BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Locoregional Therapies for Hepatocellular Carcinoma and Metastatic Liver Carcinoma and Metastatic Carcinoid Tumors of the Liver

Policy #: 070
Category: Surgical
Latest Review Date: August 2020
Policy Grade: B

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after June 1, 2015:

Blue Advantage will treat **Radio-frequency Ablation (RFA)** as a **covered benefit** for patients with one of the following indications:

- hepatocellular carcinoma (HCC)
- metastatic liver carcinoma

Blue Advantage will treat **Percutaneous Ethanol Injection (PEI)** as a **covered benefit** for patients with one of the following indications:

- hepatocellular carcinoma (HCC)
- metastatic liver carcinoma

Please refer to Policy #178 "MRI-Guided Focused Ultrasound (MRgFUS)" for coverage information on ultrasound ablation of the bone.

Please refer to Policy #119 "Radiofrequency Ablation of Solid Tumors Excluding Liver Tumors" for coverage information on radiofrequency ablation of solid tumors excluding liver.

Please refer to NCD (230.9) for Cryosurgery of Prostate.

Please refer to Policy #429 "Cryosurgical Ablation of Miscellaneous Solid Tumors Other than Liver, Prostate, or Dermatologic Tumors" for coverage information on cryosurgical ablation of these tumors.

Please refer to Policy #512 "Microwave Tumor Ablation" for coverage information on microwave tumor ablation.

Please refer to Policy MP# 737 "Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver" for coverage information on Transcatheter Arterial Chemoembolization.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Hepatic tumors can arise either as primary liver cancer (hepatocellular cancer) or by metastasis to the liver from other tissues. At present, surgical resection with adequate margins or liver transplantation constitutes the only treatments available with demonstrated curative potential. However, because most hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve; local therapy may be indicated.

Local therapy for hepatic metastasis is indicated only when there is no extrahepatic disease, which rarely occurs for patients with primary cancers other than CRC or certain neuroendocrine malignancies. For liver metastases from CRC, postsurgical adjuvant chemotherapy has been reported to decrease recurrence rates and prolong time to recurrence. Combined systemic and hepatic arterial chemotherapy may increase disease-free intervals for patients with hepatic metastases from CRC but apparently is not beneficial for those with unresectable hepatocellular carcinoma.

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 a variety of symptoms depending on the hormone produced. They are rare, with an incidence of two to four per 100,000 per year.

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

Various locoregional therapies for unresectable liver tumors have been evaluated: transhepatic arterial embolization (TACE), radiofrequency ablation, percutaneous ethanol injection, microwave ablation, cryosurgical ablation (cryosurgery), and radioembolization with yttrium-90 microspheres.

Radio-frequency Ablation (RFA)

Another alternative to surgical resection of liver tumors is RFA**.** During the procedure, a probe is inserted into the center of a tumor and heated locally by a high frequency, alternating current that flow from electrodes. The local heat treats the tissue adjacent to the probe, resulting in a 3 to 5cm 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 can be performed percutaneously, laparoscopically, or open procedure.

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).

Percutaneous Ethanol Injection (PEI)
PEI induces tumor necrosis by cellular dehydration, protein denaturation, and thrombosis of small vessels. HCC is softer than the surrounding cirrhotic liver and is often encapsulated, allowing selective diffusion of ethanol within the tumor mass. The hypervascularization of HCC also favors ethanol injection therapy by enhancing the distribution of ethanol within the network of the tumor vessels. A fine needle is inserted into the tumor under ultrasonographic guidance, and absolute ethanol is then injected slowly into the tumor until the whole area of tumor appears hypoechogenic on the ultrasound. PEI may be performed under CT guidance for tumors not visualized by ultrasounds. The injection is repeated once or twice a week for up to six to eight sessions, depending on the tumor size. PEI can be done as an outpatient procedure under local anesthesia.

KEY POINTS:
The most recent literature update was performed through June 2, 2020.

Summary
RFA
Operable Hepatocellular Carcinoma
For individuals who have primary, operable hepatocellular carcinoma (HCC) who receive RFA, the evidence includes randomized controlled trials (RCTs), meta-analyses RCTs and retrospective observational studies, and additional observational studies. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and morbid events. The majority of data found that patients undergoing surgical resection experienced longer survival outcomes and lower recurrence rates than patients receiving RFA, though complication rates were higher with surgical resection. Results from observational studies have suggested that RFA alone or RFA plus 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. Although the exact size cutoff has not been established, current National Comprehensive Cancer Network guidelines suggest use of ablation as a treatment option when tumors are 3 cm or smaller. 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 the effects of the technology RFA on health outcomes.

Inoperable Hepatocellular Carcinoma
For individuals who have primary, inoperable, hepatocellular carcinoma (HCC) who receive RFA, the evidence includes randomized trials and nonrandomized trials. Relevant outcomes are overall survival, disease-specific survival, changes in disease status, morbid events,

hospitalizations, and treatment-related morbidity. 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 (eg, with percutaneous ethanal injection or systemic therapy) compared with other nonsurgical treatments alone. Response rates demonstrate 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. Therefore, the evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

Inoperable Hepatic Metastases of Colorectal Origin

For individuals with 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, changes in disease status, morbid events, quality of life, and treatment-related morbidity. There are no RCTs comparing RFA with alternative treatments for patients with unresectable colorectal liver metastases. However, an RCT assessing RFA combined with chemotherapy found improved survival at 8 years compared with chemotherapy alone. In addition, 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 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 minimum equivalent but likely superior to historical outcomes achieved with systemic chemotherapy. Evidence from one 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. It should be noted, however, that patients treated with RFA in different series may have better prognosis than those who undergo chemotherapy, suggesting patient selection bias may at least partially explain the apparent 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 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 more than 1 ablative method or very small subsets of larger case series of patients with various diagnoses. The available evidence indicates 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 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. Complete ablation of tumors was seen in >/= 90% of tumors in most studies; however, there was tumor recurrence. Although there are only small case series available, OS was documented as being at least 90% at 1year in 2 studies. The available evidence indicates that symptom control may be achieved using RFA, therefore the evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Percutaneous Ethanol Injection
For patients who have inoperable hepatocellular carcinoma, PEI can be considered. The evidence includes several RCTs, non- randomized trials and a comparative analysis. It has been noted that to achieve complete necrosis of liver tumors using PEI, multiple treatment sessions are usually needed.

Practice Guidelines and Position Statements
RFA:
Society of Interventional Radiology
The Society of Interventional Radiology published a position statement on percutaneous radiofrequency ablation for the treatment of liver tumors in 2009. It is the position of the Society 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
The National Comprehensive Cancer Network (NCCN) guidelines recommend:

- The guidelines for Hepatobiliary Cancers (v.3.2020) 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 3-5 cm may be treated to prolong survival using arterially directed therapies, alone or in combination with ablation as long as the tumor is accessible for ablation" (category 2A).
- The guidelines for colorectal cancer metastatic to the liver (v3.2020) 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). Of all ablative techniques, the guidelines note that RFA has the most supporting evidence.
- The NCCN guidelines for Neuroendocrine Tumors (v..2019) state that ablative therapies such as radiofrequency ablation 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."

Percutaneous Ethanol Injection:
National Comprehensive Cancer Network
The 2018 NCCN guidelines (v2.2018) state that "locoregional therapy should be considered in patients who are not candidates for surgical curative treatments, or as a part of a strategy to bridge patients for other curative therapies." PEI is included in the locoregional therapies.

- Tumors should be amenable to ablation, but a margin is not expected following PEI
- Tumors should be accessible for ablation

U.S. Preventive Services Task Force Recommendations

- RFA of tumors is not a preventive service.

KEY WORDS:

Locoregional liver therapy, Locoregional liver treatment, Radio-frequency Ablation (RFA), Percutaneous Ethanol Injection (PEI), liver cryotherapy, cryotherapy

APPROVED BY GOVERNING BODIES:

Chemoembolization for hepatic tumors is a medical procedure, and as such is not subject to FDA regulations. However, the embolizing agents and drugs are subject to FDA approval.

