Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

Description

In radiofrequency ablation (RFA), a probe is inserted into the center of a tumor; then, prong-shaped, non-insulated 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 cm to 5.5 cm sphere of dead tissue. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is a local recurrence, it occurs at the edge and can sometimes be retreated. RFA may be performed percutaneously, laparoscopically, or as an open procedure.

OBJECTIVE

The objective of this evidence review is to determine whether the use of radiofrequency ablation improves the net health outcome in individuals with a range of tumors (including, osteolytic bone metastases, osteoid osteomas, renal cell carcinoma, lung cancer, breast tumors, and thyroid tumors, and others).
POLICY STATEMENT

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

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

Radiofrequency ablation may be considered medically necessary to treat localized renal cell carcinoma that is no more than 4 cm in size when either of the following criteria is met:

- When it is necessary to preserve kidney function in patients with significantly impaired renal function (ie, the patient has 1 kidney or renal insufficiency defined by a glomerular filtration rate of <60 mL/min/m^2); AND
- When the standard surgical approach (ie, 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 3 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 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart.

Radiofrequency ablation may be considered medically necessary to treat malignant nonpulmonary tumor(s) metastatic to the lung that are no more than 3 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 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery, and the heart.

(See the Policy Guidelines section 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.

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POLICY GUIDELINES

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

- 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.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

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

RATIONALE

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 radiofrequency ablation RFA, the evidence includes case series. The relevant outcomes are symptoms, change in disease status, quality of life (QOL), 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. The relevant outcomes are symptoms, change in disease status, quality of life (QOL), 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 (RCC)**

For individuals who have localized RCC that is no more than 4 cm in size who receive RFA, the evidence includes a randomized controlled trial (RCT), numerous observational studies, and systematic reviews of these studies. The relevant outcomes are overall survival (OS), change in disease status, QOL, 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 found that PN was superior to ablative techniques (the study included RFA but also cryoablation and microwave ablation) in overall mortality and local recurrence but not in cancer-specific mortality. It also found fewer complications and improved renal function with ablation. 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 Metastatic to Lung**

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. The relevant outcomes are OS, change in disease status, QOL, and treatment-related morbidity. A multicenter study found that for tumors less than 3.5 cm in size, RFA can lead to a complete response in as many as 88% of patients for at least 1 year. Two-year survival rates have been reported to range from 41% to 75% in case series, with 5-year survival rates of 20% to 27%. In general, the evidence suggests that RFA results in adequate survival and tumor control in patients who are not surgical candidates, with low morbidity rates. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Breast Tumors**

For individuals who have breast tumors who receive RFA, the evidence includes observational studies and systematic reviews of these studies. The relevant outcomes are OS, change in disease status, QOL, 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 compared 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. The relevant outcomes are symptoms, change in disease status, QOL, 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 (eg, head and neck, thyroid cancer, pancreas) who receive RFA, the evidence includes a few case series, prospective studies, and retrospective comparative studies. The relevant outcomes are OS, change in disease status, QOL, 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 technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

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Practice Guidelines and Position Statements

American College of Chest Physicians

The American College of Chest Physicians (2013) guidelines on the treatment of stage I and II non-small-cell lung cancer (NSCLC) have indicated 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. The College also collaborated with the Society of Thoracic Surgeons to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC. These 2012 consensus guidelines indicated RFA is an alternative treatment option for patients who are not surgical candidates due to severe medical comorbidity.

National Comprehensive Cancer Network

The NCCN guidelines for the treatment of non-small cell lung cancer (v.5.2019) state: "For medically operable disease, resection is the preferred local treatment modality (other modalities include SABR, thermal ablation such as radiofrequency ablation and cryotherapy)."

The NCCN guidelines for thyroid carcinoma (v.1.2019) indicate that local therapies such as RFA may be considered for locoregional recurrence of thyroid carcinoma-papillary carcinoma.

The NCCN guidelines (v.1.2020) for renal cancer indicate that "[t]hermal ablation (eg, cryosurgery, radiofrequency ablation) is an option for the management of patients with clinical stage T1 renal lesions. Thermal ablation is an option for masses <3 cm, but it may also be an option for larger masses in select patients. Ablation in masses >3 cm is associated with higher rates of local recurrence/persistence and complications." 65,

The NCCN colon cancer guidelines (v.2.2019), which are currently under discussion, state that "for the local treatment of resectable metastatic disease, patients with liver or lung oligometastases can be considered for tumor ablation therapy..." 67, Evidence on the use of RFA as a reasonable treatment option for non-surgical candidates and those with recurrent disease after hepatectomy with small liver metastases that can be treated with clear margins is growing.

The NCCN guidelines for head and neck cancers (v.2.2019) and pancreatic adenocarcinoma (v.3.2019) do not mention RFA.

National Institute for Health and Care Excellence

The NICE guidance (2004) on osteoid osteoma indicated that "current evidence on the safety and efficacy of computed tomography (CT)-guided thermocoagulation of osteoid osteoma appears adequate to support its use...."

Updated NICE guidance (2010) on renal cancer has indicated that "evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) ... in the short and medium term appears adequate to support the use of this procedure provided that patients are followed up in the long term." 70,

The NICE guidance (2010) on RFA for primary and secondary lung cancers has stated: "[C]urrent evidence on the efficacy of percutaneous radiofrequency ablation (RFA) ... is adequate in terms of tumor control." 71, The NICE also indicated RFA might "be used in patients with small, early-stage lung cancers or small numbers of lung metastases who are unsuitable for, or prefer not to undergo, surgery. It may also have a place in multi-modality treatment of more advanced primary lung cancers." The guidance warned of serious complications (eg, pneumothorax) among lung cancer patients.

The NICE guidance (2016) on benign thyroid nodules stated: "Current evidence on the safety and efficacy of ultrasound-guided percutaneous radiofrequency ablation ... is adequate to support the use of this procedure...." 72,

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U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

<table>
<thead>
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<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tr>
<td>June 2012</td>
<td>New policy</td>
<td>Policy updated with literature review, reworded not medically necessary policy</td>
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<tr>
<td>March 2013</td>
<td>Replace policy</td>
<td>statement and added thyroid as not medically necessary. References 12, 19, 29,</td>
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<td></td>
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<td>42, 50-52, 59, 62-63 added. Other references deleted.</td>
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<tr>
<td>March 2014</td>
<td>Replace policy</td>
<td>Policy updated with literature review, Policy statements unchanged. References added,</td>
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<td>March 2015</td>
<td>Replace policy</td>
<td>Policy updated with literature review; references 4, 48, and 56 added; other references deleted. Policy statements unchanged.</td>
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<tr>
<td>December 2016</td>
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<td>Policy updated with literature review; reference 13 added; references 54-56 updated; some references removed. Policy statements unchanged.</td>
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<tr>
<td>December 2017</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 20, 2017; reference 59 added. Policy statements unchanged.</td>
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<tr>
<td>December 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 26, 2018; references 5-7, 15-19, 31, 34-35, 40, 42, and 50 added. Policy statements unchanged.</td>
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<tr>
<td>December 2019</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 8, 2019; references added, references on NCCN updated. Policy statements unchanged.</td>
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