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Medical Policy

Title: **Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors**

See also: *Radioembolization for Primary and Metastatic Tumors of the Liver*
Radiofrequency Ablation of Primary or Metastatic Liver Tumors
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies
Cryosurgical Ablation of Primary or Metastatic Liver Tumors

Professional
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December 7, 2018
Current Effective Date: December 7, 2018

Populations	Interventions	Comparators	Outcomes
Individuals: • With painful osteolytic bone metastases who have failed or are poor candidates for standard treatments	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Medical management • Radiotherapy	Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Medication use • Treatment-related morbidity

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Populations	Interventions	Comparators	Outcomes
Individuals: • With painful osteoid osteomas	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Medical management • Surgical excision • Core drill excision • Laser photocoagulation	Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Medication use • Treatment-related morbidity
Individuals: • With localized renal cell carcinoma no more than 4 cm in size	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Surgical excision	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With inoperable primary pulmonary tumors or nonpulmonary tumor metastatic to the lung	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Radiotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With breast tumors	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Radiotherapy • Surgical excision	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With benign thyroid tumors	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Radiotherapy • Surgical excision	Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Medication use • Treatment-related morbidity
Individuals: • With miscellaneous solid tumors (eg, head and neck, thyroid cancer, pancreas)	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Radiotherapy • Surgical excision	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity

DESCRIPTION

In radiofrequency ablation (RFA), a probe is inserted into the center of a tumor; then prong-shaped, noninsulated electrodes are projected into the tumor. Next, heat is generated locally by an alternating, high-frequency current that travels through the electrodes. The localized heat treats the tissue adjacent to the probe, resulting in a 3- 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 can sometimes be retreated. RFA may be performed percutaneously, laparoscopically, or as an open procedure.

OBJECTIVE

The objective of this policy is to determine whether the use of radiofrequency ablation improves the net health outcome in individuals with a range of tumors (including

osteolytic bone metastases, osteoid osteomas, renal cell carcinoma, lung cancer, breast tumors, and thyroid tumors).

BACKGROUND

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.

Treatment

External beam irradiation 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 such as 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 another alternative for palliating pain from 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 its location, and although they rarely exceed 1.5 cm, 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

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 period of 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 as soon as 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

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 (as in 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 radiation treatment 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 whole body radiotherapy (SBRT) has gained more widespread use, as it is a high-precision mode of therapy that allows for delivery of 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.

Breast Tumors

The treatment of small breast cancers has evolved from total mastectomy toward 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 killing, and local recurrence. Additionally, RFA can cause burning of the skin or 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.

Miscellaneous Tumors

Radiofrequency ablation has been investigated for use in individuals with different lesions in different anatomic sites. These include, but are not limited to, breast, head, and neck.

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.

Radiofrequency Ablation

RFA was initially developed to treat inoperable tumors of the liver. Recently, reports have been published 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).

REGULATORY ISSUES

The U.S. Food and Drug Administration (FDA) issued a statement September 24, 2008, concerning the regulatory status of radiofrequency ablation. The 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 as a tool 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. The 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. The FDA has received reports of death and serious injuries associated with the use of RFA devices in the treatment of lung tumors.

POLICY

A.   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.

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

C.   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 is met:

   1.   In order to preserve kidney function; **OR**

   2.   The patient is not considered a surgical candidate.

D.   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:

1. 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**

2. Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart.

E. Radiofrequency ablation may be considered **medically necessary** to treat malignant nonpulmonary tumor(s) metastatic to the lung that are no more than 3 cm in size when the following criteria are met:

1. 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**

2. There is no evidence of extrapulmonary metastases; **AND**

3. The tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart.

    The following additional criteria have been developed by clinical judgment / consensus and existing guidelines for the use of RFA in metastatic tumors to the lung and include:

    a) No more than 3 tumors per lung should be ablated;
    b) Tumors should be amenable to complete ablation; AND
    c) Twelve months should elapse before a repeat ablation is considered.

F. Radiofrequency ablation is considered **experimental / investigational** as a technique for ablation of:

1. Breast tumors;

2. Lung cancer not meeting the criteria above;

3. Renal cell cancer not meeting the criteria above;

4. Osteoid osteomas that can be managed with medical treatment;

5. Painful bony metastases as initial treatment; AND

6. 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.

RATIONALE

The most recent literature review was performed for the period through July 26, 2018. The following is a summary of key findings to date.

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

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

Osteolytic Bone Metastases

Clinical Context and Therapy Purpose

The purpose of radiofrequency ablation (RFA) in patients who have painful osteolytic bone metastases who have failed or are poor candidates for standard treatments is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with painful osteolytic bone metastases who have failed or are poor candidates for standard treatments?

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

Patients

The relevant populations of interest are individuals with painful osteolytic bone metastases who have failed or are poor candidates for standard treatments.

Interventions

The therapy being considered is RFA.

Comparators

The following therapies and practices are currently being used to make decisions about managing painful osteolytic bone metastases: medical management (eg, chemotherapy) and radiotherapy.

Outcomes
The general outcomes of interest are overall survival, reduction in pain and medication use, fractures, functional outcomes, and quality of life.

Timing
Patients would be followed for several years given the impact of bone metastases on bone remodeling.