Radiofrequency ablation devices have been cleared through the U.S. Food and Drug Administration (FDA) 510(k) process.

Several cryosurgical devices have clearance by the U.S. Food and Drug Administration (FDA). For example, the ENDOcare™ CRYOcare Cryosurgical System (Endocare, Inc., Irvine, CA) was cleared for marketing through the 510(k) process in December 1996 for "use in general surgery, dermatology, neurology, thoracic surgery, ENT, gynecology, oncology, proctology and urology for the ablation of tissue, including liver metastases, skin lesions, warts, and removal of prostate tissue."

TheraSphere® has been granted Humanitarian Device Exception status by the FDA on December 10, 1999

SIR-Spheres was given a 510(k) PMA, March 5, 2002

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT:

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, open, of one or more liver tumor(s); percutaneous, radiofrequency
47399	Unlisted procedure, liver
77013	Computerized tomography guidance for, and monitoring of, parenchymal tissue ablation
77022	Magnetic resonance guidance for, and monitoring of, parenchymal tissue ablation
77261	Therapeutic radiology treatment planning; simple
77262	Therapeutic radiology treatment planning; intermediate
77263	Therapeutic radiology treatment planning; complex

ICD-10-CM:

C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas 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
C24.0	Malignant neoplasm of extrahepatic bile duct
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C7B.02	Secondary carcinoid tumors of liver

REFERENCES:

1. Abdalla EK, Vauthey JN, Ellis LM et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. Ann Surg 2004; 239(6):818-27.
2. Adam Rene, et al. A comparison of percutaneous cryosurgery and percutaneous radiofrequency for unresectable hepatic malignancies, Arch Surg 2002; 137: 1332-1339.
3. Al-Asfoor A, Fedorowicz Z, Lodge M. Resection versus no intervention or other surgical interventions for colorectal cancer liver metastases. Cochrane Database Syst Rev 2008; (2):CD006039.
4. Allison C. Yttrium-90 microspheres (TheraShpere and SIR-Spheres) for the treatment of unresectable hepatocellular carcinoma. Issues Emerg Health Technol 2007; 102: 1-6.

5. American Cancer Society. Liver Cancer. Available at www.cancer.org/cancer/livercancer/detailedguide/liver-cancer-what-is-liver-cancer. Accessed September 2016.
6. Arata MA, Nisenbaum HL, Clark TWI and Soulen MC. Percutaneous radiofrequency ablation of liver tumors with the LeVeen probe: is roll-off predictive of response? J Vasc Interv Radiol 2001; 12:455-458.
7. Awad T, Ghorlund K, Gluud C. Cryotherapy for hepatocellular carcinoma. Cochrane Database Syst Rev 2009; (4):CD007611.
8. Azoulay D, Castaing D, and et al. Percutaneous portal vein embolization increases the feasibility and safety of major liver resection for hepatocellular carcinoma in injured liver. Annals of Surg 2000; 232(5).
9. Bala MM, Riemsma RP, Wolff R et al. Cryotherapy for liver metastases. Cochrane Database Syst Rev 2013; 6:CD009058.
10. Bangash AK, Atassi B, Kaklamani V et al. 90Y radioembolization of metastatic breast cancer to the liver: toxicity, imaging response, survival. J Vasc Interv Radiol 2007; 18(5):621-8.
11. Bedikian AY, Legha SS, Mavligit G, et al. Treatment of uveal melanoma metastatic to the liver: a review of the M. D. Anderson Cancer Center experience and prognostic factors. Cancer. 1995; 76(9):1665-1670.
12. Berber E, Siperstein A. Local recurrence after laparoscopic radiofrequency ablation of liver tumors: An analysis of 1032 tumors. Ann Surg Oncol 2008; 15(10):2757-64.
13. Bertot LC, Sato M, Tateishi R et al. Mortality and complication rates of percutaneous ablative techniques for the treatment of liver tumors: a systematic review. Eur Radiol 2011; 21(12):2584-96.
14. Biederman DM, Titano JJ, Korff RA, et al. Radiation Segmentectomy versus Selective Chemoembolization in the Treatment of Early-Stage Hepatocellular Carcinoma. J Vasc Interv Radiol. Jan 2018;29(1):30-37 e32.
15. Biselli M, Andreone P, Gramenzi A, et al. Transcatheter arterial chemoembolization therapy for patients with hepatocellular carcinoma: a case-controlled study. Clin Gastroenterol Hepatol. 2005; 3(9):918-925.
16. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Cryosurgical ablation of unresectable hepatic tumors. TEC Assessments 2000; Volume 15, Tab 14.
17. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Radiofrequency ablation of unresectable hepatic tumors. TEC Assessments 2003: Volume 18, Tab 13.
18. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcatheter arterial chemoembolization of hepatic tumors. TEC Assessments. 2000; Volume 15; Tab 22.
19. Boehm LM, Jayakrishnan TT, Miura JT, et al. Comparative effectiveness of hepatic artery based therapies for unresectable intrahepatic cholangiocarcinoma. J Surg Oncol. Sep 1 2014.
20. Brown KT, Koh By, and et al. Particle embolization of hepatic neuroendocrine metastases for control of pain and hormonal symptoms. J Vasc Interv Radiol 1000; 10(4): 397-403.

21. Brunello F, Veltri A, Carucci P, et al. Radiofrequency ablation versus ethanol injection for early hepatocellular carcinoma: A randomized controlled trial. Scand J Gastroenterol 2008; 43(6): 727-735.
22. Burger I, Hong K, Schulick R et al. Transcatheter arterial chemoembolization in unresectable cholangiocarcinoma: Initial experience in a single institution. J Vasc Interv Radiol 2005; 16(3):353-61.
23. Bush DA, Smith JC, Slater JD, et al. Randomized clinical trial comparing proton beam radiation therapy with transarterial chemoembolization for hepatocellular carcinoma: results of an interim analysis. Int J Radiat Oncol Biol Phys. May 1 2016; 95(1):477-482.
24. Cao CQ, Yan TD, Bester L et al. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. Br J Surg 2010; 97(4):537-43.
25. Carr BI, Kondragunta V, Buch SC et al. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma. A two cohort study. Cancer 2010; 116(5):1305-14.
26. Chen S, Peng Z, Lin M, et al. Combined percutaneous radiofrequency ablation and ethanol injection versus hepatic resection for 2.1-5.0 cm solitary hepatocellular carcinoma: a retrospective comparative multicentre study. Eur Radiol. Mar 29 2018.
27. Cheng BQ, Jia CQ, Liu CT, et al. Chemoembolization combined with radiofrequency ablation for patients with hepatocellular carcinoma larger than 3 cm: A randomized controlled trial. JAMA, April 2008; 299(14): 1669-1677.
28. Cho YK, Kim JK, Kim MY et al. Systematic review of randomized trials for hepatocellular carcinoma treated with percutaneous ablation therapies. Hepatology 2009; 49(2):453-9.
29. Choi GH, Kim DH, Kang CM et al. Is preoperative transarterial chemoembolization needed for a resectable hepatocellular carcinoma? World J Surg 2007; 31(12):2370-7.
30. Choi H, Loyer EM, DuBrow RA and et al. Radio-frequency ablation of liver tumors: assessment of therapeutic response and complications. RadioGraphics 2001; 21:S41-S54.
31. Chu HH, Kim JH, Kim PN, et al. Surgical resection versus radiofrequency ablation very early-stage HCC (2 cm Single HCC): A propensity score analysis. Liver Int. Dec 2019; 39(12): 2397-2407.
32. Chua TC, Liauw W, Saxena A et al. Systematic review of neoadjuvant transarterial chemoembolization for resectable hepatocellular carcinoma. Liver Transpl 2009; 30(2):166-74.
33. Chung MH, Pisegna J, Spirt M et al. Hepatic cytoreduction followed by a novel long-acting somatostatin analog: a paradigm for intractable neuroendocrine tumors metastatic to the liver. Surgery 2001; 130(6):954-62.
34. Cianni R, Pelle G, Notarianni E et al. Radioembolization with (90) Y-labelled resin microspheres in the treatment of liver metastasis from breast cancer. Eur Radiol 2013; 23(1):182-9.
35. Cirocchi R, Trastulli S, Boselli C et al. Radiofrequency ablation in the treatment of liver metastases from colorectal cancer. Cochrane Database Syst Rev 2012; 6:CD006317.
36. Clavien PA, Kang KJ, Selzner N et al. Cryosurgery after chemoembolization for hepatocellular carcinoma in patients with cirrhosis. J Gastrointest Surg 2002; 6(1):95-101.
37. Coldwell DM, Kennedy AS, Nutting CW. Use of yttrium-90 microspheres in the treatment of unresectable hepatic metastases from breast cancer. Int J Radiat Oncol Biol Phys 2007; 69(3):800-4.

