Title: Radiofrequency Ablation of Primary or Metastatic Liver Tumors

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**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 local recurrence, it occurs at the edge, and in some cases may be retreated. RFA may be performed percutaneously, laparoscopically, or as an open procedure.

**Background**

Hepatic tumors can arise either as primary liver cancer (hepatocellular cancer [HCC]) 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. At present, surgical resection with adequate margins or liver transplantation constitutes the only treatments available with demonstrated curative potential. However most hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve.

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

Radiofrequency ablation (RFA) has been investigated as a treatment for unresectable hepatic tumors, both as primary treatment and as a bridge to liver transplant. In the latter setting, it is hoped that RFA will reduce the incidence of tumor progression while awaiting transplantation and thus maintain a patient’s 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 (FDA) through the 510(k) process. FDA product code GEI.

**POLICY**
A. Radiofrequency ablation of primary hepatocellular carcinoma (HCC) may be considered **medically necessary** as a primary treatment of HCC for patients when there are no more than 3 nodules and all tumor foci can be adequately treated (see Policy Guidelines).

B. Radiofrequency ablation of primary hepatocellular carcinoma (HCC) is considered **medically necessary** as a bridge to transplant, where the intent is to prevent further tumor growth and to maintain a patient’s candidacy for liver transplant.

C. Radiofrequency ablation of primary hepatocellular carcinoma (HCC) is considered **experimental / investigational** when there are more than 3 nodules or when not all sites of tumor foci can be adequately treated.

D. Radiofrequency ablation may be considered **medically necessary** as a primary treatment of hepatic metastases from colorectal cancer in the absence of extrahepatic metastatic disease when all tumor foci can be adequately treated.

E. Radiofrequency ablation of primary hepatocellular carcinoma (HCC) is considered **experimental / investigational** when used to downstage (downsize) HCC in patients being considered for liver transplant.

F. Radiofrequency ablation may be considered **medically necessary** as a primary treatment of hepatic metastases 5 cm or less in diameter from colorectal cancer in the absence of extrahepatic metastatic disease when all tumor foci can be adequately treated (see Policy Guidelines section).

G. Radiofrequency ablation may be considered **medically necessary** as treatment of hepatic metastases from neuroendocrine tumors in patients with symptomatic disease when systemic therapy has failed to control symptoms (see Policy Guidelines section).
H. Radiofrequency ablation for hepatic metastasis is considered experimental / investigational:
   1. for hepatic metastases from colorectal cancer or neuroendocrine tumors that do not meet the criteria above; and
   2. for hepatic metastases from other types of cancer with the exception of colorectal cancer or neuroendocrine tumors.

Policy Guidelines
1. Explicit criteria have not been established for RFA of HCC or cancer metastatic to the liver.
2. For the medically necessary indications noted above for RFA in those with primary HCC and metastatic colorectal or neuroendocrine tumors, patients should not be candidates for curative resections (eg, due to location of lesion[s] and/or comorbid conditions) and for HCC should also not be candidates for liver transplantation unless RFA is used as a bridge to transplant.
3. Candidacy for RFA treatment of HCC is based on several factors that include number of tumor foci (nodules), size of tumor foci, and accessibility. In general, the randomized trials for HCC have included patients with 3 or fewer hepatic lesions measuring 5 cm or less (and often ≤3 cm) using current technology.
4. Candidacy for RFA treatment of metastatic colorectal cancer is based on several factors that include number of tumor foci, size of tumor foci, and accessibility. In general, published studies with metastatic colorectal cancer have included patients with 4 to 5 or fewer hepatic lesions measuring 5 cm or less using current technology.

RATIONALE
This evidence review has been updated with periodic literature reviews of the MEDLINE database; the most recent update with literature review covers the period through June 13, 2016.

Radiofrequency Ablation as a Primary Treatment of Unresectable HCC Systematic Reviews
A 2003 TEC Assessment addressed radiofrequency ablation (RFA) in the treatment of unresectable primary or metastatic liver tumors. Since that time, many systematic reviews and meta-analyses have been published on RFA for hepatocellular cancer (HCC). Some of these are discussed below.

In 2016, Lan et al published a network meta-analysis comparing different interventional treatments for early stage HCC. A total of 21 RCTs were included that compared TACE, RFA, percutaneous ethanol injection, and hepatic resection, or combinations of treatments. These studies were all rated at a low to moderate risk of bias, with lack of blinding being the most substantial limitation. The primary outcome measures were overall survival at 1, 3, and 5 years post-treatment. The treatments and combinations of treatments were rank ordered according to the results on overall survival. At each time point, the combination of RFA + TACE was the number one ranked treatment. The combination of RFA + TACE ranked second highest at 1 and
3 years, and was third highest at 5 years, with hepatic resection ranked second at 5 years. RFA alone was ranked as the fourth highest treatment at 1 year and the fifth highest treatment at 3 and 5 years.

In a Cochrane review published in 2013, Weis et al reviewed studies on RFA for HCC versus other interventions. Moderate quality evidence demonstrated hepatic resection had superior survival outcomes compared with RFA; however, resection might have greater rates of complications and longer hospital stays. Other systematic reviews and meta-analyses have also found superior survival with hepatic resection but higher rates of complications than RFA. This reinforces the use of RFA for only unresectable HCC. The Cochrane review also reported finding moderate quality evidence demonstrating superior survival with RFA over percutaneous ethanol injection (PEI). Evidence on RFA versus acetic acid injection, microwave ablation, or laser ablation was insufficient to draw conclusions.

Randomized and nonrandomized trials in the 1990s reported that PEI could safely achieve complete necrosis in small HCCs, with 5-year survival rates of 32% to 38%. A systematic review of randomized trials for HCC treated with percutaneous ablation therapies was conducted by Cho et al. The authors identified 4 RCTs involving 652 patients that compared RFA with PEI. The review concluded that RFA demonstrated significantly improved 3-year survival in patients with HCC compared with ethanol injections. Most patients in these studies had 1 tumor, and more than 75% of the tumors were 3 cm or smaller in size. The 3-year survival with RFA ranged from 63% to 81%.

