast has evolved from total mastectomy to more conservative treatment options such as lumpectomy, with more acceptable cosmetic outcomes and preservation of the breast. The selection of surgical approach balances the patient’s desire for breast conservation and the need for tumor-free margins in resected tissue. Minimally invasive nonsurgical techniques such as RFA are appealing if they can produce local control and survival equivalent to breast-conserving surgical alternatives. Nonsurgical ablative techniques pose difficulties such as the inability to determine tumor size, complete tumor cell death, and local recurrence. Additionally, RFA can burn the skin and damage to muscle, possibly limiting use in patients with tumors near the skin or chest wall.

**Thyroid Tumors**
Surgical resection is the primary treatment choice for medically unresponsive, symptomatic benign thyroid tumors and thyroid carcinomas. However, techniques for ablation of thyroid tumors (eg, RFA, microwave ablation) are being investigated.
Head and Neck Cancer
In patients with head and neck cancer with recurrent disease, surgical salvage attempts are poor in terms of local control, survival, and quality of life, and these recurrent tumors are often untreatable with standard salvage therapies. Palliative chemotherapy or comfort measures may be offered. The safety and efficacy of RFA has been investigated as an option for palliative treatment in these situations.

Regulatory Status
The U.S. Food and Drug Administration (FDA) issued a statement September 24, 2008, concerning the regulatory status of radiofrequency ablation (RFA). FDA has cleared RFA devices for the general indication of soft tissue cutting, coagulation, and ablation by thermal coagulation necrosis. Under this general indication, RFA can be used to ablate tumors, including lung tumors. Some RFA devices have been cleared for additional specific treatment indications, including partial or complete ablation of nonresectable liver lesions and palliation of pain associated with metastatic lesions involving bone. FDA has not cleared any RFA devices for the specific treatment indication of partial or complete ablation of lung tumors, citing lack of sufficient clinical data to establish safety and effectiveness for this purpose. FDA has received reports of death and serious injuries associated with the use of RFA devices in the treatment of lung tumors.

Rationale
This evidence review was originally created in October 2003 and has been regularly updated with searches of the MEDLINE database. The most recent literature update was performed through July 26, 2016. The following is a summary of key findings to date.

Osteolytic Bone Metastases
Goetz et al reported on an international study (N=43) conducted at 9 centers in which patients with painful osteolytic bone metastases were treated palliatively with radiofrequency ablation (RFA). The study’s primary outcome measure was the Brief Pain Inventory–Short Form, a validated scale from 0 (no pain) to 10 (worst pain imaginable). Patient eligibility required baseline values of 4 or more from 2 or fewer painful sites. Thirty-nine (91%) of the patients had previously received opioids to control pain from the lesion(s) treated with RFA, and 32 (74%) had prior radiotherapy to the same lesion. Mean pain score at baseline was 7.9 (range, 4-10). At 4, 12, and 24 weeks after RFA, average pain scores decreased to 4.5, 3.0, and 1.4, respectively (all p<0.001). Forty-one (95%) patients achieved a clinically significant improvement in pain scores, prospectively defined as a decrease of 2 units from baseline. Investigators also reported statistically significant (p=0.01) decreases in opioid use at weeks 8 (by 59%) and 12 (by 54%).

An earlier case series showed that palliative RFA provided significant pain relief in 9 (90%) of 10 patients with unresectable, osteolytic spine metastases who had no other treatment options. Pain was reduced by an average of 74%; back pain–related disability was reduced by an average of 27%. Neurologic function was
preserved in 9 patients and improved in the other. An additional small case series of 24 patients with painful metastatic bone tumors who experienced pain-alleviating effects with RFA is consistent with other evidence.³

**Section Summary: Osteolytic Bone Metastases**
Case series have shown clinically significant pain relief and reduction in opioid use following treatment with RFA of osteolytic pain metastases in patients with no or limited treatment options.

**Osteoid Osteomas**

**Systematic Reviews**
Lanza et al reported on a systematic review of various ablative techniques for osteoid osteomas in 2014.⁴ Included in the review were 23 articles on RFA, 3 on interstitial laser ablation, and 1 with a combination of ablation techniques, totaling 27 articles (total N=1772 patients). Mean technical success was 100% and clinical success, defined as being pain-free, ranged from 94% to 98%, depending on length of follow-up. Complications occurred in 2% of patients and included skin or muscle burn in 9 patients, 4 infections, nerve lesions or tool breakage in 3 patients each, delayed skin healing, hematoma, and failure to reach target temperature in 2 patients each, and fracture, pulmonary aspiration, thrombophlebitis, and cardiac arrest in 1 patient each. Eighty-six patients had tumor recurrence.

**Longer Term Follow-up**
An observational study published in 2015 evaluated long-term clinical outcomes after computed tomography (CT)‒guided RFA in patients diagnosed with osteoid osteoma located in the upper and lower extremities.⁵ The study population included 52 patients with a typical clinical history and radiologically confirmed osteoid osteoma who received CT-guided RFA treatment from 1998 to February 2014 at Aarhus University Hospital, Denmark. The clinical outcome was evaluated based on patient-reported outcome measures and medical record review. The response rate was 52 (87%) of 60. After 1 RFA treatment, 46 (88%) of 52 patients experienced pain relief, and 51 (98%) of 52 patients had pain relief after repeat RFA. One patient underwent open resection after RFA. No major complications were reported; 4 patients reported minor complications including small skin burn, minor skin infection and hypoesthesia at needle entry point. In all, 50 (96%) of 52 patients were reported to be "very satisfied" with the RFA treatment.