38. Cucchetti A, Mazzaferro V, Pinna AD, et al. Average treatment effect of hepatic resection versus locoregional therapies for hepatocellular carcinoma. Br J Surg. Nov 2017;104(12):1704-1712.
39. Curley SA. Radiofrequency ablation of malignant liver tumors. The Oncologist 2001; 6:14-23.
40. DeAngelis CD, Fontanarosa PB. Retraction: Cheng B-Q, et al. Chemoembolization combined with radiofrequency ablation for patients with hepatocellular carcinoma larger than 3 cm: a randomized controlled trial. JAMA. 2008; 299(14):1669-1677. JAMA. May 13 2009; 301(18):1931.
41. DeVita Jr VT, Lawrence TS and Rosenberg SA. The Cancer Journal. The Journal of Principles and Practice of Oncology. March/April 2010, Vol. 16, No. 2.
42. Ding J, Jing X, Liu J et al. Comparison of two different thermal techniques for the treatment of hepatocellular carcinoma. Eur J Radiol 2013; 82(9):1379-84.
43. Ding J, Jing X, Liu J et al. Complications of thermal ablation of hepatic tumours: comparison of radiofrequency and microwave ablative techniques. Clin Radiol 2013; 68(6):608-15.
44. Duan C, Liu M, Zhang Z et al. Radiofrequency ablation versus hepatic resection for the treatment of early-stage hepatocellular carcinoma meeting Milan criteria: a systematic review and meta-analysis. World J Surg Oncol 2013; 11(1):190.
45. Dunne RM, Shyn PB, Sung JC, et al. Percutaneous treatment of hepatocellular carcinoma in patients with cirrhosis: a comparison of the safety of cryoablation and radiofrequency ablation. Eur J Radiol. Apr 2014; 83(4):632-638.
46. Ei S, Hibi T, Tanabe M, et al. Cryoablation provides superior local control of primary hepatocellular carcinomas of >2 cm compared with radiofrequency ablation and microwave coagulation therapy: an underestimated tool in the toolbox. Ann Surg Oncol. Apr 2015; 22(4):1294-1300.
47. Elias D, Goere D, Leroux G et al. Combined liver surgery and RFA for patients with gastroenteropancreatic endocrine tumors presenting with more than 15 metastases to the liver. Eur J Surg Oncol 2009; 35(10):1092-7.
48. Fairweather M, Swanson R, Wang J, et al. Management of Neuroendocrine Tumor Liver Metastases: Long-Term Outcomes and Prognostic Factors from a Large Prospective Database. Ann Surg Oncol. Aug 2017;24(8):2319- 2325.
49. Feng K, Yan J, Li X et al. A randomized controlled trial of radiofrequency ablation and surgical resection in the treatment of small hepatocellular carcinoma. J Hepatol 2012; 57(4):794-802.
50. Feng Q, Chi Y, Liu Y et al. Efficacy and safety of percutaneous radiofrequency ablation versus surgical resection for small hepatocellular carcinoma: a meta-analysis of 23 studies. J Cancer Res Clin Oncol 2015.
51. Fiorentini G, Aliberti C, Tilli M et al. Intra-arterial infusion of irinotecan-loaded drug-eluting beads (DEBIRI) versus intravenous therapy (FOLFIRI) for hepatic metastases from colorectal cancer: final results of a phase III study. Anticancer Res 2012; 32(4):1387-95.
52. Gervais DA, Goldberg SN, Brown DB et al. Society of Interventional Radiology position statement on percutaneous radiofrequency ablation for the treatment of liver tumors. J Vasc Interv Radiol 2009; 20(1):3-8. Available online at: www.sirweb.org/clinical/cpg/PS_on_Percutaneous_RF_for_the_Treatment_of_Liver_Tumors.pdf.

53. Giorgio A, Di Sarno A, De Stefano G, et al. Percutaneous radiofrequency ablation of hepatocellular carcinoma compared to percutaneous ethanol injection in treatment of cirrhotic patients: an Italian randomized controlled trial. Anticancer Res. 2012 Mar; 32(3):1117.
54. Giorgio A, Merola MG, Montesarchio L, et al. Sorafenib combined with radio-frequency ablation compared with sorafenib alone in treatment of hepatocellular carcinoma invading portal vein: a western randomized controlled trial. Anticancer Res. Nov 2016; 36(11):6179-6183.
55. Gonsalves CF, Eschelman DJ, Sullivan KL et al. Radioembolization as salvage therapy for hepatic metastasis of uveal melanoma: a single-institution experience. AJR Am J Roentgenol 2011; 196(2):468-73.
56. Gruenberger T, Jourdan JL, Zhao J et al. Reduction in recurrence risk for involved or inadequate margins with edge cryotherapy after liver resection for colorectal metastases. Arch Surg 2001; 136(10):1154-7.
57. Guenette JP, Dupuy DE. Radiofrequency ablation of colorectal hepatic metastases. J Surg Oncol 2010; 102(8):978-87.
58. Gulec SA, Mountcastle TS, and et al. Cytoreductive surgery in patients with advanced-stage carcinoid tumors. 70th Annual Meeting Southeastern Surgical Congress. February 2002.
59. Gupta S, Yao JC, Ahrar K, et al. Hepatic artery embolization chemoembolization, for treatment of patients with metastatic carcinoid tumors: the M. D. Anderson experience. Cancer J. 2003; 9(4):241-243.
60. Gupta S, Yao JC, Ahrar KHae et al. Anderson experience. Cancer J 2003; 9(4):241-3.
61. Gurusamy KS, Ramamoorthy R, Imber C, et al. Surgical resection versus non-surgical treatment for hepatic node positive patients with colorectal liver metastases. Cochrane Database Syst Rev. Jan 20 2010(1):CD006797.
62. Gurusamy KS, Ramamoorthy R, Sharma D et al. Liver resection versus other treatments for neuroendocrine tumours in patients with respectable liver metastases. Cochrane Database Syst Rev 2009; (2):CD0076060.
63. Haug AR, Heinemann V, Bruns CJ et al. 18F-FDG PET independently predicts survival in patients with cholangiocellular carcinoma treated with 90Y microspheres. Eur J Nucl Med Mol Imaging 2011; 38(6):1037-45.
64. Haug AR, Tiega Donfack BP, Trumm C et al. 18F-FDG PET/CT predicts survival after radioembolization of hepatic metastases from breast cancer. J Nucl Med 2012; 53(3):371-7.
65. Hof J, Wertenbroek MW, Peeters PM, et al. Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases. Br J Surg. Jul 2016; 103(8):1055-1062.
66. Hoffmann RT, Paprottka PM, Schon A et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. Cardiovasc Intervent Radiol 2012; 35(1):105-16.
67. Hong K, McBride JD, Georgiades CS et al. Salvage therapy for liver-dominant colorectal metastatic adenocarcinoma: comparison between transcatheter arterial chemoembolization versus yttrium-90 radioembolization. J Vasc Interv Radiol 2009; 20(3):360-7.
68. Hua YQ, Wang P, Zhu XY, et al. Radiofrequency ablation for hepatic oligometastatic pancreatic cancer: An analysis of safety and efficacy. Pancreatology. Nov - Dec 2017;17(6):967-973