In a 2013, Shen et al reported on a systematic review of 4 RCTs and quasi-RCTs (total N=766 patients), to compare RFA with PEI for treatment of HCC nodules up to 3 cm. Overall survival (OS) was significantly longer for RFA than PEI at 3 years (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.48 to 0.90; p=0.009), and local recurrence risk was lower with RFA (HR=0.38; 95% CI, 0.15 to 0.96, p=0.040). However, there was no difference in distant intrahepatic recurrence and RFA resulted in more complications.

In 2012, Xu et al reported on a meta-analysis of 13 studies to compare RFA with surgical resection for early HCC. Only 2 studies were RCTs. Surgical resection occurred in 1233 patients and RFA was used in 1302 patients. Surgical resection patients had significantly longer OS rates at 1, 3 and 5 years than RFA (odds ratio [OR], 0.60; 95% CI, 0.42 to 0.86; OR=0.49; 95% CI, 0.36 to 0.65; OR=0.60; 95% CI, 0.43 to 0.84), respectively. When only HCC tumors of 3 cm or less were analyzed, resection was still significantly better in OS than RFA at 1, 3, and 5 years. Recurrence rates were also significantly lower in the surgical resection group at 1, 3, and 5 years than RFA (OR=1.48; 95% CI, 1.05 to 2.08; OR=1.76; 95% CI, 1.49 to 2.08; OR=1.68; 95% CI, 1.21 to 2.34), respectively. Local recurrence rates did not differ significantly between procedures. Complication rates were higher with resection than RFA (OR=6.25; 95% CI, 3.12 to 12.52; p=0.000), but in a subanalysis of HCC 3 cm or less, complication rates were significantly lower with resection than RFA.

Tiong and Maddern conducted a systematic review of the literature from 2000 to 2010 and a meta-analysis of survival and disease recurrence after RFA for HCC. Studies reporting on patients with HCC who were treated with RFA, either in comparison or in combination with other interventions, such as surgery or PEI, were eligible for inclusion. Outcome data collected were OS, disease-free survival (DFS), and disease recurrence rates. Only RCTs, quasi-RCTs, and
nonrandomized comparative studies with more than 12 months of follow-up were included. Forty-three articles, including 12 RCTs, were included in the review. Most articles reported the use of RFA for unresectable HCC, often in combination with other treatments such as PEI, transhepatic arterial chemoembolization (TACE), and/or surgery. A meta-analysis of 5 RCTs showed that RFA was better than PEI, with higher OS and DFS rates. Data on RFA compared with microwave ablation were inconclusive. The authors concluded that RFA can achieve good clinical outcomes for unresectable HCC.

In a 2013 meta-analysis comparing RFA with cryoablation for HCC, Huang et al evaluated 3 prospective studies and 1 retrospective study. Included in the studies were 180 RFA and 253 cryoablation patients. RFA was significantly superior to cryoablation in rates of complications (OR=2.80; 95% CI, 1.54 to 5.09), local recurrence of patient (OR=4.02; 95% CI, 1.93 to 8.39), and local recurrence of tumor (OR=1.96, 95% CI, 1.12 to 3.42). However, mortality did not differ significantly (OR=2.21; 95% CI, 0.45 to 10.8) between groups.

**Randomized Controlled Trials**
In 2012, Feng et al reported on an RCT of 84 RFA patients compared with 84 surgical resection patients with up to 2 HCC nodules less than 4 cm in size. Patients were followed for 3 years, and OS and recurrence-free survival (RFS) did not differ statistically between groups (p=0.342 and p=0.122, respectively).

**Section Summary: RFA as a Primary Treatment for Patients with Unresectable HCC**
Randomized and nonrandomized trials have been performed comparing RFA to alternate treatments for HCC. RCTs of RFA versus hepatic resection report that resection is associated with greater overall survival, but also with more complications. RCT evidence has also established that RFA is more effective than PEI in this population, and a small amount of evidence reports that RFA may be better than cryoablation. The evidence on RFA versus TACE is limited and no conclusions can be drawn. This evidence supports the use hepatic resection as first line therapy for HCC, and the use of RFA in patients who are inoperable.

**RFA for Patients with Unresectable HCC Awaiting Transplant**
In 2002, the United Network for Organ Sharing (UNOS) introduced a new liver allocation system—Model for End-stage Liver Disease (MELD)—for adult patients awaiting liver transplant. The MELD score is a continuous disease severity scale incorporating bilirubin, prothrombin time (ie, international normalized [INR] ratio for prothrombin activity), and creatinine into an equation, producing a number that ranges from 1 to 40. Aside from those in fulminant liver failure, donor livers are prioritized to those with the highest MELD number. This scale accurately predicts the risk of dying from liver disease except for those with HCC, who often have low MELD scores because bilirubin, INR, and creatinine levels are near normal.

In considering how to allocate the scarce donor organs, UNOS sought to balance risk of death on the waiting list against risk of recurrence after transplant. Under UNOS criteria, patients with T1 lesions (1 nodule ≤1.9 cm) are considered at low risk of death on the waiting list, while those with T3 lesions (1 nodule >5.0 cm, or 2 or 3 nodules with at least 1 >3.0 cm) are at high risk of posttransplant recurrence. Patients with T2 tumors (1 nodule ≥2.0 cm and ≤5.0 cm, or 2 or 3 nodules ≥1 cm and ≤3.0 cm) have an increased risk of dying while on the waiting list compared with those with T1 lesions and an acceptable risk of posttransplant tumor recurrence. Therefore, UNOS criteria prioritize T2 HCC by allocating additional points equivalent to a MELD score.
predicting a 15% probability of death within 3 months. The definition of T2 lesions is often referred to as the “Milan criteria,” in reference to a key 1996 study that examined the recurrence rate of HCC according to the size of the initial tumor. Note that liver transplantation for those with T3 HCC is not prohibited, but these patients do not receive priority on the waiting list. All patients with HCC awaiting transplantation are reassessed at 3-month intervals. Those whose tumors have progressed and are no longer T2 tumors will lose the additional allocation points.