In 2012, Rimondi et al reported on a retrospective study of 557 patients treated with CT-guided RFA as primary treatment for nonspinal osteoid osteomas.⁶ All patients were followed for a mean of 3.5 years (0.5-9 years). Pain relief occurred in all 557 patients within the first week after RFA and continued in 533 (96%) patients who remained asymptomatic through their last follow-up. Pain recurrence occurred in 24 (4%) patients. Complications occurred in 5 patients and included thrombophlebitis, skin burn, broken electrode, and 2 procedures in which the RFA generator failed to reach maximum temperature.
Rosenthal et al reported their experience over an 11-year period with 271 RFA procedures for osteoid osteomas in 263 patients. Short-term outcome was evaluated to detect procedure-related problems; by this definition, all procedures were considered technically successful. Long-term clinical success data (defined as being free of pain without the necessity of additional procedures) were available in 126 patients, with a complete clinical success observed in 89%. For procedures performed as the initial treatment, the success rate was 91%.

Section Summary: Osteoid Osteomas
Numerous case series and a systematic review of case series have evaluated RFA for the treatment of painful osteoid osteomas. In a systematic review of thermal ablation techniques, clinical success (pain-free) was achieved in 94% to 98% of patients. Most patients (89%-96%) remained pain-free at longer term follow-up.

Localized Renal Cell Carcinoma

Systematic Reviews
In a 2014 systematic review and meta-analysis, Katsanos et al reviewed 1 RCT and 5 cohort studies (total N=587 patients) on thermal ablation (RFA or microwave) or nephrectomy for small renal tumors with a mean size of 2.5 cm. The local recurrence rate was 3.6% in both groups (relative risk [RR], 0.92; 95% confidence interval [CI], 0.4 to 2.14; p=0.79). Disease-free survival was also similar in both groups up to 5 years (hazard ratio, 1.04; 95% CI, 0.48 to 2.24; p=0.92). However, the overall complication rate was significantly lower in the patients undergoing ablation (7.4%) versus nephrectomy (11.1%; pooled RR=0.55; 95% CI, 0.31 to 0.97; p=0.04).

In another systematic review and meta-analysis from 2014, Wang et al reported on studies on RFA and partial nephrectomy for stage 1 (no more than 7 cm across) renal tumors. Included in the review were 166 studies (total N=9565 patients). The rate of local progression was greater with RFA than with laparoscopic/robotic or open partial nephrectomy (4.6%, 1.2%, 1.9%, respectively; p<0.001). RFA had more frequent minor complications than laparoscopic/robotic or open partial nephrectomy (13.8%, 7.5%, 9.5%, respectively; p<0.001). However, the rate of major complications was greater with open partial nephrectomy than laparoscopic/robotic partial nephrectomy or RFA (7.9%, 7.9%, 3.1%, respectively, p<0.001).

In 2012, El Dib et al conducted a meta-analysis evaluating RFA and cryoablation for small renal masses. Selected were 11 RFA case series (426 patients) and 20 cryoablation case series (457 patients) published through January 2011. Mean tumor size was 2.7 cm (range, 2-4.3 cm) in the RFA group and 2.5 cm (range, 2-4.2 cm) in the cryoablation group. Mean follow-up times for the RFA and cryoablation groups were 18.1 and 17.9 months, respectively. Clinical efficacy, defined as cancer-specific survival rate, radiographic success, no evidence of local tumor progression, or distant metastases, did not differ significantly between groups. The pooled proportion of clinical efficacy for RFA was 90% (95% CI, 86% to 93%) and 89% (95% CI, 83% to 94%) for cryoablation.
Kunkle and Uzzo conducted a comparative meta-analysis evaluating cryoablation and RFA as primary treatments for small renal masses.\textsuperscript{11} Forty-seven case series representing 1375 renal tumors were analyzed. Of 600 lesions treated with cryoablation, 494 underwent biopsy before treatment versus 482 of 775 treated with RFA. The incidence of renal cell carcinoma with known pathology was 71.7\% in the cryoablation group and 90\% in the RFA group. The mean duration of follow-up after RFA was 15.8 months. Local tumor progression was reported in 31 of 600 lesions after cryoablation and in 100 of 775 lesions after RFA, a difference that was statistically significant (p<0.001). Progression to metastatic disease was described in 6 (1\%) of 600 lesions after cryoablation versus 19 (3\%) of 775 after RFA (p=0.06).

**Longer Term Follow-Up**
Stern et al retrospectively compared patients with stage T1a renal tumors, confirmed by pathology to be renal cell carcinoma, treated with partial nephrectomy (n=34) or RFA (n=34).\textsuperscript{12} Mean follow-up for the partial nephrectomy group was 47 months (range, 24-93 months) and 30 months (range, 18-42 months) for the RFA group. The 3-year recurrence-free survival rate was 95.2\% for partial nephrectomy and 91.4\% for RFA (p=0.58). There were no disease-specific deaths in either group. In this small study, intermediate outcomes for patients with T1a renal cell carcinomas were similar whether treated with partial nephrectomy or RFA.

