Radiofrequency Ablation of Primary or Metastatic Liver Tumors

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.

RELATED PROTOCOLS

Cryosurgical Ablation of Primary or Metastatic Liver Tumors
Radioembolization for Primary and Metastatic Tumors of the Liver
Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors
Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

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<th>Populations</th>
<th>Interventions</th>
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<th>Outcomes</th>
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| Individuals:  
• With primary, operable hepatocellular carcinoma | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Surgical resection | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Change in disease status  
• Morbid events |
| Individuals:  
• With inoperable hepatocellular carcinoma | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Systemic therapy  
• Other locally ablative therapies | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Change in disease status  
• Morbid events |
| Individuals:  
• With inoperable hepatocellular carcinoma awaiting liver transplant | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Other locoregional therapies | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Change in disease status |
| Individuals:  
• With inoperable hepatic metastases of colorectal origin | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Chemotherapy  
• Other locally ablative techniques  
• Best supportive care | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Symptoms  
• Change in disease status  
• Morbid events  
• Quality of life  
• Treatment-related morbidity |
Protocol: Radiofrequency Ablation of Primary or Metastatic Liver Tumors

Last Review Date: 09/22

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| Individuals:  
• With inoperable hepatic metastases of neuroendocrine origin | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Chemotherapy  
• Other locally ablative techniques  
• Best supportive care | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Symptoms  
• Change in disease status  
• Morbid events  
• Quality of life  
• Treatment-related morbidity |

Individuals:  
• With hepatic metastases not of colorectal or neuroendocrine origin | Interventions of interest are:  
• Radiofrequency ablation | Comparators of interest are:  
• Chemotherapy  
• Other locally ablative techniques  
• Other therapy  
• Best supportive care | Relevant outcomes include:  
• Overall survival  
• Disease-specific survival  
• Symptoms  
• Change in disease status  
• Morbid events  
• Quality of life  
• Treatment-related morbidity |

DESCRIPTION

Radiofrequency ablation (RFA) is a procedure in which a probe is inserted into the center of a tumor and heated locally by a high-frequency, alternating current that flows from electrodes. The local heat treats the tissue adjacent to the probe, resulting in a 3 to 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 of the treated tissue and, in some cases, is retreated. Radiofrequency ablation may be performed percutaneously, laparoscopically, or as an open procedure.

SUMMARY OF EVIDENCE

PRIMARY, OPERABLE HEPATOCELLULAR CARCINOMA

For individuals who have primary, operable hepatocellular carcinoma (HCC) who receive RFA, the evidence includes meta-analyses of randomized controlled trials (RCTs) and/or retrospective observational studies and additional observational studies. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and morbid events. The majority of data found that patients undergoing surgical resection experienced longer survival outcomes and lower recurrence rates than patients receiving RFA, though complication rates were higher with surgical resection. Some meta-analyses of specifically selected populations (e.g., small tumor sizes or Child-Pugh Class A liver function or HCC within the Milan criteria) found that OS and disease-free survival (DFS) rates were not significantly different between RFA and surgical resection. Results from observational studies have suggested that RFA alone or RFA plus percutaneous ethanol injection (PEI) could be as effective as a resection for small HCC tumors, as OS and DFS rates were not significantly different between RFA and surgical resection. An exact tumor cutoff size has not been established. Some studies found that OS was similar in patients receiving RFA or resection when tumor size was 3 cm or less; however, OS was significantly longer in patients undergoing resection if the tumor size was between 3.1 cm and 5 cm. Further study in a multicenter RCT would permit greater certainty whether RFA, with or without other ablative or arterial directed therapies, is as effective as surgical resection in treating HCC tumors 3 cm or smaller. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

INOPERABLE HEPATOCELLULAR CARCINOMA

For individuals who have inoperable HCC who receive RFA, the evidence includes RCTs and several systematic
reviews and meta-analyses. Relevant outcomes are OS, disease-specific survival, change in disease status, and morbid events. When resection is not an option, nonsurgical options include RFA, PEI, transarterial chemoembolization (TACE), cryoablation, microwave ablation, and systemic therapy. Meta-analyses comparing RFA to other local ablative therapies have found that RFA and microwave ablation are similarly effective, that RFA is more effective than PEI, and that RFA may be better than cryoablation. The evidence comparing RFA with TACE is limited, and no conclusions can be drawn. RFA has also been shown to improve survival in patients with unresectable HCC as an adjunct to chemotherapy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

INOPERABLE HEPATOCELLULAR CARCINOMA AWAITING LIVER TRANSPLANT

For individuals who have inoperable HCC awaiting liver transplant who receive RFA, the evidence includes small case series. Relevant outcomes are OS, disease-specific survival, and change in disease status. A number of approaches are used in this patient population, including RFA and other locoregional therapies, particularly TACE. Locoregional therapy has reduced the dropout rate of patients with HCC awaiting a liver transplant. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

INOPERABLE HEPATIC METASTASES OF COLORECTAL ORIGIN

For individuals who have inoperable hepatic metastases of colorectal origin who receive RFA, the evidence includes an RCT, systematic reviews and meta-analyses, prospective cohort series, and retrospective case series. Relevant outcomes are OS, disease-specific survival, symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. There are no RCTs comparing RFA with alternative treatments for patients who have unresectable colorectal liver metastases. However, an RCT assessing RFA plus chemotherapy found improved survival at 8 years compared with chemotherapy alone. In addition, prospective studies have demonstrated that OS following RFA is at least equivalent to and likely better than currently accepted systemic chemotherapy in well-matched patients with unresectable hepatic metastatic colorectal cancer who do not have extrahepatic disease. Results from a number of uncontrolled case series also have suggested RFA of hepatic colorectal cancer metastases produces long-term survival that is at a minimum equivalent to but likely superior to historical outcomes achieved with systemic chemotherapy. Evidence from a comparative study has indicated RFA has fewer deleterious effects on quality of life than chemotherapy and that RFA patients recover the quality of life significantly faster than chemotherapy recipients. It should be noted that patients treated with RFA in different series might have had better prognoses than those who had chemotherapy, suggesting patient selection bias might at least partially explain the better outcomes observed following RFA. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

