Name of Blue Advantage Policy:
Radiofrequency Ablation of Solid Tumors Excluding Liver Tumors

Policy #: 119       Latest Review Date: September 2018
Category: Surgery       Policy Grade: B

Background:
Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

1. Safe and effective;
2. Not experimental or investigational*;
3. Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:
   • Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient’s condition or to improve the function of a malformed body member;
   • Furnished in a setting appropriate to the patient’s medical needs and condition;
   • Ordered and furnished by qualified personnel;
   • One that meets, but does not exceed, the patient’s medical need; and
   • At least as beneficial as an existing and available medically appropriate alternative.

*Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill Original Medicare for covered services that are related to clinical trials that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).
Description of Procedure or Service:
In radiofrequency ablation (RFA), a probe is inserted into the center of a tumor, then noninsulated, prong-shaped electrodes are projected into the tumor. Next, heat is generated locally by a high-frequency, alternating current that flows from the electrodes. The localized heat treats the tissue adjacent to the probe, resulting in a 3cm to 5.5cm sphere of dead tissue. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edge and, in some cases, may be retreated. RFA may be performed percutaneously, laparoscopically, or as an open procedure.

Renal Cell Carcinoma (RCC)
Radical nephrectomy remains the principal treatment of RCC, however, partial nephrectomy or nephron-sparing surgery has been shown to be as effective as radical nephrectomy, with comparable long-term recurrence-free survival rates, in a select group of patients. Alternative therapy such as RFA is of interest in patients with small renal tumors when preservation of renal function is necessary (e.g., 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).

Osteolytic Bone Metastases
After lung and liver, bone is the third most common metastatic site and is relatively frequent among patients with primary malignancies of the breast, prostate, and lung. Bone metastases often cause osteolysis (bone breakdown), resulting in pain, fractures, decreased mobility, and reduced quality of life. External-beam irradiation often is the initial palliative therapy for osteolytic bone metastases. However, pain from bone metastases is refractory to radiation therapy 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 10–20% of benign and 2–3% of all bone tumors. They are typically seen in children and young adults, with most diagnosed in patients between five to 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 upon its location, and although they rarely exceed 1.5cm, 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 three to seven years.
Treatment options include medical management with nonsteroidal anti-inflammatory drugs (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. Complete surgical excision has several disadvantages. A substantial incision may be necessary and removal of a considerable amount of bone (especially in the neck of the femur), increases the need for bone grafting and/or 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.

Primary Pulmonary Tumors and Metastases
Surgery is the current treatment of choice in patients with Stage I primary non-small cell lung carcinoma (NSCLC). (Stage I includes Ia: T1N0M0 and Ib: T2N0M0). Only approximately 20% of patients present with Stage I 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 I NSCLC have been reported 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 I patients, with five-year overall survival (OS) rates, ranging from 77% for small T1 tumors to 35% for large T2 tumors. Untreated, Stage I NSCLC has a five-year OS rate of 6–14%.

Patients with early stage NSCLC who are not surgical candidates may be candidates for radiation treatment with curative intent. In the two largest retrospective radiation therapy series, patients with inoperable disease treated with definitive radiation therapy achieved five-year survival rates of 10% and 27%. In both studies, patients with T1N0 tumors had better five-year survival rates of 60% and 32%, respectively.

Stereotactic whole body radiation therapy (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 three-year local control rates of Stage I 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 is being investigated in patients who are medically inoperable, with small primary lung cancers or lung metastases.
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 (e.g. RFA, microwave ablation) are being investigated.

Miscellaneous Tumors
Radiofrequency ablation has been investigated for use in individuals with different lesions in different anatomic sites. This includes, but is not limited to, breast and 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, studies have reported on the 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 guidance.

