



MASSACHUSETTS

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Medical Policy

Cryosurgical Ablation of Primary or Metastatic Liver Tumors

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Policy Number: 633

BCBSA Reference Number: 7.01.75 (For Plan internal use only)

NCD/LCD: NA

Related Policies

- Isolated Limb Perfusion, #[124](#)
- Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors, #[259](#)
- Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate or Dermatologic Tumors, #[260](#)
- Radiofrequency Ablation of Primary or Metastatic Liver Tumors, #[286](#)
- Microwave Tumor Ablation, #[912](#)
- Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies, #[634](#)
- Radioembolization for Primary and Metastatic Tumors of the Liver, #[292](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Cryosurgical ablation of either primary or metastatic tumors in the liver is [INVESTIGATIONAL](#).

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is not a covered service.
Commercial PPO and Indemnity	This is not a covered service.
Medicare HMO Blue SM	This is not a covered service.
Medicare PPO Blue SM	This is not a covered service.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code 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 as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
47371	Laparoscopy, surgical, ablation of 1 or more liver tumor(s); cryosurgical
47381	Ablation, open, 1 or more liver tumor(s); cryosurgical
47383	Ablation, 1 or more liver tumor(s), percutaneous, cryoablation

Description

Liver Metastases

Hepatic tumors can be due to primary liver cancer or metastases to the liver from nonhepatic primary tumors. Primary liver cancer can arise from hepatocellular tissue (hepatocellular carcinoma [HCC]) or intrahepatic biliary ducts (cholangiocarcinoma). Multiple tumors metastasize to the liver, but there is particular interest in the treatment of hepatic metastases from colorectal cancer (CRC) given the propensity of CRC to metastasize to the liver and its high prevalence. Liver metastases from neuroendocrine tumors present a unique clinical situation. Neuroendocrine cells produce and secrete a variety of regulatory hormones (or neuropeptides), which include neurotransmitters and growth factors. Overproduction of the specific neuropeptides by cancerous cells causes various symptoms, depending on the hormone produced. In the U.S, the incidence rates of liver cancer are estimated to continually increase through 2030. ¹ Some racial groups are more affected by liver cancer than others due to differences in the prevalence of risk factors and disparities in access to quality care; the mortality rate for African Americans with HCC is higher than other racial groups in the U.S.

Treatment

Treatment of liver metastases is undertaken to reduce endocrine-related symptoms, in addition to prolonging survival and reducing symptoms related to the hepatic mass.

Surgical resection with tumor-free margins and liver transplantation are the primary treatments available that have curative potential. Many hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, the number of lesions, or underlying liver reserve. 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 the 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.

Various locoregional therapies for unresectable liver tumors have been evaluated: cryosurgical ablation (cryosurgery); radiofrequency ablation; laser ablation; transhepatic arterial embolization, chemoembolization, or radioembolization with yttrium-90 microspheres; microwave coagulation; and percutaneous ethanol injection. Cryosurgical ablation occurs in tissue that has been frozen by at least 3 mechanisms: (1) formation of ice crystals within cells, thereby disrupting membranes and interrupting

cellular metabolism among other processes; (2) coagulation of blood, thereby interrupting blood flow to the tissue, in turn causing ischemia and apoptosis; and (3) induction of apoptosis.

Some have reported on experience with cryosurgical and other ablative methods used in combination with subtotal resection and/or procedures such as transarterial chemoembolization.

Procedure-Related Complications

Cryosurgery is not a benign procedure. Treatment-related deaths occur in approximately 2% of study populations and are most often caused by cryoshock, liver failure, hemorrhage, pneumonia/sepsis, and acute myocardial infarction. Clinically significant nonfatal complication rates in the reviewed studies ranged from 0% to 83% and were generally due to the same causes as treatment-related deaths. The likelihood of complications arising from cryosurgery might be predicted, in part, by the extent of the procedure,² but much of the treatment-related morbidity and mortality reflect the generally poor health status of patients with advanced hepatic disease.

Summary

Description

Cryosurgical ablation (CSA) involves the freezing of target tissues, often by inserting a probe through which coolant is circulated into the tumor. CSA can be performed as an open surgical technique or percutaneously or laparoscopically, typically with ultrasound guidance.