Therefore, the UNOS allocation system provides incentives to use locoregional therapies in 2 different settings:

- To prevent progress of T2 tumors while on the waiting list; or
- To downsize T3 tumors to T2 status to meet the UNOS criteria for additional allocation points.

These 2 indications are discussed further here. It should be noted that the UNOS policy addresses the role of locoregional therapy in the pretransplant setting as follows:

Organ Procurement and Transplant Network (OPTN) Class 5T (Treated) nodules are defined as any OPTN Class 5 or biopsy-proven HCC lesion that was automatically approved upon initial application or extension and has subsequently undergone loco-regional treatment. OPTN Class 5T nodules qualify for continued priority points predicated on the pre-treatment classification of the nodule(s) and are defined as:

1. Past loco-regional treatment for HCC (OPTN Class 5 lesion or biopsy proven prior to ablation).
2. Evidence of persistent/recurrent HCC such as nodular or crescentic extra-zonal or intra-zonal enhancing tissue on late arterial imaging (relative to hepatic parenchyma) may be present.

OPTN guidelines also indicate “candidates whose tumors have been ablated after previously meeting the criteria for additional MELD/PELD points (OPTN Class 5T) will continue to receive additional MELD/PELD points (equivalent to a 10-percentage point increase in candidate mortality) every 3 months without RRB [regional review board] review, even if the estimated size of residual viable tumor falls below stage T2 criteria.”

Candidates with HCC not meeting transplant criteria, “including those with downsized tumors whose original/presenting tumor was greater than a stage T2, must be referred to the applicable RRB for prospective review in order to receive additional priority.”

**RFA to Prevent Tumor Progression**

Several prior studies have reported dropout rates of wait-listed patients treated with locoregional therapy. However, lacking controlled data, it is difficult to assess contributions of locoregional therapy to time on the waiting list. In addition, in 2002, as previously discussed, UNOS revised its liver allocation policy, such that wait times for patients with HCC meeting the Milan criteria have now declined.

Most of the literature has focused either on TACE or a variety of locoregional therapies. Given these limitations, the following case series have been reported. Fisher et al reported on 33 patients who received multimodality ablation therapy, consisting primarily of RFA or TACE. Five (12%) patients were removed from the waiting list after waits of 5 to 14 months. In this protocol, patients with tumors larger than 5 cm were not considered transplant candidates until
the tumor was completely ablated using TACE, RFA, or another technique. Yamashiki et al reported on 288 patients given various ablative therapies; the dropout rate due to tumor progression at 1 and 3 years was 6.2% and 23%, respectively. Tumors greater than 3 cm affected the dropout rate due to tumor progression. Mazzaferrr et al reported on 50 patients with HCC who underwent RFA while awaiting transplantation; no patient had to be removed from the waiting list due to tumor progression over a mean wait time of 9.5 months. The median tumor size was 3 cm, and 80% of patients met the Milan criteria. Similarly, Lu et al reported on 52 patients who underwent RFA as a bridge to transplantation, 42 of whom met the Milan criteria. After a mean of 12 months, 5.8% had dropped off the waiting list due to tumor progression.

In 2008, Belghiti et al reviewed the literature reporting efficacy of local management approaches including resection, TACE, RFA, and no treatment. They concluded that RFA can induce complete necrosis in most small tumors (<2.5 cm), and that no data demonstrate that the treatment reduces the rate of dropout before transplantation or improves survival after transplant. None of the studies included data from U.S. centers for patients listed after adoption of the Milan criteria. Porrett et al retrospectively compared 31 patients treated with RFA with 33 untreated controls. Study end points included patient survival and DFS, tumor recurrence, explant tumor viability, and the ability of magnetic resonance imaging (MRI) to detect viable tumor after therapy. Both cohorts had similar demographic, radiographic, and pathologic characteristics, although untreated patients waited longer for transplantation (119 [untreated] days vs 54 [RFA] days after MELD assignment; p=0.05). Only 20% of treated tumors demonstrated complete ablation (necrosis) as defined by histologic examination of the entire lesion. Only 55% of lesions with histologic viable tumor were detected by MRI after pretransplant therapy. After 36 months of follow-up, there was no difference between the treated and the untreated groups in OS (84% vs 91%), DFS (74% vs 85%), cancer recurrence (23% vs 12%), or mortality from cancer recurrence (57% vs 25%, all respectively) (p>0.1). The authors concluded that viable tumor frequently persists after pretransplant locoregional therapy, and neoadjuvant treatment does not appear to improve posttransplant outcomes in the current MELD era.

Current UNOS policy on allocation of livers indicates that candidates whose tumors have been ablated after meeting the criteria for additional MELD/PELD (PELD – calculator for persons <12 years of age) points (OPTN class 5T) will continue to receive additional points (equivalent to a 10% increase in mortality) every 3 months without review, even if the estimated size of residual viable tumor falls below stage T2 criteria. UNOS policy also notes that candidates may be removed from the listing if they are determined to be unsuitable for transplantation based on progression of HCC.

**RFA to Downgrade HCC**

Yao et al analyzed longer term outcome data on HCC downstaging in a cohort of 61 patients with tumor stage exceeding T2 criteria enrolled between June 2002 and January 2007. Eligibility criteria for downstaging included: (1) 1 lesion larger than 5 cm and up to 8 cm; (2) 2 to 3 lesions with at least 1 lesion larger than 3 cm and not exceeding 5 cm, with total tumor diameter up to 8 cm; or (3) 4 to 5 lesions with none larger than 3 cm, with total tumor diameter up to 8 cm. TACE and laparoscopic RFA (LRFA) either alone or in combination were the main methods used: 11 patients received LRFA alone, 14 received TACE and LRFA, and 9 received TACE and percutaneous RFA. A minimum observation period of 3 months after downstaging was required before liver transplant. Tumor downstaging was successful in 43 patients (70.5%). Thirty-five
(57.4%) patients received liver transplant, including 2 with live-donor liver transplantation. Treatment failure was observed in 18 (29.5%) patients, primarily due to tumor progression. In the explant of 35 patients who underwent transplant, 13 had complete tumor necrosis, 17 met T2 criteria, and 5 exceeded T2 criteria. The Kaplan-Meier intention-to-treat survival rates at 1 and 4 years after downstaging were 87.5% and 69.3%, respectively. The 1- and 4-year posttransplantation survival rates were 96.2% and 92.1%, respectively. No patient had HCC recurrence after a median posttransplantation follow-up of 25 months. The only factor predicting treatment failure was pretreatment α-fetoprotein greater than 1000 ng/mL. From this small series, the authors concluded that successful downstaging can be achieved with excellent posttransplant outcomes.