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

**Policy:**

**Effective for dates of service on or after February 26, 2018:**

Blue Advantage will treat radiofrequency ablation as a **covered benefit** for the treatment of patients with the following conditions:

- Renal cell carcinoma
  - In order to preserve kidney function in patients with significantly impaired renal function (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate [GFR] of less than 60mL/min/m²) when the standard surgical approach (i.e., resection of renal tissue) is likely to substantially worsen existing kidney function
  - OR
    - The patient is not considered a surgical candidate
- Osteoid osteomas that cannot be managed successfully with medical treatment
- Osteolytic bone metastases that have failed or are poor candidates for standard treatments such as radiation or opioids
- Isolated peripheral non-small cell lung cancer lesion ≤3cm*, And
  - Surgical resection or radiation treatment with curative intent is considered appropriate based on stage of disease, however, medical co-morbidity renders the individual unfit for those interventions; And
  - Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
- Malignant non-pulmonary tumor(s) metastatic to the lung ≤3cm*, And
  - In order to preserve lung function when surgical resection or radiation treatment is likely to substantially worsen pulmonary status OR the patient is not considered a surgical candidate; And
  - There is no evidence of extrapulmonary metastases; And
  - Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.

*No more than 3 tumors per lung should be ablated; tumors should be amenable to complete ablation; and twelve months should elapse before a repeat ablation is considered.

Blue Advantage will treat radiofrequency ablation as a **non-covered benefit** and as **investigational** as a technique for ablation of:

- Renal cell cancer not meeting the criteria above
- Osteoid osteomas that can be managed with medical treatment
• Painful bony metastases as initial treatment
• Lung cancer not meeting the above criteria
• Breast tumors
• Other tumors outside the liver, including but not limited to the head and neck, thyroid, adrenal gland, ovary, and pelvis/abdominal metastases of unspecified origin.

Please refer to Blue Advantage Policy #178 for coverage information on ultrasound ablation of the bone
Please refer to Blue Advantage Policy #429 for coverage information on cryosurgical ablation of renal, bone, and pulmonary tumors
Please refer to Blue Advantage NCD for Cryosurgery of Prostate (230.9)
Please refer to Blue Advantage Policy #070 for coverage information on locoregional therapies for liver tumors
Please refer to Policy# 596 for coverage information on focal treatments for prostate cancer.

Effective for dates of service April 27, 2015 through February 25, 2018:
Blue Advantage will treat radiofrequency ablation as a covered benefit for the treatment of patients with the following conditions:
• Renal cell carcinoma
  o In order to preserve kidney function in patients with significantly impaired renal function (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate [GFR] of less than 60mL/min/m$^2$) when the standard surgical approach (i.e., resection of renal tissue) is likely to substantially worsen existing kidney function
  OR
  o The patient is not considered a surgical candidate
• Osteoid osteomas that cannot be managed successfully with medical treatment
• Osteolytic bone metastases that have failed or are poor candidates for standard treatments such as radiation or opioids
• Isolated peripheral non-small cell lung cancer lesion ≤ 3cm*,
  And
  o 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
  o Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
• Malignant non-pulmonary tumor(s) metastatic to the lung ≤ 3cm*,
  And
  o In order to preserve lung function when surgical resection or radiation treatment is likely to substantially worsen pulmonary status OR the patient is not considered a surgical candidate;
  And
There is no evidence of extrapulmonary metastases; 

**And**

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

*No more than 3 tumors per lung should be ablated; tumors should be amenable to complete ablation; and twelve months should elapse before a repeat ablation is considered.*

**Blue Advantage** will treat **radiofrequency ablation** as a **non-covered benefit** and as **investigational** as a technique for ablation of:

- Renal cell cancer not meeting the criteria above
- Osteoid osteomas that can be managed with medical treatment
- Painful bony metastases as initial treatment
- Lung cancer not meeting the above criteria
- Breast tumors
- Other tumors outside the liver, including but not limited to the head and neck, thyroid, adrenal gland, ovary, and pelvis/abdominal metastases of unspecified origin

Please refer to Blue Advantage Policy #178 for coverage information on ultrasound ablation of the bone
Please refer to Blue Advantage Policy #429 for coverage information on cryosurgical ablation of renal, bone, and pulmonary tumors
Please refer to Blue Advantage **NCD for Cryosurgery of Prostate (230.9)**
Please refer to Blue Advantage Policy #070 for coverage information on locoregional therapies for liver tumors
Please refer to Policy# 596 for coverage information on focal treatments for prostate cancer.