Summary of Evidence

For individuals who have unresectable primary hepatocellular carcinoma (HCC) amenable to locoregional therapy who receive cryosurgical ablation (CSA), the evidence includes two meta-analyses, one randomized controlled trial (RCT), several nonrandomized comparative studies, and multiple noncomparative studies. Relevant outcomes are overall survival (OS), disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing cryoablation with radiofrequency ablation (RFA) demonstrated lower rates of local tumor progression with cryoablation but no differences in survival outcomes between groups. Although this trial provided suggestive evidence that cryoablation is comparable with RFA, trial limitations would suggest findings need to be replicated. Nonrandomized comparative studies have failed to find consistent benefit with cryoablation in outcomes related to tumor recurrence and survival. Evidence from two meta-analyses suggests equivalent OS and progression-free survival to RFA and superiority for combined transarterial chemoembolization (TACE) plus CSA over TACE alone for OS and tumor progression. Additional randomized comparative evidence is needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable liver metastases from neuroendocrine tumors amenable to locoregional therapy who receive CSA, the evidence includes a Cochrane review and case series. Relevant outcomes are OS, disease-specific survival, symptoms, and treatment-related mortality and morbidity. The available evidence base is very limited. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable liver metastases from colorectal cancer amenable to locoregional therapy who have CSA, the evidence includes an RCT, several nonrandomized comparative and noncomparative studies, and systematic reviews of these studies. Relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing surgical resection with cryoablation was judged as high risk of bias. Some nonrandomized comparative studies have reported improved survival outcomes for patients managed with cryotherapy compared with those managed with resection alone; however, these studies were subject to bias in the selection of patients for treatments. Additional controlled studies are needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
11/2023	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
11/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
9/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
7/2017	Annual policy review. New references added.
6/2016	Annual policy review. Missing word "be" added to first sentence in Background section.
1/2016	Annual policy review. New references added.
2/2015	Annual policy review. New references added.
1/2015	Clarified coding information.
3/2014	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/2011	Annual policy review. No changes to policy statements.
10/2011	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
11/2010	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
6/2010	Annual policy review. No changes to policy statements.
9/2009	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/2009	Annual policy review. No changes to policy statements.
11/2008	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
10/2008	Annual policy review. No changes to policy statements.
9/2008	Annual policy review. Changes to policy statements.
1/2008	Annual policy review. Changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

References

1. Singh SK, Singh R. Liver cancer incidence and mortality: Disparities based on age, ethnicity, health and nutrition, molecular factors, and geography. *Cancer Health Disparities*. Mar 2020; 4: e1-e10. PMID 34164612
2. Sohn RL, Carlin AM, Steffes C, et al. The extent of cryosurgery increases the complication rate after hepatic cryoablation. *Am Surg*. Apr 2003; 69(4): 317-22; discussion 322-3. PMID 12716090
3. Kim HI, An J, Han S, et al. Loco-regional therapies competing with radiofrequency ablation in potential indications for hepatocellular carcinoma : a network meta-analysis. *Clin Mol Hepatol*. Jul 05 2023. PMID 37403319
4. Keshavarz P, Raman SS. Comparison of combined transarterial chemoembolization and ablations in patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Abdom Radiol (NY)*. Mar 2022; 47(3): 1009-1023. PMID 34982183
5. Wang C, Wang H, Yang W, et al. Multicenter randomized controlled trial of percutaneous cryoablation versus radiofrequency ablation in hepatocellular carcinoma. *Hepatology*. May 2015; 61(5): 1579-90. PMID 25284802
6. Wang Y, Li W, Man W, et al. Comparison of Efficacy and Safety of TACE Combined with Microwave Ablation and TACE Combined with Cryoablation in the Treatment of Large Hepatocellular Carcinoma. *Comput Intell Neurosci*. 2022; 2022: 9783113. PMID 35795769
7. Luo J, Dong Z, Xie H, et al. Efficacy and safety of percutaneous cryoablation for elderly patients with small hepatocellular carcinoma: A prospective multicenter study. *Liver Int*. Apr 2022; 42(4): 918-929. PMID 35065003
8. Chen L, Ren Y, Sun T, et al. The efficacy of radiofrequency ablation versus cryoablation in the treatment of single hepatocellular carcinoma: A population-based study. *Cancer Med*. Jun 2021; 10(11): 3715-3725. PMID 33960697
9. Cha SY, Kang TW, Min JH, et al. RF Ablation Versus Cryoablation for Small Perivascular Hepatocellular Carcinoma: Propensity Score Analyses of Mid-Term Outcomes. *Cardiovasc Intervent Radiol*. Mar 2020; 43(3): 434-444. PMID 31844951
10. Ko SE, Lee MW, Rhim H, et al. Comparison of procedure-related complications between percutaneous cryoablation and radiofrequency ablation for treating periductal hepatocellular carcinoma. *Int J Hyperthermia*. Nov 17 2020; 37(1): 1354-1361. PMID 33297809
11. Wei J, Cui W, Fan W, et al. Unresectable Hepatocellular Carcinoma: Transcatheter Arterial Chemoembolization Combined With Microwave Ablation vs. Combined With Cryoablation. *Front Oncol*. 2020; 10: 1285. PMID 32850395
12. 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): 1294-300. PMID 25287439
13. 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): 632-8. PMID 24529593
14. Awad T, Thorlund K, Gluud C. Cryotherapy for hepatocellular carcinoma. *Cochrane Database Syst Rev*. Oct 07 2009; (4): CD007611. PMID 19821432
15. Adam R, Hagopian EJ, Linhares M, et al. A comparison of percutaneous cryosurgery and percutaneous radiofrequency for unresectable hepatic malignancies. *Arch Surg*. Dec 2002; 137(12): 1332-9; discussion 1340. PMID 12470093
16. Yang Y, Wang C, Lu Y, et al. Outcomes of ultrasound-guided percutaneous argon-helium cryoablation of hepatocellular carcinoma. *J Hepatobiliary Pancreat Sci*. Nov 2012; 19(6): 674-84. PMID 22187145
17. 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. PMID 25849963
18. Zhou L, Yang YP, Feng YY, et al. Efficacy of argon-helium cryosurgical ablation on primary hepatocellular carcinoma: a pilot clinical study. *Ai Zheng*. Jan 2009; 28(1): 45-8. PMID 19448416
19. 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. PMID 19784786
20. Jaeck D, Oussoultzoglou E, Bachellier P, et al. Hepatic metastases of gastroenteropancreatic neuroendocrine tumors: safe hepatic surgery. *World J Surg*. Jun 2001; 25(6): 689-92. PMID 11376398