A national conference involving transplant physicians was held to better characterize the long-term outcomes of liver transplantation for patients with HCC and to discuss the policy of assigning increased priority for candidates with stage T2 HCC on the transplant waiting list in the United States. Goals of the conference were to standardize pathology reporting, to develop specific imaging criteria, to expand the Milan criteria, discuss locoregional therapy, to define criteria for downstaging transplantation, and to review current liver allocation system for HCC patients. Pomfret et al summarized the conference findings and recommendations.24

The workgroup on locoregional therapy found compelling evidence that pretransplant locoregional therapy decreases waitlist dropout, especially for patients who wait longer than 3 to 6 months for transplant. They noted that “there is a paucity of data comparing RFA with transarterial therapies for the treatment of HCC prior to liver transplant and most single-center trials have a mixture of [locoregional therapies] included in the study population” and that, while early studies suggested a high rate of tumor seeding with percutaneous RFA, it is rare in larger series from experienced centers. The workgroup considering evidence to support expansion of MELD criteria for patients with HCC reported wide regional variation in the risk of death for patients without HCC. The “MELD score of the non-HCC patients was quite low in some regions. Posttransplant survival in HCC patients ranged from 25% in regions with few non-HCC patients with high MELD scores to greater than 70% in regions in which there was a greater need for liver transplant (higher MELD scores) in the non-HCC population.” The workgroup observed that there is extreme variability of the time to transplantation of patients with HCC in the United States suggesting that management of patients on the waitlist and outcomes may vary. In addition, “Concern has been raised that short times to liver transplant may lead to an increase in posttransplant recurrence because the tumor biology [aggressiveness] has not had enough time to be expressed. The lack of national data on recurrence rates limits one’s ability to study this national experiment of nature based on the divergent waiting times for transplantation for HCC.” There was agreement that the allocation policy should result in similar risks of removal from the waiting list and similar transplant rates for HCC and non-HCC candidates. In addition, the allocation policy should select HCC candidates so that posttransplant outcomes are similar for HCC and non-HCC recipients. There was a general consensus for the development of a calculated continuous HCC priority score for ranking HCC candidates on the list that would incorporate the calculated MELD score, α-fetoprotein, tumor size, and rate of tumor growth. Only candidates with at least stage T2 tumors would receive additional HCC priority points. The article discusses pretransplant local regional therapy to allow patients to maintain transplant candidacy, as well as to downstage to meet MELD criteria. The workgroup on the role of downstaging in transplant candidates with HCC noted inconsistent outcomes reported in the literature and proposed a
definition of downstaging that would include TACE and various ablative techniques but not resection. The group noted that only 2 regions have adopted a downstaging protocol.

Yao et al reported on a case series of 30 patients with HCC who underwent locoregional therapy specifically to downstage tumors to meet the University of California San Francisco (UCSF) criteria. Eligibility for locoregional therapy seeking to downstage patients included either (1) 1 nodule between 5 and 8 cm in diameter; (2) 2 or 3 nodules with at least 1 between 3 and 5 cm in diameter, with a sum of diameters no greater than 8 cm; or (3) 4 or 5 nodules all 3 cm or less, with a sum of diameters less than 8 cm. Among the 30 patients, 21 (70%) met the criteria for locoregional therapy and 16 of these were successfully downstaged and underwent transplantation. No tumors recurred at a median follow-up of 16 months. The authors concluded that downstaging can be successfully achieved in most patients but that data regarding tumor recurrence required longer follow-up.

**RFA to Reduce Risk of Recurrence in Those With T3 Tumors**

An additional indication for locoregional therapies focuses on their use in patients with T3 tumors, specifically to reduce the incidence of recurrence posttransplant. If the incidence of recurrence can be reduced, then advocates have argued that the UNOS allocation criteria should not discriminate against patients with larger tumors. Some patients with T3 lesions apparently are cured with liver transplant, although most experience recurrent tumor. For example, in the seminal 1996 study, the 4-year RFS was 92% in those who met the Milan criteria compared with 59% in those who did not; additional studies confirm this difference in the RFS rate. However, other institutions have reported similar outcomes with expanded criteria. For example, Yao et al at UCSF reported similar RFS after transplant in patients with T2 tumors and a subset of those with T3 tumors. This T3 subset was defined as a single lesion 6.5 cm or less or 3 or fewer lesions with none greater than 3 cm and with a sum of tumor diameters 8 cm or less. These expanded criteria are known as the UCSF criteria.

The question is whether locoregional therapies (including both RFA and chemoembolization) may decrease the recurrence rate in patients meeting the UCSF criteria. Yao et al published a detailed analysis of 121 patients with HCC who underwent transplantation. Seventy-eight (64%) patients had T2 lesions, while an additional 27 (22.3%) patients met the expanded UCSF criteria, termed T3A lesions. The rest had T1, T3B, or T4 lesions. Individual patients received a variety of preoperative locoregional therapies, including TACE or ablative therapies, such as PEI, RFA, or combined therapies. A total of 38.7% of patients did not receive preoperative locoregional therapy. The 1- and 5-year RFS rates were similar in those with T2 and T3A lesions, while the corresponding RFS rates were significantly lower for those with T3B and T4 lesions.