69. Huang A, McCall JM, Weston MD et al. Phase I study of percutaneous cryotherapy for colorectal liver metastasis. Br J Surg 2002; 89(3):303-10.
70. Huang C, Zhuang W, Feng H, et al. Analysis of therapeutic effectiveness and prognostic factor on argon-helium cryoablation combined with transcatheter arterial chemoembolization for the treatment of advanced hepatocellular carcinoma. J Cancer Res Ther. Dec 2016; 12(Supplement):C148-c152.
71. Huang YZ, Zhou SC, Zhou H et al. Radiofrequency ablation versus cryosurgery ablation for hepatocellular carcinoma: a meta-analysis. Hepatogastroenterology 2013; 60(127).
72. Huppert PE, Fierlbeck G, Pereira P et al. Transarterial chemoembolization of liver metastases in patients with uveal melanoma. Eur J Radiol 2010; 74(3):e38-44.
73. Ibrahim SM, Mulcahy MF, Lewandowski RJ et al. Treatment of unresectable cholangiocarcinoma using yttrium-90 microspheres: results from a pilot study. Cancer 2008; 113(8):2119-28.
74. Jaeck D, Oussoultzoglou E, Bachellier P et al. Hepatic metastases of gastroenterohepatic neuroendocrine tumors: safe hepatic surgery. World J Surg 2001; 25(6):689-92.
75. Jakobs TF, Hoffmann RT, Dehm K et al. Hepatic yttrium-90 radioembolization of chemotherapy-refractory colorectal cancer liver metastases. J Vasc Interv Radiol 2008; 19(8):1187-95.
76. Jakobs TF, Hoffmann RT, Fischer T et al. Radioembolization in patients with hepatic metastases from breast cancer. J Vasc Interv Radiol 2008; 19(5):683-90.
77. Jakobs TF, Hoffmann RT, Schrader A et al. CT-guided radiofrequency ablation in patients with hepatic metastases from breast cancer. Cardiovasc Intervent Radiol 2009; 32(1):38-46.
78. Jia JB, Zhang D, Ludwig JM, et al. Radiofrequency ablation versus resection for hepatocellular carcinoma in patients with Child-Pugh A liver cirrhosis: a meta-analysis. Clin Radiol. Dec 2017;72(12):1066-1075.
79. Jones RL, McCall J, Adam A et al. Radiofrequency ablation is a feasible therapeutic option in the multi-modality management of sarcoma. Eur J Surg Oncol 2010; 36(5):477-82.
80. Joosten J, Jager G, Oyen W et al. Cryosurgery and radiofrequency ablation for unresectable colorectal liver metastases. Eur J Surg Oncol 2005; 31(10):1152-9.
81. Kaibori M, Tanigawa N, Kariya S, et al. A prospective randomized controlled trial of preoperative whole-liver chemolipiodolization for hepatocellular carcinoma. Dig Dis Sci. May 2012; 57(5):1404-1412.
82. Kemeny N. Management of liver metastases from colorectal cancer. Oncology (Williston Park) 2006; 20(10):1161-76.
83. Kennedy A, Nag S, Salem R et al. Recommendations for radioembolization of hepatic malignancies using yttrium-90 microsphere brachytherapy: a consensus panel report from the radioembolization brachytherapy oncology consortium. Int J Radiat Oncol Biol Phys 2007; 68(1):13-23.
84. Kennedy AS, Coldwell D, Nutting C et al. Resin 90Y-microsphere brachytherapy for unresectable colorectal liver metastases: modern USA experience. Int J Radiat Oncol Biol Phys 2006; 65(2):412-25.
85. Kennedy AS, Dezarn WA, McNeillie P et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. Am J Clin Oncol 2008; 31(3):271-9.
86. Kennedy AS, Nutting C, Jakobs T et al. A first report of radioembolization for hepatic metastases from ocular melanoma. Cancer Invest 2009; 27(6):682-90.

87. Kennedy AS, Salem R. Radioembolization (yttrium-90 microspheres) for primary and metastatic hepatic malignancies. Cancer J 2010; 16(2):163-75.
88. King J, Quinn R, Glenn DM et al. Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. Cancer 2008; 113(5):921-9.
89. Klingenstein A, Haug AR, Zech CJ et al. Radioembolization as locoregional therapy of hepatic metastases in uveal melanoma patients. Cardiovasc Intervent Radiol 2013; 36(1):158-65.
90. Knuppel M, Kubicka S, Vogel A et al. Combination of conservative and interventional therapy strategies for intra- and extrahepatic cholangiocellular carcinoma: a retrospective survival analysis. Gastroenterol Res Pract 2012; 2012:190708.
91. Kornprat P, Jarnagin WR, DeMatteo RP et al. Role of intraoperative thermoablation combined with resection in the treatment of hepatic metastasis from colorectal cancer. Arch Surg 2007; 142(11):1087-92.
92. Korpan NN. Hepatic cryosurgery for liver metastases: long term follow-up. Ann Surg. 1997; 225(2): 193-201.
93. Kulik LM, Carr BI, Mulcahy MF et al. Safety and efficacy of 90Y radiotherapy for hepatocellular carcinoma with and without portal vein thrombosis. Hepatology 2008; 47(1-Jan):71-81.
94. Kutlu OC, Chan JA, Aloia TA, et al. Comparative effectiveness of first-line radiofrequency ablation versus surgical resection and transplantation for patients with early hepatocellular carcinoma. Cancer. May 15 2017; 123(10):1817-1827.
95. Lan T, Chang L, Mn R, et al. Comparative efficacy of interventional therapies for early-stage hepatocellular carcinoma: A PRISMA-compliant systematic review and network meta-analysis. Medicine (Baltimore). Apr 2016; 95(15):e3185.
96. Lang EK, Brown CL. Colorectal metastases to the liver: selective chemoembolization. Radiology. 1993; 189(2):417-422.
97. Lawes D, Chopada A, Gillams A et al. Radiofrequency ablation (RFA) as a cytoreductive strategy for hepatic metastasis from breast cancer. Ann R Coll Surg Engl 2006; 88(7):639-42.
98. Lee HJ, Kim JW, Hur YH, et al. Combined therapy of transcatheter arterial chemoembolization and radiofrequency ablation versus surgical resection for single 2-3 cm hepatocellular carcinoma: a propensity-score matching analysis. J Vasc Interv Radiol. Sep 2017;28(9):1240-1247 e1243.
99. Lee SH, Jin YJ, Lee JW. Survival benefit of radiofrequency ablation for solitary (3-5 cm) hepatocellular carcinoma: An analysis for nationwide cancer registry. Medicine (Baltimore). Nov 2017;96(44):e8486.
100. Lencioni R, Crocetti L, Cioni D et al. Percutaneous radiofrequency ablation of hepatic colorectal metastases: technique, indications, results, and new promises. Invest Radiol 2004; 39(11):689-97.
101. Lewandowski RJ, Kulik LM, Riaz A et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. Am J Transplant 2009; 9(8):1920-8.
102. Leyendecker JR and Dodd GD. Minimally invasive techniques for the treatment of liver tumors. Medscape, May 2001, www.medscape.com/viewarticle/410856_print. Accessed October 9, 2009.