A 2016 publication by Iannuccilli et al reported a mean 34.1-month follow-up (range, 1-131 months) of RFA with intent to cure in 203 patients with renal tumors.\textsuperscript{13} Patients who were referred for RFA were either high risk or had refused surgery. Smaller tumors were treated with a single electrode with a 2- or 3-cm active tip. Larger tumors were treated with a cluster electrode with 3 active tips. Patients were assessed annually for appearance of residual tumor at the treatment site, and 26 (13\%) had residual disease. Treatment effectiveness was 87\% during follow-up. The likelihood was increased for tumors 3.5 cm or larger, clear cell subtype, and treatment temperature of 70\º or less. All-cause mortality increased with increasing tumor size. Median survival was 7 years for patients with tumors less than 4 cm, with 80\% survival at 5 years. Major complications, including urinary stricture or urine leak, occurred in 8 (3.9\%) treatments.

**Section Summary: Localized Renal Cell Carcinoma**
The evidence on RFA for renal tumors includes meta-analyses of 1 RCT, cohort studies, and case series that have compared RFA with nephrectomy or cryoablation. A 2014 meta-analysis that included 1 RCT and 5 cohort studies found RFA was as effective as nephrectomy for small renal tumors, with a reduction in complications. Another 2014 meta-analysis that included case series of stage 1 (no more than 7 cm across) renal tumors found that the rate of local progression was greater with RFA than with nephrectomy, but the rate of major complications was lower with RFA. The different results of the 2 meta-analyses may be due to differences in tumor size in selected studies as well as selection bias when comparing case series. The importance of tumor size is reinforced by a large case
series with a mean 34-month follow-up that found that residual disease and mortality increased with tumors over 4 cm.

Primary Pulmonary Tumors and Nonpulmonary Metastases

Systematic Reviews
In 2013, the Agency for Healthcare Research and Quality (AHRQ) published a Comparative Effectiveness Review of local nonsurgical therapies for stage 1 non-small-cell lung cancer (NSCLC). In this review, no comparative RFA studies were identified. The AHRQ report found that available evidence was insufficient to draw conclusions on the comparative effectiveness of local nonsurgical therapies for NSCLC, including RFA. In a 2014 systematic review of RFA, surgery, and stereotactic body radiotherapy (SBRT) for colorectal cancer lung metastases, no randomized trials were identified, and evidence was insufficient to draw conclusions on the comparative effectiveness of these therapies.

In a 2012 review of 16 studies, Bilal et al compared RFA with SBRT in patients with inoperable early-stage NSCLC. The authors found overall survival (OS) rates for RFA and SBRT were similar in patients at 1 year (68.2%-95% vs 81%-85.7%) and 3 years (36%-87.5% vs 42.7%-56%), all respectively. However, survival rates at 5 years were lower with RFA (20.1%-27%) than with SBRT (47%). These findings were drawn from comparisons of results of uncontrolled case series and retrospective reviews.

In a 2011 evidence-based review, 46 studies on RFA for lung tumors were evaluated, which included 2905 ablations in 1584 patients with a mean tumor size of 2.8 cm. Twenty-four studies reported rates of local recurrence, which occurred in 282 (12.2%) cases at a mean follow-up time of 13 months (range, 3-45 months). Primary lung cancer rates of local recurrence did not differ significantly (22.2%) from metastases (18.1%). Twenty-one studies reported mean OS rates of 59.4% at a mean follow-up time of 17.7 months. Mean cancer-specific survival rate was 82.6%, at a mean follow-up of 17.4 months. Mean overall morbidity was 24.6% and most commonly included pneumothorax (28.3%), pleural effusion (14.8%), and pain (14.1%). Mortality related to the RFA procedure was 0.21%, overall.

Comparative Studies
In 2010, Zemlyak et al prospectively compared 3 treatments for medically inoperable patients with stage 1 NSCLC: RFA in 12 patients, sublobar resection in 25 patients, and percutaneous cryoablation in 27 patients. At 3-year follow-up, survival rates did not differ significantly between groups. OS and cancer-specific 3-year survival were 87.5%, 87.1%, and 77% and 87.5%, 90.6%, and 90.2%, respectively, in the 3 groups. The authors concluded that all 3 procedures were reasonable options for treatment of lung tumors in patients unfit for major surgery. The authors also noted that because surgeons chose the treatment option with patient input for this study, selection bias limited study interpretation. In 2011, Huang et al prospectively followed 329 consecutive patients treated with RFA for lung tumors (237 primary, 92 metastatic). Complications were
experienced by 34.3% (113) of patients and were most commonly pneumothorax (19.1%). OS rates at 2 and 5 years were 35.3% and 20.1%, respectively. The risk of local progression did not differ significantly for tumors less than 4 cm but were statistically significant for tumors greater than 4 cm.