The authors also compared RFS of those who did and did not receive locoregional therapy. For those with T2 lesions, recurrence rates were similar whether or not the patient received locoregional therapy. However, for T3 lesions (including both T3A and T3B), the 5-year RFS was 85.9% for those who received locoregional therapy compared with 51.4% in those who did not. When the data for T2 and T3 lesions were grouped, the 5-year RFS was 93.8% for those who received locoregional therapy compared with 80.6% in those who did not. The authors concluded that preoperative locoregional therapy may confer a survival benefit in those with T2 or T3 lesions.
The authors also noted several limitations to the study, including the retrospective nature of the data and the marginal statistical significance of the improved survival given the small numbers of patients in each subgroup. For example, only 19 patients were in the T3A (ie, UCSF expanded criteria) subgroup. In addition, no protocol specified which type of locoregional therapy to offer different patients. These therapies are only offered to those patients with adequate liver reserve; such patients may have an improved outcome regardless of the preoperative management.

**Section Summary: RFA for Unresectable HCC in patients awaiting transplant**

The evidence on the use of RFA for HCC in patients awaiting transplant consists of case series and uncontrolled trials. There is sufficient evidence to conclude that locoregional therapy with RFA or alternatives decreases the dropout rate from the transplant list. This is especially true if patients wait more than 3-6 months for a transplant. Therefore, outcomes are improved for this group. For other uses of RFA in the transplant, such as to downgrade tumors for eligibility for transplant, and/or to prevent disease recurrence, the evidence is insufficient to make conclusions.

**RFA as a Primary Treatment of Unresectable Liver Metastases**

**Colon Cancer**

More than half of patients with colorectal cancer (CRC) will develop liver metastases, generally with a poor prognosis. A median survival of 21 months has been observed in patients with a single CRC liver metastasis; those with several unilobar lesions have median survival of 15 months; and those with disseminated metastases have median survival of less than 1 year. A number of first-line systemic chemotherapy regimens have been used to treat metastatic CRC, with a 2-year survival rate of 25% for those treated with 5-fluorouracil (5-FU) or 5-FU plus leucovorin. With the introduction of newer agents, including irinotecan and oxaliplatin, and targeted drugs such as cetuximab and bevacizumab, 2-year survival rates have increased to 30% to 39%, with marked improvement in OS duration. Because the liver is often the only site of metastases from CRC, however, locoregional therapies have been investigated. Surgical resection is considered the criterion standard for treatment of CRC liver metastases, with 5-year actuarial survival rates that historically range from 28% to 38% but may reach 58% in appropriately selected, resectable patients without widely disseminated disease. However, only 10% to 25% of patients with CRC metastases are eligible for surgical resection because of the extent and location of the lesions within the liver or because of the presence of comorbid conditions or disseminated disease. Unresectable cases or those for whom surgery is contraindicated typically are treated with systemic chemotherapy, with poor results and considerable adverse effects.

Alternatively, RFA has been proposed as an approach to treat metastatic CRC in the liver. Early clinical experience with RFA comprised case series to establish feasibility, safety, tolerability, and local therapeutic efficacy in short-term follow-up. A 2006 literature review encompassing 6 case series (N=446) showed that RFA of unresectable CRC metastases was associated with 1-, 2-, and 3-year survival rates that ranged from 87% to 99%, 69% to 77%, and 37% to 58%, respectively. While these results suggest RFA may have clinical benefit in this setting, a primary caveat is the definition of the term “unresectable” in the different series and that different surgeons may have different opinions on this issue. Further, differences in lesion size, number, distribution, prior treatments, RFA technology, and physician experience may affect results, making it difficult to compare results of different studies.
Systematic Reviews
A 2012 systematic review by Cirocchi et al analyzed 17 nonrandomized studies and 1 abstract on an RCT from a 2010 American Society of Clinical Oncology meeting on RFA for CRC liver metastases.35 The RCT reported PFS was significantly higher in 60 patients receiving RFA plus chemotherapy compared with 59 patients receiving only chemotherapy. The RCT did not report OS. This Cochrane review found different types of vulnerability in all reviewed studies. Of main concern was the imbalance of patient characteristics in the studies reviewed, as well as heterogeneity in the interventions, comparisons, and outcomes. Therefore the authors concluded the evidence was insufficient to recommend RFA for CRC liver metastasis. In a 2014 Health Technology Assessment, Loveman et al also found insufficient evidence to draw conclusions on the clinical effectiveness of ablative therapies, including RFA, for liver metastases.36

In 2012, Weng et al reported a systematic review and meta-analysis comparing RFA with liver resection for the treatment of CRC liver metastases.37 One prospective study and 12 retrospective studies were included in the analysis. OS at 3 and 5 years was significantly longer in liver resection than RFA (relative risk [RR], 1.377; 95% CI, 1.246 to 1.522; RR=1.474; 95% CI, 1.284 to 1.692, respectively). DFS was also significantly longer in liver resection than RFA at 3 and 5 years (RR=1.735; 95% CI, 1.483 to 2.029; RR=2.227; 95% CI, 1.823 to 2.720). While postoperative morbidity with liver resection was significantly higher than with RFA (RR=2.495; 95% CI, 1.881 to 3.308), mortality did not differ significantly between liver resection and RFA. Liver resection also performed significantly better than RFA when data were analyzed in 3 subgroups: tumors less than 3 cm, solitary tumor, and open or laparoscopic approach. However, hospital stays were significantly shorter (9.2 vs 3.9, p<0.01) and rates of complications lower (18.3% vs 3.9%, p<0.01) with RFA than liver resection. Interpretation of the meta-analysis is limited by the retrospective nature of most studies.