103. Li J, Zhang K, Gao Y, et al. Evaluation of hepatectomy and palliative local treatments for gastric cancer patients with liver metastases: a propensity score matching analysis. Oncotarget. Sep 22 2017;8(37):61861-61875.
104. Li JK, Liu XH, Cui H, et al. Radiofrequency ablation vs. surgical resection for resectable hepatocellular carcinoma: A systematic review and meta-analysis. Mol Clin Oncol. Jan 2020; 12(1): 15-22.
105. Li Q, Wang J, Sun Y et al. Efficacy of postoperative transarterial chemoembolization and portal vein chemotherapy for patients with hepatocellular carcinoma complicated by portal vein tumor thrombosis—a randomized study. World J Surg 2006; 30(11):2004-11.
106. Li Q, Wang J, Sun Y, et al. Postoperative transhepatic arterial chemoembolization and portal vein chemotherapy for patients with hepatocellular carcinoma: a randomized study with 131 cases. Dig Surg. 2006;23(4):235-240.
107. Li W, Bai Y, Wu M, et al. Combined CT-guided radiofrequency ablation with systemic chemotherapy improves the survival for nasopharyngeal carcinoma with oligometastasis in liver: Propensity score matching analysis. Oncotarget. Aug 8 2017;8(32):52132-52141.
108. Li Z, Fu Y, Li Q, et al. Cryoablation plus chemotherapy in colorectal cancer patients with liver metastases. Tumour Biol. Nov 2014; 35(11):10841-10848.
109. Liao M, Zhu Z, Wang H, et al. Adjuvant transarterial chemoembolization for patients after curative resection of hepatocellular carcinoma: a meta-analysis. Scand J Gastroenterol. Jun - Jul 2017; 52(6-7):624-634.
110. Lin Y, Pan XB. Differences in Survival Between First-Line Radiofrequency Ablation versus Surgery for Early-Stage Hepatocellular Carcinoma: A Population Study Using the Surveillance, Epidemiology, and End Results Database. Med Sci Monit. May 28 2020;26: e921782.
111. Liu B, Huang G, Jiang C, et al. Ultrasound-Guided Percutaneous Radiofrequency Ablation of Liver Metastasis From Ovarian Cancer: A Single-Center Initial Experience. Int J Gynecol Cancer. Jul 2017;27(6):1261-1267.
112. Liu H, Wang ZG, Fu SY, et al. Randomized clinical trial of chemoembolization plus radiofrequency ablation versus partial hepatectomy for hepatocellular carcinoma within the Milan criteria. Br J Surg. Mar 2016; 103(4):348-356.
113. Liu Y, Li S, Wan X et al. Efficacy and safety of thermal ablation in patients with liver metastases. Eur J Gastroenterol Hepatol 2013; 25(4):442-6.
114. Llovet JM, Real MI, et al. Arterial embolization or chemoembolization versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomized controlled trial. Lancet 2002; 359: 1734-9.
115. Lo CM, Ngan H, Tso WK et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology 2002; 35(5):1164-71.
116. Loveman E, Jones J, Clegg AJ et al. The clinical effectiveness and cost-effectiveness of ablative therapies in the management of liver metastases: systematic review and economic evaluation. Health Technol Assess 2014; 18(7): vii-viii, 1-283.
117. Lu MD, Xu HX, Xie XY et al. Percutaneous microwave and radiofrequency ablation for hepatocellular carcinoma: a retrospective comparative study. J Gastroenterol 2005; 40(11):1054-60.
118. Mabed M, Esmaeel M, El-Khodary T et al. A randomized controlled trial of transcatheter arterial chemoembolization with lipiodol, doxorubicin and cisplatin versus intravenous

doxorubicin for patients with unresectable hepatocellular carcinoma. Eur J Cancer Care 2009; 18(5):492-9.
119. Majumdar A, Roccarina D, Thorburn D, et al. Management of people with early- or very early-stage hepatocellular carcinoma: an attempted network meta-analysis. Cochrane Database Syst Rev. Mar 28 2017; 3:Cd011650.
120. Marelli L, Stigliano R, Triantos C, et al. Transarterial therapy for hepatocellular carcinoma: Which technique is more effective? A systematic review of cohort and randomized studies. Cardiovasc Intervent Radiol 2007; 30(1): 6-25.
121. Martin RC, Scoggins CR, Schreeder M, et al. Randomized controlled trial of irinotecan drug-eluting beads with simultaneous FOLFOX and bevacizumab for patients with unresectable colorectal liver-limited metastasis. Cancer. Oct 15 2015; 121(20):3649-3658.
122. Masaki T, Morishita A, Kurokohchi K and Kuriyama S. Multidisciplinary treatment of patients with hepatocellular carcinoma. Expert Rev Anticancer Ther, October 2006; 6(10): 1377-1384.
123. Mazzaglia PJ, Berber E, Milas M et al. Laparoscopic radiofrequency ablation of neuroendocrine liver metastases: a 10-year experience evaluating predictors of survival. Surgery 2007; 142(1):10-9.
124. McKay A, Dixon E, Taylor M. Current role of radiofrequency ablation for the treatment of colorectal liver metastases. Br J Surg 2006; 93(10):1192-202.
125. McWilliams JP, Yamamoto S, Raman SS et al. Percutaneous ablation of hepatocellular carcinoma: current status. J Vasc Interv Radiol 2010; 21(8 suppl):S204-13.
126. Meijerink MR, Puijk RS, van Tilborg AAJM, et al. Radiofrequency and Microwave Ablation Compared to Systemic Chemotherapy and to Partial Hepatectomy in the Treatment of Colorectal Liver Metastases: A Systematic Review and Meta-Analysis. Cardiovasc Intervent Radiol. 2018 Aug;41(8):1189-1204.
127. Meloni MF, Andreano A, Laeseke PF et al. Breast cancer liver metastases: US-guided percutaneous radiofrequency ablation—intermediate and long-term survival rates. Radiology 2009; 253(3):861-9.
128. Memon K, Lewandowski RJ, Mulcahy MF et al. Radioembolization for neuroendocrine liver metastases: safety, imaging, and long-term outcomes. Int J Radiat Oncol Biol Phys 2012; 83(3):887-94.
129. Michl M, Haug AR, Jakobs TF et al. Radioembolization with Yttrium-90 Microspheres (SIRT) in Pancreatic Cancer Patients with Liver Metastases: Efficacy, Safety and Prognostic Factors. Oncology 2014; 86(1):24-32.
130. Min JH, Kang TW, Cha DI, et al. Radiofrequency ablation versus surgical resection for multiple HCCs meeting the Milan criteria: propensity score analyses of 10-year therapeutic outcomes. Clin Radiol. Jul 2018;73(7):676 e615-676 e624.
131. Mocellin S, Pilati P, Lise M and Nitti D. Meta-analysis of hepatic arterial infusion for unresectable liver metastases from colorectal cancer: The end of an era? J Clin Oncol 2007; 25(35): 5649-5654.
132. Mohan H, Nicholson P, Winter DC, et al. Radiofrequency ablation for neuroendocrine liver metastases: a systematic review. J Vasc Interv Radiol. Jul 2015; 26(7):935-942 e931.
133. Molinari M, Kachura JR, Dixon E, et al. Transarterial chemoembolisation for advanced hepatocellular carcinoma: results from a North American cancer centre. Clin Oncol (R Coll Radiol). 2006; 18(9):684-692.

134. Morimoto M, Numata K, Kondou M, et al. Midterm outcomes in patients with intermediate-sized hepatocellular carcinoma: a randomized controlled trial for determining the efficacy of radiofrequency ablation combined with transcatheter arterial chemoembolization. Cancer. Dec 01 2010; 116(23):5452-5460.
135. Mouli S, Memon K, Baker T et al. Yttrium-90 radioembolization for intrahepatic cholangiocarcinoma: safety, response, and survival analysis. J Vasc Interv Radiol 2013; 24(8):1227-34.
136. Mulcahy MF, Lewandowski RJ, Ibrahim SM et al. Radioembolization of colorectal hepatic metastases using yttrium-90 microspheres. Cancer 2009; 115(9):1849-58.
137. National Cancer Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Available online at: www.nccn.org/professionals/physician_gls/f_guidelines.asp#site.
138. National Cancer Institute, Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. n.d.; https://seer.cancer.gov/statfacts/html/livibd.html. Accessed July 6, 2018.
139. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast cancer. Version 1.2019. www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 2019.
140. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. Version 2.2019. www.nccn.org/professionals/physician_gls/PDF/colon.pdf. Accessed May 2019.
141. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hepatobiliary Cancers. Version 2.2019. www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf. Accessed March 2019.
142. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine Tumors and Adrenal Tumors. Version 1.2019; www.nccn.org/professionals/physician_gls/PDF/neuroendocrine.pdf. Accessed May 2019.
143. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. www.nccn.org/professionals/physician_gls/default.asp.
144. National Comprehensive Cancer Network. Colon Cancer. Version 3.2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 2, 2020.
145. National Comprehensive Cancer Network. Colon Cancer. Version 3.2020. Accessed May 27, 2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
146. National Comprehensive Cancer Network. Hepatobiliary Cancers. Version 3.2020. https://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf Accessed June 2, 2020.
147. National Comprehensive Cancer Network. Hepatobiliary cancers. Version 2.2020. Accessed May 27, 2020. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf
148. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed June 2, 2020.
149. National Comprehensive Cancer Network. Neuroendocrine tumors. Version 1.2019. Accessed May 27, 2020. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf.