Setting
RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Case Series
Goetz et al (2004) reported on an international study conducted at 9 centers in which 43 patients with painful osteolytic bone metastases were treated palliatively with RFA.[1] 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. The 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 clinically significant reductions 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 by Gronemeyer et al (2002) 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.[2] 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. In another small case series, Kojima et al (2006) assessed 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 reductions in pain relief and reductions in opioid use following treatment with RFA of osteolytic pain metastases in patients with no or limited treatment options.

Osteoid Osteomas

Clinical Context and Therapy Purpose

The purpose of RFA in patients who have painful osteoid osteomas is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with painful osteoid osteomas?

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

Patients

The relevant populations of interest is individuals with painful osteoid osteomas.

Interventions

The therapy being considered is RFA.

Comparators

The following therapies and practices are currently being used to make decisions about osteoid osteomas: medical management, surgical excision, core drill excision, and laser photocoagulation.

Outcomes

The general outcomes of interest are reductions in pain and medication use, normal bone development, and postsurgical adverse events.

Timing

Patients would be followed through adolescents to ensure normal skeletal development.

Setting

RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria

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

Systematic Reviews

Lanza et al (2014) reported on a systematic review of various ablative techniques for osteoid osteomas.[4] Included in the review were 23 articles on RFA, 3 on interstitial laser ablation, and one with a combination of ablation techniques, totaling 27 articles (total N=1772 patients). The mean technical success was 100% and clinical success, defined as being pain-free, ranged from 94% to 98%, depending on the 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.

Retrospective Studies
In their retrospective study of the efficacy and complications of computed tomography (CT)–guided RFA of spinal osteoid osteoma, Albisinni et al (2017) concluded that CT-guided RFA is effective as first-line therapy for the disease.[5] After RFA, clinical symptoms were evaluated at 3, 6, and 12 months, with a final evaluation at the end of the study. Results showed that complete regression of osteoid osteoma symptoms in 57 (93.4%) of 61 (p=0.001) for patients observed between 2002 and 2012. Study limitations included the retrospective design and focus on a single treatment.

Lassalle et al (2017) conducted a single-center retrospective analysis of long-term outcomes for CT-guided RFA in 126 patients with suspected osteoid osteoma.[6] The study was conducted from 2008 to 2015. Phone evaluations were performed. The overall success rate was 94.3% among the 88 patients who participated in the follow-up calls. The study was limited by its retrospective design, imprecision of patients' memory over follow-up, the lack of clinical and imaging follow-up, and an inability to perform multivariate statistical analysis of factors associated with treatment failure.

Rimondi et al (2012) reported on a retrospective study of 557 patients treated with CT-guided RFA as primary treatment for nonspinal osteoid osteomas.[7] All patients were followed for a mean of 3.5 years (range, 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.

Case Series
An observational study by Knudsen et al (2015) evaluated long-term clinical outcomes after CT-guided RFA in patients diagnosed with osteoid osteoma located in the upper and lower extremities.[8] 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 2014 at a Danish university hospital. 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.

Rosenthal et al (2003) reported their experience over an 11-year period with 271 RFA procedures for osteoid osteomas in 263 patients.[9] 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 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 retrospective studies and 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. Results have indicated that most patients (89%-96%) remained pain-free at longer term follow-up.

Localized Renal Cell Carcinoma

Clinical Context and Therapy Purpose

The purpose of RFA in patients who have localized renal cell carcinoma (RCC) no more than 4 cm in size is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with localized RCC no more than 4 cm in size?

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

Patients
The relevant population of interest is individuals with localized RCC no more than 4 cm in size.

Interventions
The therapy being considered is RFA.

Comparators
The following practice is currently being used to make decisions about managing localized RCC: surgical excision.

Outcomes
The general outcomes of interest are recurrence rates and reduction in rates of renal failure.

Timing
Patients should be followed for at least ten years to monitor for tumor recurrence.

Setting
RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

In a systematic review and meta-analysis, Katsanos et al (2014) reviewed 1 RCT and 5 cohort studies (total N=587 patients) assessing thermal ablation (RFA or microwave) or nephrectomy for small renal tumors (size, 2.5 cm).[10] The local recurrence rate was 3.6% in both groups (relative risk, 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%) vs nephrectomy (11.1%; pooled relative risk, 0.55; 95% CI, 0.31 to 0.97; p=0.04).

In another systematic review and meta-analysis, Wang et al (2014) reported on studies evaluating RFA and partial nephrectomy for stage I (no more than 7 cm across) renal tumors.[11] Reviewers selected 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).

El Dib et al (2012) conducted a meta-analysis evaluating RFA and cryoablation for small renal masses.[12] Selected were 11 RFA case series (426 patients) and 20 cryoablation case series (457 patients) published through January 2011. The 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 (2008) conducted a comparative meta-analysis evaluating cryoablation and RFA as primary treatments for small renal masses.[13] Forty-seven case series representing 1375 renal tumors were analyzed. Of 600 lesions treated with cryoablation, 494 underwent biopsy before treatment and 482 of 775 treated with RFA. The incidence of RCC 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 vs 19 (3%) of 775 after RFA (p=0.06).