A 2011 systematic review by Pathak et al assessed the long-term outcome and complication rates of various ablative therapies used in the management of colorectal liver metastases.38 The literature search was from 1994 to 2010, and study inclusion criteria were minimum 1-year follow-up and more than 10 patients. In all, 226 potentially relevant studies were identified, 75 of which met the inclusion criteria. Most studies were single-arm, single-center, retrospective, and prospective. There was wide variability in patient groups, adjuvant therapies, and management approaches within individual studies. Several studies combined results for colorectal and non–colorectal metastases, often reporting combined outcomes. End points were not always reported uniformly, with varying definitions of survival time, recurrence time, and complication rates. Cryotherapy (26 studies) had local recurrence rates of 12% to 39%, with mean 1-, 3-, and 5-year survival rates of 84%, 37%, and 17%, respectively. The major complication rate ranged from 7% to 66%. Microwave ablation (13 studies) had a local recurrence rate of 5% to 13%, with a mean 1-, 3-, and 5-year survival of 73%, 30%, and 16%, respectively, and a major complication rate ranging from 3% to 16%. RFA (36 studies) had a local recurrence rate of 10% to 31%, with a mean 1-, 3-, and 5-year survival of 85%, 36%, and 24%, respectively, with major complication rate ranging from 0% to 33%. The authors concluded that ablative therapies offer significantly improved survival compared with palliative chemotherapy alone, with 5-year survival rates of 17% to 24%, and that complication rates of commonly used techniques are low.

A review by Guenette and Dupuy in 2010 summarized the literature on the use of RFA for colorectal hepatic metastases.39 Approximately 17 studies with more than 50 patients treated with RFA for colorectal hepatic metastases reported survival. Average tumor size, reported in 15
studies, ranged from 2.1 to 4.2 cm. Five-year OS, reported in 12 studies, ranged from 2% to 55.3%, with a mean of 24.5%. The largest study series (Lencioni et al) included in the review consisted of 423 patients, with average tumor size of 2.7 cm, 4 or fewer metastases, each 5 cm or less in greatest dimension, and no extrahepatic disease. OS in the Lencioni study at 1, 3, and 5 years was 86%, 47%, and 24%, respectively. Guenette and Dupuy concluded that 5-year survival rates following RFA appear to rival those following resection but that long-term data associated with RFA and colorectal hepatic metastases are sparse, randomized trials have failed recruitment, and patients with resectable disease should undergo resection if possible. However, given the efficacy of RFA compared with chemotherapy alone, RFA should be considered as a primary treatment option in patients with unresectable disease.

**Nonrandomized Comparative Studies**

Nonrandomized comparative studies in which RFA was compared with resection or systemic chemotherapy in patients with localized CRC metastases and no evidence of additional metastatic disease have been conducted. In 2016, Hof et al compared outcomes from RFA or hepatic resection in patients with hepatic metastases from CRC. There were 431 patients included from an institutional database. All patients underwent some type of locoregional treatment for hepatic metastases from CRC. Initial treatment was either hepatic resection (n=261), open RFA (n=26), percutaneous RFA (n=75), or a combination of resection plus RFA (n=69). Mean followup was 38.6 months. The overall recurrence rate was 83.5% (152/182) in patients treated with RFA, compared to a rate of 66.6% (201/302) in patients treated with hepatic resection (p<0.001). The 5 year overall survival estimate by Kaplan-Meier analysis was 51.9% for RFA compared to 53.0% for hepatic resection (p=0.98).

Abdalla et al examined recurrence and survival rates for clinically similar patients treated with hepatic resection only (n=190), resection plus RFA (n=101), RFA only (n=57, open laparotomy by hepatobiliary surgeon), and systemic chemotherapy alone (n=70). In the key relevant comparison, RFA versus chemotherapy in chemotherapy-naive patients with nonresectable CRC metastases (median, 1 lesion per patient; range, 1-8; median tumor size, 2.5 cm), OS at 4 years was 22% in the RFA group and 10% in the chemotherapy group (p=0.005). Median survival was estimated at 25 months in the RFA group and 17 months in the chemotherapy group (p not reported). Recurrence anywhere in the liver at median follow-up of 21 months was 44% in the RFA group and 11% in the resection-only group (p<0.001), although the proportion of patients with distant recurrence as a component of failure was similar (41% resection, 40% RFA, p=NS).

In a second trial, a consecutive series of well-defined, previously untreated patients (N=201) without extrahepatic disease underwent laparotomy to determine therapeutic approach. Three groups were identified: those amenable to hepatic resection (n=117); those for whom resection plus local ablation were indicated (RFA, n=27; cryoablation, n=18); and those deemed unresectable and unsuitable for local ablation (n=39) who received systemic chemotherapy. Median OS was 61 months (95% CI, 41 to 81 months) in resected patients (median, 1 tumor per patient; range, 1-9; median diameter, 3.8 cm), 31 months (95% CI, 20 to 42 months) in locally ablated patients (median, 4 tumors per patient; range, 1-19; median diameter, 3 cm per lesion), and 26 months (95% CI, 17 to 35 months) in the chemotherapy patients (median, 4 tumors per patient; range, 1-17; median diameter, 4 cm per lesion; p=NS, ablated vs chemotherapy). Results from 2 validated quality-of-life instruments (EuroQol-5D, EORTC QLQ C-30) showed that patients treated by local ablation returned to baseline values within 3 months, whereas those
treated with chemotherapy remained significantly lower (ie, worse quality of life) than baseline over 12 months posttreatment (p<0.05).

In 2011, Van Tilborg et al reported long-term results in 100 patients with unresectable colorectal liver metastases who underwent a total of 126 RFA sessions (237 lesions). Lesion size ranged from 0.2 to 8.3 cm (mean 2.4 cm). The mean follow-up time was 29 months (range, 6-93 months). Major complications (including abscess, hemorrhage, grounding pad burns, and diaphragm perforation) occurred in 8 patients. Factors that determined the success of the procedure included lesion size and the number and location of the lesions. Local tumor site recurrence was 5.6% for tumors less than 3 cm, 19.5% for tumors 3 to 5 cm, and 41.2% for those greater than 5 cm. Centrally located lesions recurred more often than peripheral, at 21.4% versus 6.5%, respectively (p=0.009). Mean survival time from the time of RFA was 56 months (95% CI, 45 to 67 months).