**Inoperable Lung Tumors**

A prospective, single-arm, multicenter trial from 7 centers in Europe, the United States, and Australia reported the technical success, safety, response of tumors, and survival in 106 patients with 183 lung tumors. All patients were considered unsuitable for surgery and unfit for radiotherapy or chemotherapy. Tumors measured less than 3.5 cm (mean, 1.7 cm; SD=1.3) and included patients with NSCLC (n=22), colorectal metastases (n=41), and other metastases (n=16). Technical success rate was 99%. Patients were followed for 2 years, and a confirmed complete response lasting at least 1 year was observed in 88% of assessable patients, with no differences in response rate between patients with primary and metastatic tumors. OS in patients with NSCLC was 70% at 1 year (95% CI, 51% to 83%; cancer-specific survival, 92% [78% to 98%]), and 48% at 2 years (95% CI, 30% to 65%; cancer-specific survival, 73% [54% to 86%]). OS in patients with metastatic colorectal cancer was 89% at 1 year (95% CI, 76% to 95%; cancer-specific survival, 91% [78% to 96%]) and 66% at 2 years (95% CI, 53% to 79%; cancer-specific survival 68% [54% to 80%]). OS in patients with other metastases was 92% at 1 year (95% CI, 65% to 99%; cancer-specific survival, 93% [67% to 99%]) and 64% at 2 years (95% CI, 43% to 82%; cancer-specific survival, 67% [48% to 84%]). Patients with stage 1 NSCLC (n=13) had OS rates of 75% (95% CI, 45% to 92%) at 2 years (cancer-specific, 92%; 95% CI, 66% to 99%). No differences in response were seen between patients with NSCLC or lung metastases.

Zhu et al assessed the incidence and risk factors of various pulmonary neoplastic complications after RFA. The authors prospectively evaluated the clinical and treatment-related data for 129 consecutive percutaneous RFA treatment sessions for 100 patients with inoperable lung tumors. There was no postprocedural mortality. The overall morbidity rate was 43% (55/129). The most common adverse effect was pneumothorax, occurring in 32% (41/129) of treatment sessions. Other significant complications included pleuritic chest pain (18%), hemoptysis (7%), pleural effusions (12%), and chest drain insertion (20%). Both univariate and multivariate analyses identified more than 2 lesions ablated per session as a significant risk factor for overall morbidity, pneumothorax, and chest drain insertion. Length of the ablation probe trajectory greater than 3 cm was an additional independent risk factor for overall morbidity and pneumothorax.

In 2009, Pennathur et al reported on 100 patients with inoperable lung tumors. Forty-six patients had primary lung neoplasm, 25 had recurrent cancer, and 29 had pulmonary metastases. Mean follow-up was 17 months. Median OS for all patients was 23 months. The probability of 2-year OS for primary lung cancer patients, recurrent cancer patients, and metastatic cancer patients were 50% (95% CI, 33% to 65%), 55% (95% CI, 25% to 77%), and 41% (95% CI, 19% to 62%), respectively.
Section Summary: Primary Pulmonary Tumors and Nonpulmonary Metastases
The evidence on RFA for primary NSCLC and nonpulmonary tumor metastatic to the lung includes prospective and retrospective case series of patients with inoperable lung tumors with over 100 patients and systematic reviews of those studies. No RCTs identified compared treatment approaches.

For inoperable lung tumors, a multicenter study found that RFA for tumors less than 3.5 cm can lead to a complete response in as many as 88% of patients for at least 1 year. Two-year survival has been reported to range from 41% to 75% in case series. Survival at 1 and 2 years appears to be similar following treatment with RFA or SART in patients with inoperable lung tumors. Survival rates at 5 years were lower with RFA (20.1%-27%) than with SART (47%), but this finding was drawn from comparisons of uncontrolled case series and retrospective reviews. Prospective comparison in an RCT would permit greater certainty for this finding, but the studies are consistent with some effect of RFA on lung tumors.

Breast Tumors
Systematic Reviews
In 2010, Zhao and Wu conducted a systematic review of 38 studies on ablation techniques for breast cancer treatment published from 1994 to 2009. Nine studies focused on RFA. They included small breast tumors ranging in size from 0.5 to 7 cm. Tumor resection was performed immediately after ablation or up to 4 weeks after RFA. Complete coagulation necrosis rates of 76% to 100% were reported. The results of this review suggested RFA for breast cancer tumors is feasible, but further studies with longer follow-up on survival, tumor recurrence, and cosmetic outcomes are needed to establish clinical efficacy.

In another 2010 review, Soukup et al examined 17 studies on RFA for the treatment of breast tumors and found RFA is feasible and promising. Even though few adverse events and complications occurred with breast RFA, incomplete tumor ablation remains a concern.

Clinical Studies
In 2012, Wilson et al reported on 73 patients with invasive breast cancer who had a lumpectomy followed immediately by RFA to the lumpectomy bed. The average breast tumor size was 1.0 cm (range, 0.2-2.6 cm) and follow-up averaged 51 months. Disease-free survival was 100%, 92%, and 86% at 1, 3, and 5 years, respectively. One patient had tumor recurrence within 5 cm of the lumpectomy site and 3 patients had ipsilateral breast recurrences.

In a 2011 phase 1/2 study, 49 patients were treated with RFA for breast tumors (mean size, 1.70 cm) followed immediately with surgical resection. Complete ablation was achieved in 30 (61%) patients as assessed by hematoxylin-eosin (H&E) staining and/or nicotinamide adenine dinucleotide (NADH) diaphorase staining. Complete ablation increased to 83% in 24 patients with tumor sizes of 2
cm or less in diameter. Adverse events related to the procedure included 3 muscle and 2 skin burns.

In 2009, Imoto et al reported on a series of 30 patients with T1N0 breast cancer who had sentinel node biopsy followed by RFA and breast-conserving surgery. Twenty-six patients showed pathologic degenerative changes in tumor specimens with H&E staining, and, in 24 of 26 cases, tumor cell viability was diagnosed as negative by NADH diaphorase staining. Two patients had skin burns and 7 had muscle burn related to RFA.