Randomized Controlled Trials

In an RCT, Liu et al (2016) analyzed the safety and efficacy of the operative effects of percutaneous RFA in early-state RCC vs retroperitoneoscopic radical operation of RCC.[14] The observation group was treated with percutaneous RFA and the control group with a radical retroperitoneoscopy. A total of 76 clinically confirmed diagnosed cases, from January 2011 to January 2013, with RCC, were randomized to the observation (n=41) or the control (n=35) groups. Operation time, blood loss during operation, length of stay, and incidence complications were lower in the control group (p<0.05). For both groups, postsurgical day at 1, 2, and 3 serum C-reactive protein, interleukin 6, and T lymphocyte counts were elevated, however, the increase in the control group was significantly greater (p<0.05). Total efficacy, tumor-free survival times,

and survival rates did not differ statistically between groups (p>0.05), however, percutaneous RFA reduced postoperative recovery time and fewer complications. Trial limitations included small sample size and brief duration of follow-up.

Retrospective Studies

A retrospective study by Park et al (2018) compared the mid-term oncologic and functional outcomes of robotic partial nephrectomy with RFA for treating T1a RCC.[15] Using propensity score-matching, the study analyzed 63 similar patient cases from each treatment group for changes in tumor location, estimated glomerular filtration rates preservation, and 2-year recurrence-free survival rate. Preservation of estimated glomerular filtration rate in the robotic partial nephrectomy group was 91.7% and 86.8% of the RFA group (p=0.088), and exophytic and endophytic RCC occurred in 73% (46/63) and 27% (17/63) of the robotic partial nephrectomy group and 52.4% (33/63) and 47.6% (30/63) of the RFA group, respectively. Two-year recurrence-free survival rate was 100% in the robotic partial nephrectomy group and 95.2% in the RFA group (p=0.029). The mismatching of RCC locations between the robotic partial nephrectomy and RFA groups is a study limitation. Other limitations included the retrospective design, the relatively small sample and the lack of long-term outcomes assessing and kidney function measures.

Dai et al (2017) conducted a retrospective evaluation of 30 patients with 31 central renal tumors who underwent percutaneous RFA between 2005 and 2010 to assess the clinical efficacy and safety of image-guided percutaneous RFA of central RCC with adjunctive pyeloperfusion.[16] Overall survival was 96.0% (95% CI, 88.4% to 100.0%) and progression-free survival at 5 years was 80.9% (95% CI, 65.8% to 95.9%). The investigators found that complications were significantly higher for tumors located within 5 mm of the renal pelvis or 0 mm of a major calyx (28.6% vs 4.0%; p<0.05) and major complications occurred in 5 (12.8%) of 39 RFA sessions. They concluded that image-guided percutaneous RFA combined with pyeloperfusion had satisfactory clinical efficacy in the treatment of renal tumor but may be associated with significant major complications. The retrospective design and the small sample base are limitations to this analysis.

Over 10 years, Dvorak et al (2017) retrospectively evaluated the technical success as well as mid-term and long-term efficacy and safety of RFA and microwave ablation with guided CT in 64 patients with small, non-central renal tumors.[17] Ninety-one ablation procedures were performed on 68 tumors, 12 to 60 mm in size. Treatment was successful in 50 (73.5%) tumors; a second procedure was successful in 13 (19.1%) cases; and for the 5 largest tumors (range, 45-60 mm; 7.4%), a third treatment was required. Investigators concluded that percutaneous ablation is safe and effective in treating small, non-central renal tumors of the T1a group. The retrospective study design is the major limitation of this study.

Pantelidou et al (2016) retrospectively compared the oncologic outcomes of RFA with robotic-assisted partial nephrectomy for the treatment of T1 stage RCC.[18] Sixty-three cases were included in each treatment group. Baseline renal function for those who received RFA was poorer; and there was an imbalance between groups in the number of patients with tumors in a single kidney (16/63 RFA patients vs 1/63 partial nephrectomy patients; p<0.001). Postprocedure renal function decline at 30 days was significantly smaller in the RFA group (-0.8 mL/min/1.73 m^2 vs -16.1 mL/min/1.73 m^2; p<0.001). The robotic-assisted partial nephrectomy group experienced more minor complications (10/63 vs 4/63, p=0.15) and the RFA group had a higher local

recurrence (6/63 vs 1/63, p=0.11). The authors concluded that both RFA and RNA offered good oncologic outcomes for T1 RCC with low morbidity. The retrospective study design, the tertiary center location's specific referral procedures, a loss of follow-up case data, and the heterogeneous patient demographics are study limitations.

A publication by Iannuccilli et al (2016) reported a mean 34.1-month follow-up (range, 1-131 months) of RFA with intent to cure in 203 patients with renal tumors.[19] Patients referred for RFA at 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 the appearance of residual tumor at the treatment site, and 26 (13%) had residual disease. Treatment effectiveness was 87% during follow-up. The likelihood of recurrence was increased for tumors 3.5 cm or larger, clear cell subtype, and treatment temperature of 70° or less. All-cause mortality increased with increasing tumor size. The 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.

Stern et al (2007) retrospectively compared patients with stage T1a renal tumors, confirmed by pathology to be RCC, treated with partial nephrectomy (n=34) or RFA (n=34).[20] The 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 RCCs were similar whether treated with partial nephrectomy or RFA.