**Neuroendocrine Tumors**

Most reports of RFA treatment of neuroendocrine liver metastases include small numbers of patients or subsets of patients in reports of more than 1 ablative method or very small subsets of larger case series of patients with various diagnoses. A systematic review of RFA as treatment for unresectable metastases from neuroendocrine tumors was published in 2016. There were 7 unique studies with 301 patients included in the review, all were retrospective case series from a single institution. The most common tumor type was carcinoid (59%), followed by nonfunctional pancreatic tumors (21%) and functional pancreatic tumors (13%). There were two peri-procedural deaths for a rate of 0.7%, and the overall rate of complications was 10% (including hemorrhage, abscess, viscus perforation, bile leak, bilio-pleural fistula, transient liver insufficiency, pneumothorax, grounding pad burn, urinary retention, pneumonia, and pleural effusion). Improvement in symptoms was reported in 92% of symptomatic patients (117/127), with a median duration of symptom relief ranging from 14 to 27 months. There was a high degree of variability in the length of followup and the surveillance used for followup, and a wide range of local recurrence rates, from less than 5% to 50%. The reported 5 year survival rates ranged from 57% to 80%.

Berber and Siperstein analyzed a large series of liver tumors treated with RFA. Of 1032 tumors in the study, 295 were neuroendocrine tumor metastases. The mean number of lesions treated was 5.6 (range, 1-16) and mean size was 2.3 cm (range, 0.5-10.0 cm). Local recurrence rates were lower in patients with neuroendocrine tumors than in patients with other tumor types: neuroendocrine tumors (19/295 [6%]), colorectal metastases (161/480 [24%]), non–colorectal, non–neuroendocrine metastases (28/126 [22%]), and HCC (23/131 [18%]). In patients with neuroendocrine tumors, 58% of the recurrences were evident at 1 year and 100% at 2 years versus 83% at 1 year and 97% at 2 years for colorectal metastases. Eight neuroendocrine tumors were eligible for repeat RFA; 7 were retreated, and 1 was not. Symptom control and survival were not reported.

Mazzaglia et al report on a series gathered over 10 years of 63 patients with neuroendocrine metastases who were treated with 80 sessions of LRFA. Tumor types were 36 carcinoid, 18 pancreatic islet cell, and 9 medullary thyroid cancer. Indications for study enrollment were liver metastases from neuroendocrine tumors, enlarging liver lesions, worsening of symptoms, and/or failure to respond to other treatment modalities and predominance of disease in the liver; however, patients with additional minor extrahepatic disease were not excluded from the study.
RFA was performed 1.6 years (range, 0.1-7.8 years) after diagnosis of liver metastases. Fourteen patients had repeat sessions for disease progression. The mean number of lesions treated at the first RFA session was 6 and the mean tumor size was 2.3 cm. One week after surgery, 92% of patients had at least partial symptom relief and 70% had complete relief. Symptom control lasted 11 months. Median survival times were 11 years postdiagnosis of primary tumor, 5.5 years postdiagnosis of neuroendocrine hepatic metastases, and 3.9 years after first RFA treatment.

Elias et al report on 16 patients who underwent a 1-step procedure comprising a combination of hepatectomy and RFA for treatment of gastroenteropancreatic endocrine tumors.47 A mean of 15±9 liver tumors per patient were surgically removed, and a mean of 12±8 were ablated using RFA. Three-year survival and DFS rates were similar to those observed in the authors' preliminary series of 47 patients who had hepatectomy with a median of 7 liver tumors per patient. Venkatesan et al reported on 6 patients treated for pheochromocytoma metastases.48 Complete ablation was achieved in 6 of 7 metastases. Mean follow-up was 12.3 months (range, 2.5-28 months).

**Breast Cancer**

A number of case series report RFA of breast cancer liver metastases. In 2014, Veltri et al analyzed 45 women treated with RFA for 87 breast cancer liver metastases of a mean size of 23 mm.49 Complete ablation was seen on initial follow-up in 90% of tumors, but tumor recurrence occurred in 19.7% within 8 months. RFA did not impact OS, which at 1 year was 90% and at 3 years was 44%.

In a retrospective review, Meloni et al assessed local control and intermediate- and long-term survival in 52 patients.50 Inclusion criteria were fewer than 5 tumors, maximum tumor diameter of 5 cm, and disease confined to the liver or stable with medical therapy. Complete tumor necrosis was achieved in 97% of tumors. Median time to follow-up from diagnosis of liver metastasis and from RFA was 37.2 and 19.1 months, respectively. Local tumor progression occurred in 25% of patients, and new intrahepatic metastases developed in 53%. Median OS, from the time of first liver metastasis diagnosis, was 42 months, and 5-year survival was 32%. Patients with tumors 2.5 cm in diameter or larger had a worse prognosis than those with smaller tumors. The authors concluded that these survival rates are comparable to those reported in the literature for surgery or laser ablation. In another series of 43 breast cancer patients with 111 liver metastases, technical success was achieved in 107 (96%) metastases.51 During follow-up, local tumor progression was observed in 15 metastases. Estimated median OS was 58.6 months. Survival was significantly lower among patients with extrahepatic disease, with the exception of skeletal metastases.

A series of 19 patients was reported by Lawes et al.52 Eight patients had disease confined to the liver, with 11 also having stable extrahepatic disease. At the time of the report, 7 patients, with disease confined to the liver at presentation, were alive, as were 6 with extrahepatic disease; median follow-up after RFA was 15 months (range, 0-77 months). Survival at 30 months was 41.6%. RFA failed to control hepatic disease in 3 patients.

**Sarcoma**

Jones et al evaluated RFA in a series of patients with sarcoma.53 Thirteen gastrointestinal stromal tumor (GIST) patients and 12 with other histological subtypes received RFA for metastatic disease in the liver: 12 of them responded to the first RFA procedure and 1 achieved stable
disease. Two GIST patients received RFA on 2 occasions to separate lesions within the liver, and both responded to the second RFA procedure. Of the other subtypes: 7 underwent RFA to liver lesions, 5 of whom responded to RFA, 1 progressed and 1 was not assessable at the time of analysis. RFA was well-tolerated in this series of sarcoma patients. RFA may have a role in patients with GIST who have progression in a single metastasis but stable disease elsewhere. The authors advised that further larger studies are required to better define the role of this technique in this patient population.