In a 2008 two-stage phase 2 clinical trial, patients with histologically confirmed noninflammatory and 3 cm or less ipsilateral breast tumor recurrence were treated with RFA followed by mastectomy. The study was ended early due to lack of efficacy of the technique tested.

**Section Summary: Breast Tumors**
Evidence has reported varied and incomplete ablation rates as well as concerns about postablation tumor cell viability. Long-term improvements in health outcomes have not been demonstrated. Additionally, available the studies do not permit comparisons with conventional breast-conserving procedures. Further studies, with long-term follow-up, are needed to determine whether RFA for small breast cancers can provide local control and survival rates comparable with conventional breast-conserving treatment.

**Benign Thyroid Nodules**

**Systematic Reviews**
In 2014 Fuller et al reported on a systematic review of studies on RFA for benign thyroid tumors. Included in the review were 9 studies (5 observational studies, 4 randomized studies) totaling 306 treatments. After RFA, statistically significant improvements were reported in nodule size reduction (29.77 mL; 95% CI, -13.83 to -5.72 mL), combined symptom improvement and cosmetic scores on the 0 to 6 scale (mean, -2.96; 95% CI, -2.66 to -3.25), and withdrawal from methimazole (odds ratio, 40.34; 95% CI, 7.78 to 209.09). Twelve adverse events were reported, 2 of which were considered significant but did not require hospitalization.

In 2012, the Korean Society of Thyroid Radiology (KSTR) developed consensus recommendations for RFA of thyroid tumors after a review of the literature found few controlled studies. The recommendations indicated RFA may be appropriate for the treatment of benign thyroid nodules, inoperable thyroid nodules, and recurrent thyroid cancers in the operation bed and lymph nodes. The KSTR recommendations also indicated RFA should not be used for primary thyroid cancers or follicular neoplasms, citing no evidence of treatment benefit.

**Longer Term Outcomes and Adverse Events**
In 2013, Lim et al reported on a case series of 111 patients treated with RFA for 126 benign nonfunctioning thyroid nodules. Mean duration of patient follow-up was 49.4 months. RFA significantly decreased the volume of the thyroid nodules
from 9.8±8.5 mL to 0.9±3.3 mL (p<0.001), for a mean volume decrease of 93.4%. Tumors recurred in 7 (5.6%) patients. Complications occurred in 4 (3.6%) patients. There was also a significant improvement in thyroid symptom scores (p<0.001).

Baek et al retrospectively reviewed RFA for 1543 benign thyroid nodules in 1459 patients at 13 thyroid centers. Thirty-eight (3.3%) complications occurred and included 20 major complications: voice changes (n=15), brachial plexus injury (n=1), tumor rupture (n=3), and permanent hypothyroidism (n=1). Twenty-eight minor complications included: hematoma (n=15), skin burn (n=4), and vomiting (n=9).

A case series of 94 elderly subjects with solid or mainly solid benign thyroid nodules was reported by an Italian center. Thyroid nodule volume, compressive symptoms, and thyroid function were evaluated at baseline and 12 to 24 months posttreatment. All thyroid nodules significantly decreased in size after RFA. Compressive symptoms improved in all patients, disappearing completely in 88% of patients. Hyperthyroidism resolved in most patients, permitting complete withdrawal of methimazole therapy in 79% of patients with pretoxic and toxic thyroid nodules (100% with pretoxic and 53% with toxic thyroid nodules).

Section Summary: Benign Thyroid Tumors
Evidence on the treatment of benign thyroid nodules includes RCTs, case series, and systematic reviews of these studies. A systematic review that included 4 RCTs and 5 observational studies found significant reductions in nodule size and withdrawal from methimazole following treatment with RFA. Reports of complications vary. The most frequent major complication from a large multicenter series was voice changes.

Evidence on the treatment of other tumors consists of small number of case series or retrospective comparative studies for each of the tumor types. Reporting on outcomes is limited. These studies are insufficient to evaluate the effect of RFA.

Miscellaneous Tumors

Thyroid Cancer
In 2016, Kim et al reported a comparative review of 73 patients with recurrent thyroid cancer smaller than 2 cm who had been treated with RFA (n=27) or repeat surgery (n=46). RFA was performed in cases of patient refusal to undergo surgery or poor medical condition. Data were weighted to minimize potential confounders. The 3-year recurrence-free survival rates were similar for RFA (92.6%) and surgery (92.2%, p=0.681). Posttreatment hoarseness rate did not differ between the RFA (7.3%) and surgery (9.0%) groups. Posttreatment hypocalcemia occurred only in the surgery group (11.6%).

Head and Neck Cancer
In 2011, Owen et al reported on RFA for 13 patients with recurrent and/or unresectable head and neck cancer who failed curative treatment. Median patient
survival was 127 days. While stable disease was reported in 8 patients after RFA, and quality-of-life scores improved, 3 deaths occurred (1 carotid hemorrhage, 2 strokes).

A case series of RFA for 14 patients with recurrent advanced head and neck malignancies was reported by Brook et al. Tumor targeting and electrode deployment was successful in all cases, and 4 of 6 patients who completed quality-of-life assessments showed improvement. Three major complications (in 27 [11%] applications) occurred 7 days to 2 weeks postprocedure. They included stroke, carotid artery rupture leading to death, and threatened carotid artery rupture with subsequent stroke. Retrospective analysis of intraprocedural CT scans revealed that the retractable electrodes were within 1 cm of the carotid artery during ablation in these cases.