---

**Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.**

**Key Points:**

The most recent literature search was performed through July 26, 2018. The following is a summary of the 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.

Renal Tumors
Systematic Reviews
In 2014, Wang et al reported on studies evaluating RFA and partial nephrectomy for Stage I (no more than 7cm across) renal tumors. Included in the review were 166 studies with a total of 9565 patients. The rate of local progression was greater with RFA than laparoscopic/robotic or open partial nephrectomy (4.6%, 1.2% and 1.9%, respectively; p<0.001.) RFA had more frequent minor complications than laparoscopic/robotic or open partial nephrectomy (13.8%, 7.5% and 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% and 3.1%, respectively, p<0.001).

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

In 2012, El Dib et al conducted a meta-analysis evaluating RFA and cryoablation for small renal masses. Included in the review were 11 RFA case series (totaling 426 patients) and 20 cryoablation case series (totaling 457 patients) published through January 2011. Mean tumor size was 2.7 cm (range from 2 to 4.3 cm) in the RFA group and 2.5 cm (range from 2 to 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, was not significantly different between groups. The pooled proportion of clinical efficacy for RFA was 90% (95% CI: 0.86–0.93) and 89% (95% confidence interval [CI]: 0.83–0.94) for cryoablation.
Kunkle and Uzzo conducted a comparative meta-analysis evaluating cryoablation and RFA as primary treatment for small renal masses. Forty-seven case series representing 1,375 renal tumors were analyzed. Of 600 lesions treated with cryoablation, 494 underwent biopsy before treatment versus 482 of 775 treated with RFA. The incidence of renal carcinoma (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 significant (p<0.0001). Progression to metastatic disease was described in six of 600 lesions after cryoablation versus 19 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. 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), 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. 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. 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. 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. 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 m² vs -16.1 mL/min/1.73 m² ; 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.

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

A 2016 publication by Iannuccilli et al reported a mean 34.1-month follow-up (range, 1-131 months) of RFA with intent to cure in 203 renal tumors. Patients who were referred for RFA were either high risk or had refused surgery. Smaller tumors were treated with a single electrode with a 2 or 3 cm active tip. Larger tumors were treated with a cluster electrode with 3 active tips. Patients were assessed annually for appearance of residual tumor at the treatment site, and 26 (13%) had residual disease. Treatment effectiveness was 87% during follow-up. The likelihood of residual disease 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. Median survival was 7 years for patients with tumors less than 4 cm, with 80% survival at 5 years. Major complications, including urinary stricture or urine leak, occurred in 8 (3.9%) treatments.
Section Summary: Renal Tumors
The evidence on RFA for renal tumors includes meta-analyses of 1 RCT, meta-analyses, retrospective and cohort studies, and case series comparing 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 that included case series of stage 1 (no more than 7 cm across) renal tumors found that the rate of local progression was greater with RFA than 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.

Osteolytic Bone Metastases
Case Series
Goetz et al. (2004) reported on an international study (n=43) conducted at nine centers in which patients with painful osteolytic bone metastases were treated palliatively with radiofrequency ablation (RFA). The study’s primary outcome measure was the Brief Pain Inventory-Short Form, a validated scale from zero for no pain to ten for worst pain imaginable. Patient eligibility required baseline values of four or more from two 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 radiation therapy to the same lesion. Mean pain score at baseline was 7.9 (range: 4 to 10). At 4, 12, and 24 weeks after RFA, average pain scores decreased to 4.5, 3.0, and 1.4, respectively (all p<0.0005). Forty-one (95%) of the patients achieved a clinically significant improvement in pain scores, prospectively defined as a decrease of two units from baseline. Investigators also reported statistically significant (p=0.01) decreases in opioid use at weeks eight (by 59%) and 12 (by 54%).

