



CIGNA MEDICAL COVERAGE POLICY

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Subject Cryoablation of Liver Tumors

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Radioembolization with Yttrium-90 (90Y) Microspheres
Radiofrequency Ablation (RFA) for Primary and Metastatic Cancers of the Liver
Transcatheter Arterial Chemoembolization (TACE) of Liver Tumors

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Coverage Policy

CIGNA covers cryoablation as medically necessary for the treatment of unresectable primary liver cancer and unresectable liver metastases.

General Background

Cryoablation, also referred to as cryosurgery or cryosurgical ablation (CSA), is the use of extreme cold, produced by liquid nitrogen or argon gas, to destroy abnormal tissue. This technique can be used for internal and external tumors. For internal tumors, liquid nitrogen or argon gas is delivered to diseased tissue through a cryoprobe. Ultrasound is used to guide the cryoprobe and monitor the freezing of cells in order to avoid damage to nearby healthy tissue. Cryoablation is primarily an open surgical procedure but may be performed laparoscopically. It may also be used as an adjuvant therapy to surgical resection. Postoperative complications may include renal failure, bile duct injury, hemorrhage, infection and, less frequently, multi-organ failure.

Hepatocellular carcinoma (HCC) is relatively uncommon in the United States, but it is the most common primary malignancy of the liver. HCC is associated with liver cirrhosis in 50–80% of patients; 5% of cirrhosis patients develop HCC. Other causes of the disease include hepatitis B and C infections, particularly in conjunction with alcohol abuse. The only potentially curative treatments are surgical resection and liver transplantation. The majority of patients with primary or metastatic liver cancers are not suitable candidates for surgical resection at the time of diagnosis due to the size, site, and number of tumors; perivascular and extra-hepatic involvement; advanced or decompensated liver cirrhosis; poor hepatic reserve and/or poor general health. In addition,

chemotherapy and radiotherapy rarely produce a complete or sustained response in patients with advanced disease.

For treatment purposes, primary liver cancer is classified as localized resectable, localized unresectable, or advanced disease. Surgery with curative intent is the treatment of choice for patients with localized resectable disease, but it is not appropriate if the patient has multifocal disease, or if the tumor is in close proximity to major vascular or biliary structures, precluding margin-negative resection. Even among patients who undergo resection with curative intent, recurrence is common. Partial hepatectomy has been reported to result in five-year survival rates ranging from 10–30%. Chemoembolization, percutaneous ethanol injection (PEI), and thermal ablation by cryosurgery or radiofrequency (RFA) are minimally invasive techniques for treating localized unresectable liver tumors. These techniques provide local control, reduce recurrence, prolong survival, and possibly even cure select patients. Local treatment is less damaging to normal liver parenchyma than chemotherapy and has fewer systemic side effects. Minimally invasive techniques may be used in patients with tumors that are < 5 cm in diameter. Liver transplantation is also a treatment option for patients with localized disease that is unresectable. There is no standard treatment for patients with advanced metastatic liver cancer. These patients should be considered for clinical trials exploring new treatment options. Despite treatment, many patients die of liver failure related to parenchymal replacement, from biliary obstruction, or from extrahepatic disease (NCI, 2009a).

The liver is a common site of metastasis from gastrointestinal tumors, probably because of dissemination via the portal vein system. In the United States, the most common extrahepatic primary cancer associated with liver metastases is colorectal cancer (CRC), with only 10–25% of patients meeting the criteria for potentially curative resection. Liver resection in the absence of extrahepatic disease can result in long-term survival in 30–35% of patients. Local treatment options include laser therapy, CSA, RFA, and ethanol ablation. Patients with metastatic disease from less common primary sites, such as neuroendocrine, small intestine and ovarian tumors, are also candidates for cryoablation (NCI, 2009b; NCI, 2008; Siperstein, et al., 2000).

U.S. Food and Drug Administration (FDA)

The Cryocare[®] Surgical System (Endo Care, Irvine, CA) was granted marketing approval by the U.S. Food and Drug Administration (FDA) via the 510(k) process on January 25, 2002. The Cryocare system is designed to freeze/ablate skin lesions, liver metastases, tumors, and prostate and kidney tissue. On November 18, 2005, the SeedNet Family (Galil Medical Ltd., Shaar Yokneam, Israel) received FDA 510(k) approval as Class II devices. Approved indications for this group of cryosurgical devices (e.g., SeedNet[™], SeedNetGold[™]) are similar to those of the Cryocare system.

