

Protocol

Radiofrequency Ablation of Primary or Metastatic Liver Tumors

(70191)

Medical Benefit		Effective Date: 01/01/19	Next Review Date: 09/20
Preauthorization	No	Review Dates: 11/07, 11/08, 09/09, 09/10, 09/11, 09/12, 09/13, 09/14, 09/15, 09/16, 09/17, 09/18, 09/19	

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"> With primary, operable hepatocellular carcinoma 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Surgical resection 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Change in disease status Morbid events
Individuals: <ul style="list-style-type: none"> With inoperable hepatocellular carcinoma 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Systemic therapy Other locally ablative therapies 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Change in disease status Morbid events
Individuals: <ul style="list-style-type: none"> With inoperable hepatocellular carcinoma awaiting liver transplant 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Other locoregional therapies 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Change in disease status
Individuals: <ul style="list-style-type: none"> With inoperable hepatic metastases of colorectal origin 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Chemotherapy Other locally ablative techniques Best supportive care 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Symptoms Change in disease status Morbid events Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With inoperable hepatic metastases of neuroendocrine origin 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Chemotherapy Other locally ablative techniques Best supportive care 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Symptoms Change in disease status Morbid events Quality of life Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> With hepatic metastases not of colorectal or neuro-endocrine origin 	Interventions of interest are: <ul style="list-style-type: none"> Radiofrequency ablation 	Comparators of interest are: <ul style="list-style-type: none"> Chemotherapy Other locally ablative techniques Other therapy Best supportive care 	Relevant outcomes include: <ul style="list-style-type: none"> 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 three to five cm sphere of dead tissue. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. If there is local recurrence, it occurs at the edge of the treated tissue and, in some cases, is retreated. RFA 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 randomized controlled trials (RCTs), meta-analyses of these RCTs, database analyses, and observational studies. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and morbid events. Results from these studies have suggested that RFA alone or RFA plus transhepatic arterial chemoembolization may be as effective as resection for small resectable HCC tumors, although the exact size cutoff has not been established. Some studies found that overall survival was similar in patients receiving RFA or resection when tumor size was three cm or less; however, overall survival was significantly longer in patients undergoing resection if the tumor size was between 3.1 cm and five cm. Further study in a multicenter RCT would permit greater certainty whether RFA, with or without transhepatic arterial chemoembolization, is as effective as surgical resection in treating HCC tumors three cm or smaller. The evidence is insufficient to determine the effects of the technology RFA on health outcomes.

Inoperable HCC

For individuals who have inoperable HCC who receive RFA, the evidence includes randomized trials and several systematic reviews and meta-analyses. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and morbid events. When resection is not an option, nonsurgical options include RFA, percutaneous ethanol injection, transarterial chemoembolization, cryoablation, microwave ablation, and systemic therapy. Meta-analyses comparing these nonsurgical options have shown improved survival outcomes with RFA alone or combined with other treatments (e.g., with percutaneous ethanol injection or systemic therapy) compared with other nonsurgical treatments alone. Response rates have demonstrated that, in patients with small foci of HCC (three or fewer lesions), RFA appears to be better than percutaneous ethanol injection in achieving complete ablation and preventing local recurrence. Three-year survival rates of 80% have been reported. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Inoperable HCC Awaiting Liver Transplant

For individuals who have inoperable HCC awaiting liver transplant who receive RFA, the evidence includes small case series. Relevant outcomes are overall survival, 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 transarterial chemoembolization. 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 a meaningful 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 overall survival, 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 eight years compared with chemotherapy alone. In addition, prospective studies have demonstrated that overall survival following RFA is at least equivalent to and likely better than for 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 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 a meaningful 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 overall survival, 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 a meaningful 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 overall survival, 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 the effects of the technology RFA on health outcomes.

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 two to four per 100,000 per year.

Treatment

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 unresect-

table at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve. Patients may also have comorbid conditions and do not qualify for surgical resection.

Treatment of liver metastases is undertaken to prolong survival and to reduce endocrine-related symptoms and hepatic mass-related symptoms.

Alternative therapies available include liver transplantation, systemic therapies, or ablation procedures (radiofrequency ablation [RFA], cryoablation, microwave ablation, percutaneous ethanol or acetic acid injection). Choice of therapy depends on the severity of underlying liver disease, size and distribution of tumors, vascular supply, and patient overall health.

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 three to five cm sphere of the electrode. RFA has been investigated as a treatment for unresectable hepatic tumors, both as a primary intervention and as a bridge to 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).

Note that RFA of extrahepatic tumors is addressed in evidence review Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors Protocol.

REGULATORY STATUS

RFA 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.

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

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.**

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

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