An earlier case series by Gronemeyer et al (2002) showed that palliative RFA provided significant pain relief in nine of ten (90%) patients with unresectable, osteolytic spine metastases who had no other treatment options. Pain was reduced by an average of 74%; back pain-related disability was reduced by an average of 27%. Neurologic function was preserved in nine patients and improved in one. An additional 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.

Section Summary: Palliation for Bone Metastases
Case series show clinically significant pain relief and reduction in opioid use following treatment of osteolytic pain metastases in patients with no or limited treatment options.

Osteoid Osteomas
Systematic Reviews
Lanza et al (2014) reported on a systematic review of various ablative techniques for osteoid osteomas. Included in the review were 23 articles on RFA, three on interstitial laser ablation and one with a combination of ablation techniques, totaling 27 articles and 1,772 patients. Technical success was a mean of 100% and clinical success, defined as being pain free, ranged from 94-98% depending on length of follow-up. Complications occurred in 2% of patients and included skin or muscle burn in nine patients, four infections, nerve lesions or tool breakage in three
patients each, delayed skin healing, hematoma, and failure to reach target temperature in two patients each and fracture, pulmonary aspiration, thrombophlebitis and cardiac arrest in one 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. 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. 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.

In 2012, Rimondi et al reported on a retrospective study of 557 patients treated with CT-guided RFA as primary treatment for non-spinal osteoid osteomas. All patients were followed for a mean of 3.5 years (0.5-9 years). Pain relief occurred in all 557 patients within the first week after RFA and continued in 533 patients (96%) who remained asymptomatic through their last follow-up. Pain recurrence occurred in 24 patients (4%). Complications occurred in five patients and included thrombophlebitis, a skin burn, a broken electrode and two procedures in which the RFA generator didn’t reach maximum temperature.

Case Series
An observational study by Knudsen et al in 2015 evaluated long-term clinical outcomes after computed tomography (CT)–guided RFA in patients diagnosed with osteoid osteoma located in the upper and lower extremities. The study population included 52 patients with a typical clinical history and radiologically confirmed osteoid osteoma who received CT-guided RFA treatment from 1998 to February 2014 at Aarhus University Hospital, Denmark. The clinical outcome was evaluated based on patient-reported outcome measures and medical record review. The response rate was 52 of 60 (87%). After one RFA treatment 46 of 52 (88%) of the patients experienced pain relief, and 51 of 52 (98%) of the patients had pain relief after re-RFA. One patient underwent open resection after RFA. No major complications were reported; four patients reported minor complications including small skin burn, minor skin infection and hypoesthesia at the entry point. In all, 50 of 52 (96%) 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. Short-term outcome was evaluated to detect procedure-related problems; by this definition, all procedures were considered technically
successful. Long-term clinical success data (defined as being free of pain without the necessity of additional procedures) were available in 126 patients, with a complete clinical success observed in 89%. For procedures performed as the initial treatment, the success rate was 91%.

**Section Summary: Osteoid Osteomas**

Numerous 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. Most patients (89% to 96%) remained pain-free at longer term follow-up.

**Primary Pulmonary Tumors and Metastases**

**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.

In a 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). 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 2012 review of evidence from 16 studies, Bilal et al compared RFA to stereotactic ablative radiotherapy (SABR) in patients with inoperable early stage non-small cell lung cancer (NSCLC). The authors found overall survival rates for RFA and SBRT were similar in patients at one year (68.2 to 95% vs. 81 to 85.7%) and three years (36 to 87.5% vs. 42.7 to 56%), all respectively. However, survival rates at five years were lower with RFA (20.1 to 27%) than with SABR (47%). These findings were drawn from comparisons of results from 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 2,905 ablations in 1,584 patients with a mean tumor size of 2.8 ± 1.0 cm. Twenty-four studies (51.2%) reported rates of local recurrence, which ranged from 0% to 64% and occurred in 282 cases (12.2%) with a mean follow-up time of 13 months (range 3-45 months of 19 studies reporting). Primary lung cancer rates of local recurrence were not significantly different at 22.2% than for metastases at 18.1%. Twenty-one studies reported rates of overall survival, which ranged from 25% to 100% with a mean of 59.4% and a mean follow-up time of 17.7 ± 12.4 months. The mean cancer-specific survival rate was 82.6%, as reported in 24 studies with a range of 55% to 100% with a mean of 17.4 ± 14.1 months follow-up. 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). 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.