Literature Review

A Cochrane review by Al-Asfoor et al. (2008) compared resection of liver metastases to no intervention and other modalities of intervention (including cryosurgery and radiofrequency ablation) in terms of the benefits and harms for each intervention. The reviewers identified only one randomized controlled trial (RCT) comparing cryoablation (n=63) to surgical resection (n=60). A greater number of patients treated with cryoablation survived at three, five and 10 years (60%, 44% and 19%, respectively) compared to patients treated with conventional surgical techniques (51%, 36% and 8%, respectively). Disease recurrence was found in 85% of cryoablation patients and 95% of those who underwent surgical resection. According to the authors, the data from this 10-year prospective RCT suggest that cryosurgery is an effective treatment for resectable and unresectable liver metastasis. It was summarized that local ablative therapies may be useful, but that there is a need for further evaluation in RCTs (Al-Asfoor, et al., 2008).

Additional evidence in the published peer-reviewed medical literature evaluating the safety and effectiveness of cryoablation for the treatment of liver cancer consists of case series and comparative studies (Xu, et al., 2008; Bageacu, et al., 2007; Seifert, et al., 2005; Joosten, et al., 2005; Kerkar, et al., 2004; Goering, et al., 2002; Bilchik, et al., 2000; [n=42–326]). Follow-up has ranged from two to five years. Most studies have included patients with unresectable primary disease or secondary liver involvement from colorectal carcinoma. However, some studies have examined and support the efficacy of this treatment modality for liver metastasis from other sites. Recurrence rates have been reported to range from 70%–80% following cryoablation, with over-all five-year survival rates between 24% and 44%.

Despite the lack of randomized controlled trials comparing cryoablation to surgical resection or other interventions, the bulk of the available evidence indicates that cryoablation is a safe and effective local ablative option for the treatment of unresectable primary and metastatic liver cancer.

Professional Societies/Organizations

According to the National Comprehensive Cancer Network (NCCN) guidelines for Hepatobiliary Cancers, all HCC patients should be evaluated for potential curative therapies (i.e., resection, transplantation). Locoregional therapy including ablation (i.e., cryoablation, RFA, microwave ablation, PEI) and transarterial embolization may be appropriate for patients who are not candidates for curative treatments. Tumors that are ≤ 3 cm are optimally treated with ablation, while those between 3–5 cm may be treated with a combination of embolization and ablation (NCCN, 2010a). Other NCCN guidelines state that local ablative techniques may also be considered for the treatment of unresectable liver metastases from colorectal and neuroendocrine cancers (NCCN, 2010b; NCCN, 2009).

Summary

Minimally invasive techniques such as cryoablation are among the standard treatment options recommended by the National Cancer Institute (NCI) for selected patients with unresectable liver cancer. The results of the available clinical studies demonstrate that cryoablation of unresectable primary hepatocellular carcinoma (HCC) or metastatic colorectal liver cancers is a relatively safe and efficacious procedure for short-term local control of single or multiple small tumors. In addition, there are some limited data from these studies to support the efficacy of cryosurgery in the treatment of small neuroendocrine metastases to the liver. Although there is limited data on outcomes for patients with metastatic disease from less common sites, cryoablation may be an option for the control of cancer-related symptoms in these patients.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT ^{®*} Codes	Description
47371	Laparoscopy, surgical ablation of one or more liver tumor(s); cryosurgical
47381	Ablation, open, of one or more liver tumor(s); cryosurgical

ICD-9-CM Diagnosis Codes	Description
154.0	Malignant neoplasm of rectosigmoid junction
155.0	Malignant neoplasm of liver, primary
194.0 – 194.9	Malignant neoplasm of other endocrine glands and related structures
197.7	Secondary malignant neoplasm of liver
230.8	Carcinoma in situ of liver and biliary system
259.2	Other endocrine disorders, carcinoid syndrome

*Current Procedural Terminology (CPT[®]) © 2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	03/15/2008	0307	Cryoablation of Liver Tumors

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