

# Protocol

## Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

(70195)

<b>Medical Benefit</b>		<b>Effective Date:</b> 01/01/14	<b>Next Review Date:</b> 11/19
<b>Preauthorization</b>	No	<b>Review Dates:</b> 11/07, 11/08, 09/09, 09/10, 09/11, 09/12, 09/13, 07/14, 07/15, 11/15, 11/16, 11/17, 11/18	

**Preauthorization is not required.**

*The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>With painful osteolytic bone metastases who have failed or are poor candidates for standard treatments</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Medical management</li> <li>Radiotherapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Symptoms</li> <li>Change in disease status</li> <li>Quality of life</li> <li>Medication use</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With painful osteoid osteomas</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Medical management</li> <li>Surgical excision</li> <li>Core drill excision</li> <li>Laser photocoagulation</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Symptoms</li> <li>Change in disease status</li> <li>Quality of life</li> <li>Medication use</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With localized renal cell carcinoma no more than four cm in size</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Surgical excision</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Change in disease status</li> <li>Quality of life</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With inoperable primary pulmonary tumors or nonpulmonary tumors metastatic to the lung</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Radiotherapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Change in disease status</li> <li>Quality of life</li> <li>Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>With breast tumors</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Radiotherapy</li> <li>Surgical excision</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Change in disease status</li> <li>Quality of life</li> <li>Treatment-related morbidity</li> </ul>

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>• With benign thyroid tumors</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Radiotherapy</li> <li>• Surgical excision</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Symptoms</li> <li>• Change in disease status</li> <li>• Quality of life</li> <li>• Medication use</li> <li>• Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>• With miscellaneous solid tumors (e.g., head and neck, thyroid cancer, pancreas)</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Radiotherapy</li> <li>• Surgical excision</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Overall survival</li> <li>• Change in disease status</li> <li>• Quality of life</li> <li>• Treatment-related morbidity</li> </ul>

## 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 a local recurrence, it occurs at the edge and can sometimes be retreated. RFA may be performed percutaneously, laparoscopically, or as an open procedure.

## 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 four cm in size who receive RFA, the evidence includes an randomized controlled trial (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 (seven cm or larger 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 one year. Two-year survival rates have been reported to range from 41% to 75% in case series, with five-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 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 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 (e.g., 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.

**POLICY**

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

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

Radiofrequency ablation may be considered **medically necessary** to treat localized renal cell carcinoma that is no more than four cm in size when either of the following criteria is met:

- When it is necessary 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 of less than 60 mL/min/m<sup>2</sup>) AND
- When the standard surgical approach (i.e., resection of renal tissue) is likely to worsen existing kidney function substantially; OR
- When the patient is not considered a surgical candidate.

Radiofrequency ablation may be considered **medically necessary** to treat an isolated peripheral non-small cell lung cancer lesion that is no more than three cm in size when the following criteria are met:

- When surgical resection or radiotherapy with curative intent is considered appropriate based on stage of disease, however, medical comorbidity renders the individual unfit for those interventions; AND
- When the tumor is located at least one cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.

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

- When it is necessary to preserve lung function because surgical resection or radiotherapy is likely to worsen pulmonary status substantially; OR
- When the patient is not considered a surgical candidate; AND
- When there is no evidence of extrapulmonary metastases; AND the tumor is located at least one cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.

(See the Policy Guidelines for additional criteria.)

Radiofrequency ablation is considered **investigational** as a technique for ablation of:

- breast tumors;
- lung cancer not meeting the criteria above;
- renal cell cancer not meeting the criteria above;
- osteoid osteomas that can be managed with medical treatment;
- painful bony metastases as initial treatment; and
- all other tumors outside the liver including, but not limited to, the head and neck, thyroid, pancreas, adrenal gland, ovary, and pelvic/abdominal metastases of unspecified origin.

**POLICY GUIDELINES**

The following are additional criteria developed by clinical judgment or consensus and existing guidelines for the use of RFA to treat metastatic tumors to the lung:

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

**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 radiotherapy often is the initial palliative therapy for osteolytic bone metastases. However, pain from bone metastases is refractory to radiotherapy in 20% to 30% of patients, while recurrent pain at previously irradiated sites may be ineligible for additional radiation due to risks of normal tissue damage. Other alternatives include hormonal therapy, radiopharmaceuticals (e.g., strontium 89), and bisphosphonates. Less often, surgery or chemotherapy may be used for palliation, and intractable pain may require opioid medications. Radiofrequency ablation (RFA) has been investigated as an alternative for palliation of bone metastases.