In 2010, Zemlyak and colleagues prospectively compared three treatments for medically inoperable patients with Stage I NSCLC: RFA in 12 patients, sublobar resection in 25 patients and percutaneous cryoablation in 27 patients. At three years follow-up, survival rates were not significantly different between groups. Overall and cancer-specific three-year survivals were 87.5%, 87.1%, and 77% and 87.5%, 90.6%, and 90.2%, respectively. The authors concluded any of the three procedures were reasonable options for treatment of lung tumors in patients unfit for major surgery. The authors noted since surgeons chose the treatment option with patient input for this study, selection bias limits interpretation of his study, and further studies are warranted.

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

Zhu et al reported on a study to assess the incidence and risk factors of various complications after RFA of pulmonary neoplasms. The authors prospectively evaluated the clinical and treatment-related data regarding 129 consecutive percutaneous radiofrequency ablation treatment sessions for 100 patients with inoperable lung tumors. In this study, there was no post-procedural mortality. The overall morbidity rate was 43% (n=55 of 129). The most common adverse effect was pneumothorax, occurring in 32% (n=41 of 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 two lesions ablated per session as a significant risk factor for overall morbidity, pneumothorax, and chest drain insertion. Length of the ablation probe trajectory greater than 3cm was an additional independent risk factor for overall morbidity and pneumothorax.

In 2009, Pennathur et al reported on 100 patients with inoperable lung tumors. Forty-six patients had primary lung neoplasm, 25 had recurrent cancer, and 29 had pulmonary metastases. Mean
follow-up was 17 months. Median OS for all patients was 23 months. The probability of two-year OS for primary lung cancer patients, recurrent cancer patients, and metastatic cancer patients was 50% (95% CI: 33–65%), 55% (95% CI: 25–77%), and 41% (95% CI: 19–62%), respectively.

Section Summary: Primary Pulmonary Tumors and Metastases
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
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. 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.

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

In another 2010 review, Soukup and colleagues examined 17 studies on RFA for the treatment of breast tumors and found RFA is feasible. However, while minimal adverse effects and complications occurred with breast RFA, the authors noted incomplete tumor ablation remains a concern.
Clinical Studies
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. 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). 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.

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

In 2011, 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. 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 do
not allow comparisons with conventional breast-conserving procedures. For small breast tumors, further studies, with long-term follow-up, are needed to determine whether RFA can provide local control and survival rates comparable with conventional breast-conserving treatment.

**Benign Thyroid Nodules**

**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. 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.

In 2014 Fuller et al reported on a systematic review of studies on RFA for benign thyroid tumors. Included in the review were nine studies (five observational studies and four 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), combined symptom improvement and cosmetic scores on the 0 to 6 scale (mean of -2.96, 95% CI: -2.66 to -3.25) and withdrawal from methimazole (OR of 40.34, 95% CI: 7.78 to 209.09). Twelve adverse events were reported of which two 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. 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**

In 2013 Lim et al reported on a case series of 111 patients treated with RFA for 126 benign non-functioning thyroid nodules. Patient follow-up was a mean duration of 49.4 ± 13.6 months. RFA significantly decreased the volume of the thyroid nodules from 9.8 ± 8.5 mL to 0.9 ± 3.3 mL (p<0.001) for a mean volume decrease of 93.4 ± 11.7%. Tumor recurrence occurred in seven patients (5.6%). Complications occurred in four patients (3.6 %). Additionally, there was significant improvement in thyroid symptom scores (p<0.001).