Section Summary: Localized Renal Cell Carcinoma
The evidence on RFA for renal tumors includes an RCT, meta-analyses, retrospective and 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 that RFA was as effective as nephrectomy for small renal tumors, with a reduction in complications. Another 2014 meta-analysis, which included case series of stage I (no more than 7 cm across) renal tumors, found that the rate of local progression was higher with RFA than with nephrectomy, but the rate of major complications was lower with RFA. The conflicting results between these meta-analyses might be due to differences in tumor sizes assessed in selected studies as well as selection bias when comparing case series. The correlation between tumor size and RFA efficacy has been reinforced by a large case series with a mean 34-month follow-up; it found that residual disease and mortality increased with tumors over 4 cm.

Primary Pulmonary and Nonpulmonary Tumors
<u>Clinical Context and Therapy Purpose</u>
The purpose of RFA in patients who have inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung?

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

Patients
The relevant population of interest is individuals with inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung.

Interventions
The therapy being considered is RFA.

Comparators
The following practice is currently being used to make decisions about managing primary pulmonary tumors or nonpulmonary tumors metastatic to the lung: radiotherapy.

Outcomes
The general outcomes of interest are overall survival, tumor recurrence, and treatment-related adverse events eg, pneumothorax).

Timing
Patients would be followed for at least five years.

Setting
RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
In a systematic review of RFA, surgery, and stereotactic body radiotherapy for colorectal cancer lung metastases, Schlijper et al (2014) did not identify any randomized trials, and evidence was insufficient to draw conclusions on the comparative effectiveness of these therapies.[21]

In comparative effectiveness review conducted for the Agency for Healthcare Research and Quality, Ratko et al (2013) assessed local nonsurgical therapies for stage I non-small-cell lung cancer (NSCLC).[22] In this review, no comparative RFA studies were identified. Reviewers found that available evidence was insufficient to draw conclusions on the comparative effectiveness of local nonsurgical therapies for NSCLC, including RFA.

In a review of 16 studies, Bilal et al (2012) compared RFA with stereotactic ablative radiotherapy in patients with inoperable early-stage NSCLC.[23] Reviewers found that overall survival (OS) rates for RFA and stereotactic ablative radiotherapy 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 stereotactic body radiotherapy(47%).

These findings were drawn from comparisons of results of uncontrolled case series and retrospective reviews.

In an evidence-based review by Chan et al (2011), 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.[24] Twenty-four studies reported rates of local recurrence, which occurred in 282 (12.2%) cases at a mean follow-up 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 of 17.7 months. The mean cancer-specific survival rate was 82.6%, at a mean follow-up of 17.4 months. The 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.

Prospective Studies
Huang et al (2011) prospectively followed 329 consecutive patients treated with RFA for lung tumors (237 primary, 92 metastatic).[25] Complications were experienced by 34.3% (113) of patients, 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 was statistically significant for tumors greater than 4 cm.

Zemlyak et al (2010) prospectively compared 3 treatments for medically inoperable patients with stage I NSCLC: RFA in 12 patients, sublobar resection in 25 patients, and percutaneous cryoablation in 27 patients.[26] At 3-year follow-up, survival rates did not differ significantly between groups. OS and cancer-specific 3-year survival rates 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 treating 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.

Inoperable Lung Tumors
In a prospective, single-arm, multicenter trial from 7 centers in Europe, the United States, and Australia, Lencioni et al (2008) reported the technical success, safety, response of tumors, and survival in 106 patients with 183 lung tumors.[27] All patients were considered unsuitable for surgery and unfit for radiotherapy or chemotherapy. Tumors measured less than 3.5 cm (mean, 1.7 cm) and included patients with NSCLC (n=22), colorectal metastases (n=41), and other metastases (n=16). The 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 those with primary and metastatic tumors. OS rates in patients with NSCLC were 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 rates in patients with metastatic colorectal cancer were 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 rates in patients with other metastases were 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 I NSCLC (n=13) had an OS rate of 75% (95% CI, 45% to 92%) at 2 years (cancer-specific, 92%; 95% CI, 66% to 99%). No differences in response rates were seen between patients with NSCLC or lung metastases.

Zhu et al (2009) assessed the incidence and risk factors of various pulmonary neoplastic complications after RFA.[28] They 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 event was a 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. The length of the ablation probe trajectory greater than 3 cm was an additional independent risk factor for overall morbidity and pneumothorax.

Pennathur et al (2009) reported on 100 patients with inoperable lung tumors.[29] Forty-six patients had primary lung neoplasm, 25 had recurrent cancer, and 29 had pulmonary metastases. The 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 and Nonpulmonary Tumors
The evidence on RFA for primary NSCLC and nonpulmonary tumors metastatic to the lung includes prospective and observational studies 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 stereotactic ablative radiotherapy in patients with inoperable lung tumors. Survival rates at 5 years were lower with RFA (20.1%-27%) than with stereotactic ablative radiotherapy (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
Clinical Context and Therapy Purpose
The purpose of RFA in patients who have breast tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with breast tumors?

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

Patients
The relevant population of interest is individuals with breast tumors.

Interventions
The therapy being considered is RFA.

Comparators
The following practices are currently being used to make decisions about managing breast cancer: radiotherapy and surgical excision.

Outcomes
The general outcomes of interest are tumor recurrence, reduction in medication, and treatment-related adverse events.