A case series of 66 patients who underwent hepatic resection (n=35), resection and RFA (n=18), or RFA alone (n=13) was reported by Pawlik et al. After a median follow-up of 35.8 months, 44 patients had recurrence (intrahepatic only, n=16; extrahepatic only, n=11; both, n=17). The 1-, 3-, and 5-year OS rates were 91.5%, 65.4%, and 27.1%, respectively. The authors recommended that patients with metastatic disease who can be rendered surgically free of disease be considered for potential hepatic resection.

Section Summary: RFA as Primary Treatment of Unresectable Liver Metastases

There are no RCTs of RFA versus alternative treatments for patients with unresectable liver metastases. Two prospective studies have demonstrated that overall survival following RFA is at least equivalent and likely better than that obtained with 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 suggest RFA of hepatic CRC metastases produces long-term survival that is at least equivalent and likely superior to systemic chemotherapy, based on historical outcomes. Evidence from 1 comparative study suggests RFA has less deleterious effect on quality of life than chemotherapy and that RFA patients recover quality of life significantly faster than chemotherapy recipients. Patients treated with RFA in different series may have better prognosis than those who undergo chemotherapy, meaning that patient selection bias may at least partially explain the better outcomes observed following RFA. Durable tumor and symptom control of neuroendocrine liver metastases can be achieved by RFA in individuals whose symptoms are not controlled by systemic therapy. For cancers other than CRC or neuroendocrine tumors, small case series are not sufficient evidence to determine whether RFA improves outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

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Summary of Evidence
For individuals who have primary, unresectable, hepatocellular carcinoma (HCC) who receive radiofrequency ablation (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, morbid events, hospitalizations, and treatment-related morbidity. Surgical resection of HCC, compared with RFA, has shown superior survival, supporting the use of RFA for unresectable HCC and for those who are not candidates for surgical resection. Response rates have demonstrated that, in patients with small foci of HCC (≤3 lesions), RFA appears to be better than 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 qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable 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 qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable hepatic metastases of colorectal or neuroendocrine origin who receive RFA, the evidence includes 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. Two prospective studies have demonstrated that overall survival following RFA is at least equivalent and likely better than that for currently accepted systemic chemotherapy in well-matched patients with unresectable hepatic metastatic colorectal cancer (CRC) who do not have extrahepatic disease, and results from a number of uncontrolled case series also have suggested RFA of hepatic CRC metastases produces long-term survival that is at minimum equivalent but likely superior to historical outcomes achieved with systemic chemotherapy. Evidence from 1 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, however, that patients treated with RFA in different series may have had better prognoses than those who underwent chemotherapy, suggesting patient selection bias may at least partially explain the apparent better outcomes observed following RFA. Durable tumor and symptom control of neuroendocrine liver metastases can be achieved by RFA in individuals whose symptoms are not controlled by systemic therapy. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable hepatic metastases other than colorectal or neuroendocrine origin who receive RFA, the evidence includes 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. The evidence is insufficient to determine the effects of the technology RFA on health outcomes.
Practice Guidelines and Position Statements

Society of Interventional Radiology
The Society of Interventional Radiology (SIR) published a position statement on percutaneous RFA for the treatment of liver tumors in 2009. It is SIR’s position that “percutaneous RF ablation of hepatic tumors is a safe and effective treatment for selected patients with HCC and colorectal carcinoma metastases” and that the current literature is insufficient to support any recommendations supporting or refuting the use of RFA in other diseases.

National Comprehensive Cancer Network
National Comprehensive Cancer Network (NCCN) guidelines recommend the following. The hepatobiliary cancers (v.2.2016) guidelines state that “ablation alone may be curative in treating tumors ≤ 3 cm. In well-selected patients with small, properly located tumors, ablation should be considered as definitive treatment in the context of a multidisciplinary review. Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, alone or with combination of an arterially directed therapy and ablation as long as the tumor is accessible for ablation” (category 2A).

The guidelines on colorectal cancer metastatic to the liver (v.2.2016) 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.” (category 2A).

The NCCN guidelines for neuroendocrine tumors (v.2.2016) state that “…ablative therapies such as radiofrequency ablation (RFA) or cryoablation may be considered if near-complete treatment of tumor burden can be achieved (category 2B). For unresectable liver metastases, … (arterial embolization, chemoembolization, or radioembolization [category 2B]) is recommended.

U.S. Preventive Services Task Force Recommendations
Not applicable.

CodiNG
The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS
47370 Laparoscopy, surgical, ablation of one or more liver tumor(s); radiofrequency
47380 Ablation, open, of one or more liver tumor(s); radiofrequency
47382 Ablation, 1 or more liver tumor(s), percutaneous, radiofrequency
76940 Ultrasound guidance for, and monitoring of, parenchymal tissue ablation

ICD-9 Diagnoses
155.0 Malignant neoplasm of liver
155.2 Liver, not specified as primary or secondary
197.7 Secondary malignant neoplasm of respiratory or digestive system; liver, specified as secondary
209.72 Secondary neuroendocrine tumor of liver
ICD-10 Diagnoses (Effective October 1, 2015)
C22.0  Liver cell carcinoma
C22.2  Hepatoblastoma
C22.3  Angiosarcoma of liver
C22.4  Other sarcomas of liver
C22.7  Other specified carcinomas of liver
C22.8  Malignant neoplasm of liver, primary, unspecified as to type
C22.9  Malignant neoplasm of liver, not specified as primary or secondary
C78.02  Secondary carcinoma tumors of liver
C78.7  Secondary malignant neoplasm of liver and intrahepatic bile duct

REVISIONS

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REFERENCES

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Radiofrequency ablation of unresectable hepatic tumors. TEC Assessments 2003: Volume 18, Tab 13. PMID