Baek et al (2012) reported on a retrospective review of RFA for 1,543 benign thyroid nodules in 1,459 patients at 13 thyroid centers. 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 2009 case series by Spiezia et al assessed 94 elderly subjects with solid or mainly solid benign thyroid nodules was reported by an Italian center. Thyroid nodule volume, compressive symptoms, and thyroid function were evaluated at baseline and 12 to 24 months after treatment. All thyroid nodules significantly decreased in size after RFA. Compressive symptoms improved in all patients and disappeared completely in 88% of patients. Hyperthyroidism resolved in most patients allowing methimazole therapy to be completely withdrawn in 79% of patients with pretotoxic and toxic thyroid nodules (100% in 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 are variable. 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 Tumors
Thyroid Cancer
In 2016, Kim et al reported a comparative review of 73 patients with recurrent thyroid cancer smaller than 2 cm who had been treated with RFA (n=27) or repeat surgery (n=46). RFA was performed in cases of patient’s refusal to undergo surgery or poor medical condition. Data were adjusted by weighted analysis to minimize potential confounders. The 3 year recurrence-free survival rates were similar for RFA (92.6%) and surgery (92.2%, p=0.681). Posttreatment hoarseness rate did not differ between the RFA (7.3%) and surgery (9.0%) groups. Posttreatment hypocalcemia occurred only in the surgery group (11.6%).

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

A case series of RFA for 14 patients with recurrent advanced head and neck malignancies was reported by Brook et al. Tumor targeting and electrode deployment was successful in all cases, and four of six patients who completed quality-of-life assessments showed improvement. Three major complications (in 27 applications, 11%) occurred seven days to two weeks after the procedure. These 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 1cm of the carotid artery during ablation in these cases.

A 2004 case series showed palliative CT-guided RFA provided subjective improvement with regard to pain, appearance, and function in 12 patients who had recurrent and advanced head and neck malignancies and were not candidates for radiation or surgery.
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. 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. From 2009 to 2013, 25 patients diagnosed with unilateral adrenal aldosterone-producing adenoma and similar tumor size (<25mm) 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.

A large series in 2015 evaluated the effectiveness and safety of RFA for uterine myomas in a 10-year retrospective cohort study. From July 2001 to July 2011, a total of 1216 patients treated for uterine myomas were divided into two groups. Group A consisted of 476 premenopausal patients (average age 36±8 years) who had an average 1.7±0.9 myomas with average diameter of 4.5±1.5 cm. Group B consisted of 740 menopausal patients (average age, 48±4 years) with an average 2.6±1.3 myomas with average diameter of 5.0±2.5 cm. Patients were followed for a mean of 36±12 months. At 1, 3, 6, 12, and 24 months after RFA, the average diameters of myomas in group A were 3.8, 3.0, 2.7, 2.4, and 2.2 cm, respectively; 48% (227/476) of patients had residual tumor at 12 months after RFA. 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 after RFA. Three months after treatment, myoma volumes were significantly reduced in both the groups (p<0.01), although group B had a higher rate of residual tumor at 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 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 RF ablation. Eleven of the 13 lesions were treated successfully with RFA, defined by follow-up CT scans and normalization of preprocedural biochemical abnormalities.

painful soft tissue neoplasms recalcitrant to conventional therapies. Patients had tumors located in a variety of sites including chest wall, pelvis, breast, perirectal, renal, aortocaval, retroperitoneal, and superficial soft tissues. All had failed conventional methods of palliation or experienced dose-limiting adverse effects from pain medication. Although not all Brief Pain Inventory scores were statistically significant, all mean scores trended down with increased time after ablation. Complications from RFA were minor or insignificant in all but one patient who had skin breakdown and infection of the ablated superficial tumor site.

