



FEP Medical Policy Manual

FEP 7.01.91 Radiofrequency Ablation of Primary or Metastatic Liver Tumors

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Related Policies:

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

Radiofrequency Ablation of Primary or Metastatic Liver Tumors

Description

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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.

OBJECTIVE

The objective of this evidence review is to determine whether radiofrequency ablation improves the net health outcome in individuals with primary hepatocellular carcinoma or hepatic metastases.

POLICY STATEMENT

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

- as a primary treatment of hepatocellular carcinoma meeting the Milan criteria (a single tumor of ≤ 5 cm or up to 3 nodules < 3 cm).
- as a bridge to transplant, where the intent is to prevent further tumor growth and to maintain an individual'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 ≤ 5 cm or up to 3 nodules < 3 cm).
- metastases are of neuroendocrine origin and systemic therapy has failed to control symptoms.

Radiofrequency ablation of primary, inoperable, hepatocellular carcinoma is considered **investigational** under the following conditions:

- when there are more than 3 nodules or when not all sites of tumor foci can be adequately treated.
- when used to downstage (downsize) hepatocellular carcinoma in individuals 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
- for hepatic metastases from other types of cancer except colorectal cancer or neuroendocrine tumors.

POLICY GUIDELINES

None

BENEFIT APPLICATION

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

FDA 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.

RATIONALE

Summary of Evidence

For individuals who have primary, operable hepatocellular carcinoma (HCC) who receive radiofrequency ablation (RFA), the evidence includes meta-analyses of randomized controlled trials (RCTs) and/or retrospective observational studies, an RCT, 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 and an RCT of specifically selected populations (eg, 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.

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.

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.

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 (CRC) who do not have extrahepatic disease. Results from a number of uncontrolled case series also have suggested RFA of hepatic CRC 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 their 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.

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.

For individuals who have hepatic metastases, not of colorectal or neuroendocrine origin who receive RFA, the evidence includes a systematic review, 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Association for the Study of Liver Diseases

The American Association for the Study of Liver Diseases (AASLD) published a guideline in 2018 on the treatment of hepatocellular carcinoma (HCC),⁷¹ which was subsequently updated in 2023.⁷² Relevant guidance statements related to radiofrequency ablation (RFA) are listed below:

- "Thermal ablation (radiofrequency or microwave ablation) should be considered the treatment of choice for patients with early-stage HCC ≤ 3 cm who are ineligible for or decline surgery (Level 1, Strong Recommendation).
 - AASLD does not advise 1 thermal ablative modality over another."

National Comprehensive Cancer Network

Several National Comprehensive Cancer Network (NCCN) guidelines are relevant to this review.

The NCCN (v1.2024) guidelines on HCC note that "locoregional therapy should be considered in patients who are not candidates for surgical curative treatments, or as part of a strategy to bridge patients for other curative therapies." The guideline further states that "ablation alone may be curative in treating tumors ≤ 3 cm. In well-selected patients with small, properly located tumors, ablation should be considered a definitive treatment in the context of a multidisciplinary review. Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, or with the combination of an arterially directed therapy and ablation as long as the tumor is accessible for ablation".⁷³

The NCCN (v2.2024) guidelines on colon cancer metastatic to the liver state that "Ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection".⁷⁴ Of all ablative techniques, the guidelines note that RFA has the most supporting evidence.

The NCCN (v1.2023) guidelines for neuroendocrine and adrenal tumors state that "percutaneous thermal ablation, often using microwave energy (radiofrequency and cryoablation are also acceptable), can be considered for oligometastatic liver disease, generally up to 4 lesions each smaller than 3 cm. Feasibility considerations include safe percutaneous imaging-guided approach to the target lesions, and proximity to vessels, bile ducts, or adjacent non-target structures that may require hydro- or aero-dissection for displacement." Additionally, "cytoreductive surgery or ablative therapies such as RFA or cryoablation may be considered if near-complete treatment of tumor burden can be achieved (category 2B). Ablative therapy in this setting is non-curative...For unresectable liver metastases, hepatic regional therapy (arterial embolization, chemoembolization, or radioembolization [category 2B]) is recommended."⁷⁵

Society of American Gastrointestinal and Endoscopic Surgeons

The Society of American Gastrointestinal and Endoscopic Surgeons with the Americas Hepato-Pancreato-Biliary Association developed guidelines (2023) for the use of microwave and radiofrequency liver ablation for the surgical treatment of hepatocellular carcinoma or colorectal liver metastases less than 5 cm.⁷⁶ A systematic review was conducted to address key questions and GRADE methodology was used to provide evidence-based recommendations. All guideline recommendations were assigned "conditional" recommendations based on the weak evidence found. The key questions and subsequent recommendations related to RFA addressed by the guideline are summarized in Table 1.

Table 1. SAGES/AHPBA recommendations for use of ablative therapy

Key questions addressed by the guideline	Recommendations
Should MWA (laparoscopic or open) vs. RFA (laparoscopic or open) be used for HCC or CRLM less than 5 cm ineligible for other therapies?	The panel suggests MWA and RFA are both safe and feasible. There was insufficient evidence to recommend one modality over another in terms of oncologic outcomes (conditional recommendation, very low certainty of evidence).

AHPBA: Americas Hepato-Pancreato-Biliary Association; MWA: microwave ablation; RFA: radiofrequency ablation; SAGES: Society of American Gastrointestinal and Endoscopic Surgeons.

Society of Interventional Radiology

The Society of Interventional Radiology (2009) published a position statement on percutaneous RFA for the treatment of liver tumors.⁷⁷ The Society indicated that "percutaneous RFA of hepatic tumors is a safe and effective treatment for selected patients with HCC and colorectal carcinoma metastases" and that the current literature does not support any recommendations for or against the use of RFA in other diseases.

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.

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

Date	Action	Description
December 2011	New policy	
December 2012	Replace policy	Policy updated with literature search; duplicate reference 29 was removed and references renumbered. References 4 and 29 added; references 5, 6 and 40-42 updated. Policy statements remain unchanged.
September 2013	Replace policy	Policy updated with literature search; References 4-5, 7-8 and 29-30 added; references 9 and 48 updated. Policy statements remain unchanged.
September 2014	Replace policy	Policy updated with literature review. References 2-6, 35, and 46 added; policy statements unchanged.
September 2015	Replace policy	Policy updated with literature review. References 2-6, 35, and 46 added; policy statements unchanged
September 2017	Replace policy	Policy updated with literature review through June 2, 2017; references 2, 5, 11-12, 14, 18, 22, and 40-41, 44 added; references 58-60 updated. Policy statements reformatted and edited for clarity and specificity, including the distinction between operable and non-operable tumors and the Milan criteria. The intent of the statements is unchanged. A statement has been added that RFA for operable HCC is considered investigational.
September 2018	Replace policy	Policy updated with literature review through May 7, 2018; references 14, 16, 18-21, 56, and 63-66 added. Policy statements unchanged.
September 2019	Replace policy	Policy updated with literature review through May 13, 2019; references on NCCN updated. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through June 2, 2020; references added. Policy statements unchanged.
September 2021	Replace policy	Policy updated with literature review through June 2, 2021; references added. Policy statements unchanged.
September 2022	Replace policy	Policy updated with literature review through June 8, 2022; 1 reference added and additional references updated. Minor editorial refinements to policy statements; intent unchanged.
September 2023	Replace policy	Policy updated with literature review through June 2, 2023. References added. Policy statements unchanged.
September 2024	Replace policy	Policy updated with literature review through May 20, 2024; references added. Policy statements unchanged.

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