INOPERABLE HEPATIC METASTASES OF NEUROENDOCRINE ORIGIN

For individuals who have inoperable hepatic metastases of neuroendocrine origin who receive RFA, the evidence includes case series and a systematic review of case series. Relevant outcomes are OS, disease-specific survival, symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. Most reports of RFA treatment for neuroendocrine liver metastases have assessed small numbers of patients or subsets of patients in reports of multiple ablative methods or very small subsets of larger case series of patients with various diagnoses. The available evidence has indicated that durable tumor and symptom control of neuroendocrine liver metastases can be achieved using RFA in individuals whose symptoms are not controlled by systemic therapy or who are ineligible for resection. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

HEPATIC METASTASES NOT OF COLORECTAL OR NEUROENDOCRINE ORIGIN

For individuals who have hepatic metastases not of colorectal or neuroendocrine origin who receive RFA, the evidence includes small nonrandomized comparative studies and small case series. Relevant outcomes are OS, disease-specific survival, symptoms, change in disease status, morbid events, quality of life, and treatment-
related morbidity. Similar to primary HCC, resection appears to have the most favorable outcomes. For patients who are ineligible for resection, RFA may provide a survival benefit. However, the evidence is limited by study designs with a high-risk of bias and small sample sizes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY
Radiofrequency ablation of primary, inoperable (e.g., due to location of lesion[s] and/or comorbid conditions), hepatocellular carcinoma (HCC) may be considered medically necessary under the following conditions:

• as a primary treatment of HCC meeting the Milan criteria (a single tumor of five cm or less, or up to three nodules smaller than three cm).
• as a bridge to transplant, where the intent is to prevent further tumor growth and to maintain a patient’s candidacy for liver transplant.

Radiofrequency ablation as a primary treatment of inoperable hepatic metastases may be considered medically necessary under the following conditions:

• metastases are of colorectal origin and meet the Milan criteria (a single tumor of five cm or less or up to three nodules smaller than three cm).
• metastases are of neuroendocrine in origin and systemic therapy has failed to control symptoms.

Radiofrequency ablation of primary, inoperable, HCC is considered investigational under the following conditions:

• when there are more than three nodules or when not all sites of tumor foci can be adequately treated.
• when used to downstage (downsize) HCC in patients being considered for liver transplant.

Radiofrequency ablation of primary, operable hepatocellular carcinoma is investigational.

Radiofrequency ablation for hepatic metastasis is considered investigational for:

• hepatic metastases from colorectal cancer or neuroendocrine tumors that do not meet the criteria above; and
• hepatic metastases from other types of cancer with the exception of colorectal cancer or neuroendocrine tumors.

BACKGROUND
HEPATIC AND NEUROENDOCRINE TUMORS

Hepatic tumors can arise as primary liver cancer (hepatocellular cancer) or by metastasis to the liver from other tissues. Local therapy for hepatic metastasis may be indicated when there is no extrahepatic disease, which rarely occurs for patients with primary cancers other than colorectal carcinoma or certain neuroendocrine malignancies.

Neuroendocrine tumors are tumors of cells that possess secretory granules and originate from the neuroectoderm. Neuroendocrine cells have roles both in the endocrine system and in the nervous system. They produce and secrete a variety of regulatory hormones, or neuropeptides, which include neurotransmitters and growth factors. Overproduction of the specific neuropeptides produced by the cancerous cells causes various symptoms, depending on the hormone produced. They are rare, with an incidence of 2 to 4 per 100,000 per year.
Treatment

Treatment options for hepatocellular carcinoma (HCC) range from potentially curative treatments, such as resection or liver transplantation, to nonsurgical options, which include ablative therapies (radiofrequency ablation [RFA], cryoablation, microwave ablation, percutaneous ethanol or acetic acid injection), transarterial chemoembolization, radiation therapy, and systemic therapy. Choice of therapy depends on the severity of the underlying liver disease, size and distribution of tumors, vascular supply, and patient overall health. Treatment of liver metastases is undertaken to prolong survival and to reduce endocrine-related symptoms and hepatic mass-related symptoms.

At present, surgical resection with adequate margins or liver transplantation constitutes the only treatments available with demonstrated curative potential for hepatic tumors. However, most hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve. Comorbid conditions may also make patients unqualified for surgical resection.

RADIOFREQUENCY ABLATION

Radiofrequency ablation (RFA) is a procedure in which a needle electrode is inserted into a tumor either percutaneously, through a laparoscope, or through an open incision. The electrode is heated by a high-frequency, alternating current, which destroys tissue in a 3 to 5 cm sphere of the electrode. Radiofrequency ablation has been investigated as a treatment for unresectable hepatic tumors, both as a primary intervention and as a bridge to a liver transplant. In the latter setting, RFA is being tested to determine whether it can reduce the incidence of tumor progression in patients awaiting transplantation and thus maintain patients’ candidacy for liver ablation, transhepatic arterial chemoembolization, microwave coagulation, percutaneous ethanol injection, and radioembolization (yttrium-90 microspheres).

REGULATORY STATUS

Radiofrequency ablation devices have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process. Food and Drug Administration product code: GEI.

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