Additional research has addressed the use of RFA in solid malignancies and in the pancreas. A systematic review by Rombouts et al. (2015) examined studies of ablative therapies, including RFA, in patients with locally advanced pancreatic cancer. No RCTs were identified in this review, and conclusions are limited by the sparse evidence available on RFA in this setting.

Stereotactic radiofrequency thermocoagulation for epileptogenic hypothalamic hamartomas is described in a retrospective analysis by Kameyama et al. (2009) who evaluated 25 patients with gelastic seizures (a rare type of seizure that involves a sudden burst of energy, usually in the form of laughing or crying). Other seizure types were exhibited in 22 patients (88.0%), precocious puberty in eight (32.0%), behavioral disorder in 10 (40.0%), and mental retardation in 14 (56.0%). Gelastic seizures were resolved in all but two patients. Complete seizure freedom was achieved in 19 patients (76.0%). These patients had disappearance of all seizure types and behavioral disorder and also demonstrated intellectual improvement.

Preliminary results of endoscopic RFA of rectosigmoid tumors have been described in a paper by Vavra et al. (2009). Twelve patients were treated with the Endoblate RFA device, with ten patients having surgical resection after ablation. Histology of the resected specimens showed that, on average, 82% (range: 60-99%) of the tumor mass was destroyed in the ablation zone.

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

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

Summary
Renal cell carcinoma
For individuals who have localized renal cell carcinoma 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 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 meta-analysis included case series of stage 1 (no more than 7 cm across) renal tumors found that the rate of local progression was greater with RFA than nephrectomy. The differing results in these meta-analyses may be due to differences in tumor size in the included studies, as well as the potential for 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. The evidence is sufficient to determine the effects of the technology on health outcomes.

**Osteolytic Bone Metastases**

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

**Osteoid Osteomas**

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

**Inoperable Primary Pulmonary Tumors and Metastases**

For individuals who have inoperable primary pulmonary tumors or non-pulmonary 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, RFA can lead to a complete response in as many as 88% of patients for at least 1 year. Two-year survival has been reported to range from 41% to 75% in case series, with 5-year survival rates of 20% to 27%. In general, the evidence shows RFA results in adequate survival and tumor control in patients who are not surgical candidates, with low morbidity rates. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Breast Tumors**

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

**Benign Thyroid Tumors**
For individuals who have benign thyroid tumors who receive RFA, the evidence includes RCTs, 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 four RCTs and five 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 have varied. While RFA has been shown to reduce thyroid tumor volume and improve clinical symptoms, complications can be common and available evidence is insufficient to determine the impact of RFA on net health outcomes. Therefore, RFA for the treatment of thyroid tumors is considered investigational.

**Miscellaneous Tumors**
For individuals who have miscellaneous tumors (e.g. head and neck and 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 each of these tumor types. 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.

**Practice Guidelines and Position Statements**
**American College of Chest Physicians**
The American College of Chest Physicians (ACCP) guidelines (2013) on the treatment of stage I and II non-small-cell lung cancer (NSCLC) indicate RFA has been used effectively in clinical stage I NSCLC. Therefore, in medically inoperable patients, peripheral NSCLC tumors less than 3 cm may be treated with RFA. ACCP also joined with the Society of Thoracic Surgeons to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC. These 2012 consensus guidelines indicate RFA is an alternative treatment option in patients who are not surgical candidates due to severe medical comorbidity.

**National Comprehensive Cancer Network**
National Comprehensive Cancer Network (NCCN) practice guidelines for the treatment of NSCLC (v.6.2018) state, “Resection is the preferred local treatment modality (other modalities include radiofrequency ablation, cryotherapy and SABR).”

NCCN guidelines for thyroid carcinoma (v.1.2018) indicate that local therapies such as radiofrequency ablation may be considered for locoregional recurrence of thyroid carcinoma-papillary carcinoma.