Timing
Patients would be followed for up to five years.

Setting
RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
Peek et al (2017) conducted a systematic review and meta-analysis of all studies evaluating the role of ablative techniques in the treatment of breast cancer published between 1994 and 2016.[30] Selection criteria included at least 10 patients with breast cancer treated with RFA, high-intensity ultrasound, or cryo-, laser, or microwave ablation; 63 studies (total N=1608 patients) were identified through PubMed and MEDLINE library databases. Fifty studies reported complete ablation, and RFA had the highest rate of complete ablation (87.1% [491/564]) as well as the shortest treatment time (15.6 minutes). A major limitation of this systematic review was the authors' inability to perform a comparative meta-analysis due to the inclusion of only 4 RCTs and 1 retrospective analysis that compared 2 or more of techniques. There was also considerable heterogeneity across included studies.

Zhao and Wu (2010) conducted a systematic review of 38 studies on ablation techniques for breast cancer treatment published from 1994 to 2009.[31] Nine studies focused on RFA. Reviewers included small 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 suggested RFA for breast cancer tumors is feasible, but further studies with longer follow-up on survival, tumor recurrence, and cosmetic outcomes would be needed to establish clinical efficacy.

In another review, Soukup et al (2010) examined 17 studies on RFA for the treatment of breast tumors and found RFA is feasible.[32] Even though few adverse events and complications occurred with breast RFA, incomplete tumor ablation remains a concern.

<u>Clinical Studies</u>
Retrospectively, Ito et al (2018) studied the safety and efficacy of percutaneous RFA of breast carcinomas in 386 patients from 10 institutions treated with RFA between 2003 and 2009.[33] Patients were followed for a median of 50 months and ipsilateral breast tumor recurrence was more frequent in patients with initial tumor sizes of 2 centimeters or more (10% [3/30]) than those with initial tumors 2 centimeters or less (2.3% [8/355]; p=0.015). Ipsilateral breast tumor recurrence rates 5 years after RFA were 97%, 94%, and 87% in patients with initial tumor sizes of 1 centimeter or less, 1.1 to 2.0 centimeters, and greater than 2 centimeters, respectively. The authors concluded that RFA was safe for tumors of 2 centimeters or less. The retrospective design and lack of data on ipsilateral breast tumor recurrence for different types of chemotherapy and endocrine therapy and analyses to ascertain whether adjuvant chemotherapy or endocrine therapy influenced outcomes are the limitations of this study.

The efficacy and safety of using ultrasound-guided RFA for multiple breast fibroadenoma as an alternative to surgical resection were retrospectively analyzed by Li et al (2016).[34] From 2014 to 2016, 65 patients with 256 nodules were treated with ultrasound-guided RFA and complete ablation was achieved for 251 nodules (98.04%) after the first month of treatment; after the first and third months, tumor volume overall was reduced by 39.06% and 75.99%, respectively. The study reported minimal to no complications such as skin burns, hematoma, or nipple discharge. The retrospective design and short follow-up time limited conclusions drawn from this study.

Wilson et al (2012) reported on 73 patients with invasive breast cancer who had a lumpectomy followed immediately by RFA to the lumpectomy bed.[35] 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 phase 1/2 study reported by Kinoshita et al (2011), 49 patients were treated with RFA for breast tumors (mean size, 1.70 cm) followed immediately with surgical resection.[36] Complete ablation was achieved in 30 (61%) patients. The complete ablation rate 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.

Imoto et al (2009) reported on a series of 30 patients with T1N0 breast cancer who had sentinel node biopsy followed by RFA and breast-conserving surgery.[37] Twenty-six patients showed pathologic degenerative changes in tumor specimens, and, in 24 of 26 cases, tumor cell viability was diagnosed. Two patients had skin burns, and seven had muscle burn related to RFA.

In a 2-stage, phase 2 clinical trial reported by Garbay et al (2008), patients with histologically confirmed noninflammatory and 3 centimeters or less ipsilateral breast tumor recurrence were treated with RFA followed by mastectomy.[38] The study was ended early due to lack of efficacy of the technique tested.

Section Summary: Breast Tumors
Systematic reviews, retrospective studies, and observational studies have 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 studies have not compared RFA with conventional breast-conserving procedures. For small breast

tumors, further study, with long-term follow-up, is needed to determine whether RFA can provide local control and survival rates comparable with conventional breast-conserving treatment.

Benign Thyroid Nodules

Clinical Context and Therapy Purpose

The purpose of RFA in patients who have benign thyroid tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with benign thyroid tumors?

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

Patients

The relevant population of interest is individuals with benign thyroid tumors.

Interventions

The therapy being considered is RFA.

Comparators

The following practices are currently being used to make decisions about managing thyroid tumors: radiotherapy and surgical excision.

Outcomes

The general outcomes of interest are reduction in nodule volume, hyper- and hypothyroidism, and treatment-related adverse events (eg, voice changes).

Timing

Patients would be followed for at least 5 years.

Setting

RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria

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

Systematic Reviews

To evaluate the efficiency of RFA for the treatment of benign thyroid nodules, Chen et al (2016) conducted a systematic review and meta-analysis of outcomes based on literature search to January 2016.[39] Meta-analysis of data from 20 articles covering the RFA treatment of 1090 patients with 1406 benign thyroid nodules showed a significant decrease in nodule volume at

months 1, 3, 6, 12, and last follow-up. Heterogeneous inclusion criteria, limited sample sizes, indirect transformation methods in the analysis, and selection bias of studies mainly from the Republic of Korea and Italy are the major limitations of this study.