**OSTEOID OSTEOMAS**

Osteomas are the most common benign bone tumor, comprising 10% to 20% of benign and 2% to 3% of all bone tumors. They are typically seen in children and young adults, with most diagnosed in patients between five 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 non-steroidal anti-inflammatory drugs. The natural history of the osteoid osteoma varies based on location, and although they rarely exceed 1.5 cm in diameter, may produce bone widening and deformation, limb length inequality, or angular deviations when near a growth plate. When located in the spine, these lesions may lead to painful scoliosis or torticollis. Sometimes, they heal spontaneously after three to seven years.

**Treatment**

Treatment options include medical management with NSAIDs, surgical excision (wide/en bloc excision or curetting), or the use of computed tomography-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 the removal of a considerable amount of bone (especially in the neck of the femur). This increases the need for bone grafting plus internal fixation (which often necessitates a second procedure to remove the metal work). Other possible risks include avascular necrosis of the femoral head and postoperative pathologic fracture. In addition, surgical excision leads to a lengthier convalescence and postoperative immobilization. Anatomically inaccessible tumors may not be completely resectable and may recur. RFA of osteoid osteoma is done with a needle puncture, so no incision or sutures are needed; further, patients may immediately walk on the treated extremity and return to daily activities when the

anesthetic effect wears off. The risk of recurrence with RFA of an osteoma is 5% to 10%, and recurrent tumors can be retreated with RFA. In general, RFA is not performed in many spinal osteomas because of possible thermal-related nerve damage.

#### LOCALIZED RENAL CELL CARCINOMA

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

#### PRIMARY PULMONARY AND NONPULMONARY TUMORS

Surgery is the current treatment of choice in patients with stage I primary non-small-cell lung cancer (NSCLC; stage I includes Ia [T1N0M0] and Ib [T2N0M0]). 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 computed tomography scans for other indications. Postsurgical recurrence rates of stage I 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 I patients, with five-year overall survival rates ranging from 77% for small T1 tumors to 35% for large T2 tumors. Untreated, stage I NSCLC has a five-year overall survival rate range from 6% to 14%.

Patients with early-stage NSCLC who are not surgical candidates may be candidates for radiotherapy with curative intent. In two large retrospective radiotherapy series, patients with inoperable disease treated with definitive radiotherapy 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 body radiotherapy has gained more widespread use as a treatment option because it is a high-precision mode of therapy that delivers very high doses of radiation. Two- to three-year local control rates of stage I NSCLC with stereotactic body radiotherapy have ranged from 80% to 95%. Stereotactic body radiotherapy 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 cancers of the breast has evolved from total mastectomy to more conservative treatment options such as lumpectomy, with more acceptable cosmetic outcomes and preservation of the breast. The selection of surgical approach balances the patient's desire for breast conservation and the need for tumor-free margins in resected tissue. Minimally invasive nonsurgical techniques such as RFA are appealing if they can produce local control and survival equivalent to breast-conserving surgical alternatives. Nonsurgical ablative techniques pose difficulties such as the inability to determine tumor size, complete tumor cell death, and local recurrence. Additionally, RFA can burn the skin and damage the 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

RFA has been investigated for use in individuals with different lesions in different anatomic sites. These anatomic sites include, but are 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; further, these recurrent tumors are often untreatable with standard salvage therapies. Palliative chemotherapy or comfort measures may be offered. The safety and efficacy of RFA have been investigated as an option for palliative treatment in these situations.

## RADIOFREQUENCY ABLATION

RFA was initially developed to treat inoperable tumors of the liver (see the Radiofrequency Ablation of Primary or Metastatic Liver Tumors Protocol). 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 (e.g., 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 (e.g., single versus 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).

## REGULATORY STATUS

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.

## RELATED PROTOCOLS

Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate, or Dermatologic Tumors

Radiofrequency Ablation of Primary or Metastatic Liver Tumors

Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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