A case series showed palliative CT-guided RFA provided subjective improvement with regard to pain, appearance, and function in 12 patients who had recurrent and advanced head and neck malignancies and were not candidates for radiotherapy or surgery. The procedure appeared reasonably safe and feasible for this indication.

**Other Miscellaneous Tumors**

A large 2015 series evaluated the effectiveness and safety of RFA for uterine myomas in a 10-year retrospective cohort study. From July 2001 to July 2011, a total of 1216 patients treated for uterine myomas were divided into 2 groups. Group A consisted of 476 premenopausal patients (average age, 36 years) who had an average of 1.7 myomas with average diameter of 4.5 cm. Group B consisted of 740 menopausal patients (average age, 48 years) with an average of 2.6 myomas with average diameter of 5.0±2.5 cm. Patients were followed for a mean of 36 months. At 1, 3, 6, 12, and 24 months after RFA, the average diameters of myomas in group A were 3.8, 3.0, 2.7, 2.4, and 2.2 cm, respectively; 48% (227/476) of patients had residual tumor at 12 months. In group B, myoma diameters were 4.7, 3.7, 3.3, 2.3, and 2.3 cm, respectively; 59% (435/740) of patients had trace disease at 12 months. Three months after RFA treatment, myoma volumes were significantly reduced in both the groups (p<0.01), although group B had a higher rate of residual tumor 12 months after RFA than group A (p<0.05). Clinical symptoms and health-related quality of life were significantly improved after RFA in both groups. The postoperative recurrence rate of uterine myomas was significantly higher in group A at 10.7% (51/476) than in group B at 2.4% (18/740; p<0.05).

One case series of 13 patients with adrenal neoplasms treated with RFA was identified. Eleven of the 13 lesions were treated successfully with RFA, defined by follow-up CT scans and normalization of preprocedural biochemical abnormalities.

A single-arm, retrospective, paired-comparison study evaluated the short-term efficacy of RFA in relation to pain and functional impact in patients with unresectable, painful soft tissue neoplasms recalcitrant to conventional
therapies. Patients had tumors located in a variety of sites including chest wall, pelvis, breast, perirectal, renal, aortocaval, retroperitoneal, and superficial soft tissues. All had failed conventional methods of palliation or experienced dose-limiting adverse events from pain medication. Although not all Brief Pain Inventory scores were statistically significant, all mean scores trended down with increased time after ablation. Complications from RFA were minor or insignificant in all but 1 patient who had skin breakdown and infection of an ablated superficial tumor site.

Additional research has addressed the use of RFA in solid malignancies and in the pancreas. A recent systematic review examined studies of ablative therapies, including RFA, in patients with locally advanced pancreatic cancer. No RCTs were identified, and conclusions limited by the sparse evidence available on RFA in this setting.

Stereotactic radiofrequency thermocoagulation for epileptogenic hypothalamic hamartomas has been described in a retrospective analysis of 25 patients with gelastic seizures (a rare type of seizure). Other seizure types were exhibited in 22 (88.0%) patients, precocious puberty in 8 (32.0%), behavioral disorder in 10 (40.0%), and mental disability in 14 (56.0%). Gelastic seizures resolved in all but 2 patients. Complete seizure freedom was achieved in 19 (76.0%) patients. These patients experienced resolution of all seizure types and behavioral disorder and also demonstrated intellectual improvement.

Preliminary results of endoscopic RFA of rectosigmoid tumors have been described by Vavra et al. Twelve patients were treated with the Endoblate RFA device, with 10 patients having surgical resection after ablation. Histology of the resected specimens showed that, on average, 82% (range, 60%-99%) of the tumor mass was destroyed in the ablation zone.

Small case series on RFA for colorectal and rectal carcinoma have demonstrated a debulking role for RFA. These case series did not permit comparison with available alternative.

**Section Summary: Miscellaneous Tumor**

Evidence on use of RFA to treat other types of tumors consists of small number of case series or retrospective comparative studies for each tumor type. Reporting on outcomes is limited. The evidence base is insufficient to evaluate the effect of RFA.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

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<th>NCT No.</th>
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<td>NCT01051037</td>
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Ablation for Medically Inoperable and Recurrent Lung Tumors Near Central Airways

Radiofrequency Ablation in Resectable Colorectal Lung Metastasis: A Phase-II Clinical Trial

NCT00776399

70
Aug 2017

Unpublished

Single Session Treatment of RFA Versus EA for Predominantly Cystic Thyroid Nodules: A Randomized Controlled Trial

NCT01778400

50
Jan 2014

Zero Ischemia Laparoscopic Radio Frequency Ablation Assisted Enucleation of Renal Cell Carcinoma With T1a Stage: Clinical Outcomes of a Randomised Controlled Trial

NCT01838720

90
Oct 2014

(unknown)

NCT: national clinical trial.