Fuller et al (2014) reported on a systematic review of studies on RFA for benign thyroid tumors.[40] Selected 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, two of which were considered significant but did not require hospitalization. The interpretation of meta-analytic results was limited by the variability in the comparator arms (percutaneous ethanol injection, percutaneous laser ablation and high-intensity focused ultrasound ablation). The only RCT included in the meta-analysis was small (N=30).

Prospective Studies
From 2010 to 2011, Jung et al (2018) conducted a multicenter prospective assessment of the efficacy and safety of thyroid RFA for benign thyroid nodules in 345 patients.[41] Volume reduction 12 months after RFA was 80.3% (n=276), and at the 24-, 36-, and 60-month follow-ups, reductions were 84.3% (n=198), 89.2% (n=128), 91.9% (n=57), and 95.3% (n=6), respectively. Therapeutic success was 97.8% overall, and mean symptom and cosmetic scores showed significant improvements (p<0.001). Lack of long-term follow-up is a limitation of this study.

Case Series
Lim et al (2013) reported on a case series of 111 patients treated with RFA for 126 benign nonfunctioning thyroid nodules.[42] The mean duration of patient follow-up was 49.4 months. RFA significantly decreased the volume of the thyroid nodules from 9.8 to 0.9 milliliters (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 (2012) retrospectively reviewed RFA for 1543 benign thyroid nodules in 1459 patients at 13 thyroid centers.[43] Forty-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 by Spiezia et al (2009) assessed 94 elderly subjects with solid or mainly solid benign thyroid nodules was reported by an Italian center.[44] 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 randomized and nonrandomized trials, case series, and systematic reviews of these studies. A systematic review that included 1 RCT, 3 randomized studies, 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. However, the comparators were variable and nonconventional. The single RCT had a small sample size of 30.

Miscellaneous Solid Tumors

Clinical Context and Therapy Purpose

The purpose of RFA in patients who have miscellaneous solid tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in individuals with miscellaneous solid tumors?

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

Patients
The relevant population of interest is individuals with miscellaneous solid tumors (eg, head and neck, thyroid cancer, pancreas).

Interventions
The therapy being considered is RFA.

Comparators
The following practices are currently being used to make decisions about managing miscellaneous solid tumors: radiotherapy and surgical excision.

Outcomes
The general outcomes of interest vary by disease state but include OS, tumor recurrence, and reductions in pain.

Timing
Patient follow-up will vary by disease state.

Setting
RFA is administered in an outpatient setting by oncologists and radiologists.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

- Studies with duplicative or overlapping populations were excluded.

Thyroid Cancer

Kim et al (2015) reported on 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).[45] 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

Owen et al (2011) reported on RFA for 13 patients with recurrent and/or unresectable head and neck cancer who failed curative treatment.[46] 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 (2008).[47] Tumor targeting and electrode deployment were 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 by Owen et al (2004) showed that 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.[48] The procedure appeared reasonably safe and feasible for this indication.

Other Tumors

Liu et al (2016) retrospectively compared laparoscopic adrenalectomy with CT-guided percutaneous RFA for the treatment of aldosterone-producing adenoma, evaluating short-term and long-term outcomes of normalized aldosterone-to-renin ratio, hypokalemia, and hypertension.[14] Of 63 patients, 27 were in the laparoscopic adrenalectomy group and 36 were in the RFA group. Primary aldosteronism was seen in 33 of 36 patients treated with RFA and all 27 who had laparoscopic adrenalectomy (p=0.180), within a median follow-up of 5 to 7 years. RFA was associated with faster recovery post procedure, but hypertension was less frequently resolved using RFA (13/36 patients) compared with laparoscopic adrenalectomy (19/27 patients; p=0.007). The use of posture test and CT for subtype classification of primary aldosteronism is the major limitation of the study, as well as the retrospective design.

Retrospectively, Yang et al (2016) compared the efficacy and safety of RFA with laparoscopic adrenalectomy in treating aldosterone-producing adenoma of the adrenal gland.[49] From 2009 to 2013, 25 patients diagnosed with unilateral adrenal aldosterone-producing adenoma and similar tumor size (<25 mm) were allocated to a control group (n=18) that underwent laparoscopic adrenalectomy and a test group (n=7) that underwent CT-guided percutaneous RFA. Complete tumor ablation on follow-up CT scan and normalization of serum aldosterone-to-renin were the

primary outcomes compared in this study. Success in the RFA group reached 100% within 3 to 6 months, compared with 94.4% in the laparoscopic adrenalectomy group, and normalization ability was statistically equivalent in both groups. The study's retrospective design and small sample are the main limitations of this study.

In a large series, Yin et al (2015) evaluated the effectiveness and safety of RFA for uterine myomas in a 10-year retrospective cohort study.[50] From 2001 to 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 an 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 an average diameter of 5.0 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 a 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 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; $p < 0.05$).