NCCN guidelines (v.4.2018) for renal cancer indicate that ablative techniques such as radiofrequency ablation “can be considered for selected patients with clinical stage T1 renal disease”. The guidelines note that ablative techniques are associated with higher rates of local recurrence than traditional surgery.
National Institute for Clinical Excellence
NICE guidance issued in 2004 indicates that “current evidence on the safety and efficacy of computed tomography (CT)–guided thermocoagulation of osteoid osteoma appears adequate to support its use, provided that the normal arrangements are in place for consent, audit and clinical governance.”

Guidance updated in 2010 indicates that “evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) for renal cancer in the short and medium term appears adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit, and provided that patients are followed up in the long term.

Guidance on RFA for primary and secondary lung cancers issued in 2010 states, “[C]urrent evidence on the efficacy of percutaneous radiofrequency ablation (RFA) for primary or secondary lung cancers is adequate in terms of tumor control.” The National Institute for Clinical Excellence Guidance also indicates RFA may “be used in patients with small, early-stage lung cancers or small numbers of lung metastases who are unsuitable for, or prefer not to undergo, surgery. It may also have a place in multi-modality treatment of more advanced primary lung cancers.” The guidance warns of complications such as pneumothorax, which can result in serious consequences among lung cancer patients.

NICE guidance issued in 2016 stated “Current evidence on the safety and efficacy of ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.”

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

Key Words:
Renal cell carcinoma, RCC, radiofrequency ablation, RF, RF ablation, RFA, percutaneous radiofrequency ablation, pulmonary tumor, lung cancer, breast cancer, head and neck, cancer, adrenal, ovary, pelvic and/or abdominal tumor, osteoid tumor, bone metastases, palliation of pain, thyroid cancer, osteoid osteoma, metastatic bone cancer

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

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

**Current Coding:**

<table>
<thead>
<tr>
<th>CPT codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>19499</td>
<td>Unlisted Procedure, Breast</td>
</tr>
<tr>
<td>20982</td>
<td>Ablation therapy for reduction or eradication of 1 or more bone tumors (e.g., metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; radiofrequency</td>
</tr>
<tr>
<td>32998</td>
<td>Ablation therapy for reduction or eradication of one or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, including imaging guidance when performed, unilateral; radiofrequency</td>
</tr>
<tr>
<td>50542</td>
<td>Laparoscopy, surgical; ablation of renal mass lesion(s)</td>
</tr>
<tr>
<td>50592</td>
<td>Ablation, one or more renal tumor(s), percutaneous, unilateral, radiofrequency</td>
</tr>
<tr>
<td>76940</td>
<td>Ultrasound guidance for, and monitoring of, parenchymal tissue ablation</td>
</tr>
</tbody>
</table>

**References:**


Policy History:
Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, January 2006 (from MP# 149)
Medical Policy Group, December 2006
Available for comment January 11-February 24, 2007
Medical Policy Group, October 2007 (from MP# 149)
Available for comment November 17-December 31, 2007 (from MP# 149)
Medical Policy Group, December 2007
Medical Policy Group, March 2009
Available for comment April 3-May 18, 2009
Medical Policy Group, October 2009 (from MP# 149)
Available for comment November 6-December 21, 2009 (from MP# 149)
Medical Policy Group, October 2010
Medical Policy Group, March 2011 (from MP# 149)
Available for comment April 4 – May 18, 2011 (from MP# 149)
Medical Policy Group, January 2012:
Available for comment February 9 – March 26, 2012
Medical Policy Group, March 2013
Medical Policy Group, October 2013
Medical Policy Group, November 2014
Medical Policy Group, February 2015
Available for comment March 12 – April 26, 2015
Medical Policy Group, April 2015
Medical Policy Group, September 2015
Medical Policy Group, September 2016
Medical Policy Group, September 2017
Medical Policy Group, December 2017
Medical Policy Group, April 2018
Available for comment April 17 through May 31, 2018
Medical Policy Group, September 2018 (4): Updates to Description, Policy, Key Points, and References. Removed policy statements effective for dates of service January 1, 2012 through April 26, 2015. No change to current policy statements.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.