21. Gurusamy KS, Ramamoorthy R, Sharma D, et al. Liver resection versus other treatments for neuroendocrine tumours in patients with resectable liver metastases. *Cochrane Database Syst Rev*. Apr 15 2009; (2): CD007060. PMID 19370671
22. 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*. Oct 2012; 35(5): 439-45. PMID 21654315
23. 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*. Dec 2001; 130(6): 954-62. PMID 11742323
24. Al-Asfoor A, Fedorowicz Z, Lodge M. Resection versus no intervention or other surgical interventions for colorectal cancer liver metastases. *Cochrane Database Syst Rev*. Apr 16 2008; (2): CD006039. PMID 18425932
25. Korpan NN. Hepatic cryosurgery for liver metastases. Long-term follow-up. *Ann Surg*. Feb 1997; 225(2): 193-201. PMID 9065296
26. Bala MM, Riemsma RP, Wolff R, et al. Cryotherapy for liver metastases. *Cochrane Database Syst Rev*. Jun 05 2013; (6): CD009058. PMID 23740609
27. 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. PMID 20091607
28. Pathak S, Jones R, Tang JM, et al. Ablative therapies for colorectal liver metastases: a systematic review. *Colorectal Dis*. Sep 2011; 13(9): e252-65. PMID 21689362
29. 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*. Mar 2007; 14(3): 1161-9. PMID 17195903
30. 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*. Jul 2007; 14(7): 2078-87. PMID 17473951
31. Joosten J, Jager G, Oyen W, et al. Cryosurgery and radiofrequency ablation for unresectable colorectal liver metastases. *Eur J Surg Oncol*. Dec 2005; 31(10): 1152-9. PMID 16126363
32. Ng KM, Chua TC, Saxena A, et al. Two decades of experience with hepatic cryotherapy for advanced colorectal metastases. *Ann Surg Oncol*. Apr 2012; 19(4): 1276-83. PMID 21913018
33. 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*. Nov 2005; 20(6): 507-20. PMID 15973545
34. 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*. Nov 2007; 142(11): 1087-92. PMID 18025338
35. Xu KC, Niu LZ, He WB, et al. Percutaneous cryosurgery for the treatment of hepatic colorectal metastases. *World J Gastroenterol*. Mar 07 2008; 14(9): 1430-6. PMID 18322961
36. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hepatocellular Carcinoma. Version 1.2023. https://www.nccn.org/professionals/physician_gls/PDF/hcc.pdf. Accessed August 8, 2023.