150. National Institute for Clinical Excellence (NICE). Radiofrequency ablation for colorectal liver metastases-guidance (IPG327). 2009. Available online at: guidance.nice.org.uk/IPG327.
151. National Institute for Clinical Excellence (NICE). Radiofrequency ablation of hepatocellular carcinoma (IPG327). 2003. Available online at: guidance.nice.org.uk/IPG2.
152. Nazario J, Gupta S. Transarterial liver-directed therapies of neuroendocrine hepatic metastases. Semin Oncol 2010; 37(2):118-26.
153. Ng KKC, Chok KSH, Chan ACY, et al. Randomized clinical trial of hepatic resection versus radiofrequency ablation for early-stage hepatocellular carcinoma. Br J Surg. Dec 2017;104(13):1775-1784.
154. Ng KM, Chua TC, Saxena A et al. Two decades of experience with hepatic cryotherapy for advanced colorectal metastases. Ann Surg Oncol 2012; 19(4):1276-83.
155. Niu R, Yan TD, Zhu JC et al. Recurrence and survival outcomes after hepatic resection with or without cryotherapy for liver metastases from colorectal carcinoma. Ann Surg Oncol 2007; 14(7):2078-87.
156. Obed A, Beham A, Pullmann K et al. Patients without hepatocellular carcinoma progression after transarterial chemoembolization benefit from liver transplantation. World J Gastroenterol 2007; 13(5):761-7.
157. Oliveri RS, Wetterslev J, Gluud C. Transarterial (chemo) embolisation for unresectable hepatocellular carcinoma. Cochrane Database Syst Rev 2011; (3):CD004787.
158. Organ Procurement and Transplant Network. Policy 9: Allocation of Livers and Liver-Intestines. 2018;https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_09. Accessed June 9, 2020.
159. Osborne DA, Zervos EE, Strosberg J et al. Improved outcome with cytoreduction versus embolization for symptomatic hepatic metastases of carcinoid and neuroendocrine tumors. Ann Surg Oncol 2006; 13(4):572-81.
160. Paprottka PM, Hoffmann RT, Haug A et al. Radioembolization of symptomatic, unresectable neuroendocrine hepatic metastases using yttrium-90 microspheres. Cardiovasc Intervent Radiol 2012; 35(2):334-42.
161. Park SY, Kim JH, Yoon HJ et al. Transarterial chemoembolization versus supportive therapy in the palliative treatment of unresectable intrahepatic cholangiocarcinoma. Clin Radiol 2011; 66(4):322-8.
162. Patel K, Sullivan K, Berd D et al. Chemoembolization of the hepatic artery with BCNU for metastatic uveal melanoma: results of a phase II study. Melanoma Res 2005; 15(4):297-304.
163. Pathak S, Jones R, Tand JMF, et al. Ablative therapies for colorectal liver metastases: a systematic review. Colorectal Dis 2011; 13(9):e252-65.
164. Pawlik TM, Vauthey JN, Abdalla EK et al. Results of a single-center experience with resection and ablation for sarcoma metastatic to the liver. Arch Surg 2006; 141(6):537-44.
165. Peng BG, He Q, Li JP, et al. Adjuvant transcatheter arterial chemoembolization improves efficacy of hepatectomy for patients with hepatocellular carcinoma and portal vein tumor thrombus. Am J Surg. Sep 2009; 198(3):313-318.
166. Peng ZW, Zhang YJ, Liang HH, et al. Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial. Radiology. Feb 2012; 262(2):689-700.

167. Piduru SM, Schuster DM, Barron BJ et al. Prognostic value of 18f-fluorodeoxyglucose positron emission tomography-computed tomography in predicting survival in patients with unresectable metastatic melanoma to the liver undergoing yttrium-90 radioembolization. J Vasc Interv Radiol 2012; 23(7):943-8.
168. Pomfret EA, Washburn K, Wald C et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. Liver Transpl 2010; 16(3):262-78.
169. Qi X, Tang Y, An D et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinoma: a meta-analysis of randomized controlled trials. J Clin Gastroenterol 2014; 48(5):450-7.
170. Qi X, Wang D, Su C, et al. Hepatic resection versus transarterial chemoembolization for the initial treatment of hepatocellular carcinoma: A systematic review and meta-analysis. Oncotarget. Jul 30 2015; 6(21):18715-18733.
171. Rhee TK, Lewandowski RJ, Liu DM et al. 90Y radioembolization for metastatic neuroendocrine liver tumors: Preliminary results from a multi-institutional experience. Ann Surg 2008; 247(6):1029-35.
172. Riaz A, Gates VL, Atassi B, et al. Radiation segmentectomy: A novel approach to increase safety and efficacy of radioembolization. Int J Radiation Oncology Biol Phys 2010.
173. Richardson AJ, Laurence JM, Lam VW. Transarterial chemoembolization with irinotecan beads in the treatment of colorectal liver metastases: systematic review. J Vasc Interv Radiol 2013; 24(8):1209-17.
174. Riemsma RP, Bala MM, Wolff R, et al. Percutaneous ethanol injection for liver metastases. Cochrane Database Syst Rev. May 31 2013(5):CD008717.
175. Rong G, Bai W, Dong Z, et al. Long-term outcomes of percutaneous cryoablation for patients with hepatocellular carcinoma within Milan criteria. PLoS One. 2015; 10(4):e0123065.
176. Rose DM, Allegra DP, and et al. Radiofrequency ablation: a novel primary and adjunctive ablative technique for hepatic malignancies. Annual meeting of the Southern California Chapter of the American College of Surgeons, January 1999.
177. Rosenbaum CE, Verkooijen HM, Lam MG et al. Radioembolization for treatment of salvage patients with colorectal cancer liver metastases: a systematic review. J Nucl Med 2013; 54(11):1890-5.
178. Ruers T, Punt C, Van Coevorden F, et al. Radiofrequency ablation combined with systemic treatment versus systemic treatment alone in patients with non-resectable colorectal liver metastases: a randomized EORTC Intergroup phase II study (EORTC 40004). Ann Oncol. Oct 2012; 23(10):2619-2626.
179. Ruers T, Van Coevorden F, Punt CJ, et al. Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial. J Natl Cancer Inst. Sep 01 2017; 109(9).
180. Ruers TJ, Joosten J, Jager GJ et al. Long-term results of treating hepatic colorectal metastases with cryosurgery. Br J Surg 2001; 88(6):844-9.
181. Ruers TJ, Joosten JJ, Wiering B et al. Comparison between local ablative therapy and chemotherapy for non-resectable colorectal liver metastases: a prospective study. Ann Surg Oncol 2007; 14(3):1161-9.
182. Ruutiainen AT, Soulen MC, Tuite CM et al. Chemoembolization and bland embolization of neuroendocrine tumor metastases to the liver. J Vasc Interv Radiol 2007; 18(7):847-55.