A case series by Mayo-Smith and DuPuy (2004) assessed 13 patients with adrenal neoplasms treated with RFA. Eleven of the 13 lesions were treated successfully with RFA, defined by follow-up CT scans and normalization of preprocedural biochemical abnormalities.[51]

A single-arm, retrospective, paired-comparison study by Locklin et al (2004) evaluated the short-term efficacy of RFA in reducing pain and improving function in patients with unresectable, painful soft tissue neoplasms recalcitrant to conventional therapies.[52] 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 over 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[53,54] and in the pancreas.[55-57] A systematic review by Rombouts et al (2015) has examined studies of ablative therapies, including RFA, in patients with locally advanced pancreatic cancer.[58] No RCTs were identified, and conclusions limited by the sparse evidence available on RFA in this setting.

Stereotactic radiofrequency thermocoagulation for epileptogenic hypothalamic hamartomas was described in a retrospective analysis by Kameyama et al (2009) who evaluated 25 patients with gelastic seizures (a rare type of seizure).[59] 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 (2009).[60] 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.[61,62] These case series did not permit comparison with an available alternative.

Section Summary: Miscellaneous Solid Tumor
Evidence on the use of RFA to treat other types of solid tumors consists of a small number of case series or retrospective comparative studies for each tumor type. Reporting on outcomes is limited. The evidence base does not support a conclusion on the effects of RFA.

SUMMARY OF EVIDENCE

Bone Tumors
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 painful osteolytic metastases. The population is comprised of patients with few or no treatment options, for whom short-term pain relief is an appropriate clinical outcome. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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 during 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 symptom relief with minimal complications, for a population for whom short-term symptom relief and avoidance of invasive procedures are appropriate clinical outcomes. The evidence is sufficient to determine 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 an RCT, numerous 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 I (≤7 cm across) renal tumors, found that the rate of local progression was greater with RFA than with nephrectomy. The differing meta-analytic results 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 and Nonpulmonary Tumors
For individuals who have inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung who receive RFA, the evidence includes prospective 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 in size, RFA can lead to a complete response in as many as 88% of patients for at least 1 year. Two-year survival rates have been reported to range from 41% to 75% in case series, with 5-year survival rates of 20% to 27%. In general, the evidence suggests that 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 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 permit comparisons with conventional breast-conserving procedures. Further studies, with long-term follow-up, should focus on whether RFA of the breast for small tumors 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, prospective studies, 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 when compared with a variety of local treatment. Reports of complications vary. The most frequent major complication in 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 few 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 these tumor types. Reporting on outcomes or comparisons with other treatments is limited. These studies do not permit conclusions on the health benefits of RFA. The evidence is insufficient to determine the impact of the technology on health outcomes.

CLINICAL INPUT RECEIVED THROUGH 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 October 2010. The input was similar to that in 2009, except support for use in lung tumors was less (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 for February 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 with regards to 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 setting of a clinical trial. The reviewers were also split with regards 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 regarding 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 guidelines (2013) on the treatment of stage I and II non-small-cell lung cancer (NSCLC) have indicated radiofrequency ablation (RFA) has been used effectively in clinical stage I NSCLC.[63] Therefore, in medically inoperable patients, peripheral NSCLC tumors less than 3 cm may be treated with RFA. The College also collaborated with the Society of Thoracic Surgeons to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC.[64] These 2012 consensus guidelines indicated RFA is an alternative treatment option for patients who are not surgical candidates due to severe medical comorbidity.

National Comprehensive Cancer Network

National Comprehensive Cancer Network (NCCN) guidelines for the treatment of NSCLC (v.6.2018) state: "Resection is the preferred local treatment modality (other modalities include radiofrequency ablation, cryotherapy and SABR [stereotactic ablative radiotherapy])."[65]

NCCN guidelines for thyroid carcinoma (v.2018) indicate that local therapies such as RFA may be considered for locoregional recurrence of thyroid carcinoma-papillary carcinoma.[66]

NCCN guidelines (v.2018) for renal cancer indicate that ablative techniques such as RFA "can be considered for selected patients with clinical stage T1 renal lesions."[67] The guidelines note that ablative techniques are associated with higher rates of local recurrence than traditional surgery.

National Institute for Health and Care Excellence
The National Institute for Health and Care Excellence (NICE) guidance (2004) on osteoid osteoma indicated that "current evidence on the safety and efficacy of computed tomography (CT)-guided thermocoagulation of osteoid osteoma appears adequate to support its use...."[68]

Updated NICE guidance (2010) on renal cancer has indicated that "evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) … in the short and medium term appears adequate to support the use of this procedure provided that patients are followed up in the long term."[69]

NICE guidance (2010) on RFA for primary and secondary lung cancers has stated: "[C]urrent evidence on the efficacy of percutaneous radiofrequency ablation (RFA) … is adequate in terms of tumor control."[70] NICE also indicated RFA might "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.