Summary of Evidence

Osteolytic Bone Metastases
For individuals who have painful osteolytic bone metastases who have failed or are poor candidates for standard treatments who receive radiofrequency ablation (RFA), the evidence includes case series. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. Case series have shown clinically significant pain relief and reduction in opioid use following treatment of osteolytic pain metastases. The population is comprised of patients with limited or no treatment options, for whom short-term pain relief is an appropriate clinical outcome. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

Osteoid Osteomas
For individuals who have painful osteoid osteomas who receive RFA, the evidence includes numerous observational studies and a systematic review of these studies. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. In a systematic review of thermal ablation techniques, clinical success (pain-free) was achieved in 94% to 98% of patients. Most patients (89%-96%) remained pain-free when assessed at longer term follow-up. Although no randomized trials of RFA for osteoid osteomas have been performed, the uncontrolled studies have demonstrated RFA can provide adequate symptomatic relief with minimal complications, for whom short-term symptom relief and avoidance of invasive procedures are appropriate clinical outcomes. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

Localized Renal Cell Carcinoma
For individuals who have localized renal cell carcinoma that is no more than 4 cm in size who receive RFA, the evidence includes 1 randomized controlled trial (RCT), a large number of observational studies, and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. A recent meta-analysis that included only an RCT and cohort studies found that RFA was as effective as nephrectomy for small renal tumors, with a reduction in complications. Another recent meta-analysis, which
included case series of stage 1 (≤7 cm across) renal tumors, found that the rate of local progression was greater with RFA than with nephrectomy. The differing results in these meta-analyses may be due to differences in tumor size in selected studies as well as potential selection bias when evaluating case series. Although inconsistent, the evidence does suggest that for small renal tumors, RFA may result in a similar rate of disease progression with a lower complication rate than nephrectomy. However, comparative trials are needed to determine with greater certainty the effects of these treatments in the same patient population. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Inoperable Primary Pulmonary Tumors and Nonpulmonary Metastases**

For individuals who have inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung who receive RFA, the evidence includes observational studies and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. A multicenter study found that, for tumors less than 3.5 cm, RFA can lead to a complete response in as many as 88% of patients for at least 1 year. Two-year survival has been reported to range from 41% to 75% in case series, with 5-year survival rates of 20% to 27%. In general, the evidence shows RFA results in adequate survival and tumor control in patients who are not surgical candidates, with low morbidity rates. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Breast Tumors**

For individuals who have breast tumors who receive RFA, the evidence includes observational studies and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Evidence has reported varied and incomplete ablation rates with concerns about postablation tumor cell viability. Long-term improvements in health outcomes have not been demonstrated. Additionally, available studies do not allow comparisons with conventional breast-conserving procedures. Further studies, with long-term follow-up, are needed to determine whether RFA of the breast for small cancers can provide local control and survival rates comparable with conventional breast-conserving treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Benign Thyroid Tumors**

For individuals who have benign thyroid tumors who receive RFA, the evidence includes RCTs, case series, and systematic reviews of these studies. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. A systematic review that included 4 RCTs and 5 observational studies found significant reductions in nodule size and withdrawal from methimazole following treatment with RFA. Reports of complications have varied. The most frequent major complication from a large multicenter series of specialty centers was voice change. The evidence is insufficient to determine the effects of the technology on health outcomes.
Miscellaneous Solid Tumors
For individuals who have miscellaneous tumors (eg, head and neck, thyroid cancer, pancreas) who receive RFA, the evidence includes a small number of case series and retrospective comparative studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. There is a limited evidence base for each tumor type. Reporting on outcomes or comparisons with other treatments is limited. These studies are insufficient to evaluate the effect of RFA. The evidence is insufficient to determine the impact of the technology on health outcomes.

Supplemental Information

Clinical Input Received 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.

2010 Input
In response to requests, input was received from 2 physician specialty societies (4 reviewers) and 2 academic medical centers (4 reviewers) while this policy was under review in 2010. The input was similar to that in 2009, except support for use of RFA to treat lung tumors was declined (only 1 respondent indicated this was an option in tumors metastatic to lung). One respondent also indicated potential use for adrenal tumors. Clinical input supported RFA ablation for localized renal cell carcinoma no more than 4 cm in size when preservation of kidney function is necessary and a standard surgical approach would likely to substantially worsen kidney function or when the patient is not considered a surgical candidate.

2009 Input
In response to requests, input was received from 1 physician specialty society (4 reviews) and from 2 academic medical centers (3 reviews) while this policy was under review in 2009. All reviewers supported the use of RFA in the treatment of painful bone metastases that have failed standard treatment and in the treatment of osteoid osteomas. The reviewers were divided on the use of RFA for lung tumors, although several agreed that, while it may be useful in a select population of patients, it should be used in the clinical trial setting. The reviewers were also split with regard to RFA in the treatment of renal tumors, with some supporting its use in a select population of patients. With the exception of 1 disagreement and 1 nonresponse, the reviewers agreed to the investigational statement on the use of RFA in all other tumors outside the liver that are addressed in this policy.

Practice Guidelines and Position Statements
American College of Chest Physicians
The American College of Chest Physicians (ACCP) guidelines on the treatment of stage 1 and 2 non-small-cell lung cancer (NSCLC) have indicated RFA has been used effectively in clinical stage 1 NSCLC. Therefore, in medically inoperable patients, peripheral NSCLC tumors less than 3 cm may be treated with RFA.\textsuperscript{51} ACCP also collaborated with the Society of Thoracic Surgeons to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC.\textsuperscript{52} These 2012 consensus guidelines indicated RFA is an alternative treatment option in patients who are not surgical candidates due to severe medical comorbidity.