183. Salem R, Lewandowski RJ, Mulcahy MF et al. Radioembolization for hepatocellular carcinoma using yttrium-90 microspheres: a comprehensive report of long-term outcomes. Gastroenterology 2010; 138(1):52-64.
184. Sato T. Locoregional management of hepatic metastasis from primary uveal melanoma. Semin Oncol 2010; 37(2):127-38.
185. Saxena A, Bester L, Chua TC et al. Yttrium-90 radiotherapy for unresectable intrahepatic cholangiocarcinoma: a preliminary assessment of this novel treatment option. Ann Surg Oncol 2010; 17(2):484-91.
186. Saxena A, Bester L, Shan L et al. A systematic review on the safety and efficacy of yttrium-90 radioembolization for unresectable, chemorefractory colorectal cancer liver metastases. J Cancer Res Clin Oncol 2013.
187. Saxena A, Chua TC, Chu F et al. Optimizing the surgical effort in patients with advanced neuroendocrine neoplasm hepatic metastases: a critical analysis of 40 patients treated by hepatic resection and cryoablation. Am J Clin Oncol 2012; 35(5):439-45.
188. Seidensticker R, Denecke T, Kraus P, et al. Matched-pair comparison of radioembolization plus best supportive care versus best supportive care alone for chemotherapy refractory liver-dominant colorectal metastases. Cardiovasc Intervent Radiol 2012; 35(5):1066-73.
189. Seifert JK and Junginger T. Cryotherapy for liver tumors: Current status, perspectives, clinical results, and review of literature, Technol Cancer Research Treatment, April 2004; 3(2): 151-63. (Abstract)
190. Seifert JK, Moris DL. World survey on the complications of hepatic and prostate cryotherapy. World J Surg. 1999; 23 (2): 109-114.
191. Seifert JK, Springer A. Baier P, et al. Liver resection or cryotherapy for colorectal liver metastases: a prospective case control study. Int J Colorectal Dis. 2005; 31 (10): 1152-1159.
192. Sharma KV, Gould JE, Harbour JW et al. Hepatic arterial chemoembolization for management of metastatic melanoma. AJR Am J Roentgenol 2008; 190(1):99-104.
193. Sheen AJ, Poston GJ, Sherlock DJ. Cryotherapeutic ablation of liver tumors. Br J Surg 2002; 89(11):1396-401.
194. Shen A, Zhang H, Tang C et al. A systematic review of radiofrequency ablation versus percutaneous ethanol injection for small hepatocellular carcinoma up to 3 cm. J Gastroenterol Hepatol 2013; 28(5):793-800.
195. Shen WF, Zhong W, Liu Q et al. Adjuvant transcatheter arterial chemoembolization for intrahepatic cholangiocarcinoma after curative surgery: retrospective control study. World J Surg 2011; 35(9):2083-91.
196. Shibata T, Iimuro Y, Yamamoto Y et al. Small hepatocellular carcinoma: comparison of radio-frequency ablation and percutaneous microwave coagulation therapy. Radiology 2002; 223(2):331-7.
197. Shiina S, Tagawa K, and et al. Percutaneous ethanol injection therapy for hepatocellular carcinomas: results in 146 patients. AJR Am J Roentgenol 1993; 160(5): 1023-8.
198. Si T, Chen Y, Ma D, et al. Preoperative transarterial chemoembolization for resectable hepatocellular carcinoma in Asia area: a meta-analysis of random controlled trials. Scand J Gastroenterol. Dec 2016; 51(12):1512-1519.
199. Siperstein AE, Berber E. Cryoablation, percutaneous alcohol injection, and radiofrequency ablation treatment of neuroendocrine liver metastases. World J Surg 2001; 25(6):693-6.

200. Smits ML, Prince JF, Rosenbaum CE et al. Intra-arterial radioembolization of breast cancer liver metastases: a structured review. Eur J Pharmacol 2013; 709(1-3):37-42.
201. Sohn RL, Carlin AM, Steffes C et al. The extent of cryosurgery increases the complication rate after hepatic cryoablation. Am Surg 2003; 69(4):317-22.
202. Sotsky TK, Ravikumar TS. Cryotherapy in the treatment of liver metastases from colorectal cancer. Semin Oncol 2002; 29(2):183-91.
203. Stuart K, Huberman M, Posner M, et al. Chemoembolization for colorectal metastases. Proc Am Soc Clin Oncol. 1995; 14:190. (Abstract).
204. Sullivan KL. Hepatic artery chemoembolization. Semin Oncol 2002; 29(2): 145-51.
205. Takayasu K, Arii S, Ikai I, et al. Prospective cohort study of transarterial chemoembolization for unresectable hepatocellular carcinoma in 8510 patients. Gastroenterology. 2006; 131(2):461-469.
206. Taniai N, Yoshida H, Mamada Y et al. Is intraoperative adjuvant therapy effective for satellite lesions in patients undergoing reduction surgery for advanced hepatocellular carcinoma? Hepato-gastroenterology 2006; 53(68):258-61.
207. TheraSphere. www.nordion.com/therasphere/home_us/index.asp.
208. Tian X, Dai Y, Wang DQ, et al. Transarterial chemoembolization versus hepatic resection in hepatocellular carcinoma treatment: a meta-analysis. Drug Des Devel Ther. 2015; 9:4431-4440.
209. Tian X, Dai Y, Wang DQ, et al. Transarterial chemoembolization versus hepatic resection in hepatocellular carcinoma treatment: a meta-analysis. Drug Des Devel Ther. 2015; 9:4431-4440.
210. Tice J. Selective internal radiation therapy or radioembolization for inoperable liver metastases from colorectal cancer. California Technology Assessment Forum 2010. Available online at: www.ctaf.org/assessments/selective-internal-radiation-therapy-or-radioembolization-inoperable-liver-metastases. Last accessed February, 2014.
211. Tiong L and Maddern G.J. Systematic review and meta-analysis of survival and disease recurrence after radiofrequency ablation for hepatocellular carcinoma. Br J Surg 2011 Sep; 98:1210-24.
212. Townsend A, Price T, Karapetis C. Selective internal radiation therapy for liver metastases from colorectal cancer. Cochrane Database Syst Rev 2009; (4):CD007045.
213. Tung-Ping Poon R, Fan ST, Tsang FH, and Wong J. Locoregional Therapies for hepatocellular carcinoma: a critical review from the surgeon's perspective. Annals of Surg 2002; 235(4).
214. U.S. Food and Drug Administration. 510(k) Summary or 510(k) Statement. Valleylab Microwave Ablation Generator. www.fda.gov.
215. Van HG, Blackwell A, Anderson J et al. Randomized phase 2 trial of SIR-Spheres plus fluorouracil/leucovorin chemotherapy versus fluorouracil/leucovorin chemotherapy alone in advanced colorectal cancer. J Surg Oncol 2004; 88(2):78-85.
216. Van Tilborg AA, Meijerink MR, Sietses C et al. Long-term results of radiofrequency ablation for unresectable colorectal liver metastases: a potentially curative intervention. Br J Radiol 2011; 84(1002):556-65.
217. Veltri A, Gazzera C, Barrera M et al. Radiofrequency thermal ablation (RFA) of hepatic metastases (METS) from breast cancer (BC): an adjunctive tool in the multimodal treatment of advanced disease. Radiol Med 2014; 119(5):327-33.