NICE guidance (2016) on benign thyroid nodules stated: "Current evidence on the safety and efficacy of ultrasound-guided percutaneous radiofrequency ablation … is adequate to support the use of this procedure...."[71]

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

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

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01051037	Phase II Study Evaluating Safety and Efficacy of Stereotactic Body Radiotherapy and Radiofrequency Ablation for Medically Inoperable and Recurrent Lung Tumors Near Central Airways	17	Dec 2017 (ongoing)
Unpublished			
NCT00776399	Radiofrequency Ablation in Resectable Colorectal Lung Metastasis: A Phase-II Clinical Trial	70	Aug 2018 (completed)

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

20982	Ablation therapy for reduction or eradication of 1 or more bone tumors (eg, metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; radiofrequency
32998	Ablation therapy for reduction or eradication of 1 or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, including imaging guidance when performed, unilateral; radiofrequency
50542	Laparoscopy, surgical; ablation of renal mass lesion(s)
50592	Ablation, one or more renal tumor(s), percutaneous, unilateral, radiofrequency
76940	Ultrasound guidance for, and monitoring of, parenchymal tissue ablation

ICD-10 Diagnoses

C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
D16.01	Benign neoplasm of scapula and long bones of right upper limb
D16.02	Benign neoplasm of scapula and long bones of left upper limb
D16.11	Benign neoplasm of short bones of right upper limb
D16.12	Benign neoplasm of short bones of left upper limb
D16.21	Benign neoplasm of long bones of right lower limb
D16.22	Benign neoplasm of long bones of left lower limb
D16.31	Benign neoplasm of short bones of right lower limb
D16.32	Benign neoplasm of short bones of left lower limb
D16.4	Benign neoplasm of bones of skull and face
D16.5	Benign neoplasm of lower jaw bone
D16.6	Benign neoplasm of vertebral column

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D16.7   Benign neoplasm of ribs, sternum and clavicle
D16.8   Benign neoplasm of pelvic bones, sacrum and coccyx
D16.9   Benign neoplasm of bone and articular cartilage, unspecified

REVISIONS

04-01-2011	Medical Policy Language section updated.
	In the policy language: • Removed "Radiofrequency ablation is considered medically necessary as an alternative to surgical resection for debulking of primary and metastatic neoplasms." • In Item #2, removed "surgery cannot be tolerated" and inserted "patient is not considered an appropriate surgical candidate" to read Radiofrequency ablation is considered medically necessary for removal of primary or metastatic malignant neoplasms when removal of the neoplasm may be curative and the patient is not considered an appropriate surgical candidate. • Added item #4, "Radiofrequency ablation may be considered medically necessary to treat osteoid osteoma that cannot be managed successfully with medical treatment."
	Rationale section updated.
	Reference section updated.
12-11-2013	Replaced medical policy reference, "Treatment of Liver Tumors" with the following references: "*Radioembolization for Primary and Metastatic Tumors of the Liver* *Radiofrequency Ablation of Primary or Metastatic Liver Tumors* *Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies* *Cryosurgical Ablation of Primary or Metastatic Liver Tumors*"
	Updated Description section.
	Updated Rationale section.
	In Coding section: • Added ICD-10 Diagnosis *(Effective October 1, 2014)*
	Updated Reference section.
01-01-2015	In Coding section: • Revised CPT Code: 20982 (Effective January 1, 2015)
11-11-2016	Updated Description section.
	In Policy section: • Removed previous Item B, "Radiofrequency ablation is considered medically necessary for removal of primary or metastatic malignant neoplasms when removal of the neoplasm may be curative and the patient is not considered an appropriate surgical candidate." • Added new Item C, "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 is met: 1. In order to preserve kidney function; OR 2. The patient is not considered a surgical candidate." • Added new Item D, "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: 1. 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 2. Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart."

	- Removed previous Item E, "Radiofrequency ablation is considered experimental / investigational for curative treatment of primary or metastatic malignant neoplasms in surgical candidates because the effectiveness of radiofrequency tumor ablation is improving clinical outcomes has not been established." - Added new Item E, "Radiofrequency ablation may be considered medically necessary to treat malignant nonpulmonary tumor(s) metastatic to the lung that are no more than 3 cm in size when the following criteria are met: 1. 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 2. There is no evidence of extrapulmonary metastases; AND 3. The tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart. The following additional criteria have been developed by clinical judgment / consensus and existing guidelines for the use of RFA in metastatic tumors to the lung and include: 1) No more than 3 tumors per lung should be ablated; b) Tumors should be amenable to complete ablation; AND c) Twelve months should elapse before a repeat ablation is considered." - Removed previous Item F, "Radiofrequency tumor ablation, excluding the liver, is considered experimental / investigational for all other indications." - Added new Item F, "Radiofrequency ablation is considered experimental / investigational as a technique for ablation of: 1. Breast tumors; 2. Lung cancer not meeting the criteria above; 3. Renal cell cancer not meeting the criteria above; 4. Osteoid osteomas that can be managed with medical treatment; 5. Painful bony metastases as initial treatment; AND 6. 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."
	Updated Rationale section.
	In Coding section: Added ICD-10 codes: C64.1, C64.2, C79.51, C79.52.
	Updated References section.
10-25-2017	Updated Description section.
	Updated Rationale section.
	Updated References section.
01-01-2018	In Coding section: - Revised nomenclature to CPT code: 32998. - Removed ICD-9 codes.
12-07-2018	Policy published to the bcbsks.com website on 11-07-2018 with an effective date of 12-07-2018.
	Updated Description section.
	Updated Rationale section.
	In Coding section: - Added ICD-10 codes: C78.01, C78.02. - Removed ICD-10 codes: C33, C68.8, C68.9.
	Updated References section.

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