National Comprehensive Cancer Network
National Comprehensive Cancer Network (NCCN) practice guidelines for the treatment of NSCLC (v.4.2016) state that “studies suggest that RFA may be an option for node-negative patients who either refuse surgery or cannot tolerate surgery” and that “optimal candidates for RFA include patients with an isolated peripheral lesion less than 3 cm.”\textsuperscript{53} Additionally, the guidelines note “RFA can be used for previously irradiated tissue and for palliation.”

NCCN guidelines for colon cancer (v.2.2016) indicate that “ablative techniques can be considered [in patients whose primary colon tumor was resected for cure when metastatic lung tumors are] unresectable and amenable to complete ablation” (category 2A).\textsuperscript{54} The guidelines also state that “ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection.”

NCCN guidelines for thyroid carcinoma (v.1.2016) indicate ablation techniques such as radiofrequency may be considered for palliative resection of symptomatic distant metastases.\textsuperscript{55} Ablation may also be considered for symptomatic or asymptomatic distant metastases when there is progressive disease.

NCCN guidelines (v.3.2016) indicate RFA is an ablative option for the treatment of kidney cancer in select patients with clinical stage T1 lesions who are not candidates for surgery, though ablative techniques have shown higher local recurrence rates than surgery.\textsuperscript{56} RFA is also an option in select patients (eg, elderly patients, others) with competing health risks.

NCCN guidelines do not address the use of RFA in head and neck cancer.

NCCN guidelines do not address RFA in the management of breast cancer.

National Institute for Clinical Excellence
Guidance issued in 2004 from the National Institute for Clinical Excellence (NICE) has indicated that “current evidence on the safety and efficacy of computed tomography (CT)-guided thermocoagulation of osteoid osteoma appears adequate to support its use, provided that the normal arrangements are in place for consent, audit and clinical governance.”\textsuperscript{57}
NICE guidance updated in 2010 has indicated that “evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) for renal cancer in the short and medium term appears adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit, and provided that patients are followed up in the long term.”

NICE 2010 guidance on RFA for primary and secondary lung cancers has stated: “[C]urrent evidence on the efficacy of percutaneous radiofrequency ablation (RFA) for primary or secondary lung cancers is adequate in terms of tumor control.”

NICE also indicated RFA may “be used in patients with small, early-stage lung cancers or small numbers of lung metastases who are unsuitable for, or prefer not to undergo, surgery. It may also have a place in multi-modality treatment of more advanced primary lung cancers.” The guidance warned of serious complications (eg, pneumothorax) among lung cancer patients.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References


**Billing Coding/Physician Documentation Information**

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<td>32998</td>
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<tr>
<td>49203</td>
<td>Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor 5 cm diameter or less</td>
</tr>
<tr>
<td>49204</td>
<td>Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor 5.1-10.0 cm diameter</td>
</tr>
<tr>
<td>49205</td>
<td>Excision or destruction, open, intra-abdominal tumors, cysts or endometriomas, 1 or more peritoneal, mesenteric, or retroperitoneal primary or secondary tumors; largest tumor greater than 10.0 cm diameter</td>
</tr>
<tr>
<td>50542</td>
<td>Laparoscopy, surgical; ablation of renal mass lesion(s), including intraoperative ultrasound guidance and monitoring, when performed</td>
</tr>
<tr>
<td>50592</td>
<td>Ablation, 1 or more renal tumor(s), percutaneous, unilateral, radiofrequency</td>
</tr>
<tr>
<td>76940</td>
<td>Ultrasound guidance for, and monitoring of, parenchymal tissue ablation</td>
</tr>
</tbody>
</table>

**ICD10 Codes.**

C34.0- C34.9 Malignant neoplasm of lung, primary, code range

C64.0- C64.9 Malignant neoplasm of kidney, except renal pelvis code range

C78.00- Malignant neoplasm of lung, secondary, code range
C78.02  Secondary malignant neoplasm of bone and bone marrow code range
C79.51-  
C79.52  
D16.0-  
D16.9  Benign neoplasm of bone and articular cartilage code range (includes osteoid osteoma)

CPT codes 47380 and 47382 describe open and percutaneous radiofrequency of liver tumors, respectively. In 2003, CPT code 20982 was introduced that specifically describes radiofrequency ablation of osteoid osteoma and other primary or metastatic bone tumors. In addition, CPT code 76940 (ultrasound guidance for, and monitoring of, parenchymal tissue ablation) might be used to describe the ultrasound guidance for radiofrequency ablation for both intra- and extrahepatic targets.

In 2006, a CPT code was added for radiofrequency ablation of renal tumors:

50592: Ablation, 1 or more renal tumor(s), percutaneous, unilateral, radiofrequency

In 2007, a CPT code was added for radiofrequency ablation of pulmonary tumors:

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, radiofrequency, unilateral.

There are no specific CPT codes for other targets of extrahepatic tumors, unlisted codes may be used.

Additional Policy Key Words
N/A

Policy Implementation/Update Information
3/1/2007  No policy statement changes.
3/1/08    No policy statement changes.
2/12/09   Interim Update. Policy statement added to indicate that use of RFA as treatment of osteoid osteomas that cannot be managed successfully with medical treatment may be considered medically necessary.
3/1/09    No policy statement changes.
3/1/10    No policy statement changes.
3/1/11    Except for minor clarification of policy statement related to preserving renal function, policy statements unchanged.
3/1/12    Policy statements changed to include medically necessary options for primary and metastatic pulmonary tumors.
3/1/13    Added thyroid as investigational.
3/1/14    No policy statement changes.
3/1/15    No policy statement changes.
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