218. Venkatesan AM, Locklin J, Lai EW et al. Radiofrequency ablation of metastatic pheochromocytoma. J Vasc Interv Radiol 2009; 20(11):1483-90.
219. Vente MA, Wondergem M, van der Tweel I et al. Yttrium-90 microsphere radioembolization for the treatment of liver malignancies: a structured meta-analysis. Eur Radiol 2009; 19(4):951-9.
220. Vietti Violi N, Duran R, Guiu B, et al. Efficacy of microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma in patients with chronic liver disease: a randomised controlled phase 2 trial. Lancet Gastroenterol Hepatol. 2018 May;3(5):317-325.
221. Vogl TJ, Gruber T, Balzer JO et al. Repeated transarterial chemoembolization in the treatment of liver metastases of colorectal cancer: prospective study. Radiology 2009; 250(1):281-9.
222. Vogl TJ, Mack MG, Balzer JO et al. Liver metastases: neoadjuvant downsizing with transarterial chemoembolization before laser-induced thermotherapy. Radiology 2003; 229(2):457-64.
223. Wang C, Lu Y, Chen Y et al. Prognostic factors and recurrence of hepatitis B-related hepatocellular carcinoma after argon-helium cryoablation: a prospective study. Clin Exp Metastasis 2009; 26(7):839-48.
224. Wang C, Wang H, Yang W, et al. A multicenter randomized controlled trial of percutaneous cryoablation versus radiofrequency ablation in hepatocellular carcinoma. Hepatology. Oct 6 2014.
225. Wang Y, Luo Q, Li Y et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinomas: a meta-analysis of randomized and nonrandomized controlled trials. PLoS One 2014; 9(1):e84484.
226. Weis S, Franke A, Mossner J et al. Radiofrequency (thermal) ablation versus no intervention or other interventions for hepatocellular carcinoma. Cochrane Database Syst Rev 2013; 12:CD003046.
227. Weng M, Zhang Y, Zhou D et al. Radiofrequency ablation versus resection for colorectal cancer liver metastases: a meta-analysis. PLoS One 2012; 7(9):e45493.
228. Wessels FJ and Schell SR. Radiofrequency ablation treatment of refractory carcinoid hepatic metastases. J of Surg Research 2001; 9(5): 8-12.
229. Xie F, Zang J, Guo X, et al. Comparison of transcatheter arterial chemoembolization and microsphere embolization for treatment of unresectable hepatocellular carcinoma: a meta-analysis. J Cancer Res Clin Oncol. Mar 2012; 138(3):455-462.
230. Xu G, Qi FZ, Zhang JH et al. Meta-analysis of surgical resection and radiofrequency ablation for early hepatocellular carcinoma. World J Surg Oncol 2012; 10:163.
231. Xu KC, Niu LZ, He WB et al. Percutaneous cryosurgery for the treatment of hepatic colorectal metastases. World J Gastroenterol 2008; 14(9):1430-6.
232. Xu KC, Niu LZ, Zhou Q et al. Sequential use of transarterial chemoembolization and percutaneous cryosurgery for hepatocellular carcinoma. World J Gastroenterol 2009; 15(29):3664-9.
233. Xu XL, Liu XD, Liang M, et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinoma: systematic review of randomized controlled trials with meta-analysis and trial sequential analysis. Radiology. May 2018;287(2):461-472

234. Yan DB, Clingan P, Morris DL. Hepatic cryotherapy and regional chemotherapy with or without resection for liver metastases from colorectal carcinoma. How many are too many? Cancer 2003; 98(2):320-30.
235. Yang Y, Wang C, Lu Y et al. Outcomes of ultrasound-guided percutaneous argon-helium cryoablation of hepatocellular carcinoma. J Hepatobiliary Pancreat Sci 2012 Nov; 19(6):674-84.
236. Yeh ML, Huang CI, Huang CF, et al. Neoadjuvant transcatheter arterial chemoembolization does not provide survival benefit compared to curative therapy alone in single hepatocellular carcinoma. Kaohsiung J Med Sci. Feb 2015; 31(2):77-82.
237. Yin Z, Jin H, Ma T, et al. A meta-analysis of long-term survival outcomes between surgical resection and radiofrequency ablation in patients with single hepatocellular carcinoma </= 2cm (BCLC very early stage). Int J Surg. Apr 30 2018;56:61-67.
238. Yu C, Wu S, Zhao J, et al. Evaluation of efficacy, safety and treatment-related outcomes of percutaneous radiofrequency ablation versus partial hepatectomy for small primary liver cancer meeting the Milan criteria: A systematic review and meta-analysis of randomized controlled trials. Clin Res Hepatol Gastroenterol. Jan 17 2020.
239. Yu SJ, Yoon JH, Lee JM, et al. Percutaneous ethanol injection therapy is comparable to radiofrequency ablation in hepatocellular carcinoma smaller than 1.5cm: A matched case-control comparative analysis. Medicine (Baltimore). 2016 Aug;95(35):e.4551
240. Zacharias AJ, Jayakrishnan TT, Rajeev R, et al. Comparative effectiveness of hepatic artery based therapies for unresectable colorectal liver metastases: a meta-analysis. PLoS One. 2015; 10(10):e0139940.
241. Zhang Z, Liu Q, He J, et al. The effect of preoperative transcatheter hepatic arterial chemoembolization on disease-free survival after hepatectomy for hepatocellular carcinoma. Cancer. 2000; 89(12):2606-2612.
242. Zhao WJ, Zhu GQ, Wu YM, et al. Comparative Effectiveness of Radiofrequency Ablation, Surgical Resection and Transplantationnfor Early Hepatocellular Carcinoma by Cancer Risk Groups: Results of Propensity Score-Weighted Analysis. Onco Targets Ther.
243. Zheng L, Zhang CH, Lin JY, et al. Comparative Effectiveness of Radiofrequency Ablation vs. Surgical Resection for Patients With Solitary Hepatocellular Carcinoma Smaller Than 5 cm. Front Oncol. 2020; 10: 399.
244. Zhong C, Guo RP, Li JQ, et al. A randomized controlled trial of hepatectomy with adjuvant transcatheter arterial chemoembolization versus hepatectomy alone for Stage III A hepatocellular carcinoma. J Cancer Res Clin Oncol. Oct 2009; 135(10):1437-1445.
245. Zhou L, Yang YP, Feng YY et al. Efficacy of argon-helium cryosurgical ablation on primary hepatocellular carcinoma: a pilot clinical study. Chin J Cancer 2009; 28(1):45-8.
246. Zhou WP, Lai EC, Li AJ et al. A prospective, randomized, controlled trial of preoperative transarterial chemoembolization for resectable large hepatocellular carcinoma. Ann Surg 2009; 249(2):195-202.
247. Zhou Y, Zhang X, Wu L et al. Meta-analysis: preoperative transcatheter arterial chemoembolization does not improve prognosis of patients with resectable hepatocellular carcinoma. BMC Gastroenterol 2013; 13:51.
248. Zhu GQ, Sun M, Liao WT, et al. Comparative efficacy and safety between ablative therapies or surgery for small hepatocellular carcinoma: a network meta-analysis. Expert Rev Gastroenterol Hepatol. 2018 Sep;12 (9):935-945.

POLICY HISTORY:

Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, September 2008
Medical Policy Group, October 2009
Available for comment October 20-December 3, 2009
Medical Policy Group, August 2010
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Medical Policy Group, October 2010
Medical Policy Group, July 2011
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Medical Policy Group, July 2012
Medical Policy Group, June 2013
Medical Policy Group, September 2013
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Medical Policy Group, December 2013
Medical Policy Group, January 2014
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Medical Policy Group, November 2014
Medical Policy Group, February 2015
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Medical Policy Group, August 2015
Medical Policy Group, September 2015
Medical Policy Group, October 2015
Medical Policy Group, December 2015
Medical Policy Group, September 2016
Medical Policy Group, September 2017
Medical Policy Group, July 2018 **(4)**: Updates to Description, Key Points, Coding and References. No change to policy statement. Removed ICD 9 diagnosis codes from Current Coding. Removed radioembolization HCPCS code and CPT codes from Current Coding (77300, 77370, 77470, 77750, 77778, 77790, 79445, 79900, S2095). Removed CPT code 37204 (deleted 2014) from Previous Coding. Changed policy statement for microwave ablation (per 5) since it is referred to in the Blue Advantage policy #512. Also deleted Policy statements prior to November 2015.
Medical Policy Group, October 2019
Medical Policy Group, August 2020: Removed CPT codes 37243 and 75894. Policy statement updated to remove TACE. See medical policy #737 for TACE.
Medical Policy Group, September 2020

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.